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DIGITAL EUROPE: DIGITISING INDUSTRY, EMPOWERING PEOPLE

ANDRUS ANSIP, EUROPEAN COMMISSION VP FOR
THE DIGITAL SINGLE MARKET OUTLINES WHY
SCIENCE AND RESEARCH PLAY AN INTEGRAL
ROLE IN CREATING A DIGITAL EUROPE



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FOREWORD

Markku Markkula

Vice President

European Committee of the Regions

For many political leaders at the local, regional, national, and European level, the most tangible evidence of EU solidarity is its cohesion policy. It is a policy that helps rich and poor regions alike – and that narrows the development gap between Europe’s east and west. But, cohesion policy is not only about solidarity; it also makes economic sense. Cohesion policy is about capacity-building, co-creating, and applying innovative solutions tailored to tackle local societal challenges – increasingly through European partnerships of cities and regions that are using the best knowledge available.

The European Commission has shown that for €1 invested through cohesion funds, €2.7 is created. In the wake of Brexit, the EU will be under more pressure than ever to spend wisely and efficiently by focusing on results. This is why the European Committee of the Regions (CoR) has called for a cohesion alliance, in order to mobilise all stakeholders to make visible the impact of this policy and build its future based on stronger awareness and partnerships. We want a strong, effective, yet reformed cohesion policy, a cohesion policy that is fit for purpose.

The European Commission's investment plan for Europe – which is expected to trigger €500 billion – also aims to contribute to a more cohesive Europe. We are convinced that the cohesion policy and the investment plan each have unique but not opposing philosophies. They must be complementary and act in synergy. This was also a clear message in our committee's official position on the future cohesion policy, drafted by Michael Schneider and adopted in May.

When I took the reins of the CoR Presidency in February 2015, I set boosting the economy through investment and entrepreneurship as our number one political priority: Europe needs to be renewed based on a bottom-up approach. Our flagship Summit of Regions and Cities in Bratislava in July 2016 showed that the challenge of 'connecting Europe' needs targeted investment and more partnership. We have seen many signs for optimism and renewal as the economy slowly starts to return to growth. This is also thanks to the tireless work of mayors, regional presidents and councillors who are using their regions and cities as test-beds for innovation in Europe.

The CoR's most valuable asset is its membership, local and regional political leaders who know their citizens' needs and are on the frontline when it comes to introducing new projects, ideas, and concepts. To give one example: at the same time as the violent extremist attacks in Paris and Brussels, we learnt that, just 30 miles away from Brussels, the mayor of Mechelen had developed a successful model of integration. Despite similar demographics to Brussels and Antwerp, Mechelen has not produced a single 'foreign fighter' in Syria or Iraq. My CoR colleague, Bart Somers, was this February awarded the World Mayor Prize for 2016.

In short, following a formal referral – the first of its kind – from the European Council's President Donald Tusk, we are increasingly mobilising our members to be the face of the EU on the ground. Our initiative called "Reflecting on Europe" is the best example of the difference that local and regional governments can make in wider EU reflections. Based on, to date, 135 citizen dialogues and town-hall debates held throughout Europe, we will have clear messages and proposals for the EU's decision-making bodies.



We need to showcase the added value of our Union better, using innovative processes and solutions. Together we will build a Europe for and with our citizens.

Markku Markkula was president until late July 2017 and is now the 1st Vice-President of the European Committee of the Regions, the EU's assembly for local and regional politicians. It has a consultative role in the EU's decision-making. ■



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INTRODUCTION

Welcome to the August edition of Open Access Government. Following the snap general election in June, there is still a sense of uncertainty in the UK. Also, as Brexit talks get underway, it is unclear what the future holds for the relationship between Europe and the UK. However despite a sense of unknowing, there are still a number of positive areas to focus on and our summer publication kicks off with a foreword from Markku Markkula, Vice-President of the European Committee of the Regions (CoR).

In his introduction, Markkula looks at how, following Brexit, the EU will be under more pressure to spend wisely and efficiently. He discusses in particular cohesion funds and the need for a cohesion alliance.

Also in this issue, Commissioner for Regional Policy, Corina Cretu, explains how cohesion policy must be tailored to help low-income regions and ensure growth. A piece by Kieran McCarthy, a member of the CoR also highlights upcoming challenges of the European Union and why instead of looking at the negatives we should be focusing on the positive activities being done.

With many current challenges at the forefront of policy, our health section highlights a number of them. A speech by the Commissioner for Health and Food Safety, Vytenis Andriukaitis outlines a new Action Plan to tackle antimicrobial resistance (AMR). He discusses why AMR is not only a European issue, but a global one. Following on from that, Jane Philpott, Minister for Health in

Canada outlines how the government of Canada are also tackling the issue.

Cyber security is another area we look at in the latest issue. Several articles in the security section highlight this global problem, including a piece by MP Meg Hillier, Chair of the Public Accounts Committee. She discusses the government's efforts to tackle cyber-attacks and what more needs to be done to protect the UK. We also shed light on the National Cyber Security Centre (NCSC) and their work to reduce threats and protect the public, as well as business community.

Other areas we shine the light on include, the EU Clean Energy Package, smart cities, biodiversity, gender equality in research, as well as Huntington's disease and vascular dementia.

As always, I do hope that you find this edition of Open Access Government thought provoking and welcome any comments you may have. ■

Laura Evans
Editor

 @Laura_AdjDigPol



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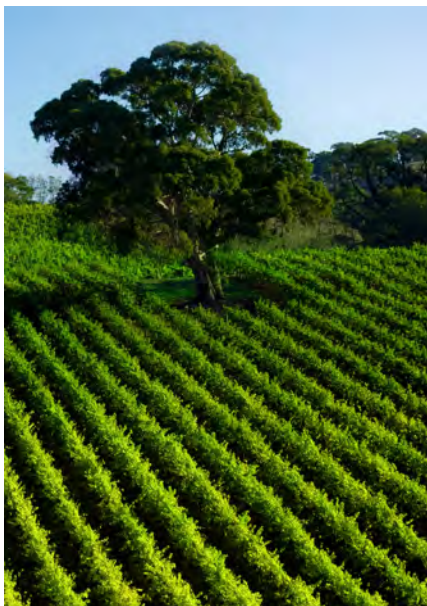
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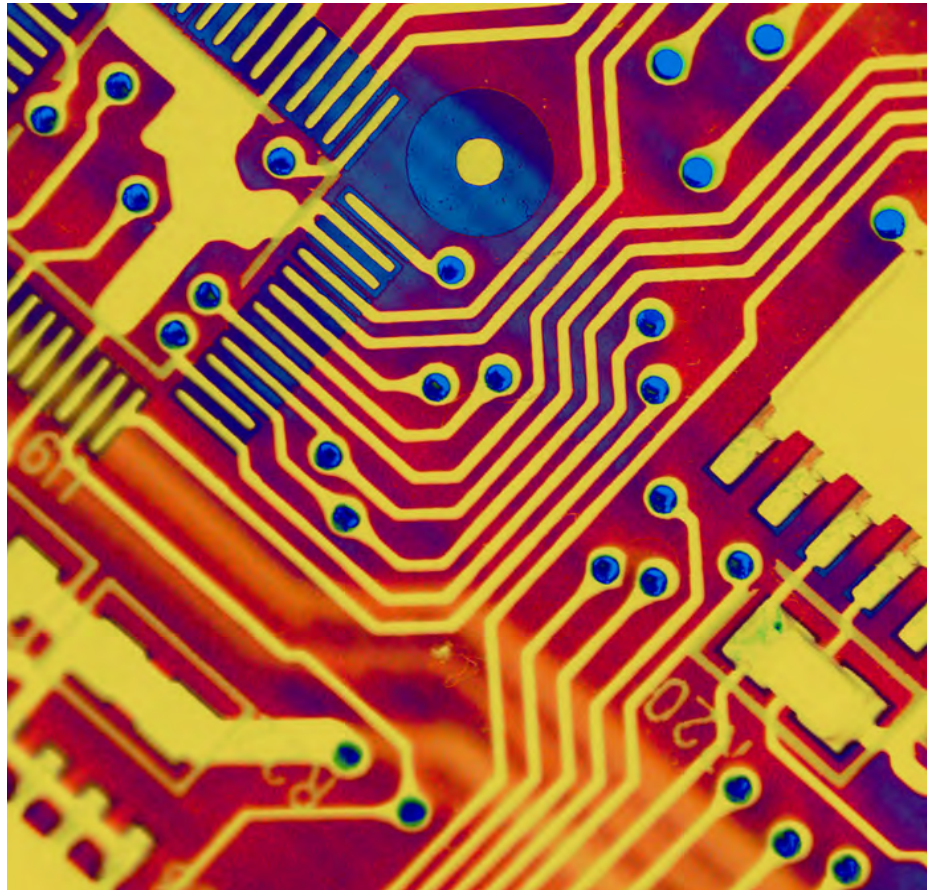


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 OPEN ACCESS
GOVERNMENT

Fighting against antimicrobial resistance

Antimicrobial resistance is a global problem that requires commitment to tackle it, shares EU Health Commissioner Vytenis Andriukaitis in a speech

Antimicrobial resistance (AMR) is a global health threat that continues to grow throughout the EU and worldwide. The European Commission has recently launched a new Action Plan to tackle the growing threat as part of the One Health approach that addresses resistance in both humans and animals. The new Action Plan will also aim to boost research and further incentivise innovation between Member States, as well as public and private sectors across Europe and beyond.

Here, EU Commissioner for Health and Food Safety, Vytenis Andriukaitis, highlights in a speech in Washington DC, the Commission's commitment to tackling AMR.

"My principal role as European Commissioner with responsibility for health and food safety is to support the 28 European Union countries towards achieving common objectives. But many of these, particularly in the field of health, are not confined within the borders of the European Union.

It is clear that this is not only a European issue. Bacteria do not respect national borders or walls and this is why AMR is a truly global health problem.

The burden of AMR

The social and economic burden of AMR is already unacceptably high with an annual human death-toll estimated to be in excess of 700,000 people.

By 2050, antibiotic resistant bacteria are projected to kill 10 million people a year.

Furthermore the long-term economic damage of AMR could be worse than the 2008 financial crisis.

In the European Union alone, it is estimated that AMR

annually costs €1.5 billion in additional healthcare expenses and productivity losses.

The case for urgent action on a global scale is plain for all to see.

Last year I attended the United Nations General Assembly in New York, where a number of countries, including the United States – made the commitment to implement activities of the WHO Global Action Plan on AMR.

Since the adoption of this Global AMR Action Plan and the United Nations Declaration on AMR, many countries have made significant progress in tackling AMR – and these achievements should be recognised and applauded.

This has been the case for the USA and also the EU.

In the EU, we take pride in the fact that the EU banned the use of antibiotics for growth promotion in animal production as long ago as 2006. I am a firm believer in this policy and would like to see its further adoption beyond the EU.

An external evaluation of the Action Plan that we have launched back in 2011 highlighted considerable achievements – in areas such as harmonised surveillance in food producing animals. However, it also concluded that greater efforts were needed to tackle AMR and in a more concerted manner.

This explains my firm commitment to stepping up current efforts. At the end of this month, I will present a new European Union One Health Action Plan. It will focus on 3 strategic pillars:

- Making the EU a best-practice region;

- Boosting research and innovation; and
- Shaping the global agenda.

I hope that this Plan will serve as the principal vehicle for the EU to contribute towards implementation of current global commitments – particularly those under the WHO Global Action Plan.

International action

Let me expand a little bit on international action under the third pillar that is ‘shaping the global agenda’.

I see the US as a key strategic partner in addressing AMR. In addition to cooperating within international organisations – such as the World Health Organization (WHO), the World Organisation for Animal Health (OIE) and the Food and Agriculture Organization (FAO), and international forums such as the G7 and G20 – I want to reinforce bilateral relations between the US and the EU.

Indeed, the US and the EU share many interests on AMR and there is already good collaboration at technical level within the Transatlantic Partnership on Antimicrobial Resistance (TATFAR).

A key guiding principal underpinning our EU actions to fight AMR continues to be “one health approach” – bringing together the health and veterinary sectors in a unified and coherent effort to tackle AMR. As diseases can spread between humans and animals, these 2 sectors are undoubtedly interconnected.

Let me stress that I am under no illusion as to the magnitude of the task ahead.

I recognise that there is still a mountain to climb if we are to successfully defeat AMR.

To this end, more needs to be done to address AMR across all relevant sectors with a one-health approach applied at national, regional and international level.

Finally, I want to stress that citizens have an important role to play in this multi-lateral effort.

Let me tell you about a little experiment my trainees have done on the occasion of the European Antibiotic Awareness Day.

My trainees went to 3 pharmacies around the building where our offices in Brussels are and asked a simple question: how many packs of Antibiotics do you sell a day?

What they learnt is the following: on average these 3 pharmacies sell 41 packages a day.

If we imagine that these trends are common, there are 5000 pharmacies in Belgium... 5000 times 41 is 205 000 packs a day!

I am not claiming it is a real study, though I am sure I could ask to put it on my twitter with a claim: ‘last study shows 41 packs of antibiotics are sold in Brussels per day’.

I reassure you I won’t do this, as a medical doctor I know that doing real study takes a bit more than visiting 3 pharmacies...

Many people out there really need these drugs, therefore we should not stigmatise anyone.

But what we are interested in – is what all the pharmacists said. They said that they sell too much and way too often the prescriptions are inadequate. They also added that people tend to get angry if they don’t get antibiotics prescriptions and often is the question of knowledge, education... and awareness. People do not know that antibiotics do not kill viruses, or that they are ineffective against colds. This little experiment is just a snapshot illustration, in its relative capacity of course.

That’s why citizens matter. We need to change the perception of how antibiotics are used.” ■

This is an edited version of a speech, which can be found [here](#).

Vytienis Andriukaitis
Commissioner for Health and Food Safety

European Commission

www.ec.europa.eu/commission/commissioners/2014-2019/andriukaitis_en

www.twitter.com/V_Andriukaitis

An insight into *Escherichia coli*

Understanding *Escherichia coli* ecology and evolution in the gut as a commensal is a prerequisite to fight this opportunistic pathogen

E*scherichia coli* is one of the most characterised bacterial species. It has been a workhorse of molecular biology for more than 80 years. Yet over the last 2 decades, *E. coli* has also become a major public health concern. *E. coli* has been known as a dangerous pathogen for a long time, mostly through its intra-intestinal pathogenicity, that lead to various forms of diarrhoea from benign to lethal, but the toll of these pathologies has been drastically reduced in recent years. While, in the late 70s, about 1 million infants died yearly from Shigella, a member of the *E. coli* species, this number has now been decreased by more than an order of magnitude (Bardhan et al. 2010). The new concerns about *E. coli* are now due to its extra-intestinal pathogenicity and antibiotic resistance that are promoted by changes in the epidemiology of the species. Strains loaded with extra-intestinal virulence factors and carrying multiple antibiotic resistances are more and more common as commensals of the gut of individuals both in the community and in the hospital. Patients arrive therefore to the hospital with an enemy within that takes any opportunity to challenge their immune systems and generate a wide diversity of extra-intestinal diseases ranging from urinary tract infections, pyelonephritis, peritonitis and bacteraemia to new born meningitides. These diverse extra-intestinal pathologies kill close to a million people every year (Russo & Johnson 2003).



IAME

This dynamic evolution of the species has convinced us at the Infection, Antimicrobial, Models and Evolution (IAME) Unit Inserm U1137, that an ecological perspective with both basic and applied approaches is required to apprehend *E. coli* as an infectious agent. Moreover, as extra-intestinal diseases are opportunistic infections, we are also persuaded that the determinants of the species evolution are to be found in its commensal habitat. Along those lines, years of epidemiology by Erick Denamur, has revealed that the prevalence of the different genetic group that structure the species, varied and that the most equipped for extra-intestinal virulence, B2 group, increased in frequency in Europe over the last 3 decades (Massot et al. 2016). Interestingly, work with animal models have also

revealed that many of the so called virulence factors that are required for extra-intestinal diseases are indeed providing some selective advantages in the gut, suggesting that pathogenesis is a by-product of commensalism (Le Gall et al. 2007).

To use an evolutionary perspective requires an understanding of bacterial adaptation, its dynamics, and its constraints. Thanks to an ERC grant, my team Quantitative Evolutionary Microbiology, in IAME unit, has focused on different facets of *E. coli* adaptation. One of our first goals was to unravel the molecular determinants of bacterial adaptation using experimental evolution coupled to whole genome sequencing. Working with bacteria evolved in the laboratory, notably the Long-Term Experimental Evolution initiated by Richard Lenski in 1988, we

showed that the flux of beneficial mutations that accumulate in the genomes slowed down after a few thousand generations, but remained high even after 50,000 generations of adaptation (Tenaillon et al. 2016). This strong adaptation results in an excess of nonsynonymous mutation genome wide that is unheard of in natural settings. We have therefore adapted *E. coli* for a year to the mouse gut (Lescat et al. 2017). The genomic signature of adaptation was still present but much weaker, and the activation of metabolic pathways was part of the response. Finally, to go to even more natural conditions, we sampled *E. coli* from human faeces at different times. In these conditions, we could not detect so far any traces of adaption over a year of evolution. These experiments revealed on the one hand that *E. coli* can adapt extremely fast to new challenges and on the other that it is highly adapted to the human gut, such that de novo adaptation may not be dominant in that context.

Another process, by which *E. coli* evolution occurs, is through changes in prevalence of the diverse clones that constitute the species (Tenaillon et al. 2010). Indeed, within a human host, a clone may suddenly replace another, or at a human population level, we may find that some phylogroups change in frequencies over the years. Diet and microbiota composition could contribute to both short and long-term changes. To investigate their role, we are now studying how different *E. coli* strains, with different potential for extra-intestinal diseases, behave and

evolve in the gut of mice having different diets. Preliminary results suggest that Western diet may favour the maintenance of strains from B2 group. We also developed tools to confront the composition of *E. coli* population to the composition of the microbiota within a host. Using close to 500 healthy individuals (Goodrich et al. 2014), we have so far not found any specific association, suggesting that the time scale of the changes in microbiota and the ones *E. coli* may differ.

While *E. coli* is becoming an increasing public concern, *E. coli* is also a very important component of the human microbiota. This duality prevents an eradication-like strategy and necessitates a deeper understanding of the ecological factors that contribute to *E. coli* evolution in the gut. Over the last few years we have initiated these approaches in IAME, but deeper and more frequent sampling of individuals fully characterised in terms of diet, immunity and microbiota will be needed to go further.

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NRD.E1 – a treatment for diabetic related neuropathic pain

Novaremed's Dr Eli Kaplan shares research on NRD.E1 and explains how it can help to treat diabetic related neuropathic pain

Founded in 2008, Novaremed is an Israeli pharmaceutical company developing a pipeline of compounds for treatment of various diseases. At the top of the list is NRD.E1, the proposed treatment for neuropathic pain: A first in class, efficacious and safe remedy which has a unique mechanism of action.

The company is headed by Dr. Eli Kaplan, and supported by a staff with vast professional expertise.

There are 2 types of pain: Chronic and acute. Chronic pain can also be divided into 2 types: Nociceptive and Neuropathic, depending on the body organ affected. Nociceptive Pain comes from damage to the body tissues, to muscles, joints and bones, whereas Neuropathic Pain is a continuous pain resulting from damage to the nervous system. The specific cause of Neuropathic Pain is often difficult to classify and treat, such as back pain, peripheral neuropathy associated with diabetes, shingles etc.

Global health problem

Neuropathic Pain, is a significant global health issue and a growing medical challenge as a consequence of aging population, rising incidences of diabetes and shingles, the treatment for which presents a significant unmet need. In the US, an estimated 100 million people having experienced at least one chronic pain episode in the last 12

months. This results in an annual cost of around \$600 billion in medical treatment and lost productivity.

Pain affects more people than cancer, diabetes and heart disease combined.

Numbers show that in 2008 there were between 9 and 16 million sufferers in the US and Western Europe, expected to increase to between 16 and 22 million by 2018, totalling an expected market size of between 7 and 10 billion US dollars.

“Novaremed's discovery is a medical breakthrough that, if proved to be effective, has the potential to bring relief to a large population suffering from a problem that has not yet been adequately addressed.”

“Moderate-to-severe pain has been and continues to be dominated by opioids, which are increasingly being reformulated to offer abuse-resistance, whereas mild pain is effectively treated with non-steroidal anti-inflammatory drugs (NSAID). However, significant unmet needs remain, as chronic pain subtypes – and particularly neuropathic pain – do not respond well to existing therapies:

“The drugs that are available today in the market have not been developed specifically for neuropathic pain and their effect on them has been discovered by chance,” says Kaplan, “but

because they work on the central nervous system, they have so many side effects that many patients avoid them and prefer to suffer the pain”.

Neuropathic pain

Neuropathic pain is caused by damage to the nervous system. 15% of people with diabetes develop neuropathic pain over the years due to poor blood supply, which causes nerves to continue to transmit pain to the brain via an intracellular enzyme.

Once this enzyme was found, the pathway to developing the drug in question was paved: the molecule Kaplan discovered – NRD.E1 – inhibits the enzyme, thus preventing the feeling of pain from reaching the brain.

In June 2016, the Company completed successfully the Phase IIa study. The main objectives were to assess the safety and tolerability of NRD.E1 as well as finding the effective dose. The study was conducted in Israel at 10 sites (both medical and health care centres). 88 diabetic patients with chronic neuropathic pain were randomly recruited into four treatment groups: low dose (10 mg / day), medium dose (40 mg / day), high dose (150 mg / day) and placebo treatment.

At the end of 3 weeks of treatment, NRD.E1 moderate-dose (40 mg/day) showed clear preference over the other groups:



- It reduced the mean daily pain score by 29.7% vs. placebo (2.6%) which was the study's primary end point. (p=0.034)
- The highest impact of pain reduction was noted in the sub-group of strong pain (NPS of 7-9 at screening): An improvement of 38.5% vs. worsening of 5.03% in the placebo group. (p=0.0048)
- NRD.E1 is well tolerated: The numbers of adverse events in the 40 mg/day group was less than in the placebo and in the high dose group.

As all secondary study endpoints showed the same trend of improvement as the primary end point indicating positive totality of the data – we concluded that the dose of 40 mg/day

is the best choice for further development of NRD.E1 as a drug candidate for the treatment of Diabetes Related Neuropathic Pain.

“Numbers show that in 2008 there were between 9 and 16 million sufferers in the US and Western Europe, expected to increase to between 16 and 22 million by 2018, totalling an expected market size of between 7 and 10 billion US dollars.”

Currently – Novaremed is planning its Phase IIb study in which the effect of NRD.E1 will be tested on 3 treatment groups, (2 doses of NRD.E1 vs. Placebo), app. 100 Diabetic patients with related neuropathic pain per group.

Novaremed's discovery is a medical breakthrough that, if proved to be

effective, has the potential to bring relief to a large population suffering from a problem that has not yet been adequately addressed.



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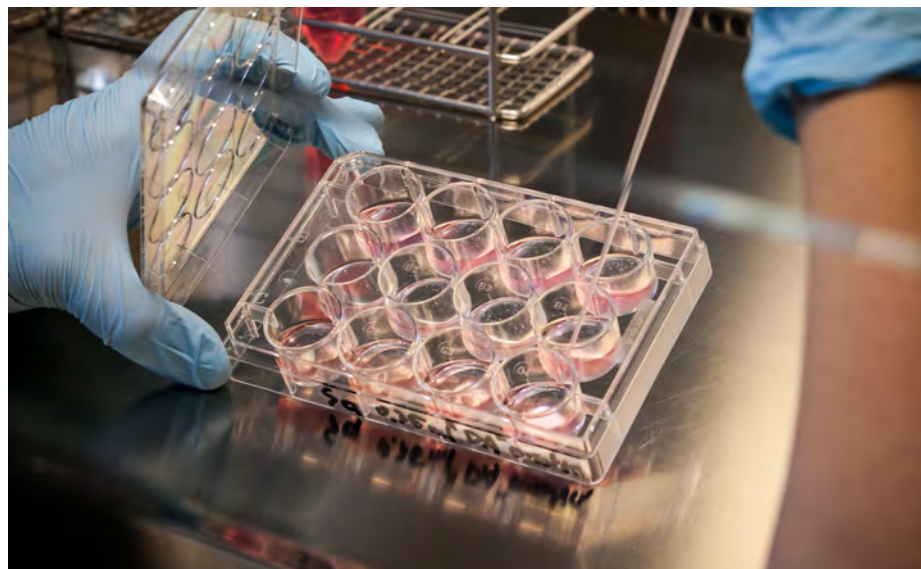
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Understanding cancer through molecular cell biology

Progress in Targeted Therapy and Immunotherapy of Cancer Requires Rethinking of European Reimbursement Practices for Mutation Testing

Molecular cell biology has changed the understanding of cancer. From a mysterious condition, with empirical and descriptive attributes, an explosion of knowledge occurred in the past 15 years concerning precise somatic acquired mutations linked to both solid and hematologic cancers. In certain cases mutations are at the origin of the disease. In others, mutations contribute to evolution of the malignant condition and are relevant for prognosis. The World Health Organization (WHO) has integrated molecular testing into the formal criteria of diagnosis. The identification of the precise mutational picture of every patient can significantly help therapeutic decisions, as targeted therapies are being developed and act specifically on cells carrying a particular mutant protein.

An example of the importance of mutation testing for medical practice is given by blood cancers called myeloproliferative neoplasms (MPNs). In these diseases hematopoietic stem cells acquire mutations in essentially one of 3 genes, coding for JAK2, the receptor for thrombopoietin (TpoR/Mpl) or calreticulin (CALR). The mutated proteins tell precursors of blood cells to survive, grow and differentiate continuously. Detection of these “driver” mutations (responsible for main features of disease) at diagnosis begins to be reimbursed, but the problem is that their changes during disease (in dynamics)



are usually not, and those are important for follow-up.

And the plot thickens. A substantial fraction of the patients with MPNs carry in their malignant clone other mutations that favor progression to severe conditions, like ultimately secondary acute leukemia. Such mutations concern epigenetic regulators and are usually loss-of-function, which is the mutation that impairs the normal tumor suppressive effects of those proteins. Examples are mutations in TET2, EZH2, ASXL1, DNMT3a or mutations in the gene that guards our genome against lesions, p53. The presence of several such mutants along with a driver mutation is usually a sign of a more severe disease that needs rapid intervention. Yet, mutations in those genes are not routinely tested, and are examined only too late after

progression to leukemia. This again comes from reimbursement policies.

The molecular progress was even more effective for chronic myeloid leukemia (CML) associated with the BCR-ABL fusion product. A series of molecules developed in the past 17 years targeting ABL kinase almost cures the patients and allows survival comparable to the normal population. Such molecules also are active against other cancers, which are triggered by mutated proteins, also sensitive to the same molecules.

The principles detailed above on MPNs and CML could be similar to many other conditions, cancers, autoimmune and degenerative diseases, for which deep molecular understanding is emerging. To give a few more examples, mutational testing is becoming

routine for lung, colon, breast and prostate cancer, lymphoid and myeloid leukemia, glioblastoma and several other cancers. Frequently tested mutations like BRAF V600E, N- and K-RAS gene mutations, ALK and EGFR mutations, mutations in TET2, IDH1/2 are just a few examples. Genetics is beginning to identify more and more predisposing mutations for several diseases. Next generation sequencing of peripheral blood DNA from pregnant women allows not only the discovery of fetal anomalies in chromosomes 21, 18, 13 and others, but can also reveal characteristics of the maternal DNA. These can concern the fetus or identify diseases such as undetected tumors. Genome-wide non-invasive detection of genomic alterations both in the fetus and mother is an area of major potential.

Immunotherapy

Besides targeted therapies, there is another area of enormous potential for cancer treatment, the area of immunotherapy. In this area, discoveries spanning the past 60 years have now blossomed into incredibly positive clinical results in cancer. It turns out that our immune system can recognise tumor cells, because such cells express either mutated proteins (their genome makes mistakes), or proteins that are not normally expressed in adults, as they are expressed only in the embryonic life. Discoveries in this area are changing the treatment of several cancers, for example melanoma. Success of immunotherapy appears to hinge on the capacity of tumors to generate mutations. These can be different from patient to patient, and expression of certain genes might predict response. So, for immunotherapy to work and develop, we would need massive muta-

tional and gene expression testing of tumors. Are we ready for this?

Every country in the EU has its own mechanisms of deciding which molecular/genetics test is reimbursed and how frequently. An incredible heterogeneity in the rules of reimbursement exists in the EU, which negatively influence both patient care and scientific progress, as untested patients will not be included in clinical studies. The situation is even more complex for former communist Eastern European countries that have financial difficulties. An exception is the Czech Republic where there is an impetus to both reimburse molecular testing and support research efforts to develop in-house validated molecular tests. At the opposite end, Romania begins to use an un-conventional system whereby pharmaceutical companies are asked to support molecular testing that directly relates to drugs they commercialise. This system can lead to an enormous conflict of interest as pharmaceutical companies cannot substitute themselves to hospitals and medical professional bodies, and will certainly not invest in resistance mechanisms and testing for scientific purposes.

In conclusion, progress made on targeted therapies and on immunotherapies hinge in the future on the capacity to obtain mutational and gene expression information, and ultimately whole genome sequence on a patient per patient basis. Results must be generated rather fast, as patients with acute conditions cannot wait for complicated bioinformatics to unfold, so standardisation must follow. All this appears very costly at the moment. However, broad application of immunotherapy would

dramatically lower costs because immunotherapy leads to long-lasting effects, like vaccines against infectious diseases, with immunological memory that would not require repetitive administration.

The question then is, how we re-think reimbursement policies and how can we get to a more uniform system in Europe? This reflection, I would say, is urgent.



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Understanding the process of intravenous access

Virginia M Stewart, Forsythe Emergency Services outlines when intravenous access may be needed and how the skilful process should be undertaken

Patients coming to the Emergency Department (ED) with shortness of breath may have characteristics that impede intravenous (IV) access. Such characteristics may include hypotension, dialysis dependence, morbid obesity, history of diabetes, sickle cell disease, or IV drug use. One prospective observational study identified nearly 1 in every 9 to 10 adults coming to an urban ED had difficult venous access requiring 3 or more IV attempts.¹ If peripheral IVs are not established, patients may need a central venous catheter placed for life-saving medications administered. In addition to requiring physician skill, central venous catheter insertion carries a risk of complications including infection, arterial puncture or an aneurysm, and pneumothorax. Ultrasound-guidance for peripheral IV placement (UGPIV) has prevented the need for central venous catheter placement in 85% of patients with difficult intravenous access.² UGPIV has been performed by Emergency Medical Technicians (EMTs) in prehospital settings, as well as nurses and physicians. Patients who have been identified as having difficult access have higher patient satisfaction scores when ultrasound is used in peripheral IV access attempts.³

Frequently, the large veins of the antecubital fossa are sufficient to place large bore peripheral IVs needed for resuscitation. The brachial and basilic

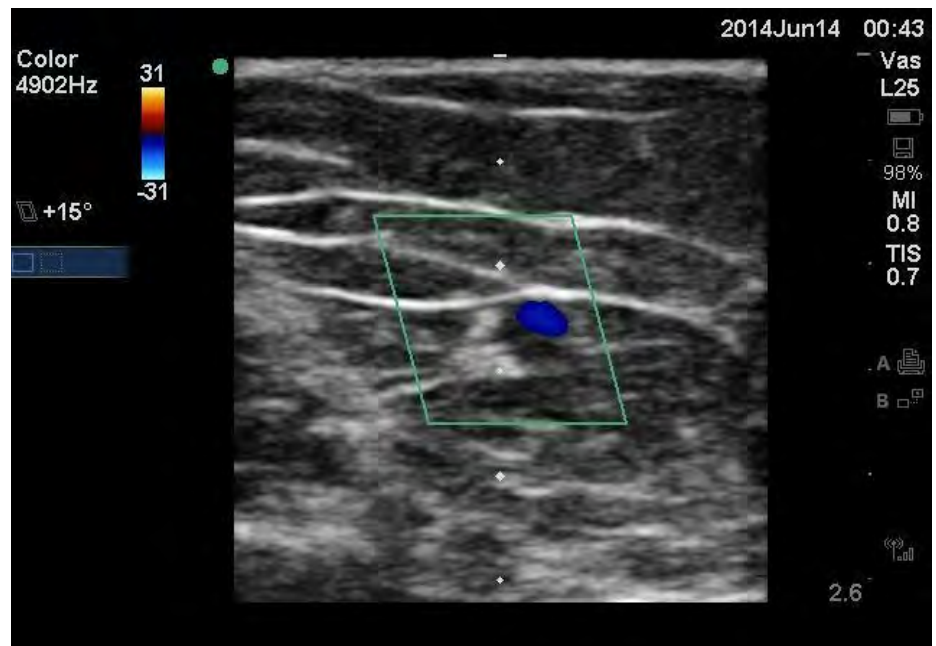


Figure 1: Short axis view of a peripheral vessel visualised with Colour Doppler (blue). The scale on the right of the screen demonstrates a total depth of 2.6 cm. A guide (white dots) in the centre of the screen marks each 0.5cm of depth. Therefore the depth of the vessel is between 1-1.5cm deep to the skin surface.

veins are easy to locate. The brachial artery is generally flanked by 2 smaller veins and the median nerve. Anatomically, these structures are medial to the insertion of the medial biceps tendon. This tendon is palpable in the antecubital fossa as the patient flexes the elbow. The basilic vein is located medial to the brachial vessels. Generally, it is more superficial, larger, and does not have an accompanying artery or nerve at the level of the antecubital fossa. As you move proximally up the arm (towards the head) the basilic vein dives deeper toward the humerus, and longer angi catheters may be required for cannulation.

When considering vascular access, there are 2 views, a short and long axis view. Cannulation from the short axis is considered 'out of plane' since the needle is perpendicular to the probe. A short axis approach 'looks' at a cross section of the vessel. Long axis uses an 'in plane' approach with the needle entering from the probe marker end, and 'looks' along the length of the vessel. Figure 1 identifies a vessel using colour Doppler in the short axis view. Figure 2 demonstrates a long axis view with a hyperechoic angiocatheter. Figure 3 is the same vessel in long axis with the angi catheter placed. While both approaches may be used for UGPIV placement, the



Figure 2: Long axis view of a peripheral vessel. The hyperechoic needle is visualized approaching from the top left of the screen into the vessel lumen.

benefit for the short axis is the ability to identify target veins as well as accompanying non-target (arteries and nerve) structures.

Identify the vein: remember the two C's

The two C's to remember for UGPIV access or for central venous cannulation are compression and colour (or Power) Doppler. Veins are thinner-walled and more easily compressed than arteries. This author advocates for finding a vessel first in the short plane, and compressing the vessel to ensure it is indeed a vein, rather than a less or non-compressible artery. Colour or Power Doppler may be utilised to determine if the pulsatile flow is consistent with an artery or vein. Colour Doppler uses red and blue to determine flow towards or away from the probe respectively. Power Doppler detects flow without concern for direction. Colour should not be relied on alone to determine arterial or venous flow due to the colour scale setting can be flipped or reversed, or aliasing can occur. Arterial flow is more pulsatile than venous. Venous flow may require distal augmentation (by squeezing the forearm distal to the probe) to appreciate the blush of colour.

Once the target vein is identified, the

depth from the skin surface should be noted. A common mistake is to use an angiocatheter that is too long or too short. A general rule of thumb is to use a catheter length that is more than twice the depth of the vessel to ensure at least half the catheter lies within the vein. Sterile ultrasound gel should be used, with a covered probe to prevent infection. To prevent the risk of multiple punctures, this author advocates for first bouncing the needle on the skin over the point of entry. The tissue should deform at the top of the screen, and confirm the needle is over the target vessel. Once the skin is punctured, the needle tip is kept in view by angling the ultrasound probe until the target vessel is punctured.

To confirm placement, either a 'bubble study' with agitated saline may be performed or Colour (or Power) Doppler utilised to visualise saline flow through the cannulated vessel. A vessel that is not properly cannulated will demonstrate extravasation of saline around the vessel into the tissue before the tissue swells to a degree which is palpable on the surface of the skin. Figure 4 demonstrates confirmation of intraosseous (IO) lines utilise Power Doppler. A 10cc saline flush is rapidly pushed through the line, and flow is demonstrated beneath



Figure 3: In this long axis view of a peripheral vessel the catheter has been threaded and is seen within the lumen of the vessel.



Figure 4: Power Doppler (orange) confirms placement of an intraosseus line within the distal tibia. The bright white line of the tibia cortex (in long axis view) is visualised at the top of the screen, with flow confirmation from a 10cc saline flush immediately distal (below) to the hyperechoic cortex.

the bony cortex in this adult tibia. If the line is improperly placed, the blush of colour using Doppler would appear in the soft tissues. For further information about UGPIV placement, visit: <http://rmgultrasound.com/piv-access/>

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Gluten friendly technology fixes proteins in wheat kernels

Professor Carmen Lamacchia is the inventor of a new gluten friendly technology that promises to make bread and pasta safe for people with coeliac disease

Scribbling notes in a cosy kitchen, Professor Carmen Lamacchia observed the slow rotation of wheat kernels in her microwave oven. It was 2011 and the food chemist from the University of Foggia in southern Italy was going on a hunch.

Could gluten, the protein that causes intestinal damage in people with coeliac disease, be disarmed inside the kernel? Could its toxicity be reduced before it became flour? Tapping into her intimate knowledge of gluten proteins, Lamacchia began testing her hypothesis away from the university labs. She was at home expecting her third child, yet she was equipped with the essentials: water, heatwaves, and a stopwatch.

"I soon realised that time was key to achieve detoxification," said Lamacchia. "I was applying high temperatures and humidity in synergy, but I needed to find the right tempo to induce a steady conformational change at the molecular level of the wheat kernels."

Gluten Friendly™

Just 6 years later, Lamacchia's early hypothesis has become a patented technology, called Gluten Friendly™. Her formula disarms the toxic component of gluten inside wheat kernels, through cycles of heat, soaking and resting. As a result, gluten proteins crystallise into a new shape, making them unrecognisable to the immune system of coeliac patients.



The Gluten Friendly™ method is a cost-efficient, chemical-physical process that also maintains all the precious organoleptic properties of wheat. The detoxified flour leavens and bakes into fluffy bread, pizza and cookies. The discovery is at the heart of the food-tech startup New Gluten World, a partnership among Professor Lamacchia, the University of Foggia and cereal giant Casillo Group.

In Lamacchia's native region of Apulia, wheat fields extend into the horizon. Come summer, the panorama puffs smoke. Farmers set wheat stubbles ablaze to prepare their land for a new agricultural cycle. What is left behind in the furrows caught Lamacchia's attention. She discovered that gluten proteins inside burnt kernels behaved differently.

"Glutenins and gliadins, which make up gluten, did not mingle in the kernel after exposure to strong heat, but stayed separate," said Lamacchia, "the opposite of what gluten does in the dough during baking." These early investigations became the entry point for the Gluten Friendly™ discovery. The scientist began thinking that, through heat, gliadins and glutenins could be moulded, without burning the kernel.

From kitchen tests, to *in vitro* lab analysis, Professor Lamacchia has now reached the ultimate phase testing her detoxified flour on humans. New Gluten World has partnered with a hospital in southern Italy, Casa Sollievo della Sofferenza, to conduct the clinical study. Fifty coeliac volunteers are now eating 3 or 6 grammes of detoxified

gluten daily, for 3 months. Neither doctors nor patients know who is eating Gluten Friendly™ bread rolls, and who is instead in a third control group that eats gluten-free.

Around 6 grammes of gluten is found in 2 slices of pizza. Previous medical studies show that coeliac patients ingesting such quantities of gluten suffer from diarrhoea, vomiting, and other serious symptoms within 3 days, and intestinal damage within a month.

“My coeliac patients are well and are not reporting symptoms,” said Lamacchia. “This is very reassuring, however, we won’t have the full picture of how the gluten friendly bread has interacted with coeliac patients until all the data comes in.”

Intestinal biopsies sampled before and after the 12-week period will be sent to an independent laboratory in Finland for in-depth analysis. Results are expected in early 2018.



New Gluten World has received funding from the European Union’s Horizon 2020 Research and Innovation Programme, under grant agreement no 732640. With EU support, New Gluten World is already developing a line of industrial ovens for gluten detoxification, with the ambitious goal of bringing the Gluten Friendly™ technology to milling companies around the world.

“To close the nutritional gap between people with coeliac disease and the general population, you need millers, bread and pasta makers from around the globe,” said Lamacchia. “We’ll disseminate our technology and know-how through an international licensing program,” she said, “so licensees can make fresh products that are safe for everyone.”

Coeliac disease

The World Gastroenterology Organisation estimates that one percent of the global population suffers from coeliac disease. That is about 70 million people. Affecting children and adults with a genetic predisposition, the autoimmune condition is for life. In people with coeliac disease, gluten triggers an inflammatory reaction that destroys the villi of the small intestine, causing malabsorption of nutrients and collateral illnesses like anaemia, dermatitis herpetiformis, osteoporosis and infertility. One-third of humanity carries genetic markers that indicate a risk of developing the disease.

Currently, the only therapy for coeliac patients is the gluten free diet. That means cutting out wheat, barley, rye, and certain oats. Still, the danger of gluten contamination is always around the corner. Eating socially can become a real source of anxiety.

“I don’t want to speak for coeliac patients, but I believe that many would much rather take a pill than stay away from pasta, bread or pizza,” said Lamacchia. “Unfortunately, this pill does not exist.”

The gluten free industry is conservatively estimated at \$8bn. But coeliac’s are not the biggest buyers. The largest chunk of consumers of gluten free products are people with non-coeliac gluten sensitivity (NCGS). They are those who without coeliac disease associate gluten consumption with symptoms of bloatedness, headaches and irritable bowel. Whether as a therapy or a lifestyle, eating gluten free products, comes with a cost.

While nature provides a plethora of healthy gluten free options, industrial gluten free substitutes of wheat-based foodstuff are often enriched



Carmen Lamacchia, PhD is President and CEO of New Gluten World

with starches, fatty acids and sugars in an attempt to mimic the original taste and texture of wheat flour. Consequently, they bring more calories and a higher glycaemic index, while costing significantly more than the original wheat-based food.

Gluten Friendly™ foods could offer a natural, safe alternative that is also appealing to the wallet. New Gluten World promises that Gluten Friendly™ licensees will sell their products for one-third of the price of gluten free.

“We are shifting the paradigm, from over pricing to fair pricing,” said Lamacchia, “and from fixing the intestine to fixing gluten itself.”



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Tackling the threat of antimicrobial resistance in Canada

As antibiotics become less effective against infection, Minister of Health, Jane Philpott, outlines the response to antimicrobial resistance in Canada

Antimicrobial resistance (AMR) is one of the most serious global health threats today. Existing antimicrobials, such as antibiotics, are becoming less effective as AMR is outpacing the development of new drugs to treat infections.

AMR happens naturally when bacteria that cause illness become resistant to the antimicrobials used to treat infections. However, inappropriate use of antimicrobials in health care, agriculture and veterinary settings can increase AMR. Resistant infections that are more difficult to treat can lead to long-term illness, increased healthcare costs and death. It is estimated that, with no action, annual worldwide human deaths attributable to AMR could reach 10 million by 2050¹.

Tackling AMR in Canada

Canada must be prepared to detect and respond to the threat of AMR to lessen the health risks to Canadians in the face of rising rates of drug-resistant infections around the world.

The Government of Canada created a Federal Framework and Action Plan, which has laid out the concrete actions we have been taking in recent years to address AMR and antimicrobial use (AMU). We are using a “One Health” lens with coordinated effort across human health, animal health and agri-food sectors, among others, to help prevent and control AMR.

We are strengthening surveillance systems to help identify new threats or changing patterns of AMR and AMU in humans and animals. For example, the Public Health Agency of Canada’s Canadian Antimicrobial Resistance Surveillance System integrates information about AMR and AMU in humans and animals to inform public health action. It draws on relevant data from both the human health and animal health domains



**Jane Philpott, Canada’s
Minister of Health**

through partnerships with specialised surveillance systems and laboratories.

Our government is strengthening the responsible use of antimicrobials in human and veterinary medicine, through the development of regulatory and non-regulatory initiatives, including public health guidelines, best practices and widespread communication to health professionals and the public. In May, Health Canada announced changes to the Food and Drug Regulations that strengthen rules to control access to veterinary antimicrobial drugs to better promote their prudent use in food-producing animals. Complementary measures are being developed to ensure that a veterinarian’s prescription will be required to obtain antimicrobial drugs for animal use. The Canadian Food Inspection Agency is also working with the animal feed industry to ensure prudent AMU through changes in the Compendium of Medicating Ingredient Brochures.

The government is also collaborating with national and international partners to advance policy, research and innovation in Canada and abroad. For example, the Canadian Institutes of Health Research (CIHR) invests in the Joint Programming Initiative on AMR, a global

research network made up of 23 member countries. CIHR is also investing in Canadian research teams that are developing innovative diagnostic tools to help clinicians quickly identify whether prescribing antibiotics will be effective.

Our Government plays a role in developing and disseminating information and guidance, and encouraging prudent AMU by public health and healthcare professionals, food producers, veterinarians and the Canadian public. Public awareness activities help Canadians to understand the benefits and risks of antimicrobials and why their use is not always warranted for treatment of infectious diseases.

“Our government is strengthening the responsible use of antimicrobials in human and veterinary medicine, through the development of regulatory and non-regulatory initiatives, including public health guidelines, best practices and widespread communication to health professionals and the public.”

Working with our Partners

Addressing AMR requires sustained efforts across multiple sectors and organisations. Provinces and territories, academia, animal and human health professionals, food production stakeholders and pharmaceutical and livestock industries each hold essential levers for reducing AMR.

A Pan-Canadian Framework for Action is being developed jointly with the provinces and territories and other key partners to guide our collective action in tackling AMR in Canada. This high-level Framework will identify strategic objectives, opportunities for action and desired outcomes under 4 pillars: surveillance, stewardship, infection prevention and control, and research and innovation.

Some key opportunities identified for future action include:

- Establishing coordinated ways to link AMR and AMU data from human health, animal health and agriculture sectors;

- Engaging all levels of government and stakeholders to deliver communication, education and training programs and tools on evidence-based infection prevention and control practices and strategies;
- Building knowledge about antimicrobial stewardship through enhanced and coordinated education for prescribers, dispensers and end-users of antimicrobials; and,
- Establishing a fast-tracked, cost-effective process for licensing antimicrobial drugs, alternatives to antimicrobials and new diagnostic tools in Canada to incentivise pharmaceutical investment without compromising safety, efficacy and quality.

Once the Framework has been completed, we will focus on developing an action plan that lays out concrete actions and timelines to meet the Framework’s objectives.

Looking to the Future

Significant work remains to be done to protect Canadians from the threat of AMR and to minimise the impact on human and animal health.

Everyone has a role to play and it is through collective actions that we will make real progress in tackling AMR in Canada and around the world. ■

¹ “Tackling Drug-Resistant Infections Globally: Final Report and Recommendations” The review on antimicrobial resistance chaired by Jim O’Neill, May 2016 https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf

Jane Philpott
Canada’s Minister of Health

Health Canada
www.canada.ca/en/health-canada.html
[www.twitter.com/HealthCanada](https://twitter.com/HealthCanada)

Queueing theory: the solution to unsustainable wait list practices

David Stanford, Richard Boucherie, and Peter Taylor outline how queueing theory could help tackle some of the challenges in the healthcare sector

Most readers can appreciate that governments are continually challenged by demand for new services and medications while striving to limit health care from consuming an ever-increasing proportion of public revenues. Increasing demand is, in part, due to an ageing population, but it is also due to the cost of new drugs and high-tech treatments. Arguing whether or not these increasing costs should be avoided is an important debate in many countries, including the Netherlands, where it has resulted in a reduction of the number of treatments being reimbursed by healthcare insurers.

As shown in [Global Health Observatory \(GHO\)](#) data, delayed access to care is known to reduce the quality of that care. While the Netherlands' healthcare quality is at the top of many worldwide rankings, the Dutch Healthcare Authority (NZa) recently sounded the alarm about increasing access times. Various reasons, including the insufficient numbers of medical specialists, were listed as common causes.

Increasing the numbers of medical specialists or diagnostic facilities has often been employed to reduce access times in healthcare. However, the cost increases of such solutions are unsustainable. Widely in the Western world, healthcare costs already represent about 10-15 % of the GDP, making healthcare the largest indus-

try in these countries. In contrast, a proper implementation of queueing principles in the healthcare system often yields better performance for less cost than additional resources do. Consider the following example: In 2006, the Academic Medical Centre Amsterdam (AMCA) scanning facility approached the Center for Healthcare Operations Improvement & Research (CHOIR) at University of Twente for help with scheduling. Patients for the two non-emergency CT scanners were waiting up to four weeks for treatment. The AMCA intended to add a third CT scanner to reduce waiting times.

CHOIR

When CHOIR researchers looked at the logistics of the patient flow, they observed large variability in both the arrival times of patients from other facilities in the hospital and in CT scanner occupation times, since a small proportion of patients required the administration of contrast fluids. In queueing theory, variability is known to be one cause of access delay. The CHOIR team advised that patients should arrive ten minutes earlier than scheduled and that the contrast fluid should be administered in an adjacent room when necessary. These two measures reduced both the mean time the CT scanners were occupied and its variability, thereby reducing the average CT access time to two days with the two existing scanners. Ongoing collaboration with CHOIR currently enables AMCA to run the CT

facility as a walk-in facility, with negligible access time.

The above story is a good example of what can be achieved when queueing theory is brought to bear on problems of congestion in healthcare facilities. Queueing theory is the branch of mathematics which models congested systems in which randomness features prominently. The first such models, from the early 1900s, responded to needs in the rapidly-expanding telephone network. Since then queueing theory has been used for applications as diverse as design of production lines, theme park operations, and Internet data traffic.

Randomness is a key factor confounding a health facility's ability to provide timely access to care. The times when people need health services are not predictable, and there is considerable variability in both the service duration and the resources required to provide appropriate treatment. The relative acuities of the patients present and how they evolve over time, the interactions between distinct health services, and the number of nurses, doctors, beds, and ancillary facilities available are all aspects that can vary widely.

The fact that variability is among the main factors influencing access is well-known to queueing theorists; in fact, it is a key aspect considered in queueing practice. In healthcare, however, variability is too often ignored.



Averages are treated as if they occur with certainty, leading to degradation of medical care, as illustrated in the CT example above.

In recent decades, queueing theorists have had success in improving health system delivery. Along with academics interested in scheduling, they have impacted areas as diverse as emergency room waiting times, operating room schedules, medical short-stay units, and the connectedness of the emergency/acute care/subacute care pathway.

Organ transplantation

One frequent challenge is the fact that waiting times for organ recipients of the 'universal donor' blood type O used to be notably longer than those of other blood groups, because too many O organs are cross-transplanted into recipients of other blood types. In November 2010, this led to the Euro-transplant zone insisting upon ABO-identical transplantation of kidneys. This strategy penalises recipients with

rarer blood types (in Europe, B and AB) due to their much smaller number of donor organs. A queueing solution that balances the needs of both large and small-populated blood-type pools was presented in a [ScienceDirect article](#).

Clearly, continual increases in the fraction of government revenues devoted to healthcare are unsustainable. A proven alternative which can no longer be ignored is to improve the logistics processes, invoking operations research techniques such as queueing theory and simulation. These models give solid evidence to wary practitioners of the effectiveness of new working methods in a safe setting.

We close with one further call. It is still widely true that doctors and nurses receive no training in health system congestion and its impacts upon timely delivery of healthcare. This lack of any training in queueing principles tends to lead to repeated re-inventing of the wheel, often based upon faulty intuition. For meaningful improve-

ments in access, this must change. With no such training for doctors and nurses, the natural fault line between patient care and system efficiency will only be exacerbated; with it, evidence-based arguments can be made, and the improvements in access that we all seek are much more likely to occur.

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Pushing scientific fact over public opinion in Italian healthcare

Open Access Government's Giara Ruane explores the challenges facing the Italian healthcare system and the need for an evidence-based approach

The Italian Minister for Health, Beatrice Lorenzin, has been faced with many controversial issues since she came to the position in 2003. Italy is a country with a chequered political past, and passions can come to the surface when debating issues as personal as those involving health. The Ministry of Health is faced with maintaining a standard of innovation in the face of varied public opinion.

Vaccinations

In recent years vaccines have become a big issue in central Europe, particularly in Italy. An outbreak of

measles lead to the government making 12 vaccines mandatory for children of school age, with [Lorenzin stating that](#) proof would be required of vaccination for children to be permitted to attend school. Claims that vaccines were linked to autism have been widely discredited, however, some in Italy are still wary when it comes to vaccinating their children. Lorenzin called these ideas 'anti-scientific', and praised the legislation in a [statement](#), saying the government has a duty to reassure the public. However, the legislation has proved controversial, with many families expressing anger and some even considering emigration.



Italian healthcare, requiring an updating of health processes for new arrivals. Again, Lorenzin emphasised that the new guidelines would be strictly ‘evidence-based’ in her [statement](#) on the issue. These guidelines included vaccination for all migrants and refugees, and immediate treatment for infectious disease. The main concern is ensuring that the European healthcare systems has the resources available to provide adequate emergency care and prevent infection from spreading. Conditions like pregnancy have been made a priority, as well the diagnosis of degenerative illnesses in their early stages.

“The legislation came after a measles outbreak in the country which killed 35 people. In 2012 an Italian court ruled in favour of a family who claimed their child’s autism had been caused by an MMR jab, leading to a deep rooted distrust of vaccines in the country. The move to make them mandatory has sparked backlash and protests throughout the country.”

The perilous journey refugees are often forced to take, overseas with little support and supplies, often leads to conditions such as burns, dehydration, infections, and lesions. Along with non-profit organisations [Italy’s healthcare system](#) aims to immediately examine new arrivals. If required, care is provided in purpose-built structures, and arrivals are airlifted to hospitals if additional specialised care is required. Mothers with young children and pregnant women are given special attention, an ultrasound scan when they arrive possibly being the first piece of assurance on their baby’s health they have received in months. However, as the crisis worsens, the scale of work needed is increased. [Dr Pietro Bartolo](#) leads migrant medical care and has done so for 2 decades. He is not optimistic about the future, saying “We do what we can, because it’s right to do it. We want to save as many lives as we can, but in the end it’s the system that’s broken.” Lorenzin [has faced](#) criticism for issues surrounding migrant healthcare, and has continued with her ‘evidence based’ approach to this and similar issues. ■

The legislation came after a measles outbreak in the country which killed 35 people. In 2012 an Italian court ruled in favour of a family who claimed their child’s autism had been caused by an MMR jab, leading to a deep rooted distrust of vaccines in the country. The move to make them mandatory has sparked backlash and protests throughout the country. Lorenzin has reassured parents, even tweeting an image of her own [3-month-old twins](#) receiving the jabs. She has accused negative press of being ‘fake news’, and has urged people to stick to just the facts surrounding the issue. She has asserted that science is separate from politics and shifted public opinion, urging a bipartisan approach to ensure all children starting school are immunised.

Evidence-based healthcare

This emphasis on pushing scientific fact over public opinion extends beyond the Italian government’s vaccination legislation. Something as personal and far-reaching as health will always involve deeply emotional involvement from the public. Recent arrivals of refugees and migrants have created a greater strain on

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The DIDO Project: autoimmune disease therapies research

University of Perugia's Ursula Grohmann and Antonio Macchiarulo share the work of the DIDO project in understanding cancer and autoimmune disease therapies

As proposed by Burnet and Thomas in their theory of 'cancer immune-surveillance' more than 50 years ago, our immune system is endowed with the capacity to identify and eliminate tumour cells. However, immune responses must be properly controlled in order to prevent the destruction of organism's cells and tissues, as it occurs in autoimmune diseases. Such physiological control mechanisms, or 'brakes' of the immune system, are commonly known as check-points. Whereas, defects in check-points can lead to autoimmune diseases, cancer cells have learnt how to successfully exploit such brakes in order to escape from an immune attack. The generation of check-point inhibitors, i.e., drugs releasing critical brakes of the immune system, has revolutionised the therapeutic treatment of certain cancers, such as melanoma, kidney and small cell lung tumours. Nevertheless, the low percentage of responsive patients, as well as the limited number of tractable tumours would require innovative inputs to the check-point inhibitor field. On the other hand, no therapeutic approach has been developed so far on the basis of a potentiation of check-point activity in autoimmune diseases.

An important mechanism of immune escape in tumors involves the metabolism of tryptophan (Trp), the rarest essential amino acid found in food. More than 90% of Trp entered with diet is metabolised via a pathway

that produces several biologically active molecules, collectively known as kynurenines. Both Trp degradation and the production of kynurenines are involved in the brake effects of Trp metabolism on the immune system and, in this regard, the main enzyme involved is indoleamine 2,3-dioxygenase 1 (IDO1). The highest expression of IDO1 can be found physiologically in dendritic cells (DCs), sentinels of the immune system that instruct T lymphocytes to either mount an effective immune response to destroy the foreign invaders or tolerate (not respond to) the antigens. A deficiency in IDO1 activity, particularly in DCs, has been observed in several experimental models, as well as human diseases of chronic inflammation and autoimmunity. On the other hand, tumour-bearing animals as well as neoplastic patients are often characterised by an overexpression of the IDO1 enzyme, thus dampening anti-tumour immunity. Hence, IDO1 may represent an additional check-point molecule and, indeed, a combination of pembrolizumab (a 'classical' check-point inhibitor) and epacadostat, (a potent inhibitor of IDO1 catalytic activity) has recently reached phase III in clinical trials (ClinicalTrials.gov: NCT02752074).

In 2011 (1), we discovered that IDO1 is not just an enzyme metabolising Trp, but once phosphorylated by other enzymes, can trigger a signalling pathway that completely reprograms an immunostimulatory DC into a tolero-

genic cell. Notably, we also discovered that, whereas the tolerogenic effects of IDO1 as an enzyme degrading Trp are transient, a DC reprogrammed via the IDO1 signalling pathway will be capable to maintain tolerance and thus keep in check auto- and also anti-tumour immunity over the long-term. Thus our data suggested that the positive or negative modulation of IDO1 signalling by small molecules rather than catalytic activity could be more effective in the control of two chronic diseases such as autoimmunity and neoplasia, respectively (Figure 1).

"The DIDO project thus appears to have great potential to generate highly innovative drugs for the treatment of both autoimmunity and neoplasia, two wide disease classes so different in their pathologic nature."

The DIDO Project

DIDO is a 5-year project funded by the European Research Council and led by Prof. Ursula Grohmann (principal investigator) and Prof. Antonio Macchiarulo (team member). It started in early February, 2014 and is due to end in late January, 2019. The aim of DIDO is to identify small molecules capable of acting over the long-term by either favouring (thus useful in the therapy of chronic inflammation and autoimmune disease) or inhibiting (useful in neoplasia) the IDO1 signalling. To this purpose, the expertise in pharmacology/immunology/biology (PI's group) has been integrated with the expertise

IDO1 Signaling Modulators (Autoimmunity, Neoplasia)

VIS-110
University of Perugia
PRECLINICAL STAGE

Long-Term Immunotherapy

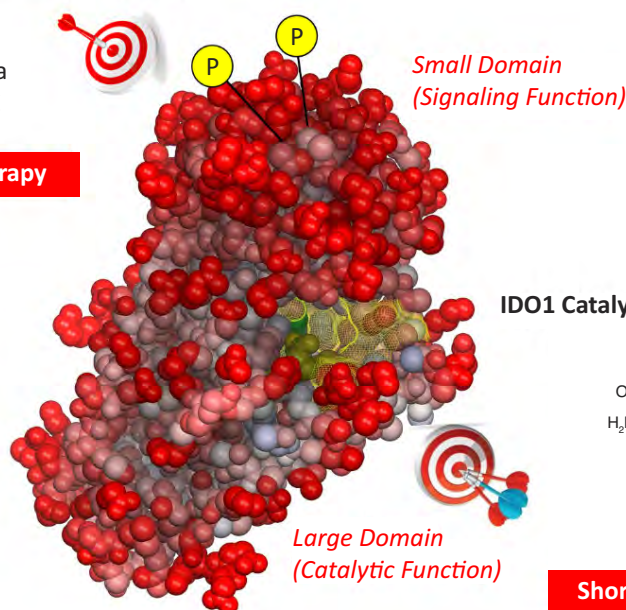
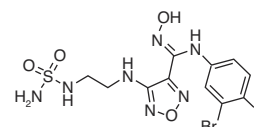


Figure 1: IDO1 is an enzyme metabolizing Trp (catalytic function) that, once phosphorylated (P), triggers a signalling pathway to reprogram immunostimulatory DCs into tolerogenic cells

IDO1 Catalytic Inhibitors (Neoplasia)



Epacadostat
Incyte
PHASE III

Short-Term Immunotherapy

in medicinal chemistry/molecular and computational modelling (team member's group) to develop such innovative drugs.

In the first 30 months of the project, we established a novel, integrated method capable of screening hundreds of compounds with the potential of modulating IDO1 signalling. We screened more than 200 structurally diverse compounds selected from a structure-based virtual screening of ~600.000 small molecules endowed with drug-like or lead-like properties. Of these, dozen compounds were so far proven to be novel, potent IDO1 catalytic inhibitors. We also identified chemical structures capable of modulating the signalling and not catalytic activity of IDO1. Specifically, one of these, VIS-110, did not show significant inhibitory effects on IDO1 catalysis but did promote the IDO1 signalling and, when used in DC cultures, conferred long-term tolerogenic properties capable of blocking the presentation of an autoantigen in vivo in an IDO1-dependent fashion. Moreover, the same molecule was capable to protect mice from experimental

autoimmune encephalomyelitis, a preclinical model of human multiple sclerosis.

Finally, we unexpectedly discovered an IDO1 catalytic enhancer, i.e., VIS-119, capable of increasing the affinity of IDO1 for its substrate Trp in both cell and biochemical (using a recombinant IDO1 protein) assays. VIS-119 was also effective in protecting mice from the development of experimental autoimmune encephalomyelitis. Very recently, we have also identified an additional novel method that allows for the identification of inhibitors of IDO1 signalling. All selected molecules are currently subjected to studies of structure activity relationships, early ADME profiling, pharmacokinetics, toxicity and efficacy in tumour models and additional experimental disease models of autoimmunity and also allergy.

The DIDO project thus appears to have great potential to generate highly innovative drugs for the treatment of both autoimmunity and neoplasia, two wide disease classes so different in their pathologic nature.

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Understanding speech and language disorders

OAG Editor Laura Evans talks to NIDCD's Deputy Director Dr. Judith Cooper about the research strides being made in speech and language disorders

The National Institute on Deafness and Other Communication Disorders (NIDCD), part of the National Institutes of Health (NIH), reports that nearly 1 in 12 children ages 3 to 17 has a disorder that is related to voice, speech, language or swallowing. As defined by the NIDCD, a childhood communication disorder can include a child's voice that may be too weak, hoarse or strained; how a child speaks; problems making speech sounds; or problems with how a child learns, understands and uses words or sentences.

Statistics from 2015 revealed that nearly 8% of children between 3 and 17 years experienced a communication or swallowing disorder within a 12-month period. Among those, 55% of children received treatment during the same 12-month period. It was reported that 5% had speech problems, 3.3% of children had language problems, and 1.4% had a problem with their voice.

In order to gain a better understanding of communication disorders in children as well as adults, Editor Laura Evans speaks to Dr. Judith Cooper, Deputy Director of the NIDCD, to shed further light on research in this area and the challenges that arise.

"Speech and language disorders can occur in both children and adults throughout the life span. With children, if you're talking about speech disorders, that term usually refers to difficulty pronouncing speech sounds. There may be a problem in articulating or forming consonants and vowels in the language," Dr. Cooper explains. "Some children have such severe problems that they are literally unintelligible, which means they are talking but you can't understand what they are saying."

"Adults can also have speech disorders. These are usually the result of some sort of neurological event,

perhaps a brain injury, stroke, or Parkinson's disease. Usually these adults had normal speech up until they had the neurological problem, but then find that they have difficulty speaking and being understood.

"Another speech disorder found in both children and adults is stuttering, or problems with fluent speech."

"Language disorders are problems in comprehending (understanding) or using words and sentences. With children, what you may see is a child who is very slow to talk, with delays in first words, or they've got single words but they don't seem to be able to put the words together, or they put the words together but their grammar or syntax is off."

"For adults, language problems typically occur, again like speech problems, as a result of stroke or another kind of neurological problem."

In order to gain further knowledge and develop treatments to help people living with speech and language disorders, research plays a vital role. As Dr. Cooper explains, research is improving the process of early identification of children who are at risk of developing these disorders, and lessening problems that could arise.

"For children who have speech and language disorders, sometimes it's hard to tell them apart from other children until speech and language should be appearing, at which time it becomes really hard to understand them compared to their peers, or they don't seem to be doing very well in language," she says.

"We do have speech and language treatments: for young children, preschoolers, and all the way up to adults. What many of our treatment studies show us is that one treatment doesn't solve the problem for all

individuals. So what research is trying to address is what kind of treatment works for what kind of profile for that disorder, and how often do they need the intervention. These are questions we can only answer through rigorous research.”

The role of research

According to Dr. Cooper, the mission of the NIDCD is to improve the lives of people with communication disorders. Through both basic and clinical research, the Institute is continually looking to improve methods of identifying, treating, and preventing communication disorders, all with an ultimate goal of helping people with these speech and language disorders and their families.

“We make a huge effort to get the results of our research out to the public, as well as to healthcare providers and clinicians,” says Dr. Cooper. “We do that through the [NIDCD public website](#), on which we have publications that are developed to convey research results. Many of our staff go out to scientific meetings and to professional organisation meetings to talk about the findings of research.”

The Institute’s commitment to research and delivering the results to patients and healthcare providers is crucial. Challenges come with any type of research, however, and communication disorder research is no different. Dr. Cooper says that there are key challenges in this area of research, and she underlines the importance of understanding what works best for each individual.

“One challenge for the future is individualised intervention: How do we figure out what’s going to work best for a particular individual with a particular type of disorder? For the longest time, our studies would take a group of people with similar disorders and treat them similarly. More individualised intervention is the way of the future.”

Finding populations and individuals to take part in research can also be a problem, as there are more people who don’t have communication disorders than do. Dr. Cooper notes, “Researchers have rigorous cri-

teria about the kind of population they are studying in a particular research project, and one of the challenges is for investigators to find sufficient numbers of individuals who are willing to participate. Many times, our investigators have to involve multiple sites, multiple hospitals, and multiple collaborations, and that’s often a challenge.

“Another challenge is making our findings relevant to as diverse a population as possible,” she adds. “For a long time, many less well studied populations were not included in some of our research. Thus, there was limited relevance of our findings to individuals not included, for example, those from low socio-economic status or individuals from diverse ethnic or racial groups. Expanding the diversity of the populations included in our research is a priority.

“This is also the case for particular populations with communication impairments. For example, much of the research in communication and autism was previously focused on individuals who were at the higher end of the autism spectrum. So who got left behind? Minimally verbal children with autism. Now our Institute has been encouraging and trying to push forward the need for that kind of research, and we are certainly making some progress.”

The NIDCD sponsors a broad range of research to better understand the development of speech and language disorders, improve diagnostic capabilities, and fine-tune more effective treatments. ■

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Specific language impairment: what do we know?

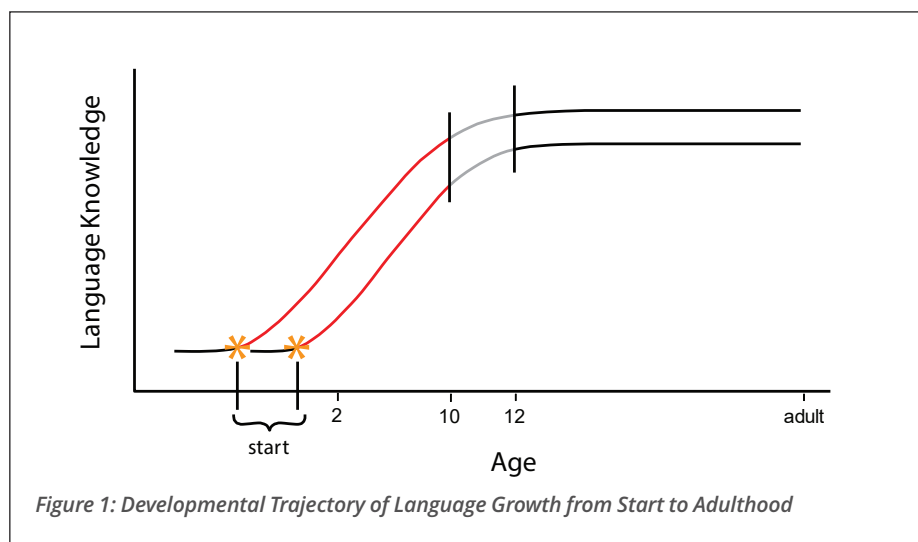
Mabel L Rice, University of Kansas details how the language of children with specific language impairment differs from typical children

A recent paper in this publication introduced the condition of Specific Language Impairment (SLI) as a largely unrecognised yet high impact common disorder of childhood (7-10% of children) that persists into adulthood and warrants further consideration by public health experts. SLI is a language disorder that delays the mastery of language skills in children who have no hearing loss or other developmental delays. Recent studies reveal the ways in which language development in children with SLI is not the same as unaffected children, yet also shows many of the same strengths.

These 3 findings are crucial to understanding the differences and similarities across the age span of 1 to 20 years of age. To sort this out, we need to consider the developmental arc of children's acquisition of language, from first words as toddlers, through childhood, and into adulthood. We also need to consider different dimensions of language; single words appear first, followed by simple sentences that adhere to grammatical rules. Some features of the adult grammar are relatively late-appearing in English-speaking children and those features are especially late for children with SLI.

Finding 1: Children with SLI are likely to be late language learners

Most children start producing words between 1 and 2 years of age, and then follow an accelerated rate of lan-



guage acquisition. As shown in Figure 1, children with SLI can be delayed by 1 or even 2 years in this early start-up period. Studies of preschool children report that the language of 5-year-old children with SLI resembles that of 3-year-old typically developing children, a notable delay at a time of rapid change. Yet when their language system begins to grow, it does so at a rate and pattern of change much like that of younger children. Children with SLI seem prepared to learn language in much the same way as other children, only with a delayed start. Because the rate and pattern of change in children with SLI parallels that of unaffected children, they are not likely to 'catch up' to their age peers. Yet when children with SLI reach preadolescence they, like typically developing children, slow their rate of language acquisition and then level off into adulthood, the stable end-state for much of language development¹.

Finding 2: Delayed vocabulary development can follow the pattern of late start + similar growth trajectories

Not all children with SLI have vocabulary deficits beyond the preschool years, but if so, the pattern holds over many years. Vocabulary growth is shown in Figure 2². This figure charts children's understanding of words, from 4 to 20 years of age, in a study that tested the same children annually. The SLI group is at the bottom 15% for their age and, in this study, the typical group is in the top 15%. At 4 years the SLI children, on average, know fewer words than children at higher levels for their age. This is not surprising; what is of interest is that the children at the low end learn new words at the same rate over time as the comparison group, but they don't close the gap. Instead, for both groups the rate of new word learning markedly slows with age, beginning at

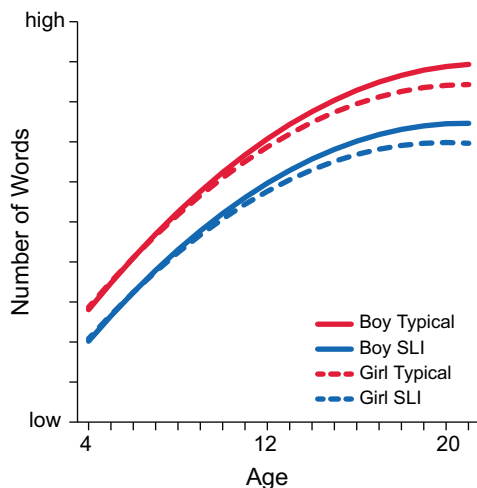


Figure 2: Growth of Word Comprehension from Childhood to Adulthood

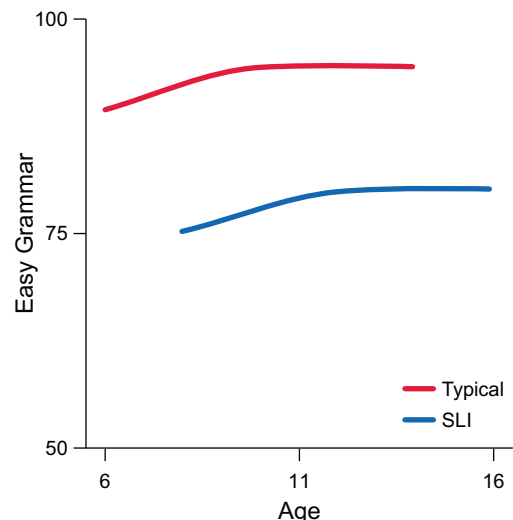


Figure 3: SLI Children's Judgment of Omitted Tense and Agreement Markers in Childhood

10-12 years of age and maintaining a slower rate into adulthood. Although before 4 years of age girls tend to have larger vocabularies than boys, this study found girls to have a slower rate of word acquisition than boys in adolescence, which left a marked disadvantage for girls with lower levels of vocabulary in the crucial time of education for preparation into the work place or higher education.

Finding 3: Tense and agreement marking on verbs is a grammar requirement likely to be difficult for children with SLI

This is evident in the use of forms of auxiliary or copula BE, as in "He is happy" and "Are the girls here?" as well as Auxiliary DO, as in "Does he want a cookie?" past tense, as in "Patsy walked home" and third person singular, as in "He wants a cookie." The persistent problem is that children with SLI, on average, omit these parts of the sentence as if the requirement were optional instead of obligatory. Figure 3 shows how persistent this tendency is in children with SLI³. As expected, between the ages of 6 and 16 years typically developing children recognise in judgement tasks that omission of

these parts of the grammar render a sentence ungrammatical. Even at 6 years this is an easy task. Yet children with SLI, on average, persist in considering omissions as optional and OK for grammar. It is as if they are stuck with an immature form of the grammar into adolescence.

Interpretation: SLI is a persistent language disorder that is evident early in development and has many similarities to younger language profiles with steady gains in language, levelling off in adolescence. This makes it likely that a child with SLI will become an adult with weak language skills, particularly in some, but not all, parts of the grammar. Much of the weakness in language can be hidden under compensatory social skills, and thereby goes undetected as a likely contributor to poor reading skills or avoidance of social interactions in adolescents and adults. Current studies investigate genetic influences on the causal pathways, as inherited language abilities can drive the strong language growth trajectories, yet selective inherited differences operative at key times could account for persistent and unresolved delays¹.

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The burden of non-communicable diseases

The Swiss Federal Office of Public Health shares the strategies in place for non-communicable diseases and the importance evidence-based prevention policy

One quarter of the Swiss population, or about 2 million people, already have a non-communicable disease (NCD), and the trend is increasing. Around 80% of direct health-related costs (CHF 50 billion in 2013) are caused by non-communicable diseases. Treatment of the 5 most common NCDs – cardiovascular diseases, diabetes, and cancer, respiratory and musculoskeletal disorders – accounts for around 40% of direct health-related costs, and this situation will intensify as society ages.

The strategy for prevention of non-communicable diseases in Switzerland

A “National strategy for the prevention of non-communicable diseases” has been developed in Switzerland to deal with these challenges. It is based on established approaches used in prevention work but at the same time strikes out in new directions. For example, prevention will be intensified in the healthcare setting with support from general practitioners and therapists. A further aim of the NCD strategy is to promote the health-related skills of the individual whilst also creating conditions that make it easier to adopt healthier behaviours on a daily basis. It is a fact that a large proportion of non-communicable diseases could be avoided or at least delayed by a healthy lifestyle.

Scientific principles in the service of an evidence-based prevention policy

An effective prevention policy for non-communicable diseases requires a sound scientific basis. The national NCD monitoring system is intended to show where needs exist and where progress has been made. The monitoring system comprises of 99 indicators that are derived mainly from existing national data sources and describe the disease burden, risk factors and social determinants. It involves the systematic collection of comparable and nationally representative data that

allow current health developments to be observed more effectively.

The monitoring system will also create a basis for comparing the situation in Switzerland with that in other countries. Additional surveys will be designed and carried out to fill any major gaps in the data. The monitoring system will also permit the targeted promotion, funding and scientific follow-up of prevention projects that are tested and evaluated on a regional basis or for a limited period before possibly being launched nationwide or for the long-term.

“Attention was paid to give equal consideration to themes relating to the risk factors alcohol, tobacco, nutrition, physical activity and overweight. In this way the monitoring system provides a sound basis for an evidence-based evaluation of the strategy and enables it to be adapted to new challenges.”

The NCD monitoring system

The Global Monitoring Framework (GMF) published by the World Health Organization (WHO) creates the important foundation needed to develop the monitoring system and select the indicators. The indicators contained in the GMF are being modified to suit Swiss needs and resources and are being optimised. They have been divided into key and additional indicators in line with the WHO’s proposal. The 99 indicators have thus been prioritised and categorised as follows:

- 13 strategic lead indicators that show whether the objectives of the NCD strategy have been achieved.
- 32 key indicators for central dimensions of the NCD strategy (e.g. differentiation according to target groups of the NCD strategy: children and adolescents, adults, the elderly).



- 54 additional indicators for specific information that is important for developing, reviewing and optimising measures adopted within the NCD strategy.

“Treatment of the 5 commonest NCDs – cardiovascular diseases, diabetes, and cancer, respiratory and musculoskeletal disorders – accounts for around 40% of direct health-related costs, and this situation will intensify as society ages.”

Attention was paid to give equal consideration to themes relating to the risk factors alcohol, tobacco, nutrition, physical activity and overweight. In this way the monitoring system provides a sound basis for an evidence-based evaluation of the strategy and enables it to be adapted to new challenges.

Knowledge transfer from research to field and informing the public

It is important to make the population as a whole, and vulnerable individuals in particular, aware of what causes non-communicable diseases. The monitoring system and departmental research will provide the

data and outcomes needed to inform people about the causes and consequences of NCDs and about the important role played by living, working and environmental conditions. At the same time, healthcare professionals will be assisted in their efforts to implement situation-appropriate prevention in the healthcare setting. Switzerland's NCD strategy actively supports the efforts of the WHO and work being done to prevent and control non-communicable diseases. ■

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Focusing on paediatric cancers

Epigenetic changes play a critical role in the development of paediatric cancers. Ivan Stamenkovic, Professor of Pathology, explains

Most paediatric malignancies develop and behave in ways that differ from those of adult cancers, largely due to genetic and epigenetic differences. In contrast to the majority of adult cancers, which develop years or even decades following the transformation of a single cell, paediatric cancers, particularly those that occur in the first few years following birth, emerge far more rapidly. Genetic analyses have shown that whereas most adult cancers accumulate numerous genetic mutations, paediatric cancers are for the most part genetically “quiescent”, meaning that they harbour few and sometimes only single mutations. Many mutations can contribute to adult cancer growth and different mutations may drive progression of any given cancer at different stages of its evolution. It may therefore be difficult to determine which mutation(s) is/are driving an adult cancer at the time of diagnosis. In contrast, mutations responsible for paediatric cancer development are easier to identify, which facilitates exploring the pathogenesis of these tumours and obtaining clues as to potential therapeutic targets and options.

Although genetic mutations have long been thought to play the key role in the pathogenesis of cancer, it is becoming increasingly clear that in many malignancies, posttranslational and epigenetic modifications may play an equally important role, sometimes



even dominating that of the genetic mutations. “Epigenetics” was originally coined to describe heritable changes in a cellular phenotype that were not due to alterations in DNA sequence. It is most commonly used to describe chromatin-based events that regulate DNA-templated processes such as gene expression. Chemical modifications, such as methylation, of DNA within gene promoters and of histones (acetylation and methylation), which are proteins intimately associated with DNA provide mechanisms that control gene expression. Histone modifications determine whether DNA segments assume a compact or relaxed structure. Activating histone marks are associated with relaxed DNA that is accessible to transcription factors, allowing the expression of genes within the corresponding DNA

segments. Repressive histone marks induce DNA compaction rendering it inaccessible to the transcriptional machinery and resulting in the silencing of genes located in the corresponding DNA segments. As the genes in question may control cell division, growth and survival, regulation of their expression by epigenetic modifications may be a key determinant of cancer development, behaviour and response to treatment.

Fusion proteins

Increasing evidence suggests that epigenetic changes play a critical role in the development of paediatric cancers. Many solid paediatric malignancies, particularly of bone and soft tissues, known as sarcomas, arise as a result of unique reciprocal chromosomal translocations that give rise to

fusion genes, which encode fusion proteins found only in the cancer cells. These fusion proteins provide a diagnostic signature for these particular types of cancer, and, more importantly, are responsible for their pathogenesis. In the majority of cases, the fusion proteins behave as aberrant transcription factors or transcriptional regulators. They alter the gene expression repertoire of the cells, augmenting the expression of genes that promote cell survival and growth and silencing those that induce differentiation and quiescence. To execute their functions, these aberrant transcription factors may form complexes with chromatin-modifying enzymes and instruct them to reconfigure DNA structure, opening domains that in normal cells remain compact and therefore inaccessible to transcription, while condensing domains that are open in normal differentiated cells. Chromatin modification may thus contribute to critical changes in the gene expression profile of the cells, rendering them more susceptible to uncontrolled division, inhibiting their differentiation and maintaining them in an undifferentiated, pluripotent, state, which resembles that of stem cells. Aberrant transcription factor-driven chromatin modification may therefore recapitulate a developmental state and establish a cellular hierarchy within the tumour, which mimics that of normal developing tissues, albeit in an aberrant fashion.

Whereas the presence of the aberrant fusion proteins can provide clues as to the mechanisms underlying the development of the corresponding tumours, understanding paediatric tumour development also requires identification of the cells from which these tumours originate. Most normal cells are resistant to transformation.

If a mutation that activates an oncogene, occurs in a differentiated cell, the cell undergoes what is referred to as oncogenic stress, which induces genes that cause the cells to stop proliferating and guide them toward a state of permanent growth arrest known as senescence. Senescence thus constitutes a powerful tumour suppressive mechanism and a safeguard against transformation. However, some cells, particularly stem cells, are constantly engaged in the cell cycle, which requires suppression of some of the key growth inhibitory genes. These cells thereby already display some of the properties that transformed cells recapitulate. Various types of stem cells, from embryonic stem cells to more lineage-committed variants, are more susceptible to transformation than differentiated cells and may constitute the origin of a variety of cancer types. Although transformation can occur in a differentiated cell, it requires reprogramming that many potentially oncogenic events may not be able to fulfil. A specific oncogenic event would first need to alter the chromatin structure, reprogramming the cell to acquire stem cell features, including the suppression of growth inhibitory genes, to provide permissiveness for transformation. In contrast an oncogenic event that occurs in a stem cell does not need to induce reprogramming as permissiveness for transformation may be a by-product of the pluripotency with which the cell is endowed.

Our quest is to understand the mechanisms that underlie paediatric cancer formation and to identify those that may be targetable for a therapeutic stand point. We are focusing on paediatric sarcomas whose pathogenesis is driven by unique fusion proteins

described above. We have identified a particular population of committed stem cells, known as mesenchymal stem cells, which give rise to fatty tissue, bone, cartilage and other connective tissues, as the most likely cells of origin of several sarcomas. We have begun to understand how the fusion proteins associated with defined paediatric sarcomas transform these particular cells and unravel the mechanisms whereby they drive tumour development and progression. Because they are unstructured proteins, the aberrant transcription factors that underlie sarcoma pathogenesis cannot be readily neutralised by specific drugs. It is therefore essential to identify the downstream events that they initiate, which could be amenable to drug targeting. To that end, we have identified some of the key posttranslational and epigenetic mechanisms induced by the fusion proteins that underlie transformation and tumour progression and are now exploring approaches to target these particular mechanisms and develop new and effective ways to treat these tumours.



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New concepts for the pathogenesis and asthma therapy

Prof Dr. Michael Roth, University Hospital Basel looks at how asthma therapy can reduce the effects of airway wall remodelling

Asthma is still defined as chronic inflammation of the airways and its prevalence has increased worldwide over the last few decades. The EU Symposium on the Awareness of Allergy (2016) stated: 'Chronic airway diseases are a major and growing health problem in Europe' (Muraro 2017), and in the same year the World Health Organisation announced that the worldwide increase of asthma is linked to air pollution

Asthma patient's symptoms can include chest tightness, shortness of breath, and coughing which can be caused by: inhaled pollen, dust or dandruff, skin, hair, metal, wood, stone, flour, or volatile chemicals leading to allergic asthma reaction. In addition, an asthma attack can be triggered by psychological or physical stress, sudden changes in temperature, humidity, or air pressure. The underlying mechanism is not well investigated or understood.

Most text books, and the research guidelines of the European Respiratory Society on asthma, are still focused on the allergic aspect and inflammation, ignoring the fact that tissue remodelling occurs within days in the airways of most asthma patients. None of the available asthma drugs show significant reducing effects on airway wall remodelling, while they can well control inflammation. Bronchial thermoplasty, which is used



for severe or difficult to control asthma, is the only asthma therapy which can lastingly reduce airway wall remodelling through a cell type specific reduction of airway smooth muscle cells. The majority of patients can reduce their inhaled steroids, have fewer hospitalisations, and are symptom-free over long periods. The mechanism of action of thermoplasty must be more than burning cells, as this effect is restricted to smooth muscle but not to epithelial cells, and its beneficial effect is lasting.

Airway wall remodelling

Contrary to the long-held hypothesis, airway wall remodelling does not result from chronic inflammation, but can be induced within a few days (Grainge 2011, Ijpm 2017, Rao 2017). The increase of the epithelial cell

layer thickness and the formation of smooth muscle cell spiral-like structures around the airways were first documented in rhesus monkeys and have now been demonstrated to exist in humans. A spiral-like muscle arrangement will constrict more forcefully than normal muscle bundles, which are arranged without any specific pattern, and limit air flow in the bronchi. These results, combined with new studies in childhood asthma, indicate that airway wall remodelling is independent of inflammation, but may lead to inflammation. Furthermore, we and others have shown that smooth muscle cells of asthma patients release more pro-inflammatory cytokines attracting mast cells, macrophages, eosinophils and neutrophils to infiltrate the airways and exacerbate inflammation.

It is indicated that airway wall remodelling is caused by the loss of communication between epithelial cells, fibroblasts and smooth muscle cells in the airway wall, which was first described by Davies and Holgate (2002). Today, we are still far from understanding how the integrity of this network is maintained and how the cell types affect each other in the healthy airway. Thus, we do not understand what goes wrong in the asthmatic airway. Airway wall remodelling in asthma consists of several independent events including:

- the loss of epithelium integrity;
- thickening of the basement membrane;
- increased sub-epithelial extracellular matrix deposition;
- modified extracellular matrix composition;
- increase of sub-epithelial cell layer vascularisation;
- sub-epithelial fibrosis;
- increased smooth muscle mass.

The available literature neither allows us to conclude which event occurs first nor which event leads to another. Unfortunately, except in rhesus monkeys, none of the animal models can simulate human asthma adequately. As a result, experimental therapies that work in animals often fail to achieve the expected result in humans.

Based on studies performed in isolated primary human airway cells obtained from patients with chronic inflamma-

tory lung diseases, we provided novel aspects to explain the asthma specific pathogenesis and the beneficial mechanisms of drugs. These findings explained the molecular mechanism of the beneficial combination of inhaled steroids with long acting β_2 -agonists, which is to synchronise transcription factor activity leading to improved anti-inflammatory and anti-proliferative action. However, in asthma this anti-proliferative action of the drugs is not effective due to the lack of a protein needed for smooth muscle differentiation and function. The lack of protein was due to reduced protein production, but not to low gene expression; this was the first hint that epi-genetic events are relevant to the pathogenesis of asthma. Most importantly, the production of this protein (C/EBP- α) could be reduced by well-known asthma triggers including house dust mites, cigarette smoke and IgE; thus, providing a novel mechanism leading to asthma associated airway wall remodelling.

Together with our colleagues from the Jiaotong University in Xi'an (PR China), we observed that another enzyme, PRMT1, was constitutively up-regulated in asthmatic airway smooth muscle cells and fibroblasts due to the lack of microRNA 19a. The compensation of low microRNA 19a reduced Erk1/2 signalling and PRMT1 expression and thereby adjusted pathologic cell proliferation, extracellular matrix deposition and mitochondria mass in asthmatic human airway wall cells. In theory, small peptide drugs could be used to compensate the deregulation of signalling and PRMT1 expression, but as these target cells are located behind the layer of epithelial cells, the delivery of such drugs presents a problem.

In conclusion, there is a list of new therapeutic targets for asthma: (i) specific pro-inflammatory elements of the extracellular matrix such as collagen type I or fibronectin, (ii) semaphorins which communicate between cell types, (iii) cell membrane bound glycosaminoglycans, which regulate cell-cell communication and receptor function, (iv) specific microRNAs which are over- or under-expressed in asthma, (v) protein methylating proteins such as PRMTs, and (vi) protein acetylating proteins such as histone acetylases. However, these new targets for asthma therapy are not being followed up and investigated as airway wall remodelling is still recognised as causative and the chance of securing research funding for such studies is minimal. Most of these new targets affect both inflammation and on remodelling; thus, they present the basis for finding new asthma therapies. However, the funding for these new targets is limited as described above.



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Asthma: How to treat and prevent the high impact disease

Sereina de Zordo from the aha! Swiss Allergy Centre outlines the global burden of asthma and how through various methods and programmes it can be managed

Wheezing, chest tightness, shortness of breath and cough – these are typical symptoms of allergic asthma. It is characterised by a chronic airway inflammation and spasmodic narrowing of the airways. Symptom frequency, intensity and their impact on quality of life vary individually. Asthma is a potentially serious and sometimes fatal chronic disease¹.

A global burden

Furthermore, asthma is a major health problem, affecting around 300 million people worldwide and causing annual costs of €17.7 billion in Europe. In Switzerland,

around 12% of children and 6% of the adult population are suffering from the disease.

Allergies mainly against indoor and outdoor allergens originating from pollens, house dust mites, domestic animals or moulds, as well as occupational allergens are the most common causes of allergic asthma. Viral infections, dust, odours, smoke, pollutants or exercise are factors which enhance or trigger the asthma symptoms. Untreated or poorly treated allergic rhinitis (e.g. caused by pollen allergy) leads to asthma in around 30% of the allergic patients. Consequently, with proper diagnosis

and treatment of allergies and asthma, €142 billion could be saved per year in Europe. An appropriate diagnosis by specialists apparently is of fundamental importance^{2,3}.

Asthma-management

The ultimate goal of an adequate asthma therapy are no exacerbations, no restrictions in everyday life, no nocturnal awakenings, optimum lung function and any necessary emergency treatments.

First and foremost, contact with the allergen has to be avoided or reduced as much as possible. Therefore the first imperative is to identify the allergens and triggers and, if possible, to eliminate them in order to prevent asthma attacks.

Medical treatment to reduce symptoms may include individually tailored medicines, which dilate the airways and e.g. steroids for a long-term treatment to ease swelling and inflammation.

After thorough investigation, specific immunotherapy is often recommended for allergic asthma. This is a causal treatment by increasing the tolerance to a specific allergen and no longer triggering an allergic reaction. For this subcutaneous or sublingual treatment, a well-controlled or rather intermittent or mildly persistent asthma is required, dependent on the eliciting allergen. On an economic level, the cost-effectiveness of immunotherapies in allergic asthma patients overweighs the pharmacotherapies on a long-term basis⁴.

The need for educational programmes and prevention

Effective asthma-management has to be completed by additional education on a patient's level. Structured patient's education programmes lead to improved clinically relevant conditions, better self-management and symptom control, as well as higher life quality. Combined with exercises for symptom recognition, adaptations in therapy and emergency treatments as well as in the inhalation techniques are essential⁵. Recent Swiss studies show that 6 out of 10 asthma patients do not use their inhalation devices correctly and that there is a need for educational programmes⁶.

In Switzerland, aha! Swiss Allergy Centre together with the Lung Association are leading project partners by offering such patient's asthma courses.

There is a worrying increase in asthma and allergy prevalence almost worldwide. To take into account not only the economic costs but also, in particular, the burden of the disease in all affected people, the consideration of prevention factors related to atopic diseases is crucial. Based on the German guidelines on allergy prevention, there is data for different preventive factors against the development of asthma. Regarding allergy prevention, the following exposures should be avoided: active and passive tobacco smoke exposure, obesity, indoor air pollution and outdoor air pollution like nitrogen oxides or particulate matter (e.g. PM2.5 or PM10)⁷.

There is further need for information in the population regarding allergy and asthma prevention. An appropriate diagnosis, as well as an effective short and long-term treatment, is also a crucial factor. This is where patients, doctors, as well as health organisations should closely work together – to treat and prevent the high impact disease. ■

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Pancreatic cancer: A three-pronged attack

Science Information Officer Dr Catherine Pickworth outlines the work being carried out by Cancer Research UK to fight against pancreatic cancer

Over the last 40 years, we've seen overall cancer survival double. But while some cancer types have seen an even bigger improvement in survival, in others, survival remains stubbornly low. To achieve our goal of 3 in 4 people surviving cancer for 10 years or more by 2034, we need to change that.

Pancreatic cancer is one of these cancers where survival remains low. Almost 10,000 people in the UK are diagnosed with pancreatic cancer every year, and less than 5% of people will survive beyond 5 years of their initial diagnosis.

Three-pronged approach

We are using a three-pronged approach to help improve the outlook for pancreatic cancer patients – we want to prevent the disease, diagnose it earlier and develop new and better treatments for it.

The first approach is to reduce the number of people developing pancreatic cancer. While age and genetics both affect a person's risk of pancreatic cancer, and are factors we can't control, 37% of cases could be prevented.

Many people are aware of the link between smoking and lung cancer, but there is also evidence that about a third of pancreatic cancers may also be linked to smoking. Being overweight or obese is also linked to the disease.

For those people who do develop pancreatic cancer, we want to ensure they are diagnosed as early as possible. One of the main reasons that pancreatic cancer is so hard to treat is because it's often diagnosed late when treatment is less likely to be successful. By studying how healthy cells become cancer cells, researchers hope to find new ways to spot pancreatic cancer earlier.

Our final angle is to improve the treatments we have and develop new ones. Right now, we're running clinical trials looking at ways to combine treatments to make them more effective. We are also working on tailoring existing treatments to individual patients so that each person gets the best treatment for them.

In March 2017, we invested £10 million in a programme of research to do just that. PRECISION-Panc is an ambitious study that aims to make it quicker to recruit pancreatic cancer patients to the most appropriate clinical trial for them.

But alongside getting the best treatment to every patient, we need innovative ideas and research projects that will develop new ways to treat pancreatic cancer.

Among the innovative projects we're funding, is a study on how pancreatic cancer cells 'talk' to the cells around them and to the body's own immune defences. Understanding and interfering with this communication could lead to new treatments that are desperately needed.

Together with Stand Up To Cancer (SU2C) and the Lustgarten Foundation, we've invested a total of £8 million which will help international scientists connect and collaborate, to stimulate new thinking and speed up progress.

By funding big, bright ideas and strong collaborations, we hope to revolutionise understanding of pancreatic cancer, find innovative ways of treating the disease and ultimately help more people survive their cancer. ■

Dr Catherine Pickworth
Science Information Officer

Cancer Research UK
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Childhood cancer trends: how to interpret new findings

Dr Eva Steliarova, Scientist at IARC's Section of Cancer Surveillance explains how research results can be used to reduce the burden of cancer in children

IARC's international study on the incidence of cancer in childhood found a global increase of 13% in childhood cancer between 2001-2010 compared to the 1980s. The percentage increase compares the incidence rates of 124 per million for the earlier period and 141 per million for the more recent one. With the exception of sub-Saharan Africa, the increase affected all the world regions we studied, and ranged between 3% (Central America and Caribbean) and 30% (South-east Asia). What could this increase be attributed to?

The challenge of data collection

Although the 2 studies used comparable methods and provided the best estimates of incidence for their respective periods, the covered populations differed. Data were not available for some areas included in the earlier study, while new areas were included in the more recent statistics.

It was important to ensure that data collected in different countries are comparable, so that we can draw conclusions from the observed differences in incidence rates. The established data flow system, motivated staff in cancer registries around the world, a set of international standards and extensive communication between the contributors were required for conducting this study. Our main aim was to define the level of cancer occurrence in the young populations, the most important determinant for cancer control planning and for further research into the causes of cancer in this young population. The produced information does not suffice, however, to explain the causes of the observed patterns. Further focused investigations are required in this direction.

The role of improved diagnosis

Future detailed examination of the incidence trends for specific cancer types could indicate the role of improved diagnosis. For example, a rise in the CNS tumours could be attributed to the implementation of magnetic resonance imaging (MRI) in the 1980s in high-resource countries, and their gradual uptake in less privileged areas. The lack of CNS tumours as well as sophisticated imaging technology on the African continent supports indirectly the role of diagnosis in the temporal trends. Over the time, diagnoses are increasingly based on molecular and genetic analyses, new entities are being recognised and changes in tumours classification proposed. More tumours may be counted as malignant. The novel imaging techniques may detect tumours earlier in life, which would contribute to higher rates within the childhood age-range. On the other hand, the increase in incidence rates was seen in the areas with advanced, as well as with developing diagnostic facilities, which may suggest that the improved diagnosis does not explain the observed increase entirely.

Improved awareness and referral system

More cancers may be detected also because of improved awareness among primary healthcare providers and more frequent referral of suspected cancers for correct diagnosis and treatment. The role of professional associations such as the [International Society of Paediatric Oncology](#) (SIOP), as well as charitable actions of patients' families may drive a better or faster access to diagnostic facilities.

Registration of diagnosed cases might have improved

with the accumulation of local expertise and maturation of international cooperation. A legal requirement to register (childhood) cancer cases, instituted in numerous registration areas during the 3 decades would definitely enhance the registration completeness.

A role of exposure to risk factors?

The data assembled in our study cannot confirm or refute an increased exposure to various risk factors of childhood cancer identified in other studies. The early life onset and the association of some childhood cancers with a number of inherited syndromes may explain some 5% of cancers in children. Multiple external risk factors have also been examined. While ionising radiation from atomic bombs, industrial accidents or medical interventions may cause leukaemia, thyroid and possibly other childhood cancers, the levels and opportunities of these exposures are relatively limited, as is the proportion of cases due to radiation. Some wide-spread viruses (Epstein-Barr or Human immunodeficiency virus, HIV) together with other co-factors may also lead to cancer development, such as Burkitt lymphoma or Kaposi sarcoma, both highly prevalent in sub-Saharan Africa. Environmental pollution, exposure to pesticides or other carcinogens and some dietary constituents of children or their parents were also associated with childhood cancer in some studies, but not in others. The barriers to a better knowledge of the causes lie in the low frequency of cancer in children, difficulty of accurate exposure assessment, as well as in isolation of potential risk factors from the multitude of simultaneous exposures.

Geographical and ethnic differences in childhood cancer occurrence

Our large international study characterises the geographical and ethnic differences in childhood cancer occurrence and suggests possible associations worthy of further study. One example may be the high relative incidence of childhood leukaemia in South-East Asia, the area which is also known for the wide-spread use of pesticides in agriculture. Another illustration is the drop in the incidence rates in sub-Saharan Africa, at least in part attributed to a reduction of HIV infection load through antiretroviral therapy in the exposed childhood population. This observation implies that external factors may be involved in childhood cancer development and also that preventive measures may result in a reduction of incidence.

Cancer prevention and control is a recognised priority by the WHO¹ and integrates continued surveillance to help with planning childhood cancer care. Our study also serves as a springboard for detection of associations which, if confirmed, may lead to taking preventive actions and possibly reducing childhood cancer incidence in the future.

The International Agency for Research on Cancer (IARC) the specialised agency of the WHO, is coordinating the International Incidence of Childhood Cancer study in collaboration with [International Association of Cancer Registries](#) (IACR) and with a financial support of [The Union for International Cancer Control](#) (UICC). The first bulk of results of the study were released online on the occasion of the International Childhood Cancer Day on 15 February 2017 and at <http://iicc.iarc.fr/> and they will be followed by a printed publication later in 2017 with a complete background on data sources and methods. An overview paper summarising and interpreting the main findings by world regions for period 2001-2010 was published in June by The Lancet Oncology (<http://www.sciencedirect.com/science/article/pii/S1470204517301869>). ■

About the author

Dr Eva Steliarova is a senior scientist, at IARC's Section of Cancer Surveillance. She coordinates the work on the third volume of the International Incidence of Childhood Cancer (IICC-3), presented at <http://iicc.iarc.fr/> and other international studies of cancer in children. She relies on active collaboration of hundreds of data contributors, the international boards of advisors and editors, as well as the support by her IARC colleagues.

1 http://apps.who.int/gb/ebwha/pdf_files/WHA70/A70_R12-en.pdf

International Agency for Research on Cancer



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The dilemma of over diagnosis of pancreatic cysts

Dr. Annabelle L. Fonseca et al explain the problems created by current medical guidelines for diagnosing pancreatic cysts

More than 2% of abdominal computed tomography (CT) scans will show a cyst in the pancreas. What to do about these cysts can sometimes leave us in a quandary.

Intraductal papillary mucinous neoplasms (IPMNs) are the most common type of pancreatic cyst that may harbour cancer or develop into cancer. This is a relatively new disease, first identified in 1982, and while our approach to these tumours has evolved since then, many patients still receive unnecessary treatment and we clearly still have a long way to go.

What are IPMNs?

IPMNs are cystic tumours that grow within the pancreatic duct and are characterised by the production of thick viscous mucous. The main pancreatic duct runs down the centre of the pancreas and gives off smaller branching ducts. IPMNs arise from either the main pancreatic duct or one of the branching ducts.

With the increasing use of CT scans, IPMNs are being diagnosed more frequently. Because we did not know enough about the natural history of the disease, and because of the terrible prognosis associated with pancreatic cancer, our tendency was to resect most IPMNs.

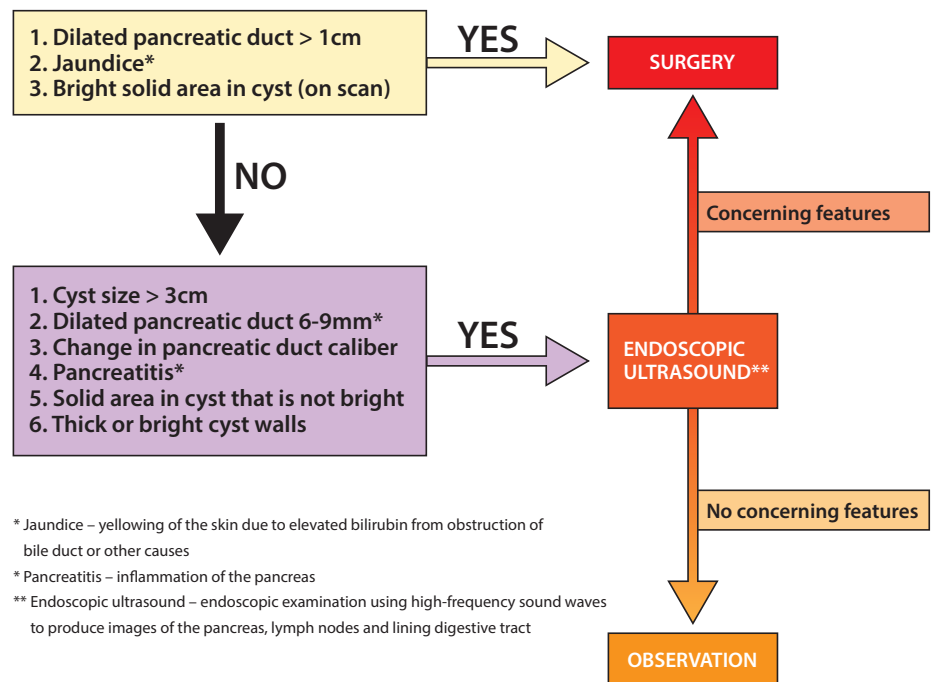


Figure 1: Algorithm for management of IPMNs (based on expert consensus guidelines)

What do we know about IPMNs and the risk of cancer currently?

IPMNs with high grade dysplasia or a cancer component are ideally the ones to remove. Over the past decade we have learnt that specific findings on CT or other imaging can be used to help us with our decision (Figure 1). We currently follow recommendations based on expert consensus to help us decide which of these tumours we should take out. We know that IPMNs that develop from the main duct are at a higher risk of developing into

cancer. We use imaging criteria and clinical findings to decide whether to operate, proceed with additional investigation, or to continue to monitor patients (Figure 2).

Current guidelines have created a dilemma

These guidelines help us to decide which patients would benefit from an operation. However, they also lead to us operating on many patients with IPMNs that would likely have never turned into cancer. The ability of current guidelines to accurately diagnose the

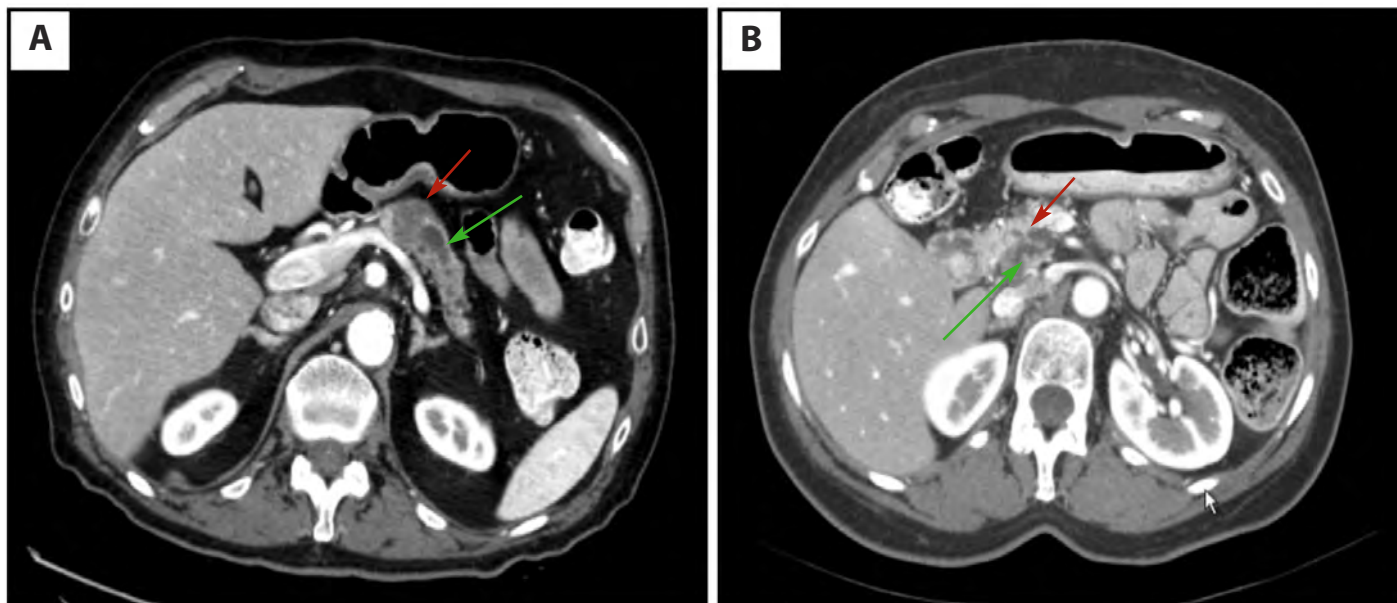


Figure 2: CT scans demonstrate high grade IPMNs (red arrows). Green arrows depict dilated pancreatic duct in (Fig A) and enhancing mural nodule inside IPMN in (Fig B)

presence or absence of high grade dysplasia or cancer ranges from 50-80% according to studies. This means that when we use these guidelines, the proportion of patients that we “over treat” is not insignificant, and we will also miss some patients that do have IPMNs with high grade dysplasia or cancer. This is a problem that we, and several other researchers around the world, are studying.

Current areas of research:

We know that IPMNs are associated with specific genetic mutations. However, these do not necessarily differentiate between those with different risks of becoming cancer. Additionally, this information is usually obtained from the tissue after resection, and this does not help us to decide who needs an operation. Cyst fluid analysis is an exciting area of research, where fluid is obtained during an endoscopic ultrasound, and can then be tested for different biological markers that may

help in our pre-operative decision making. Radiographic imaging is also being studied at a more granular level in the field of radiomics, which is the high throughput analysis of large amounts of quantitative features from imaging. This is based on the hypothesis that the underlying patterns at the genetic and cellular level are reflected in the imaging. Our approach is to integrate all of these sources of information to help us differentiate between these tumours. This data also feeds into mathematical models of tumour growth that may help us to understand the specific mechanisms that contribute to carcinogenesis in IPMNs. In the next article we will describe these exciting areas of research in more detail.

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Photodynamic Therapy – radiotherapy for the 21st Century

Photodynamic Therapy is a treatment that combines a photosensitizing drug, visible light and oxygen to kill cancer cells. Professor Eli Glatstein explains

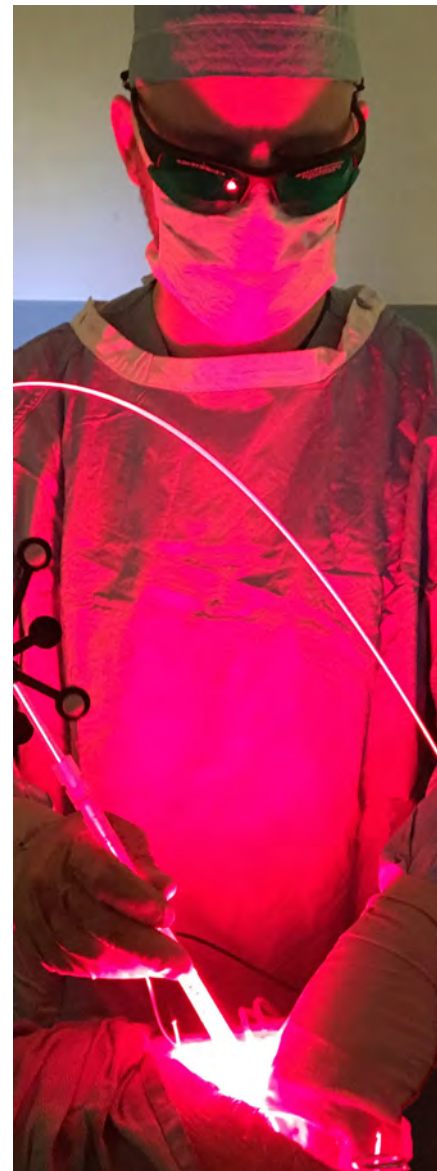
For this treatment to have a biological impact, these 3 factors must be together at the same time, in the same place. Because PDT depends on visible light, the treatment naturally spares critical normal tissues that lie beneath the cancer. Red (or near-infrared) light is the most penetrating in human tissues. This can be simply illustrated by the classic ‘experiment’ of placing one’s fingers together over the head of a flashlight turned on; only red light gets through where the fingers come together. With recent innovations in diode laser and fibre-optic technologies, it is now relatively straightforward to deliver light of a suitable wavelength to match the desired depth of tissue penetration and the absorption spectrum of the photosensitiser.

“In practical terms, the only real limitation to the application of PDT for the treatment of cancer is the imagination required to get the light where it is needed. For this purpose, treatment at the time of surgery provides an opportunity to deliver light internally where the cancer is most likely to recur following removal.”

When the photosensitising agent is administered IV, it goes ubiquitously into virtually all cells and tissues. However, most tumour tissues appear to take longer to clear the photosensitiser, leading to a modest (~2-3 fold) tumour selectivity. Porfimer sodium is the only intravenous photosensitiser

that is currently FDA approved for cancer treatment in the USA. In the EU, Temoporfin is also approved for cancer treatment, but both photosensitisers are retained in normal skin and require the patient to avoid bright (sun) light for about 6 weeks after drug delivery. Nevertheless, these photosensitisers have been successfully used to treat a wide variety of tumours, including head and neck, lung, oesophageal, bladder, cervical and skin cancers, as well as malignant pleural mesothelioma. This selectivity can be enhanced by encapsulating the photosensitiser in a nanoparticle that targets molecular abnormalities specific to tumours. Verteporfin, an early version nanoparticle photosensitiser has been highly successful at treating age related (wet) macular degeneration and is currently in clinical trials as a treatment for prostate and pancreatic cancers.

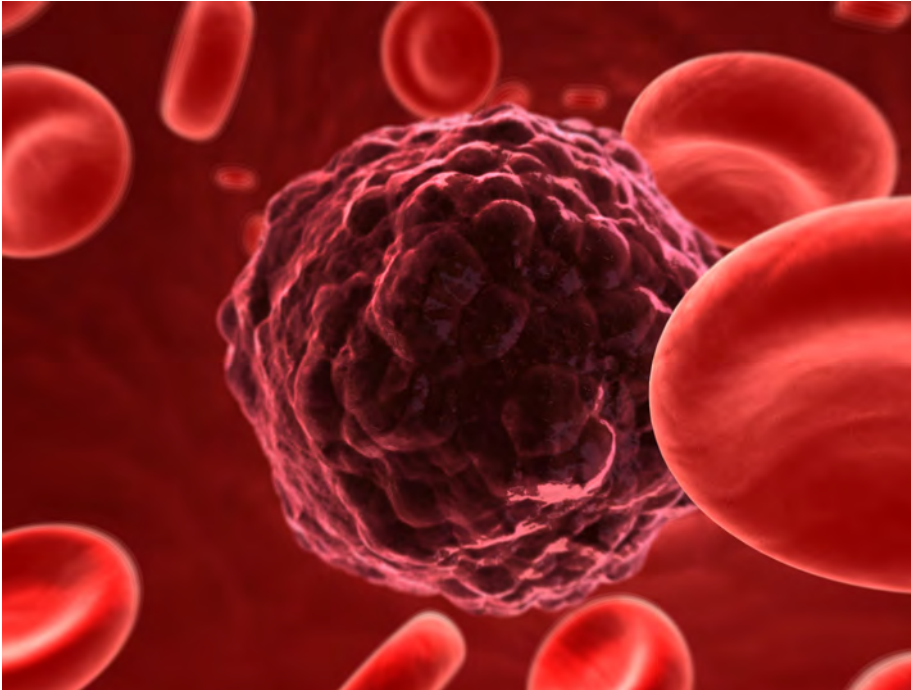
Except at specialised centres of excellence, most of the PDT throughout the world is aimed at relatively small non-melanomatous skin cancers or GI surface lesions that can be approached by endoscopic techniques. At Penn, we are using PDT to ‘light up’ the entire pleural cavity at the time of surgical resection for patients who have malignant miliary seeding of the pleural surface, which is generally considered an incurable condition. With this approach, we have extended the median survival of patients with advanced stage malignant pleural



mesothelioma to more than 3 years (from 12-18 months) while allowing a surgical procedure that spares the underlying normal lung.

Advantages of PDT

While PDT is nonionising radiation therapy, this treatment primarily tar-



gets intracellular membrane structures such as mitochondria and lysosomes. Unlike ionising X-ray therapy, DNA does not appear to be the target for PDT, so that PDT does not induce new mutations into cancers during treatment. PDT also kills cancer cells through different mechanisms than traditional chemotherapy. Thus, PDT's advantages are that it can spare normal tissues far better than other forms of cancer treatment and, because DNA is not its target, treatment induced cancer is unlikely to occur. Moreover, techniques to accurately measure light and photosensitiser in real time can even provide the ability to continuously readapt the treatment either before or even during an individual treatment session to further optimise treatment outcomes. Combined with targeted photosensitisers, PDT presents a unique opportunity for a more personalised, rational approach to cancer therapy.

Limitations of PDT

In practical terms, the only real limitation to the application of PDT for the treatment of cancer is the imagination required to get the light where it is needed. For this purpose, treatment at the time of surgery provides an opportunity to deliver light internally where the cancer is most likely to recur following removal. Relatively simple modifications can be used to avoid unintentional skin burns during surgery, such as using optical filters on the operating room lights and making sure to cover all of the patient's skin with sterile drapes/towels. In addition, light can be introduced directly into a tumour mass by interstitial techniques. This means inserting fibre-optic delivery devices directly into a tumour mass through sterile techniques similar to those that have been employed for brachytherapy, a form of ionising radiation therapy in which radioactive sources are introduced

directly into tumours. For PDT, instead of inserting radioactive isotopes, fibre-optics are used to deliver light from an appropriate laser source. This method has been used to successfully treat head and neck, prostate and pancreatic cancers, but could extend to assist the minimally invasive treatment of brain, breast, lung, bladder and gastrointestinal cancers. Thus, PDT is a critical weapon in the war on cancer. Like all cancer therapies, PDT should not be considered as "the" answer for cancer treatment but rather as an important tool in the medical armamentarium that can be adapted to an individual's cancer to provide personally optimised cancer therapy.



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Poverty and its impact on the health of children

One of the main risks to children's health is living in poverty, says Royal College of Paediatrics and Child Health's Professor Russell Viner

It's a well-known adage that the way a society treats its most vulnerable members is the measure of its humanity.

In 1942 Sir William Beveridge identified squalor, ignorance, want, idleness and disease as the 5 "Giant Evils" in our society. In a climate of post-war relief and a longing for a more just society, the Labour Party swept to victory in 1945 on a pledge to eradicate these 'evils' and provide for the people of the UK "from the cradle to the grave". It was this moment that our modern welfare state was born, and a major element of this was the formation of a brand new National Health Service a few years later. The NHS had one radical core principle; that good healthcare should be available to all, free at the point of delivery, regardless of personal wealth.

Today, we refer to Beveridge's evil of 'want' in terms of poverty and it is the shocking extent to which poverty is affecting our children of today – society's most vulnerable – that should instil a great sense of shame in us all.

Almost 1 in 3 of the UK's children – a total of 4 million – live in poverty. It's a statistic that perhaps many people hear without really appreciating the implications.

Living in poverty can have all sorts of damaging effects on a child, not least on their health. Put simply, poverty makes children sick; we know that children living in the most deprived areas have far worse health outcomes than those from the most affluent. They are more likely to be overweight or obese, suffer from asthma, have poorly managed diabetes and experience mental

health problems. In the most extreme example, infant mortality is more than twice as high in the lowest compared with the highest socio-economic groups.

Such large numbers can be a little abstract and it's only when we look at the impact on actual children, with real life stories, that reality begins to hit home.

Comments from over 250 paediatricians across the UK on the impact of poverty on child health were gathered as part of [a survey conducted by the RCPCH and Child Poverty Action Group \(CPAG\)](#). With more than two-thirds of them saying poverty and low income contribute 'very much' to the ill health of children they work with, it makes for sobering reading.

Poor housing

One doctor in London commented that 'overcrowded, damp or unsuitable housing amongst our patients is the rule rather than the exception', conditions which can cause respiratory problems such as asthma and bronchiolitis. Another said that one of his patients is a '2 year old with recurrent seizures, living in a house with no heating'. Poor housing is one of the main reasons for delays in discharging children. One paediatrician spoke of how they were 'unable to discharge a chronically unwell child requiring constant use of electrical equipment, as the house only has one socket' whilst another said: 'I have seen a number of babies being unable to be discharged from the Special Care Babies Unit due to parents being homeless.'

Food insecurity

Many respondents said their patients struggle to afford healthy food – with one doctor observing that 'many of [our] patients are from low-income families who rely on food banks'. Another said they 'see parents in A&E who are limiting their eating to care for their children. Children are worried, scared and upset'.

Worry, stress and stigma

Stress and worry caused by poverty affects not only parents, but children too. One respondent observed: 'I think that the biggest impact of poverty on the children and parents I encounter is insecurity, inferiority and stress. Through biological and psychological factors these undoubtedly lead to poor health.'

Political will

The one thing that really stands out when reading these stories from the front line is that what we're seeing is a return to 'old-fashioned' poverty relating to crowding and nutrition for our children. This is not a situation any one of us can be happy with so attention must turn to fixing this scourge of child poverty as a matter of real urgency.

We cannot continue papering over the cracks and only treat the symptoms of poverty. It's quite clear that if poverty levels were reduced, the impact on child health – and therefore the future health of the nation – would be radical.

It is then disappointing to see the government recently set out their policy agenda for the next 2 years without any mention of tackling poverty in this country. Urgent action is required to transform the lives of those 4 million children who live every day in poverty, and with this number set to rise to 5 million by 2020, there is simply no excuse for dragging our heels.

The Queen's Speech should have contained policies such as the restoration of binding national targets to reduce child poverty, backed by a national child poverty strategy and the adoption of a 'child health in all policies' approach to decision making and policy development, with Her Majesty's Treasury disclosing information about the impact of the Chancellor's annual budget statement on child poverty and inequality. These, coupled with the immediate reversal of public health cuts, could make a real difference.

Whilst child health is not only a measure of our society's humanity today, it is also a measure of our society's health tomorrow. As one doctors in the survey said, 'we cannot expect to have a healthy future for the UK if we leave our children behind.' ■

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Environmental health science: reducing the risk

Virginia Guidry and Kimberly Gray from the NIEHS outline how environmental health science can help to identify potential hazards in a child's environment

Now able to crawl and curious to discover all that's around her, little Emma reaches for a dusty toy under the table and, just like any infant would, immediately puts it into her mouth.

What chemicals are in the toy, and is there lead in its worn paint? Do the baby's pyjamas, or perhaps her crib mattress, contain flame retardant chemicals? Has the home been treated with pesticides, now lingering as residue in the dust? Does it matter?

These are the questions that drive environmental health science.

Parents, grandparents, and caregivers have enough to focus on regarding the needs and well-being of their children – making sure they are nourished, clean, and sleeping soundly. The National Institute of Environmental Health Sciences (NIEHS), part of the National Institutes of Health (NIH), funds scientists to methodologically study the silent factors that we often cannot see or smell in a child's environment.

These environmental toxicants can be in the water, food, dust, or air in children's homes, schools, and neighbourhoods. NIEHS-funded scientists determine the likelihood of harm, the sources if unknown, and how to reduce exposure or mitigate potential damage.

Why focus on children?

One thing is clear from NIEHS-funded research – children are more vulnerable to environmental toxicants than adults, particularly while in the womb¹. External substances can interfere with the complex processes of growth and development, which involve rapid cell division and intricate hormonal signals. Additionally, children don't have the mature defense systems that adults do, such as fully functional liver detoxification¹.

Sometimes changes that occur during childhood can have permanent effects².

For example, NIEHS-funded research shows the potential for environmental toxicants to harm brain development. Lead is the best-known example, but there are many others. When pregnant mothers are exposed to high levels of flame retardant chemicals, such as polybrominated diphenyl ethers (PBDEs), their offspring may be more likely to have decreases in IQ, problems with fine motor skills, and symptoms of ADHD³.

Environmental scientists are using MRIs and related technologies to study the brain regions of children exposed to common air pollutants called polycyclic aromatic hydrocarbons (PAHs), which come from fossil fuel combustion⁴. The structural and functional changes they have observed in the brain may explain why exposure to PAHs while in the womb has been linked to lower IQ and symptoms of anxiety, depression, or ADHD^{5, 6}.

Technologies help identify hazards

However, it can be difficult to know what toxicants a child has been exposed to in the womb or as a baby. Some scientists are analysing naturally shed baby teeth to reconstruct early-life exposure to lead and other metals that are incorporated into teeth as a child grows⁷. By comparing exposure information with later diagnoses, the scientists have shown that increased lead uptake, and decreased uptake of the essential nutrients zinc and manganese, may be related to autism⁸.

NIEHS-funded researchers also are developing wearable or mobile technologies to help caregivers recognise hazards in a child's environment. Scientists have designed wearable wristbands that can detect exposure to organic chemicals, such as flame retardants



or pesticides, over the course of a few hours or days⁹. Others are collaborating on an [app](#) that will help children, their parents, or healthcare providers track real-time air quality conditions so that asthma triggers can be avoided.

New programme to study children's health

Fortunately, there is a new, national effort that will allow scientists to study a variety of environmental influences on children's health. In 2016, NIH launched the 7 year Environmental influences on Child Health Outcomes ([ECHO](#)) programme. ECHO is focused on 4 important children's health outcomes: illnesses like asthma in the upper and lower airways, obesity, neurodevelopment, and health around the time of birth. ECHO is pooling resources from many NIH-funded studies to increase researchers' ability to study how a child's environment, from pregnancy through adolescence, may affect the immediate or long term health of our children.

ECHO and NIEHS-funded research will continue to point to ways that we can advance lifelong health by improving the environmental conditions around pregnant women and children. We already know that when air quality improves, children have better lung growth¹⁰ and decreased bronchitis-like symptoms¹¹. Similarly, women at the end of their pregnancies during the 2008 Beijing Olympics had babies with healthier birth weights than women exposed to higher, typical air pollution levels during the same dates in 2007 and 2009¹².

These studies show the potential health benefits of reducing environmental toxicants. These improvements matter – especially for children. ■

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Environmental chemicals: factors for neurodevelopmental disorders?

Pamela Lein, University of California, looks at whether environmental chemicals influence individual risk for the diagnosis of neurodevelopmental disorders

Neurodevelopmental disorders (NDDs) are a group of clinically heterogeneous conditions characterised by impaired growth and development of the brain. These include autism spectrum disorders (ASD), attention-deficit hyperactivity disorder (ADHD), schizophrenia, learning and intellectual disabilities, and sensory impairments. The current prevalence of ASD is estimated to be at least 1.5% of children in developed countries; the worldwide prevalence of ADHD is estimated to be 5.3% of children and adolescents; and learning and intellectual disabilities are more common than ASD and ADHD combined. Considered in the context of the tremendous costs these conditions exact on the affected individual, their families and society, these statistics underscore the urgent need to identify factors that confer risk for NDDs.

Until recently, research on the aetiology of NDDs has focused largely on genetic causes. However, this research has clearly shown that even for ASD, which is considered one of the most heritable of the complex NDDs, single genetic anomalies can account for only a small proportion of cases and, overall, genetic factors seem to account for at most 30-40% of all NDD cases. Such observations have contributed to a paradigm shift such that many NDDs are now largely thought to result from complex gene-environment interactions.

Why do we think environmental factors influence NDD risk?

Compelling evidence in support of an environmental contribution to NDD aetiology includes the rapid increase in the prevalence of ASD and ADHD over the past several decades. This is unlikely to have been caused by evolutionary shifts in the human genome. While some have questioned whether this represents a true increase in the number of affected children, studies to address this question have uniformly concluded that the broadening of diagnostic criteria, increased awareness and improved detection can only partially account for the increased prevalence of NDDs.

Genetic studies also support a role for environmental factors in determining NDD risk. Incomplete monozygotic concordance is a consistent finding in twin studies of both ASD and ADHD, and even in genetic syndromes highly associated with ASD, a significant percentage of individuals carrying the ASD-linked gene do not express autistic phenotypes. More recently, a study of 192 mono- and dizygotic twin pairs, and another of 14,000 children with autism, independently concluded that 50% or more of cases could be attributed to environmental causes. Collectively, these studies are consistent with a model in which environmental factors modify genetic risk to significantly influence not only susceptibility to NDDs, but also the variable expression of phenotypic traits. This model

provides a biologically plausible explanation for both the dramatically increased prevalence and clinical heterogeneity that are characteristic of complex NDDs.

Environmental factors associated with increased NDD risk

Observations of a high incidence of autism associated with congenital rubella were among the first reports demonstrating that an environmental factor could influence NDD risk. Subsequently, prenatal infections were linked to an increased risk for other NDDs, particularly schizophrenia, and the range of non-genetic NDD risk factors was expanded to include intrauterine stresses, increased paternal age, maternal nutrition and metabolic status, and endocrine disruption. The first indication that chemical exposures may also influence NDD risk were reports that in utero exposure to valproic acid or thalidomide during critical periods of development was associated with increased expression of autism-related traits. Subsequent epidemiological studies reported increased NDD risk associated with maternal use of various medications and drugs of abuse, including alcohol, as well as prenatal or early postnatal exposure to diverse environmental chemicals. Environmental chemicals postulated to confer risk for NDDs include legacy chemicals known to be toxic to the developing human nervous system, such as lead, mercury and polychlorinated biphenyls (PCBs), as



well as more contemporary contaminants such as pesticides, including organophosphorus (OP) and organochlorine (OC) pesticides, neonicotinoids and pyrethroids, flame retardants including the polybrominated diphenyl ethers (PBDEs), plasticisers such as phthalates and bisphenol A, and complex environmental mixtures such as air pollution and cigarette smoke.

Current challenges in the field, and a potential path forward

Current epidemiological data support the hypothesis that chemicals in the human environment contribute significantly to NDD aetiology, but also highlight the difficulty of establishing causal links between environmental exposures and NDDs. Recent reviews have concluded that, with the possible exception of tobacco and alcohol, there are insufficient numbers of epidemiological studies and/or studies are too limited in scope to either infer causality or to rule out the possibility that specific environmental factors confer NDD risk. The challenges of using epidemiological approaches to identify environmental risk factors include obtaining accurate measures of exposure, particularly for chemicals with short half-lives such as some of the pesticides, phthalates and BPA, controlling for confounding factors, especially socioeconomic stressors that tend to co-vary with environmental exposures, and are known to influence neurodevelopment independent of chemical exposures, and dealing with

multiple exposures, a not insignificant issue in light of reports that 250 environmental chemicals were detected in biological samples from a 2013 representative sample of the United States in the National Health and Nutrition Examination Survey. Epidemiological approaches must also deal with the phenotypic heterogeneity and complex multigene aetiologies that are likely to create a range of sensitivities to environmental factors, which will further mask clear associations between exposure and diagnosis.

To overcome these challenges, it will be necessary to invest resources in basic mechanistic research using experimental models to understand how environmental factors modify genetic predispositions to influence individual susceptibility and/or severity for NDDs. While a number of mechanisms have been proposed to explain gene-environment interactions, one fundamental way in which heritable genetic vulnerabilities can amplify the adverse effects triggered by environmental exposures is if both factors (environmental and heritable) converge to dysregulate the same neurotransmitter, signalling system or neurodevelopmental process during a critical developmental window. Genetic studies have identified convergent molecular mechanisms for many NDDs, which provide a biological framework for developing cell and animal models to identify and study specific gene-environment interactions

that confer susceptibility. Such mechanistic insights can then be used to inform and focus epidemiological studies.

Clearly, research is urgently needed to better predict which combination of defective genes and environmental exposures pose the greatest risk for NDDs. The fact that environmental factors are modifiable risk factors, in contrast to currently irreversible genetic risks, suggests that identification of specific environmental risk factors may provide rational approaches for the primary prevention of NDDs, which provides a compelling reason to invest in this endeavour.



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New Foot-and-Mouth Disease virus vaccines

University of St Andrews' Martin Ryan PhD talks about zoonotic diseases such as Foot-and-Mouth Disease and importance of vaccinations

What Price Animal Viruses?

Quite naturally, viruses which infect humans – such as HIV and Ebola – generate huge public concern and necessitate huge resource for treatment and control. Such viruses are originally animal viruses which have been transmitted to humans ('zoonosis'). Alongside zoonotic diseases, however, human health is also affected by viruses which infect only animals. Losses in animal productivity affect human nutrition: poor diet during pregnancy and childhood affects health prospects throughout life. The foot-and-mouth disease virus (FMDV) infects cloven-hoofed domesticated animals (cows, pigs, sheep, goats etc.), but also many types of wild animals (confusingly, there is also a human disease – Hand, Foot-and-Mouth Disease – is caused by a different virus). In 2001 the UK suffered a huge outbreak of FMDV which cost the UK economy billions of pounds, affecting not only the agricultural but the tourism sectors. Such outbreaks within developed economies do not materially affect overall food supply, but this is may not be the case for many low-to-middle income countries (LMICs) – where FMDV may be endemic. Furthermore, a much higher proportion of the population within LMICs are directly involved in agriculture than in developed countries. The increasing affluence of highly populated countries such as India and China raises demand for meat products, having a progressive effect on

the World prices of both meat and animal feedstocks: UK food security is intimately linked to global markets.

Animal Vaccines

Aside from subsistence farming, agriculture is a business and disease control via vaccines or drugs must conform to the economic factors in play. The extraordinary cost of drug development (\$billions) effectively precludes them as a way forward – most especially for farmers in LMICs, but much research is being conducted to develop new animal vaccines. Three main types of vaccine are used. 'Killed' vaccines are made by chemical 'inactivation' of the virulent virus which must be grown in bulk – with the attendant costs of highly biosecure production facilities and the hazard of virus escape. The inactivated, killed, vaccine is inert (does not grow within the recipient) and must be administered by injection to elicit the protective immune response. 'Sub-unit' vaccines comprise purified, immunogenic, virus proteins. They do not contain any virus and are, therefore, biosecure. The production of these proteins is, however, expensive and, like killed vaccines, they are inert and administration requires injection. 'Attenuated' virus vaccines are made by genetically altering the virus genome such that it can still grow with the target host species to elicit a protective immune response, but the attenuated virus can no longer cause disease. To date, two viruses have

been completely eradicated from nature: the human virus smallpox and the animal virus rinderpest – with poliovirus eradication close by. In each of these cases live, attenuated, virus vaccines were used.

"In 2001 the UK suffered a huge outbreak of FMDV which cost the UK economy billions of pounds, affecting not only the agricultural but the tourism sectors. Such outbreaks within developed economies do not materially affect overall food supply, but this is may not be the case for many low-to-middle income countries (LMICs) – where FMDV may be endemic."

Live, Attenuated FMDV Vaccines

Historically, viruses were attenuated by serial rounds of growth in mice or tissue-cultured cells. During this process mutations accumulated in the genome (by chance) such that some of the individual viruses became attenuated in the natural host. A major problem with attenuated vaccines is, however, that when the attenuated vaccine virus strain is grown in bulk during the vaccine production process, there can be spontaneous mutation of the virus genome back to a virulent form ('back mutation' or 'reversion'). For example, the attenuated poliovirus vaccine strains in use today were developed in the 1950s – long before the genome sequences were known, or what the attenuating mutations were present.



There has been a complete transformation in the techniques available in molecular biology during the past two decades: it is now possible to design and synthetically create such virus genomes at will. New techniques are available to attenuate viruses by genome modifications such that they are genetically 'stable': no reversion to virulence. The challenge facing molecular virologists is that unlike poliovirus (with a single, human, host), FMDV is able to infect a wide range of species. 'Designing' or engineering the right level of attenuation suitable for eliciting protection within multiple species (pigs / cows / sheep etc.) may prove to be problematic. The advantages of producing such a genetically stable live, attenuated, FMDV vaccine in comparison to killed vaccines are however,

considerable: increased biosecurity during production, cheaper vaccines, superior immune response, potential 'cross-vaccination' between domestic animals by transmission of attenuated virus – potentially vaccine transmission into wild-animal reservoirs of disease.

Adoption of such vaccines will, however, require changes in policy: routine, rather than 'emergency' vaccination and changes to the restrictions upon trade in animals with anti-FMDV antibodies. What is clear is that any such changes should be driven only by firm data obtained by experiments initially using animals housed under containment conditions then, if successful, controlled field trials. What I think is clear is that the policy of disease control by mass-slaughter of infected and

susceptible animals is not sustainable and is certainly unacceptable for sociological and economic reasons in many areas of the world.



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Huntington's disease: Understanding the impact

Jennifer Simpson of the Huntington's Disease Society of America highlights the disease and how there is still a long way to go before it can be truly understood

Since the discovery of the gene that causes Huntington's disease in 1993, exponential progress has been made in elucidating the true scope of Huntington's disease, but there are still miles to go to truly understand the impact of symptoms of HD families. Huntington's disease (HD), is an autosomal dominant neurological disease caused by an expanded CAG repeat in the Huntingtin gene. The disease is characterised by progressive functional decline and motor, psychiatric and cognitive symptoms, in addition to weight loss, sleep disturbances and dysregulation of the autonomic nervous system¹. Each child of a person who carries the gene mutation that causes HD has a 50% chance of inheriting the faulty gene.

“Although we currently have no cure for this disease, we do have the ability to allow individuals to access treatments to help them manage this debilitating illness. While we work on a cure and find hope for tomorrow, we have to ensure that families affected by HD can access the help they need today.”

Cognitive and behavioral symptoms are most impactful to HD patients and families

In preparation for a Patient Focused Drug Development meeting with the U.S. Food and Drug Administration, the Huntington's Disease Society of America (HDSA) surveyed the HD community in the U.S. on topics related to HD symptoms and treatments. Between two surveys, more than 3,600 responses were collected from individuals affected by HD, Juvenile Huntington's disease (JHD) and caregivers for those with HD and JHD. In reviewing the data collected, clear trends began to emerge between caregivers and HD/JHD patients alike. Caregivers responded most frequently that chorea was the most impactful symptom of HD (30%), but in aggregate, behavioral and cognitive symptoms were

reported as the most impactful to their lives by more than 50% of both caregivers and HD/JHD patients².

Huntington's disease has long been classified as a movement disorder, though prodromal features encompass cognitive and behavioral symptoms of HD³. Although classified as “prodromal”, the cognitive and behavioral symptoms of HD are major elements of the disease and its impact on the individual and their families. Cognitive and behavioral symptoms can manifest as much as a decade before motor symptoms develop, and as a result often go undiagnosed as symptoms of HD. It is not uncommon for individuals with HD to be misdiagnosed with a variety of psychiatric disorders before being correctly diagnosed with HD at the onset of motor symptoms. Delayed diagnosis may unfairly disadvantage people with HD and cognitive-behavioral symptoms, especially in terms of accessing the kind of care and benefits people with HD really need to best manage the progression of their disease⁴.

For Huntington's disease patients, treatment options are lacking

In the world of HD, treatment options are few and far between. As of the publication of this article, only two medications exist that are FDA approved for the treatment of HD, and both treat chorea symptoms associated with the disease. Currently, there are no disease-modifying treatments or cures. When surveyed on availability and efficacy of current treatments for cognitive symptoms of HD, more than 80% of respondents noted that they or their loved one were not taking any kind of medication for symptoms like deterioration of memory and thinking². For behavioral symptoms like anxiety, depression and irritability, individuals responded most frequently that they or their loved one was not taking any kind of medication



to treat those symptoms². The lack of treatment options, especially for cognitive symptoms of HD, stands in stark contrast to the impact those symptoms have on the lives of people with Huntington's disease.

Access to care early on is critical to managing Huntington's disease

As patients with HD become symptomatic, it is key that those individuals have access to comprehensive care with doctors who are knowledgeable in HD. HD patients in early to middle stages of the disease need coordinated multidisciplinary healthcare services, including assessment of cognitive function and counselling by (neuro) psychologists, rehabilitation programmes, active physiotherapeutic interventions, speech therapist training and occupational therapy⁵. Lack of access to care for families with HD means unmanaged or poorly managed symptoms, higher rates of caregiver burnout, potential unnecessary hospitalisations and early entry into long-term care facilities. With access to specialists knowledgeable in HD, families can avoid unnecessary additional emotional and financial burdens. In the U.S., HDSA has created a

clinical care model through the Center of Excellence programme, awarding grants to HD clinics around the country to provide an all-in-one service center for families affected by Huntington's disease. HDSA currently funds 41 Centers of Excellence around the U.S.

“In the world of HD, treatment options are few and far between. As of the publication of this article, only two medications exist that are FDA approved for the treatment of HD, and both treat chorea symptoms associated with the disease. Currently, there are no disease-modifying treatments or cures.”

Expanded access to government programmes can help HD families

Individuals with HD access multiple forms of governmental support as their disease progresses. Because HD symptom onset commonly occurs during prime working years, many families are devastated financially, and need to rely on programmes like Social Security Disability Income (SSDI), Medicaid and Medicare. Utilising these programmes can help families access professionals like neurologists, neuropsychiatrists,

speech therapists and physical therapists. Expansion of Medicaid programmes has resulted in a reduction of unmet need for mental health services, in addition to positive impacts on the budgets of states that expanded Medicaid as states no longer needed to use some of their general funds to pay for behavioral health treatment for the uninsured⁶. Individuals with HD are included amongst those who have benefitted from the expansion of programmes like Medicaid, and would further benefit from expedited access to Medicare through the Social Security Disability Income programme. HDSA has been advocating, alongside the HD community, for a waiver of the two-year Medicare waiting period for individuals who are disabled by Huntington's disease and utilising the SSDI programme. The Huntington's disease Parity act of 2017 is a bi-partisan solution to an HD shaped hole in the social safety net. It is one step of many to help ensure access to important behavioral health services and specialist neurologists who can assist families maintain quality of life for folks with HD for as long as possible. Although we currently have no cure for this disease, we do have the ability to allow individuals to access treatments to help them manage this debilitating illness. While we work on a cure and find hope for tomorrow, we have to ensure that families affected by HD can access the help they need today. ■

“The disease is characterised by progressive functional decline and motor, psychiatric and cognitive symptoms, in addition to weight loss, sleep disturbances and dysregulation of the autonomic nervous system¹. Each child of a person who carries the gene mutation that causes HD has a 50% chance of inheriting the faulty gene.”

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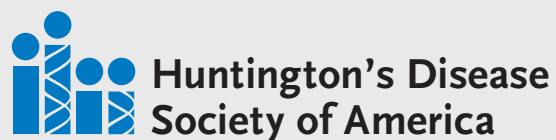
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Huntington's disease: Investigating pathogenic mechanisms

New York University School of Medicine's Naoko Tanese explores the pathogenic mechanisms and therapeutic strategies for Huntington's disease

Mutation in the huntingtin (HTT) gene causes Huntington's disease (HD), a dominant, heritable, neurodegenerative disease. The normal human HTT gene encodes a large protein whose function remains elusive. Extensive studies of the normal and mutant HTT protein have identified roles in the maintenance of proper cell structure and function, transport of key molecules within cells, regulation of gene expression, among others. HD is characterised by the appearance of aggregates visible in cells under a microscope, and degeneration of specific regions of the brain. Although the HTT protein is expressed throughout life, most patients develop symptoms in mid-life. Current evidence suggests that mutant HTT protein causes significant dysfunction of neurons as the disease progresses, ultimately resulting in cell death.

Altered RNA metabolism is linked to neurological disorders

Mutations in a variety of genes cause neurological disorders. Of particular interest are genes that encode proteins that bind RNA. RNA molecules are so-called messengers of DNA, the blueprint of genetic information stored in each cell. RNA molecules are copies of DNA with instructions to make proteins specified by the DNA, a process termed gene expression. There are many proteins whose function is to bind RNA and regulate different steps in gene expression. These proteins

bind RNA and control its stability and location within the cell. RNA binding proteins also regulate efficiency with which proteins are made by the ribosome, the machine that synthesises proteins. In response to stressful conditions, RNA binding proteins and RNA can form granules inside the cells. Under normal conditions, these types of granules also serve to transport RNA to distal sites where protein synthesis takes place locally in response to specific stimuli. RNA binding proteins whose mutations have been linked to several neurological disorders have been localised to granules found in neurons. It is tempting to speculate that mutant RNA binding proteins in these granules accumulate and become converted to irreversible toxic aggregates over time.

Aggregates contain proteins and RNA

Protein aggregation is a hallmark of many neurodegenerative diseases. They are characterised by an irreversible accumulation of mutant proteins that are toxic and impair neuronal functions. Age-associated diseases such as Alzheimer's disease involve protein misfolding and propagation of misfolded proteins. Mutations in proteins that bind RNA have been implicated in diseases such as amyotrophic lateral sclerosis, spinal muscular atrophy, and fragile X syndrome. Normally, granules formed inside cells are reversible protein-RNA assemblies comprised of RNA associated with the



Naoko Tanese, PhD, Associate Dean for Biomedical Sciences, and Director, Sackler Institute of Graduate Biomedical Sciences

protein synthesis machinery and RNA binding proteins. Mutant RNA binding proteins, however, show altered biophysical properties. They have increased propensity to interact with one another and affect the formation and function of the granules. At high concentrations, mutant RNA binding proteins may contribute to the formation of an irreversible toxic aggregate seed that triggers cell death.

Potential role of HD protein in RNA metabolism

Our lab reported a new role for the normal HTT protein in the transport of RNA and maintenance of RNA granules in neurons^{1,2}. We found HTT protein to co-localize and co-traffic with RNA

expressed in neurons. The involvement of HTT in the regulation of RNA could explain the specific pattern of cell loss and symptoms seen in HD. In the presence of mutant HTT, select groups of RNA may be more adversely affected over other RNA. An emerging body of evidence suggests regulated transport of select RNA and local synthesis of proteins from the RNA play a critical role in establishing connectivity between neurons. Our findings implicate normal HTT in these important dynamic neuronal processes. We hypothesise that HTT protein associates with a subset of RNA and regulate their fate in response to synaptic activity. It is possible that mutant HTT perturbs the process in some way, contributing to a loss of cellular homeostasis and disease pathogenesis. Thus, like other RNA binding proteins linked to neurodegenerative diseases, HTT may play a role in RNA metabolism in neurons and share mechanisms and common pathways that lead to their death. Identification and characterisation of RNA bound and regulated by normal and mutant HTT will help to uncover underlying molecular mechanisms. Interestingly, our lab discovered that HTT protein binds its own RNA³, suggesting a mechanism of self-regulation that may go awry in cells harbouring a mutation in the HTT gene.

Therapeutic strategies to treat HD

Since the gene that causes HD was discovered more than two decades ago, scientists around the world have invested monumental time and effort towards the development of therapies

and cures for HD, which has been incredibly challenging. Therapeutic approaches that show most promise to date involve lowering the levels of mutant HTT RNA and protein in affected cells^{4,5}. This may be achieved by advanced technologies developed to silence genes. Most patients have one normal copy and one mutant copy of the HTT gene. Normal HTT is required for proper maintenance of neurons. Although selective silencing of the mutant HTT gene is desirable, this is difficult to achieve because normal and mutant genes are very similar in their DNA sequence. However, even partial silencing of mutant HTT (accompanied by partial silencing of normal HTT) seems to have beneficial effects in mouse models of HD⁶. Such therapeutic approaches are being pursued in hopes of delaying the onset and progression of the disease in patients.

Disruption of irreversible aggregates may be another way to slow or reverse disease progression. A new study reports the formation of RNA aggregates (termed RNA foci) in cells that accumulate RNA containing expanded repeat sequences⁷. The RNA was shown to aggregate when the repeat expansion reached a certain threshold. The resulting RNA foci changed properties from liquid to that resembling gelatine. The study suggests that gelatine-like assemblies are similar to aggregates associated with HD. Moreover, designing chemicals that disrupt the foci may be another avenue for effective therapy to treat this incurable disease.

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Nutrition research is vital for healthy outcomes

Dr Christopher Lynch, Director of the Office of Nutrition Research explores the links between diet and health in an interview with Editor Laura Evans

The U.S. Center for Disease Control (CDC) reports that in America more than 2 in 3 adults are considered to be overweight or obese, with more than 1 in 20 adults seen as having extreme obesity. They also say that one-third of children and adolescents aged 6 to 19 are considered to be overweight or obese.

Poor nutrition is a problem that can have devastating effects on someone's health, contributing to heart disease, some forms of cancer, stroke and Type 2 diabetes. Four out of 10 causes of death in America are said to be diet related, according to the American Society for Nutrition.

Understanding the importance of nutrition is key to ensuring good health. Having relevant information and knowing the risks that come with making unhealthy food and beverage choices could help prevent many diseases from developing.

Research plays a key role in understanding the health problems related to nutrition. The Office of Nutrition Research (ONR) at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), NIH is responsible for leading nutrition research efforts across NIH Institutes and Centres. To gain insight into this topic, Editor Laura Evans speaks to Dr. Christopher Lynch, director of the ONR, about the value of nutrition research and the many challenges in this field.

"In the US, chronic diseases account for 75% of the National Health Expenditure and diet and nutrition is a major factor in those diseases," and according to Dr. Lynch, about 170 million Americans have one or more diet-related chronic disease (diabetes, obesity, diet related cardiovascular diseases, stroke and certain cancers). "The public is very interested in nutritional research because many recognize that there is a link between diet and disease.

Nutrition research funded by NIH assists other federal agencies, such as the Food and Drug Administration, to create policies and make regulatory decisions. “Nutrition research is also important for national security”, he says. In the US, we have the National School Lunch Program. It was implemented around the time of the Second World War to safeguard the health and well-being of the nation’s children. A factor in establishing the programme was the number of malnourished young draftees that were turning up to serve in the military. Presently, we have the converse problem. Although we no longer have a draft for the military, we still have health requirements to join. Now, many young people who are applying are too overweight to join. In fact, one quarter of America’s youth are too overweight to serve in the military.”

Strategic plan for nutrition

In order to develop their first NIH-wide strategic plan, the NIH formed the Nutrition Research Task Force (NRTF) to coordinate and accelerate progress in nutrition research. That group will guide the development of the nutrition research plan for the next 10 years. They hope to complement and enhance ongoing research efforts on diseases and conditions affected by nutrition, such as diabetes and cardiovascular diseases.

“While each of our institutes and centres at NIH may focus on particular organs, diseases or aspects of health, nutrition is a scientific discipline that crosses institutional boundaries. That’s why coordination and strategic planning is important,” adds Lynch. “Research will be coordinated between NIH Institutes and Centres through the strategic plan to ensure the teams are working toward common agreed upon goals.”

Challenges and Opportunities

The Nutrition Research Task Force is considering many challenges and opportunities in nutrition research. One opportunity is to improve the reproducibility and scientific rigor of nutrition research. At times, research findings and media reports can be at odds with one another. Research from different studies can be at odds with one another too.

“Understandably, people get upset if they find out that a food that they enjoy could promote disease, after previously being told it was safe. This then creates a

ground for people to condemn the scientific process more broadly,” says Lynch.

“Getting the correct information about nutrition and the elements of a healthy eating plan out to the public is essential.” This, Lynch explains, is one of the many challenges that the public faces when trying to adopt a healthy diet. “Therefore, developing approaches to improve communication, reproducibility, and rigor of scientific data will be a focus of our efforts”

Presently, many nutrition studies only rely on the participants’ recall of what they consumed. “This is something that our task force has to address,” explains Dr Lynch. “We need to develop new approaches for assessing nutritional intake and status that don’t rely entirely on people self-reporting. New tools and technologies are emerging that could help address this, so now is a good time to start taking full advantage and apply these tools to nutrition research.”

“Another key scientific gap we hope to address pertains to the nutritional requirements for pregnant moms and children from birth to 2 years of age for healthy development. Early life exposures to dietary components or feeding practices may have long term consequences for susceptibility to chronic diseases later in peoples’ lives, and even inter-generationally, through a process known as nutritional programming or epigenetics. We need to understand the permanency, and reversibility of these phenomena.”

Recent studies suggest that some dietary patterns are healthier than others. A challenge will be to understand the physiological mechanisms through which these diets effect health. Another concept is that people’s responses to diet interventions may be “personal”. As is the case for precision and personalised medicine, people’s responses to dietary patterns or even specific foods within those patterns appears to vary between individuals. So, a key challenge is to understand the mechanisms through which healthier dietary patterns, such as the Mediterranean Diet, work, and the basis of interpersonal variability in physiological/metabolic responses to certain foods.

“Our task force is also exploring how to best harness data from many sources that are collected today

| Typical values | 100ml contains | 250ml contains | %GDA* | typical adult |
|-------------------------------------|-----------------|------------------|-------|---------------|
| Energy | 199kJ 47kcal | 500kJ 120kcal | 6% | 2000kcal |
| Protein | 0.5g | 1.3g | | |
| Carbohydrate of which sugars | 10.5g | 26.3g | 29% | 90g 70g |
| Fat of which saturates | 10.5g | 26.3g | | |
| Fibre | trace | trace | | |
| Sodium | trace | trace | | |
| Salt equivalent | trace | trace | | |

*Guideline daily amounts

Vitamins/Minerals

100ml contains
25.0mg (42% RDA) 62.5mg

(grocery store inventories, federal databases keeping epidemiological and molecular data, global positioning systems (GPS) data, personal health information, social media, credit card purchases etc.), so called 'big-data', to help us address questions about nutrition, diet behaviours, and food insecurities of the population."

Finally, Lynch explains, "it has long been known that microbes co-habitat our bodies. Some of these are felt to be beneficial whereas others are potentially detrimental. There is emerging evidence that those that make our gut their home may be releasing substances or otherwise communicating with us, their hosts, and having an impact on disease or eating behaviour.

"It is likely, therefore, that a focus of the strategic plan will also be the relationship between diet and the gut microbiome along with the microbiome's relationships

to behaviour and disease, and the underlying mechanisms involved. Obviously, our strategic plan also must address how to train the next generation of nutrition research scientists in some of the emerging methodologies, informatics and technologies to address our strategic goals." ■

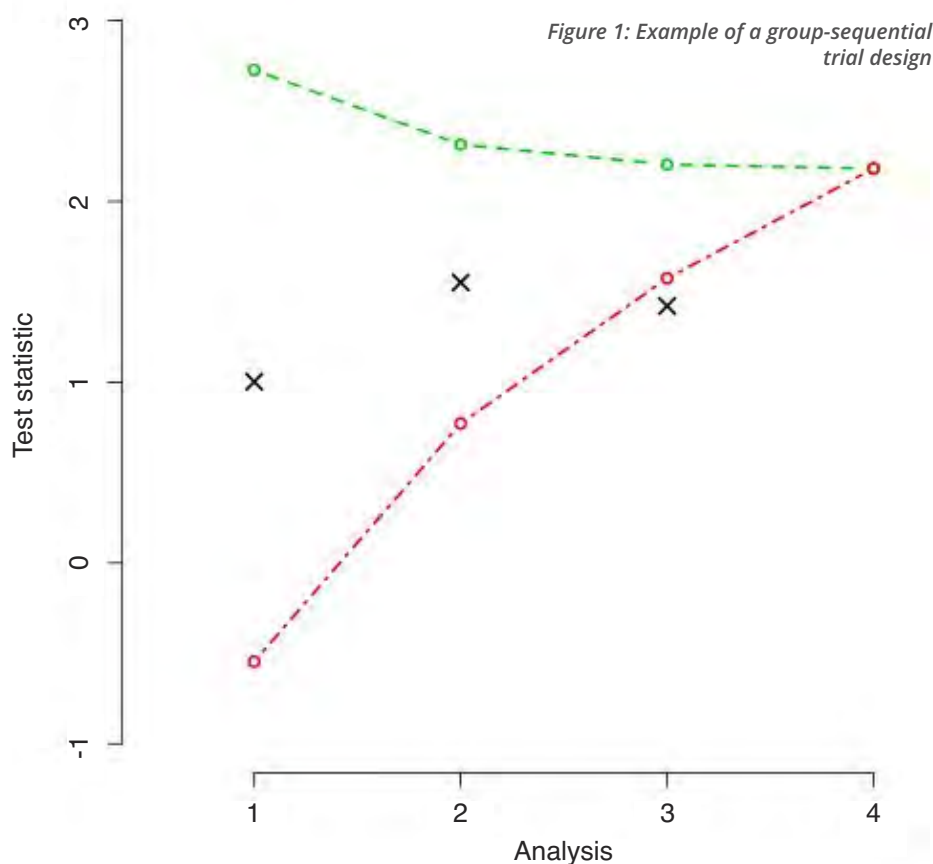
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Adaptive clinical trials: Ethical and efficient

Prof Thomas Jaki at the Medical and Pharmaceutical Statistics Research Unit, Lancaster University outlines the benefits of adaptive clinical trials

The development of new medicinal products and health technologies is time consuming and expensive. For pharmaceutical products, it is estimated that it takes 10-15 years to develop a novel compound and costs several hundred million pounds on average. The reason for the long duration is that, even after a potentially useful compound has been identified, the product needs to undergo pre-clinical animal studies, first-in-man studies and a series of clinical trials addressing different questions such as safety, dosing, and efficacy. The largest contributor to both time and cost are confirmatory (Phase III) clinical trials that often involve thousands of patients with a follow-up period frequently lasting years. Recently only about 50% of confirmatory clinical trials have been able to show that the treatment under investigation has a good enough risk-benefit trade-off to achieve a license by a regulatory authority. At the same time only around 20% of phase II clinical trials are successful in showing an improvement in the primary endpoint of the study.

The reasons for these unsuccessful trials are thought to be the taking forward of treatments that should have been abandoned earlier, and insufficient precision when determining the optimal dose, assessing safety, or when determining the patient population to be studied further.



One of the fundamental concepts of traditional clinical trials is that, once the study has been designed and recruitment started, no changes to the design are allowed and no analyses of the study data that require knowledge about treatment allocation by the study team are typically allowed until all patients have been recruited and observed in the study. This means that, for example, even if the data would already clearly show that the novel treatment is not promising, further patients will be exposed to this potentially harmful treatment.

One way to overcome this inherent dilemma are adaptive clinical trials. The US FDA defines an adaptive clinical trial as: "A study that includes a prospectively planned opportunity for modification of one or more specified aspects of the study design and hypotheses based on analysis of data (usually interim data) from subjects in the study". In other words, an adaptive design allows decisions about the study to be made on the basis of the study data while the trial is still ongoing. This allows early decisions about the utility of the intervention under

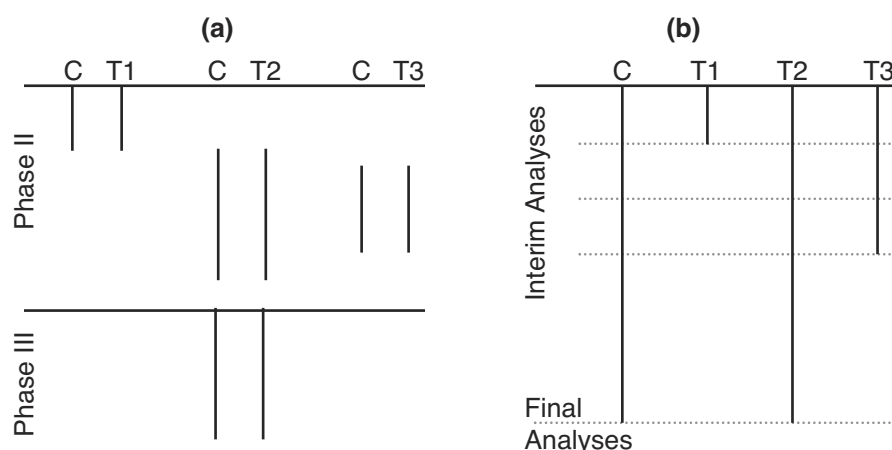


Figure 2: Schematic of traditional drug development (a) and a multi-arm multi-stage design (b)

study but also allows other changes to improve the properties of the design.

Typically, only a small number of design changes are permitted – after all, these designs are not a remedy for poor planning. Analyses of the data that inform decisions to alter the design are at prospectively planned time points called interim analyses. Although ideally the interim analyses are conducted in a blinded manner, the nature of the potential adaptations often necessitates unblinding. In either case it is crucial that the validity and integrity of the study remains intact.

Adaptive designs are ethical

One of the most common adaptive designs are (group-) sequential design. These designs allow stopping the trial early either because results so far are not promising or because the advantage of the treatment under investigation is already established. Specifically, they include a number of interim analyses at each of which a test statistic quantifying the advantage of the experimental treatment over control is found. If the test statistics is below a lower bound, the trial is stopped for lack of benefit as the treatment does

not look promising. If the test statistic exceeds an upper bound, the trial is stopped for proven efficacy. Otherwise further patients are recruited into the study. Figure 1 illustrates such a design and we find that no decision is made at the first 2 analyses, while the treatment is deemed not sufficiently promising at the third and hence the trial terminated.

This example clearly shows why adaptive trials are ethical: In a traditional trial, the decision that the treatment is not promising would have been made later and hence additional patients would have been exposed to a treatment that has no additional benefit (but potentially worse safety) than the current standard. More generally, we do expect that the number of patients in the study is smaller for a sequential design compared to a traditional design which means that we expect to stop treatments that are not promising earlier or identify promising treatment quicker.

Adaptive designs are efficient

The group-sequential design above is also efficient as a decision about the utility of a treatment can be made

quicker. Multi-arm multi-stage designs, are another highly efficient adaptive design.

Traditionally multiple treatments are evaluated, in separate trials initially, and then one is taken forward for definitive testing (Figure 2a). A multi-arm multi-stage design (Figure 2b) combines the screening of treatments with the confirmatory stage in one trial thereby removing the time gap between the 2 different phases of development. Moreover, they compare multiple novel treatments against a common control group reducing the number of patients on the control treatment and hence the total sample size.

The Medical and Pharmaceutical Statistics Research Unit at Lancaster University develops and evaluates novel statistical methods of study design (such as adaptive designs) and tailors the methods to the needs of specific trials.



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Leisure beyond the leisure centre

Cheryl Hersey of Action PR highlights how the role of leisure centres are changing to become key community hubs which deliver a range of services

Fitness has become significantly more sophisticated in recent years, with the operator forming a better understanding of their customer. Customers have greater access to information about fitness, and opportunities to be active in so many ways. With it, the leisure centre itself has also changed, and leisure operators are aspiring to create community hubs, from which they can deliver a wider range of services beyond the traditional; gym, studio and swimming. Whilst physical space inside the centre may be fixed, operators are recognising the opportunity to offer leisure services which extend beyond the 4 walls of the gym.

“Offering activities which extend beyond the physical leisure centre is essential in targeting hard to reach groups who don’t want to use the gym,” says Duncan Jefford, Regional Director for Everyone Active. “Entry level activities such as walking groups help to break down barriers to exercise.” According to Jefford, bringing people into the building and making them feel comfortable is the first step to getting them to embrace a more active lifestyle. “They will often have misconceptions of what a leisure centre is like and once they arrive they are pleasantly surprised,” he explains.

Everyone Active has 30 community development managers with a remit to facilitate more community engagement. They run regular outreach sessions, often for free, where they take fitness to different corners of the community. “Outreach activity is our bread and butter when it comes to engaging the local community,” says Jefford. “This approach helps members of the community start to feel positive about exercise, and connect with our brand.”

Working as a strategic leisure development partner to dozens of local authorities nationwide, the Pulse Group are instrumental in getting councils to look at opportunities beyond the walls of the facility.

“Community engagement is always high on the agenda for local authorities,” says Chris Johnson, Managing Director of the Pulse Group. “They want to appeal to users from 0-99. We know that an 85-year-old is unlikely to become a regular gym visitor but they might be attracted to a walking group or tea dance in a community space. Offering additional activities for traditionally hard to reach groups allows local authorities to apply for government funding to cover staffing costs which is win win.”

“Everyone Active operate 3 leisure centres on behalf of Chichester District Council. So far in 2017 they have run 10 activity programmes off site with the aim of engaging more of the community in physical activity. The centres have an excellent relationship with the local authority’s community and health teams, as well as local schools, colleges, universities and GP surgeries.”

External activity is not just for low intensity or entry level options. Following a partnership with British Triathlon in 2010, Everyone Active started to offer outdoor cycling and running training. “We recognised a shift in consumer desire to exercise outdoors and knew we needed to start thinking about how we catered for this, so as not to lose members,” explains Jefford. “The London 2012 Olympics did a huge amount to invigorate consumer interest in sport, particularly cycling and – with the success of the Brownlee brothers – triathlon. We have noticed that consumers want to challenge themselves more, so it’s vital we give them opportunities which extend beyond what we can offer in-centre.”

When involved in the build for a new centre, Everyone Active look for opportunities to build more facilities outside, to meet the demand for outdoor training. “This also allows us to create a value-added offering



which sets us apart from the competition,” says Jefford. “At Hart Leisure Centre in Fleet, we added 4G football pitches, hockey pitches and a gym trail which has meant we can launch walking and running groups. It makes commercial sense; a 4G pitch with floodlights can generate an income of 100k per year, while a gym trail costs virtually nothing to build yet brings a huge amount of added value,” he adds.

Pulse take a similar approach. “Before advising on facility mix we carry out full latent demand and demographic studies,” says Johnson. “We encourage councils to look strategically at the demographic of the community and the location of the facilities within that community. Not everyone can travel 4 miles to get to the leisure centre so we encourage clients to look actively at other locations where they can develop outreach activities. We get them to consider public parks, community centres and even schools. At Waterlane Leisure Centre in Lowestoft we identified a disused building on the side of a football pitch, several miles from the main centre, which has now been transformed into brand new changing and showering facilities to create a complete football offering. It’s smart to extend the leisure

brand, building an offering and brand presence which spans the whole community.”

According to Jefford, this is very much an area in which the public sector operator has an advantage over the private operator. “We can tap into the local authority connections with schools, health authorities, local charities, sports clubs and County Sports Partnerships,” he explains.

Pulse recommend local authorities link more closely with public health organisations. “Leisure operators have a huge skilled staffing resource who can get out into the community and support GPs and health workers,” says Johnson. “One of our clients, for example, sends their PTs to run sessions in care homes and organises care home visits to the centre to ensure they truly are taking the activity to all corners of the community,” he adds.

For Jefford, the public sector leisure operator is perfectly placed to continue to build on their outdoor offering. “We have staff and the facilities – from pools to cafes – to offer activities which go above and beyond the norm.”



Everyone Active Chichester Contract

Everyone Active operate 3 leisure centres on behalf of Chichester District Council. So far in 2017 they have run 10 activity programmes off site with the aim of engaging more of the community in physical activity. The centres have an excellent relationship with the local authority's community and health teams, as well as local schools, colleges, universities and GP surgeries. This allows them to truly cater for all segments of the community.

A weekly free walking programme led by a member of the Active for Health team is providing an excellent route into exercise for traditionally inactive groups, while activity scheme 'First Steps to Fitness' – a free 12-week activity programme designed to fit individual needs – is in its third successful year. Gym teams from the centres visit various locations as an outreach activity engaging as many of the local community as possible.

Creating opportunities to get involved with sporting activities is also high on agenda and Everyone Active are facilitators of everything from a mini Olympics for school children to organising the Chichester Triathlon

for almost 900 participants. Earlier this year the operator delivered #ThisGirlCan activity at the University of Chichester and Midhurst Rother Colleges to get females 13-21 training towards taking part in a fun triathlon. They also run ongoing free sports sessions for 12-17-year-olds in family neighbourhood areas in the Chichester District.

The working population of Chichester are also catered for, with Everyone Active working in partnership with local businesses to train up 'running leaders' who will engage their colleagues in lunch time sessions. ■

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Therapies for weak muscles

Research into personalised interventions is helping pave the way for a new generation of therapies for weak muscles at the Balgrist Campus

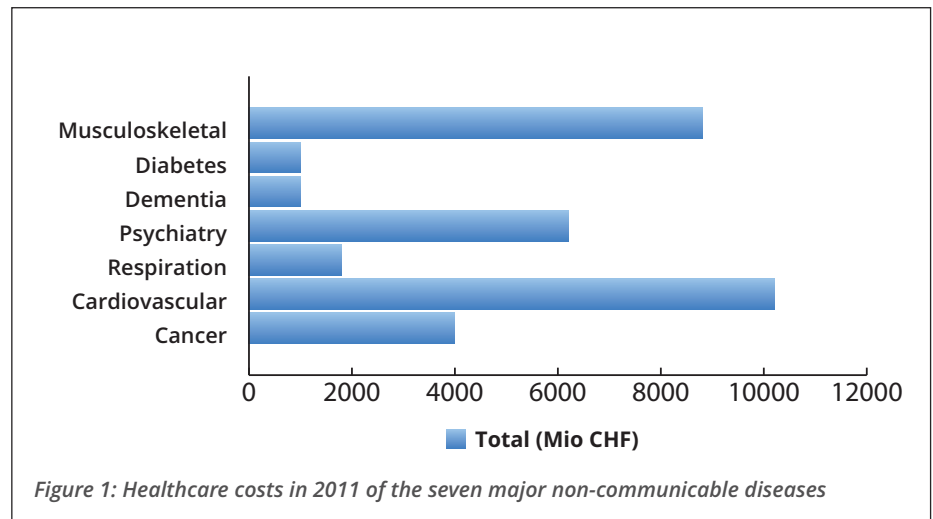
It is estimated that 10% of the cost of healthcare in Switzerland (or the equivalent of €500 billion per annum in the EU) being associated with lost work is related to injury or dysfunction of the musculoskeletal system (Fig. 1). Surgical and subsequent rehabilitative interventions are important part of the therapy that re-establishes musculoskeletal function.

The Laboratory for Muscle Plasticity at Balgrist University Hospital aims to shed light on the underlying mechanisms in skeletal muscle with the goal of translating the findings into more effective clinical applications.

Skeletal muscle plays a major part in control of movement and posture and affects whole body metabolism through its effects on energy expenditure. Affections ranging from simple overuse injury to rupture of tendons and bones, or disease, lead to deconditioning of skeletal muscle as a result of inactivity and damage signals. The consequent loss in muscle strength and fatigue resistance exerts a distinct negative impact on the quality of life and may render the affected individual dependent. In these situations a surgical intervention and rehabilitation may be indicated, yet may come too late as irreversible changes may have resulted.

Focus on muscle plasticity

The Laboratory for Muscle Plasticity investigates the mechanisms that



underlie the conditioning of skeletal muscle structure and function during recovery from surgical interventions and rehabilitation. As shown through research on sport performance, this process is driven by mechanical and metabolic stimuli. It is mediated through a gene response that instructs adjustments in muscle composition with the repeated impact of exercise during training. In consequence, force production and fatigue resistance of muscle may be improved or maintained.

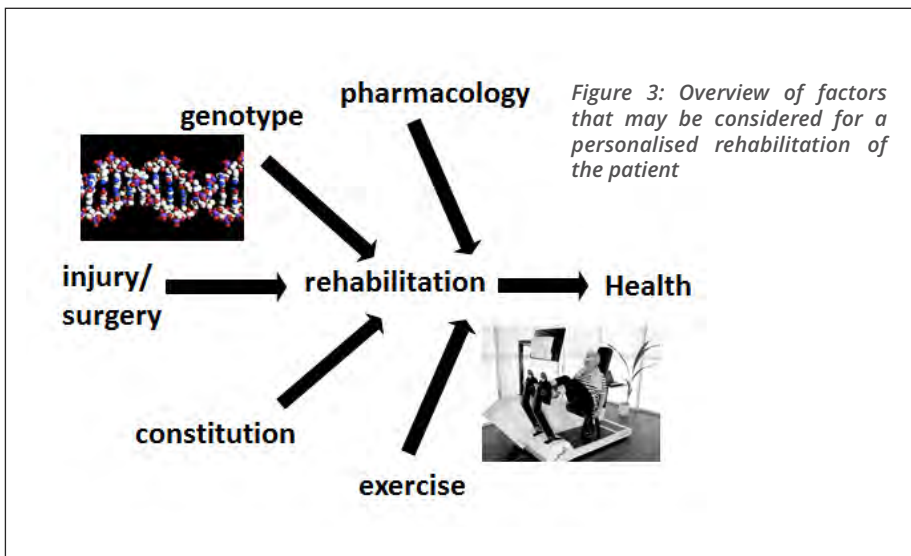
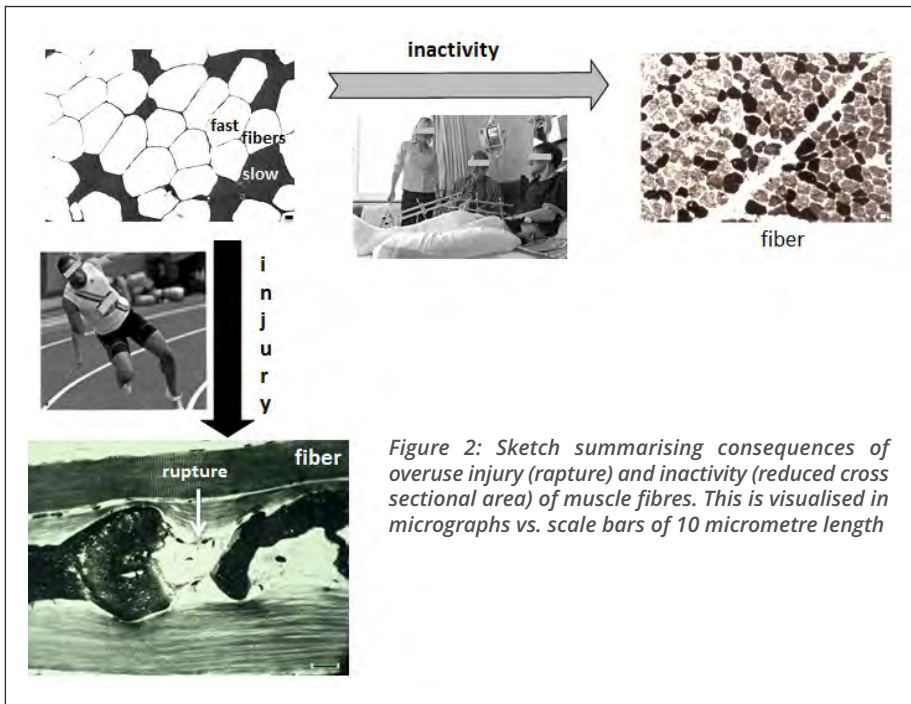
By contrast, a muscle's functional capacity is reduced in the absence of a physiological stimulus by a reduction in the size of muscle fibres and their content in mitochondria (Fig. 2).

In fact, while the safety and effectiveness of physical factors for muscle conditioning are well established, the dose-effect relationship between

exercise and muscle adaptation is often not fully respected in clinical practice. An example of this biological regulation is the important role of muscle contraction and loading in preserving muscle mass of the bedridden musculoskeletal patient after surgery, who would otherwise lose muscle mass at a pronounced rate. Genetic factors (so called gene polymorphisms) significantly affect this adaptation. This indicates that gene polymorphisms contribute to the inter-individual variability of the response to surgical interventions and rehabilitation.

Research projects

The emphasis of the research team lead by Prof Martin Flück at Balgrist is on major musculoskeletal affections that arise in the context of the orthopaedic clinics at Balgrist Hospital. A special focus is put on resolving the contribution of gene polymorphisms



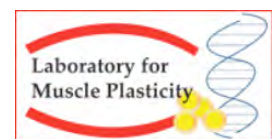
to inter-individual differences in the healing of muscle with re-attachment of the ruptured rotator cuff tendon, and the strengthening of skeletal muscle with rehabilitative exercise in patients.

The aim is to develop personalised forms of intervention that maximise muscle adaptation (Fig. 3). The latter approach is based on previous investigations pointing out the important exercise-intensity and exercise-type related influence of gene polymor-

phisms on muscle response to leisure-type sports activities. This opens a venue to tailor the therapeutically effective exercise intervention for patients which otherwise would demonstrate little plasticity to a generic exercise stimulus and for which pharmaceuticals alone do not work due to the importance of activity-induced muscle metabolism for muscle adaptations. In this regard, the clinical investigation ACE-REHAB into personalised rehabilitation of cardiac patients has been initiated.

Patient-led research

The laboratory is situated in state-of-the-art research facilities at the Balgrist Campus. A key ingredient of this research facility is an open-space landscape where research and development into musculoskeletal medicine is integrated under one roof between clinicians, biologist, engineers, and industry. The facility situates in the vicinity of the orthopaedic hospital at Balgrist; thus providing a pipeline for a reality-driven approach that re-integrates questions from bedside to bench and returns to the patient. The Laboratory for Muscle Plasticity is looking for potential partners that may want to exploit the research options presented in the future campus in the frame of collaboration.



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Has austerity made healthcare a political football?

There are recent examples where healthcare has been used to win over voters, says Dorli Kahr-Gottlieb, Secretary General, European Health Forum Gastein

Health has become a highly politicised issue. Whether we're talking about President Macron and the French dentist fees, the relocation of the European Medicines Agency or Farage's claim written on a bus that Brexit would save £350,000m a day; national health systems are often at the heart of contentious political debates. But whilst healthcare is often viewed by politicians as a bargaining tool to win over voters, we have a long way to go before it is truly put at the heart of national and European policies.

“Access to health is a fundamental European value that European voters expect to have a right to. But health systems are increasingly under pressure as they try to adapt to an increased burden of chronic diseases, migration and ageing populations.”

The concept of “Health in Policies” (HiAP) is not a new one; politicians across Europe have embraced it, however, the real question is whether it is actually put into practice. At this year's 20th anniversary of the European Health Forum Gastein we set to explore how we can take this concept to the level of political implementation – and the sooner, the better, as it becomes increasingly clear that globalisation, climate change and other major political, economic and societal challenges all have an impact on our physical and mental health.

Rewind 20 years and Europe's future has a very different outlook – it was a world before austerity, we were launching the Euro and integration of new members was a possible reality. It was at this time that technical and political experts first travelled to the Gastein valley, Austria, to explore the social and health benefits of living in Europe. And so began the first European Health Forum Gastein (EHFG) – which has grown to become a ‘must have’ event on the agendas of politicians, decision-makers, and experts from the public



Dorli Kahr-Gottlieb, Secretary General, European Health Forum Gastein

and private sectors, science and academia, and civil society. It's a ‘go-to’ event for prominent stakeholders to come together and share knowledge, expertise and views on Europe and its policies.

Fast forward to today, the EU is struggling with populism that, among other factors, often stems from austerity. Where there is austerity, you can be sure that social sectors are the first to feel the pinch. None more than national healthcare systems. We only need to glance at recent headlines in the UK and French press to understand the importance of functioning healthcare systems to Europeans. Access to health is a fundamental European value that European voters expect to have a right to. But health systems are increasingly under pressure as they try to adapt to an increased burden of chronic diseases, migration and ageing populations. All this, with a squeezed healthcare budget and a shrinking workforce. Whilst health is, for the most part, a competence of EU Member States, it's



worth noting that combatting these challenges could be much faster by leveraging shared experiences.

Access to health

Europeans may have a lot to complain about when it comes to their own national healthcare systems and the role of the EU in their daily lives. But whilst we may be quick to squabble, we mustn't forget the benefits that Europe provides. Travel across Europe, for example, and you will carry close to hand your European Health Insurance Card (EHIC), granting you the right to access state-provided healthcare in any of the EEA countries. What about food security? Thanks to the EU we can be sure that the food on our plates is safe for consumption. Collaboration between EUROPOL and INTERPOL tackles food fraud on a global scale, ensuring that the food entering Europe is what it says on the tin. As we see a dangerous rise in childhood obesity, type 2 diabetes and cardiovascular disease, discussion at EU level on nutrition, physical activity, marketing of foods and healthy lifestyles is incredibly relevant to everyday Europeans.

As we look towards this year's Gastein Forum, it is clear that the debate on Europe and its policies on health will be rife. All this with a squeezed healthcare budget and a shrinking workforce. Whilst health is, for the most part, a competence of EU Member States, it's worth

noting that combatting these challenges could be met much faster by leveraging shared experiences. The European Health Forum Gastein is an ideal setting for sharing these experiences.

With the main theme of 'Health in All Politics', this year's Forum will be structured around 4 distinct tracks: Health in All Policies, health systems, access to medicines and innovation, Big Data & ICT. A series of sessions and workshops in these tracks will address a number of topics such as pricing of medicines, vaccines hesitancy, health literacy, the environmental implications on health, personalised healthcare, the future of cancer treatments, big data and many more. With so much ground to cover, I hope you will join us on 4-6 October 2017 in Austria and celebrate EHFG's 20th anniversary.

Dorli Kahr-Gottlieb has been actively involved in the field of public health over the last 15 years. ■

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Using ATP cleaning methods to reduce HCAs

Healthcare Associated Infections (HCAs) could be prevented using adequate cleaning methods. Here Martin Easter of Hygiena International Ltd explains

Healthcare Associated Infections (HCAs) are preventable, with World Health Organization (WHO) statistics showing a prevalence of 7.1% in Europe, affecting 4.1 million patients and costing €7 billion and 37,000 deaths per annum. In the UK the prevalence is 6.4% affecting 300,000 patients and costing £1 billion.

“If we have an area of concern with a particular infection or organism – we use ATP as part of the investigation. The benefit is that with ATP we can react immediately to the results on site and put any necessary interventions into immediate effect. That way we’re safeguarding patients, which is what it’s all about.”

Cleaning is one of the primary preventative measures against HCAs. The NHS spends £725m per annum on cleaning and the NHS Productivity Review (2016) showed that £93m could be saved from a better control of cleaning. However cleaning is inadequately measured by visual assessment methods that are highly subjective and only detects gross lapses of practice. The visual assessment gives a “misleading over-estimate of cleaning that undermines infection control strategies” (Jones 2009).

The National Institute of Health Research recognises that “NHS places greater reliance on visual assessment of surface cleanness. However,

reliance on observational evidence in judging cleaning efficacy is subjective and may be of questionable validity. ... The use of ATP bioluminescence can provide this, giving an instant indication of total surface contamination and importantly an objective assessment of cleanliness. ATP detects invisible contamination and tells us that the surface has been cleaned.”

ATP bioluminescence is a simple rapid method for measuring organic soil. It requires a small hand held instrument and an all-in-one sample collection and testing device and generates giving a numerical result in 15 seconds. The use of ATP bioluminescence for cleaning verification is well established and has also been the highest recommendation by the Rapid Review Panel of the Department of Health and Public Health England in support of the fight against HCAs. The test is also recognised by the CDC in the US and is written into a standard for cleaning in Denmark and Sweden. The test is simple and easy to use giving a numerical result in 15 seconds.

Earlier adopters such as North Tees and Hartlepool Trust have shown a consistent and marked improvement in cleanliness and reductions in infection rates since its introduction in 2008. The results have shown a more than 20% improvement in pass rates and a large reduction in fail scores to fewer than 5% with a corresponding decrease of 35% in *C. difficile* cases



and a 39% reduction in infections per 10,000 occupied bed days. Monitoring officers, independent from nursing and environmental services staff, are assigned to act as project champions for individual facilities, reporting to departmental managers wherever poor cleaning was discovered and where corrective action is required. Monthly reports are circulated for cross-functional team meetings of nursing, facilities and infection control staff. This allows for open discussions on all cleaning and maintenance related issues and stimulates actions for improvement.

HOW IT WORKS



Hygiena SystemSURE Plus

The Hygiena SystemSURE Plus received the highest recommendation for the Department of Health and Public Health England's Rapid Review Panel in 2009 and it has many different applications within hospitals including the routine testing of the patient room, identification of hotspots and hazard management, training of cleaning staff, and hand wash training and verification.

The benefits of the ATP cleaning verification system including a dramatic improvement in hospital cleanliness, optimised cleaning performance and personnel training, increased productivity commitment and morale of cleaning staff and reduced infections rates.

Southport and Ormskirk NHS Trust have been using the ATP technology for over 5 years for several applications and departments from medical equipment library, ITU, IP&C, domestic services, planned care, catering and operating theatres. It is also used for hand hygiene training and compliance monitoring. Andrew Chambers explained: "We also use Hygiena ATP monitoring when we may have had an

incidence of VRE, for example after a clean the area might look clean but a number of spot ATP tests might show that the area is, in fact, not clean.

"Cleaning is one of the primary preventative measures against HCAs. The NHS spends £725m per annum on cleaning and the NHS Productivity Review (2016) showed that £93m could be saved from a better control of cleaning."

"ATP gives you a clean hospital," said Val Hulme (Domestic Services Team leader). "When you're doing a deep clean the staff know they are going to be tested they do everything to a very high standard. ATP has helped us to achieve that. When you have a number – like the ATP machine gives you – it's more objective than subjective. You can't argue with it."

Andrew explained "If we have an area of concern with a particular infection or organism – we use ATP as part of the investigation. The benefit is that with ATP we can react immediately to the results on site and put any necessary interventions into immediate effect. That way we're safeguarding patients, which is what it's all about".

Andrew added: "Low numbers mean it's a safe environment for patients to be in".

Regular objective monitoring of cleaning increases compliance of cleaning policies from 40% to 82%. This decreases contamination levels, reduces infection rates, maximises the use and value of existing resources thus saving time, money and lives.



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How can technology safeguard quality of care?

DiaGraphIT's Managing Director, Tone Birkenes, explains how technology can revolutionise the quality of care delivered in healthcare settings

Since 1978, Lise Kristiansen has been suffering from arthritis. When her local hospital improved and simplified patient care by introducing software to systematically measure the impact of medical treatment, it created a whole new world for rheumatic patients.

In need of a means to get a quick and graphic overview of the development of disease activity in relation to the medical treatment, the Norwegian rheumatologist Glenn Haugeberg developed software to help. "It simply wasn't enough to ask patients how they were feeling. Patient response, such as "better then yesterday", was imprecise and vague.

Such ICT tools enable patients to log information about their medical situation online, which have great value for both health professionals and patients. With such ICT tools, health professionals don't have to perform unnecessary duplicate registrations and the clinic saves both time and money. Patients can actively participate in their own health by registering data about their health status into the system wherever they are – and these data are monitored by highly qualified health professionals who can take action if necessary. Initially, Haugeberg's specific ICT tool was developed for rheumatic diseases. However, since then other medical disciplines have been added to the product portfolio.

In close collaboration with Glenn Haugeberg, Lise Kristiansen has been involved in the development of the healthcare software since the beginning. By evaluating software from a user's point of view, Lise contributed with feedback on usability and the graphic overview of the development of disease activity in relation to the medical treatment.

"I'm impressed", said Lise. When using the software, patients can track changes about their own health and well-being and have ownership of their own health." When Lise was diagnosed with rheumatism back in 1978, there were 64 beds in the Department of Rheumatology at Sørlandet Hospital HF in Kristiansand. Today there are none. "The medication is so much better than it used to be. Very few people are disabled by rheumatism, the treatment is amazing. That's why research is so important, that's what moves science and development further."

Using technology to ensure better outcomes

When healthcare software was introduced to the Department of Rheumatology at Sørlandet Hospital HF, it brought a new reality of technology for the patients. "Many of us hadn't even seen a computer before, now suddenly a click could show the status of the disease related to the medical treatment, which was very exciting."

Sørlandet Hospital HF still uses software in treating their patients, collecting specific and relevant clinical information for patients and health care professionals. Information related to disease activity, health status, quality of life and medical intervention, provides a common platform for patients and doctors to communicate, thus securing the best possible treatment. Data recorded in the software is reused for medical records, for systematic quality work in the clinic, for the national quality registers and for research.

Tuulikki Sokka-Isler, Head of Rheumatology at Jyväskylä Central Hospital in Finland, is extremely happy with the new functionality for data extraction. He said, "It expands the use of the software from being a clinical tool to a clinical research tool. Data that are collected in a real-world setting can now easily be extracted in an analysable format for collaborative and comparative research among all users around the world."

At Jyväskylä Central Hospital, the software feature for remote monitoring is also in use. "As the first step, all referrals and return patients are informed about the option to complete the software remotely. This week several young people completed the software at home before the visit. This is a great step forward! The web self-assessment is simply up-to-date and fantastic", concludes Sokka-Isler enthusiastically.

For Hanne Vestaby, a nurse in the Department of Rheumatology at Sørlandet Hospital HF, such new technology caters for a much more targeted way of working. "I work as a nurse in rheumatology care in the outpatient clinic where I conduct my own patient consultations. With the new technology, I can rely on explicit outcome measures and use that as a solid foundation for the conversation I'm having with the patient.

"The system provides status per patient, and I use that information actively when communicating with the patient. This often motivates the patients and gives them confidence in what they are doing themselves, indeed has an effect. After having used online patient self-assessment questionnaires, many patients report a sense of finally being taken serious, as the status information they provide, is direct, and not filtered through healthcare professionals. My experience is that it makes us all work more efficiently, and gives us better time to follow up on other patient needs or concerns."

Lise Kristiansen requests extensive use of such software in more clinics. "The software generates patient involvement and I believe more clinics should apply this type of technology to secure the best possible treatment. It is user participation at its best." ■

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What's new in Parkinson's rating scales?

Parkinson's rating scales are a vital assessment tool, but have their limitations. Jennifer Stratten explains how and why the EPDA developed a new one

Parkinson's rating scales help to evaluate a patient's clinical symptoms. They typically assess a person's responses – usually the person with Parkinson's or a healthcare professional on their behalf – to a scale questionnaire.

The answers to the questions offer medical teams patient-driven insights into a person's condition, and help them to evaluate the severity of their symptoms and their quality of life. They can also be used to support healthcare professionals in monitoring the disease progression, developing treatment and management strategies. This can, in turn, be useful to researchers and support hospital benchmarking.

So why did the EPDA develop a new scale?

Several rating scales are already available to assess the severity of Parkinson's manifestations and the effect of treatment, such as MDS-UPDRS, NMSS, UDysRS, and MoCa.

While these are useful to explore different aspects of the condition, they don't provide a holistic overview of the disease from the patient's perspective. This meant that a new scale measuring motor, non-motor symptoms and treatment-related complications was needed.

The EPDA's new Parkinson's Disease Composite Scale (PDCS) measures the severity of symptoms experienced by people with Parkinson's in a timely way. It combines motor symptoms, non-motor symptoms and treatment-related complications; it is also simple and relatively fast to use. Designed to complement existing scales, the Composite Scale is the first to offer a holistic view of Parkinson's.

The Composite Scale can be conducted in roughly 15 to 20 minutes, and in advance of a consultation with a

neurologist, freeing up time within the consultation to discuss other things important to the individual. In addition, it grades the relative importance of particular symptoms, taking into account people with Parkinson's perspectives, which are critical in the delivery of timely and effective treatment and care.

How the project was developed

The Composite Scale was developed by Parkinson's specialist neurologists Professors Pablo Martinez Martin (Spain) and Fabrizio Stocchi (Italy).

The initial pilot study took place in 2015, and generated satisfactory outcomes in terms of the tool's acceptability and hypotheses testing. A first validation study took place in October 2015 with 194 patients from 5 countries. The study proved the Composite Scale to be:

FEASIBLE AND ACCEPTABLE

– the extent to which the Composite Scale could be used successfully in a clinical setting.



VALID

(hypothesis testing validation)
– the extent to which the scale assessed the underlying theoretical construct it was designed to measure.



RELIABLE

(internal consistency and stability)
– how much the scale was free from random errors.



PRECISE

– the scale's ability to distinguish between small differences in symptoms.



The Composite Scale was introduced to EU policymakers in the European Parliament in Brussels in February 2016.

A second validation study began in February 2017. There are 19 centres, from 14 countries participating in the extensive validation study and seeks to reaffirm the scale's findings among a larger group of people with Parkinson's and clinicians.

In March of this year, the EPDA hosted a high-level workshop with political, clinical and patient stakeholders in the European Parliament. The aim was to better understand the role policy can play in facilitating the scale's uptake in clinical settings.

EPDA President Knut-Johan Onarheim explained to EU decision makers that:

"This scale aims to provide a new, holistic and patient-centric tool to measure Parkinson's symptoms by offering a comprehensive view of a person's conditions. While it should be used primarily by neurologists and healthcare professionals within the multidisciplinary team – and is not a self-assessment tool – we believe it can and should aid people with Parkinson's to better understand their condition."

Dr Fabiana Radicati, who is currently coordinating the scale's second validation study, commented:

"Any person with Parkinson's will tell you that non-motor symptoms such as sleep disturbances, anxiety and depression are almost as bad – if not worse than – the more recognisable motor-symptoms, like tremor. This scale is designed to give a voice to those symptoms in clinical consultations, and make sure that people living with this chronic condition feel confident enough to discuss all of their symptoms with their doctors and have their treatments and care tailored accordingly."

The EPDA aims to roll out the Composite Scale as a new tool to neurological and clinical bodies, policymakers, and patient organisations across Europe in 2018. The Composite Scale was developed as part of the EPDA-led My PD Journey coalition. For more information about the new Composite Scale or My PD Journey, please contact secretariat@mpdj.eu . ■

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Parkinson's disease: are conventional treatments working?

Ramón Cacabelos, President of EuroEspes Biomedical Research Centre looks at conventional pharmacological treatments for Parkinson's disease

Parkinson's disease (PD) is the second most important age-related neurodegenerative disorder in developed societies, after Alzheimer's disease. It has a prevalence ranging from 41 per 100,000 in the fourth decade of life to over 1,900 per 100,000 in people over 80 years of age. As a movement disorder, the PD phenotype is characterised by rigidity, resting tremor, and bradykinesia. PD-related neurodegeneration is likely to occur several decades before the onset of the motor symptoms. Potential risk factors include environmental toxins, drugs, pesticides, brain micro-trauma, focal cerebrovascular damage, and genomic defects. PD neuropathology is characterised by a selective loss of dopaminergic neurones in the substantia nigra pars compacta, with widespread involvement of other CNS structures and peripheral tissues. Pathogenic mechanisms associated with genomic, epigenetic and environmental factors lead to conformational changes and deposits of key proteins due to abnormalities in the ubiquitin-proteasome system together with dysregulation of mitochondrial function and oxidative stress.

Conventional pharmacological treatments for PD are dopamine precursors (L-DOPA), and other symptomatic treatments, including dopamine agonists (amantadine, apomorphine, bromocriptine, cabergoline, lisuride, pergolide, pramipexole, ropinirole, rotigotine), monoamine oxidase

(MAO) inhibitors (selegiline, rasagiline), and catechol-O-methyltransferase (COMT) inhibitors (entacapone, tolcapone). The chronic administration of anti-parkinson drugs currently induces the 'wearing-off phenomenon', with additional psychomotor and autonomic complications. In order to minimise these clinical complications, novel compounds have been developed. Novel drugs and bioproducts for the treatment of PD should address dopaminergic neuroprotection to reduce premature neurodegeneration in addition to enhancing dopaminergic neurotransmission.

Biopharmaceutical compounds

An example of this is E-PodoFavalin-15999 (Atremorine®), a novel biopharmaceutical compound, obtained by means of non-denaturing biotechnological procedures from structural components of *Vicia faba* L., for the prevention and treatment of Parkinson's Disease. Preclinical studies (in vitro) revealed that Atremorine is a powerful neuroprotectant in (i) cell cultures of human neuroblastoma SH-SY5Y cells; (ii) hippocampal slices in conditions of oxygen and glucose deprivation; and (iii) striatal slices under conditions of neurotoxicity induced by 6-OHDA. In vivo studies showed that Atremorine (i) protects against 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine (MPTP)-induced dopaminergic neurodegeneration; (ii) inhibits MPTP-induced microglia activation and neurotoxicity in the

substantia nigra; and (iii) improves motor function in mice with MPTP-induced neurodegeneration. Clinical studies in untreated patients who receive Atremorine for the first time (never treated before with antiparkinsonian drugs) revealed that Atremorine enhances dopaminergic neurotransmission and increases plasma dopamine levels by 200-500-fold. In patients chronically treated with L-DOPA or other antiparkinsonian drugs, Atremorine induces a dopamine response of similar magnitude to that observed in previously untreated patients. This pro-dopaminergic effect can be attributed to the rich content of natural L-DOPA (average concentration 20 mg/g) in the composition of Atremorine.

However, the neuroprotective effect of this nutraceutical product on dopaminergic neurones, as demonstrated in in vitro studies and in animal models of PD, cannot be attributed to L-DOPA alone, but to other intrinsic constituents (selective neurotrophic factors) of the compound. 100% of untreated PD patients exhibit a dramatic hypodopaminemia, with plasma levels of DA below 20 pg/mL, and PD patients under long-term treatment with L-DOPA and/or conventional antiparkinsonian drugs experience a hyperdopaminemic status which might be responsible for (i) the clinical improvement of PD cardinal symptoms in the short-term, (ii) the 'wearing-off' phenomenon, (iii)

motor fluctuations and dyskinesia, (iv) systemic complications (gastrointestinal disorders, cardiovascular problems, hormonal dysregulation), and (v) neuropsychiatric disorders (depression, anxiety, toxic psychosis). Atremorine is an option to minimize the 'wearing-off' phenomenon, extending the therapeutic effect of conventional antiparkinsonian drugs, and reducing potential side effects, since the co-administration of Atremorine with other antiparkinsonian drugs allows a dose reduction of conventional drugs by 25-50% with enhancement of clinical benefits and reduction of short- and long-term adverse drug reactions.

Atremorine is a powerful enhancer of plasma catecholamines (noradrenaline, adrenaline, dopamine), with no apparent effect on serotonin. Catecholamines are processed by 3 main nuclei (A8-retrobulbar, A9-substantia nigra pars compacta, A10-ventral tegmental area) arranged in the mesencephalic region where the mesostriatal, mesolimbic, and mesocortical pathways are organised. Midbrain dopaminergic neurones in the ventral tegmental area and noradrenergic neurones in the locus coeruleus are major sources of dopamine and noradrenaline to the prefrontal cortex, where these amines regulate cognition, behaviour, and psychomotor function. Noradrenaline, adrenaline, dopamine, and serotonin play a central role in CNS and gut pathophysiology. Dopamine and noradrenaline are involved in the chemical structure of neuromelanins in the substantia nigra and the locus coeruleus, respectively. Dopamine, 3, 4-dihydroxyphenylacetic acid (DOPAC), 3, 4-dihydroxyphenylethanol (DOPE), and 3, 4-dihydroxyphenylalanine (DOPA) are mainly responsible for the structure of neuromelanin from substantia nigra, while noradrenaline, 3, 4-dihydroxymandelic acid (DOMA),

and 3, 4-dihydroxyphenylethylene glycol (DOPEG) are responsible for the structure of neuromelanin from locus coeruleus.

Deficiencies in these monoamines are currently found in Parkinson's disease. Hypoactivity of the dopaminergic and noradrenergic systems in the brain stem are related to non-motor and motor symptoms in PD. Dysregulation of these neurotransmitters is also involved in a variety of gastrointestinal symptoms in PD, and all of them appear to contribute to neurotransmitter and autonomic dysfunctions in PD, including mechanisms of L-DOPA-induced dyskinesia and cardiovascular dysautonomia. Therefore, appropriate doses of Atremorine alone, or in combination with low doses of conventional anti-PD drugs may benefit PD patients in whom the biosynthetic apparatus of the catecholaminergic system is damaged. The increase in noradrenaline induced by Atremorine may contribute to clinical improvement and neuroprotection since the noradrenergic neuronal loss in the locus coeruleus is exacerbated in PD. Lewy pathology in the locus coeruleus, the brain's main source of noradrenaline, precedes that of the substantia nigra, and may be one of the very first pathogenic events in PD. Oxidised noradrenaline exerts a neuroprotective effect and may even prevent the formation of toxic and higher molecular weight α -synuclein oligomers associated with PD. Noradrenergic neurones innervate the substantia nigra. The locus coeruleus orchestrates the other major catecholaminergic nuclei, such as the substantia nigra and raphe nuclei. In this regard, it has been suggested that neuronal loss in the locus coeruleus and the accompanying noradrenergic deficiency constitute an important pharmacological target for the treat-

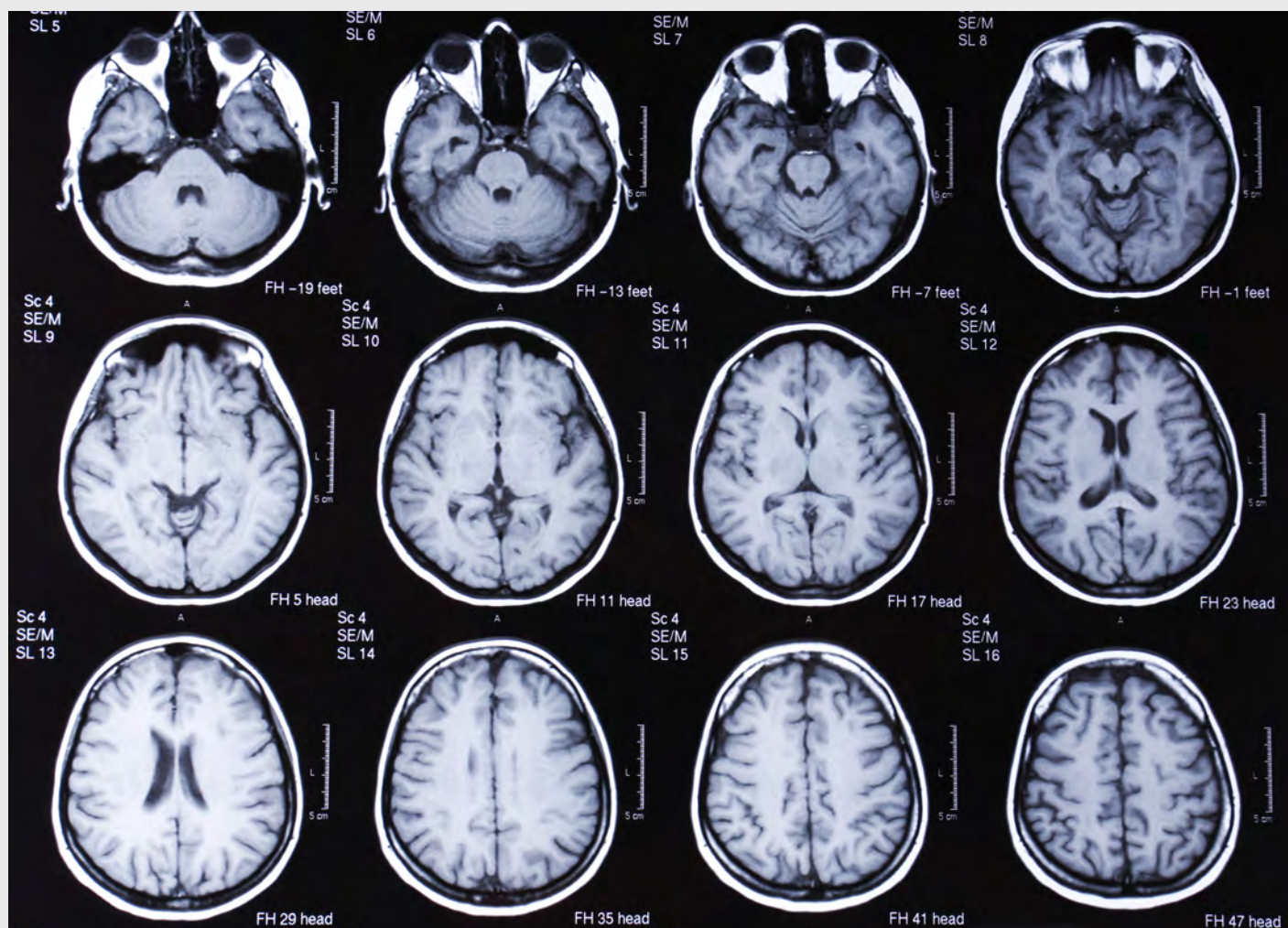
ment of PD. Atremorine also regulates hormones which appear altered in PD.

The real potency and pharmacodynamic and pharmacokinetic properties of Atremorine are highly influenced by genetic and pharmacogenetic factors. The condition of extensive (EM), intermediate (IM), poor (PM) or ultra-rapid metaboliser (UM) associated with different CYP variants, and the inheritance of the APOE-4 allele as well, influence the Atremorine-induced dopamine response in PD patients. Although practically 100% of the patients respond to Atremorine, the magnitude of the response is modulated by the pharmacogenetic profile of each patient. For instance, in absolute values, CYP2D6-PMs exhibit the lowest basal dopamine levels and a response to Atremorine which is lower than that of CYP2D6-EMs or IMs; however, CYP2D6-UMs show the highest basal dopamine levels and the most spectacular response to Atremorine. The 3 major CYP2C19 genophenotypes show a similar response to Atremorine; in contrast, comparatively, CYP2C9-IMs and CYP3A4/5-IMs are the best responders and CYP2C9-PMs and CYP3A4/5-RMs are the worst responders to Atremorine.



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Finding effective treatments for vascular dementia

Dr Doug Brown, Director of Research, Alzheimer's Society provides details on the research into vascular dementia and explains why more work is needed

Vascular dementia is the second most common type of dementia, accounting for almost one fifth of all cases. By 2025, it is estimated there will be 250,000 people living with vascular dementia in the UK. Despite the scale of this condition, we are still largely in the dark about its underlying causes and there are no effective treatments available to people receiving a diagnosis. Research into vascular dementia currently makes up less than 5% of all UK dementia research, and progress has been stifled by a lack of funding.

The condition is characterised by a reduced supply of blood to the brain, but the underlying cause can vary. It can be due to diseased blood vessels, blood clots, bleeding in the brain or a mix of these problems. Having a stroke doubles a person's risk of developing vascular dementia, and 30% of all stroke survivors will go on to develop the condition. However, the pervading lack of knowledge around the co-existing and co-developing relationship between strokes and vascular dementia has highlighted the urgent need for more research.

Investigating vascular dementia

Giving a much needed boost to this area of research, the Alzheimer's Society has united with the British Heart Foundation and the Stroke Association to make a £2.2m investment. Three studies will investigate different aspects of the relationship between strokes and vascular dementia to fill critical gaps in our knowledge. From this, we hope to begin devising ways to treat or prevent this common form of dementia.

“Having a stroke doubles a person's risk of developing vascular dementia, and 30% of all stroke survivors will go on to develop the condition.”

The first study will focus on a disease of the small blood vessels in the brain, called cerebral small vessel disease (SVC). This disease is found in approximately one quarter of all stroke victims and is the most common cause of vascular dementia. Little is known about it, and therefore there are no treatments currently available. Researchers will develop new disease models to try to better understand what causes SVC. These may also help to develop and screen new treatments that will prevent or slow the progression of the disease.

The next study will follow 2,000 patients from 8 leading hospital centres in England and Scotland. By interrogating hospital records and performing thinking and memory tests for up to 2 years following a stroke, researchers will compare those who do and do not develop vascular dementia to understand what causes the condition and how it can be prevented. The findings from this research could help health professionals to deliver better follow-up support and may help develop improved methods for identifying and treating memory problems caused by brain blood vessel diseases.

The final study is taking an alternative approach. Not only do blood vessels supply blood to the brain, they

also remove waste. Researchers will test the theory that the inability of damaged blood vessels to effectively remove waste from the brain is critical in the development of vascular dementia. If it is, the future goal will be to develop vascular dementia treatments that can enhance waste removal from the brain.

New treatment approach necessary

As there are no licensed treatments for people living with vascular dementia, many people are prescribed the same drugs used in Alzheimer's disease. Recent trials have shown that repurposing these drugs does not work, so a new approach must be taken. The implications of these new research programmes could therefore be vast. However, the studies will run for 3 to 5 years before we can interrogate the findings and derive how these learnings may help people at risk of developing vascular dementia in future.

With dementia set to be the 21st century's biggest killer, the time to act is now. By uniting against vascular dementia, these three leading charities are paving the way in working collaboratively to tackle the biggest health crisis of our time. ■

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Tackling cognitive decline in Alzheimer's disease

Ai-Ling Lin PhD, of The Lin Brain Lab talks about the reversal of cognitive decline in Alzheimer's disease with comprehensive and personalised nutrition

Alzheimer's disease (AD) represents the most common cause of dementia, accounting for 60% to 80% of all dementia cases. There are currently only a few interventions that have been approved for the treatment of AD, but none have shown a clear effect on disease progression. Between 2002 and 2012, 99.6% of clinical trials on AD failed, showing the highest failure rates of any disease area. In the last 14 years, no new drugs have been released and existing drugs only stabilise symptoms temporarily in some patients, but do not slow progression of the disease. One of the major contributors for the failure is to focus on the wrong target. Until now, companies have mostly gone after the same target – amyloid-beta ($A\beta$) proteins that form aggregates or plaques in the brain of AD patients. This has led some to question whether treating AD with a single target-based approach is an optimal one.

Accumulating evidence shows that decades before the aggregation of $A\beta$, cognitively normal individuals had developed metabolic deficits, including significantly reduced brain glucose utilisation. Failure to maintain brain metabolism has been shown to lead to neuronal death, brain volume shrinkage, and ultimately, dementia. Therefore, interventions that are able to restore brain metabolism would be critical to preserve cognitive functions. In particular, therapies that target on



multiple metabolic networks, rather than a single target-based approach, may be potentially more effective for the treatment of cognitive decline due to AD.

MEND

In a recent exciting study, Dr. Dale Bredesen (Buck Institute, CA, USA) demonstrated that cognitive decline due to AD is reversible using comprehensive and personalised nutritional interventions (Bredesen, 2014). The report described a therapeutic programme that involves multiple modalities designed to achieve metabolic enhancement for neurodegeneration (MEND). The first 10 patients who have utilised this program include patients with memory loss associated with AD, amnesic mild cognitive impairment, or subjective cognitive

impairment. Nine of the 10 displayed subjective or objective improvement in cognition beginning within 3 to 6 months, with the one failure being a patient with very late stage AD. Six of the patients have had to discontinue working or were struggling with their jobs at the time of presentation, and all were able to return to work or continue working with improved performance. Take one case as an example – a 67-year-old woman presented with 2 years of progressive memory loss. She held a demanding job that involved preparing analytical reports and traveling widely, but found herself no longer able to analyse data or prepare the reports, and therefore was forced to consider quitting her job. She noted that when she would read, by the time she reached the bottom of a page she would have to start at the

top once again, since she was unable to remember the material she had just read. She was no longer able to remember numbers, and had to write down even 4-digit numbers to remember them. She also began to have trouble navigating on the road: even on familiar roads, she would become lost trying to figure out where to enter or exit the road. She also noticed that she would mix up the names of her pets, and forget where the light switches were in her home of years.

She enrolled in the MEND program with the following therapeutic protocols:

- Eliminated all simple carbohydrates, leading to a weight loss of 20 pounds;
- Eliminated gluten and processed food from her diet, and increased vegetables, fruits, and non-farmed fish;
- Began yoga to reduce stress;
- Began to meditate for 20 minutes twice per day to reduce stress;
- Took melatonin 0.5mg po qhs;
- Increased her sleep from 4-5 hours per night, to 7-8 hours per night;
- Took methylcobalamin 1mg each day;
- Took vitamin D3 2000IU each day;
- Took fish oil 2000mg each day;
- Took CoQ10 200mg each day;
- Optimised oral hygiene using an electric flosser and electric toothbrush;

- Fasted for a minimum of 12 hours between dinner and breakfast, and for a minimum of 3 hours between dinner and bedtime;
- Exercised for a minimum of 30 minutes, 4-6 days per week.

The MEND programme has helped her restore systematic metabolism, including the brain. After 3 months she noted that all of her symptoms had abated: she was able to navigate without problems, remember telephone numbers without difficulty, prepare reports and do all of her work without difficulty, read and retain information, and, overall, she became asymptomatic. She noted that her memory was now better than it had been in many years. Two and a half years later, she remained asymptomatic and continued to work full-time. Similarly, in another 8 patients, improvements were sustained; even after 2 and a half years follow-up, the patients still showed sustained and marked improvements.


The results suggest that at least early in the course, cognitive decline is driven in large part by metabolic processes. With comprehensive and personalised nutrition, memory loss in patients with early phase of AD, may be reversed, and improvement sustained, with the therapeutic program such as MEND. Given the failure of monotherapeutics in AD to date, the results raise the possibility that MEND might be a future solution for restoring cognitive functions and preventing the onset of AD.

As mentioned in our previous reports, brain metabolic function changes can be early detected using non-invasive

neuroimaging. The combination of neuroimaging technology and personalised nutritional interventions could be a powerful strategy to prevent AD in the future. To achieve these innovative and paradigm-shifted treatments compared to the monotherapeutics (e.g., with single-targeted drugs), there is an urgent need to increase funding for epidemiological and clinical studies, focused on the impact of metabolic dysfunction in relation to progression of AD. With awareness in society as a whole (researchers, governments, and general population), it is our hope that the risk of AD can be reduced and the onset of AD will ultimately be prevented.

Reference:

Bredesen, D.E. (2014). Reversal of cognitive decline: a novel therapeutic program. *Aging* (Albany NY) 6, 707-717.

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Time for a change of tack on drug development for neurodegenerative diseases

UCB's Duncan McHale outlines why reclassification might be a good idea to boost drug development for neurodegenerative diseases like Alzheimer's and Parkinson's

Neurodegenerative diseases are a growing global challenge, as medical advances ensure more individuals live longer. By 2020 there will be more than 40 million people in the world with Alzheimer's disease (AD) and by 2040, without the development of disease modifying drugs, this will rise to more than 80 million. Discovering and developing disease modifying drugs is proving very challenging, with many programmes failing. November 2016 saw another phase 3 failure with Lilly's solanezumab failing at the final stages of development. Is this the end of the amyloid hypothesis or a case of too little, too late and too broad?

been thought of as a disease of amyloidosis. Multiple potential therapies targeting amyloid processing have been developed and studied, with several still in the development stages. These therapies have all demonstrated an ability to reduce amyloid load in preclinical models, but this has so far not been beneficial to humans.

Amyloid is undoubtedly associated with AD and its presence has been a core part of the diagnosis, either post mortem or, more recently, through imaging techniques. However, the amount of amyloid does not correlate with disease severity and many subjects have significant amyloid deposits

but no symptoms. Despite these anomalies, the majority of current potential therapies have been targeting this mechanism. The community eagerly awaits the results of a clinical trial using Biogen's aducanumab as the most promising agent so far, but given the failure of other admittedly less potent molecules targeting amyloid deposition, many are pessimistic about a good result.

Drug development for neurodegenerative diseases at a turning point

The failure of these therapies to date could be because the amyloid hypothesis is flawed and, despite the

“AETIONOMY is an Innovative Medicine Initiative (IMI) funded consortium established to develop a mechanistic based classification of neurodegenerative diseases, with an initial focus on Alzheimer’s and Parkinson’s disease.”

The amyloid hypothesis

Alzheimer's disease is a chronic neurodegenerative disease which usually presents in the seventh or eighth decade of life. However, earlier onset is not uncommon. The cause(s) of AD are not fully understood but the presence of amyloid (protein) plaques in the brain was demonstrated in 1911 and since this time the disease has



association, amyloid is a downstream consequence of the disease process and not pathogenic in its own right. However, the presence of familial forms of the disease caused by genes involved in amyloid processing make this unlikely. For example, the presenilin 1 gene is part of a protein complex which degrades amyloid, creating the pathological 42 amino acid peptide.

“By 2020 there will be more than 40 million people in the world with Alzheimer’s disease (AD) and by 2040, without the development of disease modifying drugs, this will rise to more than 80 million.”

It is much more likely that, for most individuals, amyloid is not the sole cause and additional pathological mechanisms are involved. Indeed we now know that the Tau protein is one of these additional mechanisms. It is therefore time to start focussing on some of these other mechanisms to find the causes of AD, which we can then target with new therapies. We need to look for mechanisms that are important in later stages of the disease process and/or can still be successfully modified once the very early symptoms appear. AETIONOMY is a consortium with the sole purpose of identifying these other mechanisms involved in AD and reclassifying neurodegenerative disease using these discriminatory mechanisms, which will help us develop new treatments.

At AETIONOMY we have been taking the totality of research in AD and, using our knowledge base, integrating this information into a common framework to search for other potential mechanisms. By looking for these other mechanisms we hope to find sub-populations of patients who can be treated by targeting the cause in



them which is present with the amyloid plaques. Success will result in a new way to classify AD beyond just the presence of memory problems and plaques. Success will also result in new mechanisms for targeting and precision medicines for AD.

AETIONOMY

AETIONOMY is an Innovative Medicine Initiative (IMI) funded consortium established to develop a mechanistic based classification of neurodegenerative diseases, with an initial focus on Alzheimer’s and Parkinson’s disease. This public private partnership is co-led by myself and Martin Hofman-Apitius from SCAI Fraunhofer. The premise behind the project is that, although large sums have been invested in research in neurodegeneration and a lot of data generated, the co-ordination and integration of this data across the community has been less well addressed. The consortium has brought together experts in

informatics, computing, engineering, mathematical modelling of disease, neuroscience and clinical neurology from leading academic centres, as well as neuroscience, informatics and neurology drug development experts from the EFPIA Industry partners.

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What is the European drug situation in 2017?

Jane Mounteney, Alexis Goosdeel and Paul Griffiths from the EMCDDA highlight key findings from the 2017 European Drug Report and new threats emerging

June 2017 saw the launch of the European Drug Report¹, the European Monitoring Centre for Drugs and Drug Addiction's annual review of the European drug situation. Overall the 2017 analysis shows how the drug problems Europe faces are increasingly influenced by, and interact with, global developments.

Overdose deaths on the rise for third consecutive year

The increasing number of drug overdose deaths in Europe, which has risen for the third consecutive year, is a particular concern. A total of 8,441 overdose deaths, mainly related to heroin and other opioids, are estimated to have occurred in Europe in 2015, with the region's 1.3 million problem opioid users among the most vulnerable. This is an area where effective interventions exist, including the provision of opioid substitution treatment, the dissemination of 'take-home' naloxone (opioid overdose-reversal drug) to opioid users, their peers and families, and supervised drug consumption rooms, now operating in 6 EU countries. Opioids other than heroin – primarily methadone and buprenorphine – are also regularly found in toxicological reports in some countries underlining the need for good clinical practice to prevent diversion of these substances from their legitimate use.

New drugs emerging at a slower pace, but fentanils a growing health threat

New psychoactive substances (NPS) remain a considerable public health challenge in Europe. Not covered by international drug controls, they include a broad range of synthetic substances, including cannabinoids, cathinones, opioids and benzodiazepines. In 2016, 66 NPS were detected for the first time via the EU Early Warning System (EWS) – a rate of over 1 per week. Although there has been a slowing of the pace at which new substances are being introduced onto the market, the overall number of substances now available

remains high. The 2017 report highlights the high risk use of NPS by particular groups in Europe including among opioid injectors, men who have sex with men, prisoners, and homeless populations⁴. In addition, highly potent synthetic opioids represent a growing health threat in Europe, with fentanils a particular concern. 18 of these substances have been detected in Europe since 2009 and they pose a serious risk of intoxication, not only to users but also to anyone accidentally exposed to the drugs. In early 2017, the EMCDDA carried out risk assessments of two fentanils, acryloylfentanyl and furanyl-fentanyl^{2, 3}, after over 50 deaths associated with these substances were reported.

EU and US: school students – less smoking and drinking but cannabis stable

The publication of major school surveys in both the US and Europe in 2016 allows interesting comparisons to be made on long-term patterns of substance use among European and American students (15–16 years). The surveys show smoking and drinking among school students in Europe and the US to be declining, while trends in cannabis use appear to be more stable (figure 1). Last-month cannabis use among the European school students surveyed was around half the level (8%) of that reported in the US (15%). Last-month tobacco use was almost 4 times higher among students in Europe (23%) and last-month drinking double that of their US counterparts. Understanding what has led to the reductions in cigarette smoking in both the United States and Europe may offer insights for addressing the use of other substances, such as cannabis.

Cannabis: more people entering treatment

Cannabis remains Europe's most commonly used illicit drug and around 88 million European adults (15–64 years) have tried cannabis in their lifetime. Of particular concern are the 1% of European adults who are daily or almost daily cannabis, and the drug is now responsible

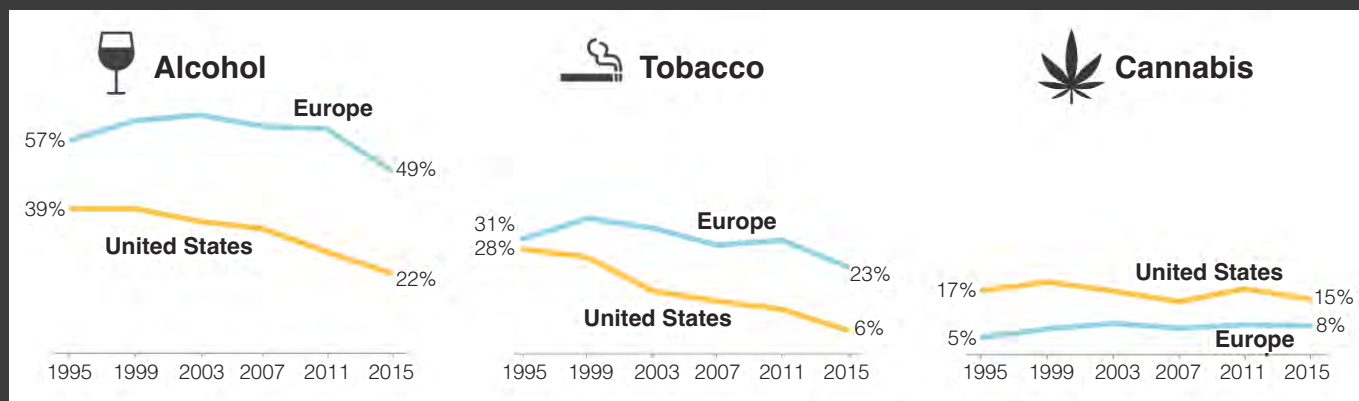


Figure 1: Substance use among school students in Europe and the United States

NB. Trends in last-month substance use among 15-16 year-old school students in Europe and the US. European averages (unweighted) are based on data from 21 EU countries and Norway (source ESPAD: <http://www.espad.org/report/home>). US averages are based on samples of 10th grade students (source: Monitoring the future: <http://www.monitoringthefuture.org/>).

for the greatest share of new entrants to drug treatment in Europe, which rose from 43 000 in 2006 to 76 000 in 2015. Multiple factors are likely to lie behind this increase, including higher prevalence of cannabis use, more intensive users, the availability of stronger products and increases in treatment referral and levels of provision. Understanding trends in cannabis use and related risks is important to the debate on what constitutes the most appropriate policy responses to this drug.

Here we note that recent changes in the regulatory framework for cannabis occurring in parts of the Americas have generated interest among policymakers and the public in Europe. Importantly, there is a need for robust evaluations before the relative costs and benefits of differing cannabis policy approaches can be assessed. In European countries, current approaches to cannabis regulation and use are diverse, ranging from restrictive models to the tolerance of some forms of personal use. Regardless of any wider impact on drug policy, the existence of a commercially regulated cannabis market in some countries outside Europe is fuelling innovation and product development (e.g. vaporisers, edible products), which may, in time, impact on consumption patterns in Europe.

Acknowledgements

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by EMCDDA scientific staff and the Reitox network of National Focal Points. ■

The report can be accessed in its entirety at: www.emcdda.europa.eu .

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European Monitoring Centre for Drugs and Drug Addiction (EMCDDA)
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Illicit drugs know no borders, neither should policy making

Simone Korff de Gidts, The Netherlands Organisation for Health, Research and Development highlights the ERANID project for illicit drugs research

The negative impact of illicit drugs on the lives of people and communities is a transnational problem. The European Commission recognised this in 2012 and committed a budget to set up a European Research Network Area on Illicit Drugs (ERANID).

A consortium of 11 partners from 6 EU member states was established.

Partners in the ERANID project are:

- Liverpool John Moores University, UK
- Department of Health, UK
- Home Office, UK
- BELSPO (Belgian Federal Public Planning Service Science Policy), Belgium
- Flanders Fund for Scientific Research, Belgium
- MILDECA, France
- Dipartimento per la Politiche antidroga, Presidenza del Consiglio dei Ministri, Italy
- General Directorate for Intervention on Addictive Behaviours and Dependencies (SICAD), Portugal
- Ministry of Health, Netherlands
- The Dutch Organisation for Health Research and Development (ZonMw), Netherlands



The first Strategic Research Agenda

The first achievement of the Network was the publication of the first Strategic Research Agenda (SRA), which provides a framework for multi-national collaboration in the field of illicit drugs research focusing on socio-economic and humanities research and both supply and demand. Drawn up as part of ERANID, the European Research Area Network on Illicit Drugs primary purpose was to identify common research priorities representing the areas of greatest need for society, and that have the greatest potential to improve our understanding of the drug situation and support effective responses to it.

Based on the SRA two transnational joint calls were published: the first call was called 'Understanding Drug Use Pathways' and resulted in the funding of three projects, the second call 'Society and Responses to Drug Use', resulted in four projects (for more detailed information on the SRA and the projects please visit the ERANID website, www.eranid.eu)

Having been written in 2014, there is no misunderstanding about the need for an update of the SRA but the "core" of the document is still relevant and many of the described priorities in research have not been covered yet.

The funding of seven excellent projects



is a good outcome of all the efforts undertaken by the partners in the ERANID network, but it would be a waste of opportunity if the existing network would not be able to be developed to a sustainable long-term cooperation between EU Member States and other countries, including policy makers, research institutions and other stakeholders.

The problems related to illicit drugs are widespread, all countries are

facing similar problems. Policy changes in one country effects other countries, the problems can affect any individual in some time in their life, directly or indirectly.

So with help of e.g. the European Monitoring Centre for Drugs and Drugs Addiction (EMCDDA) in which most of the European countries participate it would be great if ERANID could be the first step in the establishment of that longer term cooperation.



Funded projects:

First call

ImagenPathways: Understanding the Interplay between Cultural, Biological and Subjective Factors in Drug Use Pathways

ATTUNE: Understanding Pathways to Stimulant Use: a mixed-methods examination of the individual, social and cultural factors shaping illicit stimulant use across Europe

ALAMA-nightlife: Understanding the dynamics and consequences of young adult substance use pathways, a longitudinal and momentary analysis in the European nightlife scene

Second call

REC-Path: Recovery pathways and societal responses in the UK, Netherlands and Belgium

STANDUP: Sensory Processing Sensitivity AND drug Use recovery Pathways

IDPSO: Illicit drug policies and social outcomes: a cross-country analysis

D.U.R.E.S.S: Drug Use Recovery, Environment and Social Subjectivity



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Parasitic infection: Animal health matters too

Professor Colin J Suckling explains how teams at the University of Strathclyde and University of Glasgow are challenging global parasitic infection

Cows, horse, camels

When people talk about drug discovery the automatic reaction is to consider human health. In most countries with stable food supplies that's an understandable response. However in countries vulnerable to variable climatic conditions and with limited quality pasture, as is typical of north and sub-Saharan Africa, food supply from domestic animals is at risk from diseases of cattle in particular. The bovine equivalent of human sleeping sickness in Africa is known as nagana, or Animal African Trypanosomiasis, and is caused by a number of species of parasites of the genus *Trypanosoma*. Like the human disease, it is also spread by the tsetse fly. Nagana can be devastating to communities dependent upon cattle, even breeds adapted to the African environment.

In more affluent environments around the world, animals at risk of trypanosomal infections are also found. In Arabia and North Africa, camel racing is a hugely popular sport, but both camels and dromedaries are susceptible to trypanosomiasis. Away from the race track, camels are well known to be at the heart of the rural economies in these regions. In South America, another species of trypanosome causes a similar disease in horses, which are also important in rural areas. In both Africa and South America there are species of trypanosome that affect both humans and animals.

New drugs for old

The old drugs available for treatment are losing their efficacy because of developing resistance in the trypanosome parasite. In any case, the old drugs are unpleasant in use and require prolonged treatment, which in rural African environments are difficult to manage. This is the sadly familiar 21st century story of antimicrobial resistance, threatening animal and human life and well-being. When we started our anti-infective drug discovery programme at the University of Strathclyde more than 10 years ago, we did not know what the most significant applications might be. Naturally, as I noted above, we started to screen compounds against human bacterial and fungal pathogens but as the scope of our screening expanded, we found with the help of many collaborating laboratories that a subset of our compounds is particularly active against trypanosome parasites.

In addition to the potential economic benefit of new and effective treatments for animal trypanosomiasis, in several parts of the world the range of species of economically important animals that can be affected is surprisingly large. Here's a short selection of *Trypanosoma* species with the host animal noted beside:

- *T. brucei*, sleeping sickness in humans and nagana in cattle;
- *T. cruzi*, Chagas disease in humans; also infects cattle and horses;



Thomas Graham Building at the University of Strathclyde, Glasgow, where our compounds are made

- *T. congolense*, nagana in ruminant livestock, horses and a wide range of wildlife;
- *T. equinum*, in horses;
- *T. equiperdum*, in horses and other equidae;
- *T. evansi*, in horses, camels, deer: from Atlantic North Africa right across to Arabian peninsular;
- *T. lewisi*, in rats;
- *T. melophagium*, in sheep;
- *T. simiae*, nagana in pigs;
- *T. vivax*, nagana in cattle, also infects camels, horses, and antelope.

The Strathclyde and Glasgow programme

With so many infective agents (and there are more) it might be expected that a single new drug would be difficult to find. However, the similarities between the different species of trypanosomes are such that there is a

reasonable chance of success. A key test of this point is whether the potential new drug is active against *Trypanosoma brucei* and closely related species, principally from Africa, and against the relatively distantly related *Trypanosoma cruzi*, which occurs in South America. Results that arrived just this week (26th June) have prompted me to write this piece, to show convincingly that we can treat both types of trypanosome with our new compounds. This seems to me to be a major advance for our programme. So what can our compounds do?

The first hint that we might have useful compounds came from studies in Michael Barrett's laboratory at our neighbours, the University of Glasgow. He and his colleagues showed that there was significant activity against the human parasite, *T. brucei*, and were able to study some features of the mechanism of action. The team went on to show that our compounds were also active against one of the key species that infects cattle, *T. congolense*, with activity sufficiently high to suggest that development into an effective medicine would be possible. Later, in work being prepared for publication, his team importantly showed that our potential new drugs were effective against strains of parasite resistant to the most used old drugs, pentamidine and diminazine.



New drug synthesis in action in the Thomas Graham Building at the University of Strathclyde

Animal infections

In rural Africa, animal infections are commonly caused by either *T. congolense* or *T. vivax* or both. To have an effective new drug our compounds would clearly have to be active against both species. Mike's team was not in a position to screen against *T. vivax* because the parasite cannot be cultured. We were therefore introduced with the help of the not-for-profit animal and veterinary health company GalvMed, based here in Scotland, to Kirsten Gillingwater at the Swiss Tropical and Public Health Laboratory in Basel. She evaluated our compounds against *T. vivax* and we were very pleased to find that some were active, from which we selected two for further evaluation, MGB234 and MGB360.

It's all very well having compounds that work in a laboratory assay but will they cure disease in an animal? Having established that MGB234 and MGB360 were not acutely toxic in mice, Mike Barrett's team was able to begin to answer this question. Over the last six months we've been greatly encouraged by clear evidence from his team's experiments that MGB360 is able to cure mice of a *T. vivax* infection at reasonable doses. Also important was that the mice survived the course of treatment and there were no deaths due to drug treatment. MGB360 is just the pilot compound; by making small modifications to its structure we think we have a still better one, MGB402, but time and experiment will tell.

Will MGB360 and its relatives have a sufficient range of effectiveness world-wide? That's where this week's results from South America come in. Ariel Silber and his students at the University of São Paulo have just reported to us that MGB402 is very

effective at killing the South American species of trypanosome, *T. cruzi*, which causes Chagas disease in humans and also infects livestock widely. This means that not only do we have world-wide coverage with our compounds but we also most probably can attack all species in the *Trypanosoma* genus. In clinical use, therefore, it would not be necessary to identify the species, which would be a great advantage for the farmer working with the veterinarian and for the human clinician. So we're now working hard to expand the profile of our compounds to find out whether they are genuine candidates for full-scale development towards clinical use. That's not bad from one small chemistry team.

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The impact of clinical research in rare diseases

Kit C.B. Roes from the University Medical Centre, Utrecht outlines why clinical research in rare diseases requires swift implementation of new methodology

Efficient clinical research in rare diseases is crucial for new (drug) treatments to reach patients for whom there is often no treatment available. Design and conduct of clinical trials in these diseases is challenging, due to the smaller number of patients available to participate. The European Union has made a substantial investment into research for new methodologies for clinical research in small populations, with three funded projects completing in 2017. Results were obtained, a network was built, and there is strong support both from patient organisations and regulatory authorities to implement innovative methods across industry and academic clinical research. A call for concerted action to all of us to make this happen.

Clinical trials as cornerstone for development of new treatments

The combined clinical and socio-economic impact of rare diseases is huge. An estimated 30 million European patients suffer from a rare disease. Of the more than 6000 rare diseases known, many are chronic, potentially very disabling and typically affect children. The unmet need for patients suffering from a rare disease is well recognised. Over the past decades, the European Union – as well as other jurisdictions such as the United States and Japan – have taken on numerous initiatives to stimulate the development of new therapies to treat rare diseases. These initiatives range from regulatory legislation to stimulate

research by pharmaceutical companies and accelerated regulatory pathways, to funding research and building strong research networks across Europe for rare diseases. The incentives towards industry appear to be successful, with many more drugs being granted orphan designation.

A cornerstone to bringing new drug treatments to patients are clinical trials to assess efficacy and safety, and ultimately, the benefit-risk balance. These trials still face substantial challenges. The first obvious challenge is the inherently small number of patients that can be recruited into clinical trials. Secondly, there is often a substantial heterogeneity in disease course between patients suffering from the same rare diseases. Thirdly, exploration of these challenges in clinical research for rare diseases has triggered a re-think in terms of whether the usual standards of evidence (number of trials, control of false positives (type 1 error rates), and the role of meta-analysis) are adequate.

This calls for innovative approaches, including: new concepts for clinical endpoints, more advanced data analysis, (pharmaco-metric) modelling, trial designs with multiple treatments and approaches to leverage the data from registries and routinely collected clinical data. And – specifically for very rare diseases – a fundamental rethink how much evidence is actually needed

to make new treatments available to patients.

A joint meeting with regulatory authorities, patient representatives, academia and industry towards implementation

Three major EU funded projects in this area, *Asterix*, *IDeAI* and *InSPiRe*, have made major progress in these areas over the past 4 years. The progress was presented at the ‘Seventh Framework Programme (FP7) small-population research methods projects and regulatory application workshop’, March 29th & 30th 2017, which was jointly organised by the European Medicines Agency (EMA) and the 3 EU projects. At this meeting, it was clear that:

The progress across the 3 projects is impressive, and the joint challenge for patients stimulated collaboration across the 3 projects to a level that is unique for such programs.

The EMA is strongly supportive of innovative methods in this field.

Part of the results is ready for broad(er) implementation, which can be stimulated by regulatory instruments such as the EMA Guidance on Small Populations, and the EMA Qualification Procedure.

Innovative methods that may have even stronger breakthrough impact need further investigation, including real life application on a smaller scale.

Patient representatives appreciated the opportunity to truly engage actively in advancing research methodology for clinical trials.

There is a strong call from the patient perspective to move to implementation to accelerate the availability of new but proven, therapies for patients suffering from a rare disease.

Highlights and the action already envisioned

The full workshop is available online (see www.ema.europa.eu/ema/, under News and Events) and the results of the project are presented with a discussion. A few highlights are the following;

In view of the limited number of rare disease patients available for clinical trials, it is crucial that information on new treatments from other sources (animal experiments, earlier healthy volunteer trials, trials in different populations) can be used to infer efficacy and safety. Developments such as the 'scepticism' factor for extrapolation from one population to another and pharmacometric modelling now allow a more quantitatively justified approach to do so. This will strongly aid in researching new treatments within the constraints of small samples.

A second development that sparked discussion and enthusiasm, concerned a new approach to clinical endpoints. To accommodate the potential large heterogeneity between patients, Goal Attainment Scaling allows patient to have individualised outcomes that nevertheless can be summarised across comparative groups of patients to assess the treatment effect. This may resolve the problem of choosing appropriate endpoints for diseases such as Duchene's Muscular Dystrophy. Currently, the so-called 6 minute walking test is used as default

endpoint. But boys suffering from Duchene's become wheelchair bound at the age of about 8-10, hence with such endpoints many patients are excluded from trials – although they might very benefit from treatment.

A look into the future

The network of experts across the 3 projects covers large parts of the EU, and many researchers are engaged in clinical research for rare diseases. Hence, new methods gradually find their way to practice. This is, however, not enough and not quick enough from the patient perspective. The three project leads, Prof. dr. R-D Hilgers, Prof. N. Stallard and Prof. K. Roes assessed that 2 crucial objectives can be pursued simultaneously. The first and foremost objective is to ensure broad implementation of the new findings in clinical research for rare diseases, across academia and company research and across all relevant types of interventions. This directly contributes to the IRDiRC objective of regulatory approval of 150 new drug therapies in the period 2017-2027. Secondly, aiming for truly breakthrough improvements requires continuation of the research network to expand on the most innovative methods, as well as tailor these to the specific nature of the vastly diverse rare conditions.

The first objective is already on its way. In addition to engaging in clinical research projects across the EU, it is anticipated that the project leads will submit a selection of methods – such as Goal Attainment Scaling - for EMA scientific advice, e.g. for qualification of methods. This will stimulate pharmaceutical companies to use the methodology. In addition, general guidance for trials in small populations will likely be revised to include the most recent findings.

Furthermore we foresee that a target education program can be developed. The core principle is to link education directly with implementation: training is to be aimed at clinical research teams in the process of designing a clinical trials for a rare condition. Their protocol under development can then be actively used in the educational program to implement the learnings. Hence, clinical research protocols are optimised for real, important clinical trials. It can be highly beneficial if these efforts are connected to the recently established European Reference Networks for rare diseases.

Finally, the direction, content and urgency of the research has truly benefitted from patient representative involvement. Although we may not have found the optimal language and process yet, it is clear to all involved that we need to step-up our effort to include patients across all our clinical research phases, including the methodology underlying the design and ultimately the assessment of evidence from clinical trials.



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Innovation in the healthcare sector

France's Ministry of Solidarity and Health say innovation in the healthcare sector is imperative and that decision makers must work to transform the system

Innovation in the field of healthcare – including access to digital tools – is set to deeply modify its traditional organisation and practices. It will reinforce access to medical knowledge for patients and healthcare professionals, contribute to finding new knowledge and let our organisation adapt to new needs linked to the population ageing process or the increase of chronic diseases, for instance. It will also provide solutions that fit our current human and financial constraints.

For us and all the healthcare decision makers, it's a multiple regulation challenge. The good balance must be found between the necessary orientation towards our priorities and the liberty we must grant to innovators. Our evaluation methods must improve and adapt to new solutions regarding technology, organisation skills and professional practices. Regulation and funding models must evolve in order to implement and expand these solutions. There is also a new reflection for us to

adopt on our healthcare system – which we must start to consider as a value which will create jobs and wealth.

Innovation as a tool to address our healthcare system's current challenges

France has always been at the forefront of medical progress – in the field of fundamental discoveries, as well as regarding practical applications. However, the challenges we face today ask for more than just encouraging medical progress as we know it.

First of all: the healthcare system. Despite limited resources, our system must transform to deliver adapted services to the patients' chronic conditions. Beyond the quality and safety of every intervention, we must develop anticipation, coordination and follow-ups to improve them. We must also fight territorial inequalities and guarantee access to medical expertise wherever it is necessary – in particular in rural areas.

We must develop new digital tools and services for patients and healthcare professionals, as well as self-evaluation procedures and simplified information exchanges. They will have to be integrated into the existing system. France's excellence in the area of "health tech" will contribute to the success of this integration.

The clinic appropriateness is also a major issue regarding the quality of the healthcare and its economic implications. A revolution is expected in this area – it does not mean that professionals will be replaced by artificial intelligence but they must be given new tools to take care of every patient in a more personalised way.

The formation of our professionals is a crucial challenge as well. Remarkable evolutions have been seen – notably with the help of healthcare simulation – and must improve human reaction in difficult situations, teamwork and relations with the patients. Our universities' excellence in this area is well-known as they benefit from much international cooperation.

Innovation in healthcare: a regulation challenge

In this context, we have to seize this opportunity to adapt our institutional environment in order to let innovation bring genuine, sustainable and accessible medical progress for our patients.

Innovation is always linked with entrepreneurs' creativity and talent – it happens unexpectedly and we don't choose where it does. However, we can give incitation and good indications to these innovators in order to orientate their work towards our needs and values.

We must continue further investment efforts in performance ecosystems in which new ideas can be found – Station F is one of them. But we also have to determine our priorities, for example telemedicine programmes for our most fragile territories, healthcare in nursing homes, the struggle against chronic pathologies like diabetes.

Our evaluation models must evolve to fully prove the value created by innovations – that are by essence not to be compared with existing standards – and to properly remunerate them. Then, our databases must be able to inform us about the impact of these innovations in real life after their commercialisation.

Image: © Moya Angelsen



Agnès Buzyn, Minister of Solidarity and Health in France

We have to accept to lessen regulation in order to let innovations unfold. At the same time we must guarantee a global securitised canvas that respects professional cultures. It is a challenge regarding legislative conception and collective concertation with all the parties concerned.

Conclusion

Progress is and always will be a cardinal value to our medicine and healthcare system – in which innovation is necessary and encouraged. A special office is dedicated to innovation at the Ministry of Health and Social Affairs and billions of euros of public funds are dedicated to it every year in France. However, universality, equity and security are equally important values. Our duty is to make progress profitable for everyone, make sure that it responds to existing needs instead of creating new ones and guarantee that it does not bring commercial or ethical dangers for patients and professionals. ■

Minister's Cabinet
Ministry of Solidarity and Health – France
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[www.twitter.com/MinSoliSante](https://twitter.com/MinSoliSante)

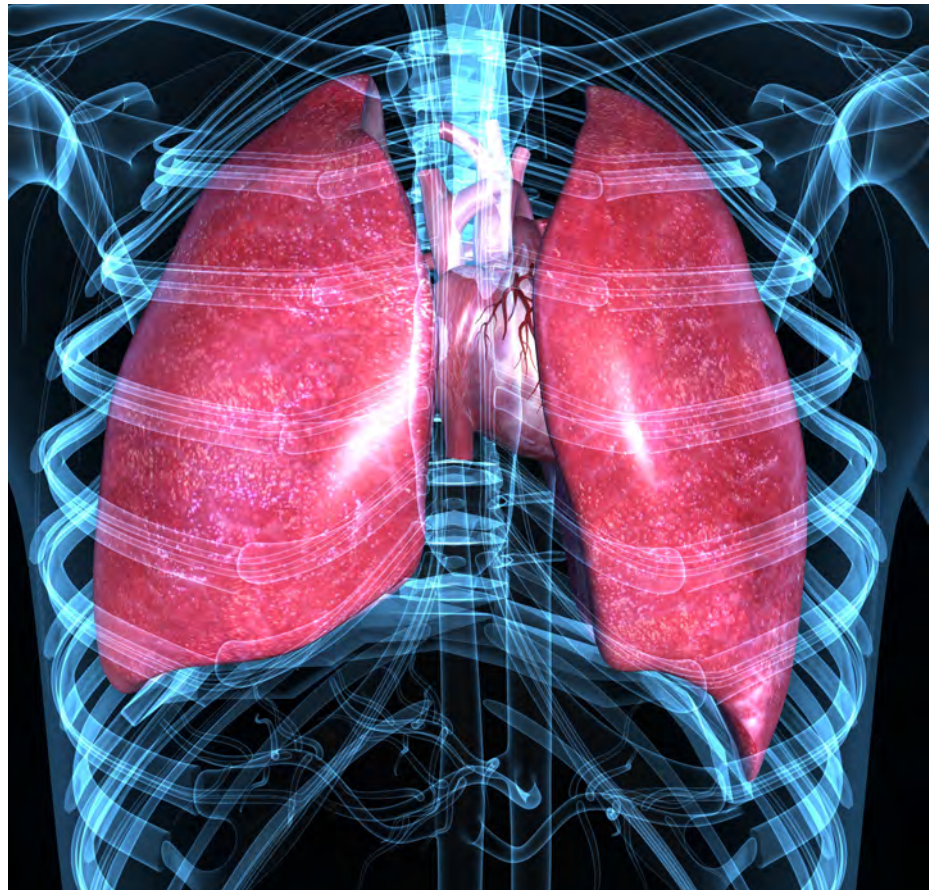
Understanding acute respiratory distress syndrome

TAURA is a research project that aims to fill in knowledge gaps in acute respiratory distress syndrome. Associate Professor Matthieu Jabaudon explains

Acute respiratory distress syndrome (ARDS) is a life-threatening condition characterised by widespread inflammation of the lung. It usually develops in critically ill patients, as a complication of an existing condition and occurs when the lungs become severely inflamed due to infection or injury, for example, after pneumonia, extra pulmonary sepsis, blood poisoning or severe chest trauma. As a result, gas exchange in the lungs is impaired, thus resulting in low arterial oxygenation and acute respiratory failure. There is no specific test to diagnose the syndrome; instead, an in-depth assessment is performed with a view to diagnosing the underlying cause. In spite of therapeutic advances in ventilation strategy and fluid management, morbidity and mortality remain high, with hospital mortality rates ranging from 35 to 45%. Unfortunately, no disease modifying pharmacologic therapies for the syndrome have been identified to date. Therefore, a better understanding of the disease, particularly its pathogeny, is required.

Translational Approach

Our research teams at Clermont-Ferrand University Hospital and Université Clermont Auvergne, France, have recently embraced a highly translational and collaborative project that seeks to fill a part of this knowledge gap. TAURA (Translational Approach to Understanding RAGE pathway in acute respiratory distress syndrome) is a four-year project funded by the



French National Research Agency (ANR), with additional support from the Auvergne Regional Council, French Ministry of Health (DGOS) and Clermont-Ferrand University Hospital. Therefore, we have set out to contribute to the assembly of many pieces of a puzzle designed to explore the pathophysiologic, diagnostic and therapeutic implications of the receptor for advanced glycation end-products (RAGE) in ARDS. The reason our teams have chosen to focus on RAGE is that the receptor was recently identified as a promising marker of alveolar type I

cell injury. The receptor is hypothesised to have a causative effect in a number of inflammatory diseases and, based on recent data, we believe targeting RAGE may attenuate lung injury. We are therefore working on gaining and enhancing knowledge about the ligands and basic mechanisms of RAGE in lung injury and repair, in an effort to pave the way for identifying new biomarkers and therapeutic options.

In order to characterise the roles of the RAGE pathway during ARDS, a

translational approach that comprises preclinical and clinical studies has been developed. Firstly, observational and interventional clinical studies have been designed to test plasma soluble RAGE (sRAGE) as a biomarker of alveolar epithelial injury in ARDS. Its diagnostic, prognostic and predictive values, its correlation with lung injury severity, and its value as a tool to tailor therapy were therefore evaluated. Our teams then used cultures of epithelial cells, macrophages, and a translational mouse model of acid-induced lung injury to describe the effects of the RAGE pathway on alveolar fluid clearance and inflammation, two major pathophysiological features that are associated with worse prognosis in ARDS. Subsequently, acid-injured mice were treated with an anti-RAGE monoclonal antibody or recombinant sRAGE, with the goal to test in vivo the impact of RAGE inhibition on alveolar fluid clearance and features of experimental ARDS. An additional motivation behind investigating the RAGE pathway is to propose new markers of epithelial injury and alveolar inflammation, including soluble proteins, membrane or intracytoplasmic proteins, gene regulatory mechanisms or polymorphisms. Similarly to the processes being undertaken with sRAGE, the methodology is also aimed at validating each specific feature of a biomarker, with new biomarkers being tested alone or in combination with others.

The multidisciplinary consortium on which relies the TAURA project comprises clinical researchers, clinicians, and biologists from Clermont-Ferrand University Hospital and scientists, as well as academics from the Université Clermont Auvergne who are specialists in medicine, molecular biology, physiology, pathology, animal models,

and/or in vitro studies. The project is coordinated by Matthieu Jabaudon, MD, PhD, who is an associate professor of medicine, anaesthesiology, and critical care. The presence of an international expert team leading the field in RAGE research (Pr Ann Marie Schmidt, New York University, USA) further strengthens the consortium, and allows, among others, studies involving knockout animals in addition to providing additional, highly valuable expertise into project design and analyses.

The design of our project is based on a translational approach. First, sRAGE is assessed as a reliable biomarker in clinical ARDS. Then, roles of the RAGE pathway in lung epithelial integrity and alveolar fluid clearance (AFC) are investigated using in vivo and in vitro experiments. The aim of this approach is to better understand the endotypes associated with phenotypes of patients with ARDS, the degree of AFC impairment, and inflammatory profiles, in order to further enhance ARDS recognition, assess response to therapy, and ultimately improve patient care. Clinical validations are performed within the project through mono-centre and multi-centre investigations involving regional, national and international networks.

Although we believe there is still much work to be done, particularly to better understand the implications of our results to date, we have already accomplished a significant number of achievements. Among these findings are: 1) that sRAGE is a biomarker of ARDS; 2) the pathophysiologic implications of the RAGE pathway in ARDS, with special emphasis on alveolar fluid clearance and alveolar inflammation; 3) that the RAGE pathway is a promising therapeutic target in ARDS.

Future objectives for the team include the development of a bedside sRAGE measurement tool and a therapeutic agent to improve epithelial function in ARDS. However, these ultimate goals extend beyond the remit of TAURA. Although the results from the TAURA project (including collected data and specimens) are valuable sources for such a development, patent projects are out of the scope of TAURA itself, and other sources of funding are under study. We are doing our best to move from strength to strength, with bigger plans to ultimately improve patient management and impact clinical outcomes. Hopefully, the future for those affected by ARDS might be significantly brighter, may we succeed in our aims.



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Managing a respiratory condition

British Lung Foundation's Dr Penny Woods provides advice on how to manage a respiratory condition and highlights the strides being made into lung research

It never fails to shock me that there are 12 million people in the UK who have been diagnosed with a lung condition, and that one person dies from lung disease every 5 minutes. It is unacceptable, and at the British Lung Foundation, we believe that prevention, earlier diagnosis and awareness of lung conditions could help improve these statistics.

We know that there are many people in the UK who may have a lung disease, but have not had a diagnosis. You could be one of them. Do you feel breathless on a daily basis, but have not asked for professional advice? Breathlessness could be an important sign of respiratory disease, and making an appointment with a GP should be a priority.

“Research is vital in the fight against lung disease. It will help us develop new treatments and cures – saving, prolonging and improving lives. In 30 years, the British Lung Foundation has spent £26m on hundreds of wide-ranging research projects.”

We've created a free interactive online breath test. It's designed to help identify who should see a medical professional and get their overall health checked.

To take the breath test visit: www.blf.org.uk/breathtest

Managing a lung condition

Of course, millions of people already know that they have a lung condition. Many come to us, seeking advice on a range of issues, including how to look after their lungs in hot weather, and how to cope with high levels of air pollution.

During very warm weather, if you have a lung condition, you may find high temperatures mean your symptoms get worse. This can be because you're too hot, you're



Dr Penny Woods, Chief Executive

dehydrated, or because of high ozone levels in the air. Near the ground, ozone is made by a chemical reaction between the sun's rays and organic gases and oxides of nitrogen, emitted by cars, power and chemical plants, and other sources.

High ozone levels can make breathing difficult, causing wheezing and coughing. And if you have asthma, you may need to use your reliever inhaler more.



Our advice is to keep out of the sun, avoid the heat, and reduce or avoid strenuous, outdoor exercise. The benefits of exercise are great if you do have a lung disease, so we suggest indoor exercise instead, in a well-ventilated room or gym.

Check Defra's air pollution forecasts and pollen forecasts if you go out and carry your medication with you. You should stay away from pollution hotspots. If you're getting wheezy or coughing from walking outside, get in touch with your doctor.

“Our advice is to keep out of the sun, avoid the heat, and reduce or avoid strenuous, outdoor exercise.”

Poor air quality contributes to the equivalent of 40,000 early deaths a year across the UK. Tiny pollution particles get deep into your lungs, making you feel out of breath, irritating the airways, and increasing the chances of developing lung disease. They can even pass through your lungs into your bloodstream, meaning air pollution could be linked to many other health problems too.

We're all put at risk from dirty air. But the most vulnerable are hit hardest - people with a lung condition, the elderly, and children.

Research

We are campaigning for greater investment in respiratory care, and into avoidable causes, such as air pollution. We're calling for more clean air zones, reduced use of diesel vehicles through an ambitious and fair diesel scrappage scheme, and more air pollution monitoring.

Research is vital in the fight against lung disease. It will help us develop new treatments and cures – saving, prolonging and improving lives. In 30 years, the British Lung Foundation has spent £26m on hundreds of wide-ranging research projects.

Lung disease is taking a huge financial toll on our health service, businesses, and society. Governments and NHS in both England and Scotland must take action. We are now leading an independent taskforce for respiratory health to improve outcomes for patients and the nation's lung health. ■

Dr Penny Woods **Chief Executive**

British Lung Foundation
www.blf.org.uk
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Image-guided surgery as an emerging treatment for lung cancer

Sumith A Kularatne, Vice President of Research & Development at On Target Laboratories discusses the scope of image-guided surgery in treating lung cancer

Lung cancer remains one of the major cause of cancer related death worldwide, resulting in over 1.4 million deaths per year. Treatment for lung cancer has been estimated at \$20 billion per year, in the US. Smoking (85%), genetic factors (8%), exposure to radon gas, asbestos, polluted air, and second-hand smoking can be considered as the major causes of lung cancer. Based on morphology of cancer cells, lung cancer has been classified into small-cell lung cancer and non-small-cell lung cancer. Non-small-cell lung cancer can further subdivided into adenocarcinoma, squamous-cell carcinoma and large-cell carcinoma subtypes. Lung cancer is diagnosed by a chest X-ray or computed tomography (CT) scans followed by a biopsy. Depending on the stage of the disease, treatment of non-small-cell lung cancer commonly involves surgery, chemotherapy, and/or radiotherapy whereas treatment of small cell lung cancer is more often limited to chemotherapy and radiotherapy.

Surgery plays an important role as a therapeutic method in non-small-cell lung cancer and over 70% of stage I and II non-small-cell lung cancer patients undergo surgery. Therefore, to accomplish optimal surgical resection of the tumor, it is important for the surgeon to locate and identify tumor margins accurately. Since surgery may be the primary therapeutic modality for substantial proportion of non-small-cell lung cancer patients, it is imperative that all cancerous tissues are excised with negative margins.

On the other hand, since the majority of the lung cancer patients are smokers, it may also be important that to leave non-cancerous lung tissue intact. The lymph node status is also important to determine the therapeutic options for the lung cancer patients. For example, metastasis to the mediastinal lymph nodes would be an indicator of not to proceed with excisional therapeutic surgery.

Unfortunately, this can only be seen once the thoracic cavity is open and this process can delay the needed chemotherapy. Moreover, spread to the lymph nodes determines adjuvant therapy. It is important to note that lymph nodes harbor metastatic cancer cells often feel and look normal, and may not detect by pre-operative techniques like X-ray or CT scans. In addition to that, those pre-operative imaging techniques will not provide real time information during surgery as they are confined to static images.

Intra-operative pathological procedures such as a frozen section are time consuming and often miss tumors due to miss-sampling, as well as poor tissue preparation, etc. Thus, there are imperative medical demands to develop new innovative technologies that help to remove a tumor completely with negative margins, identify micro-metastases including lymph nodes harboring metastatic cancer cells and leave intact non-cancerous lung tissues.

Image-guided treatment

Image-guided surgery is an emerging technique that aids surgeons to identify malignant tissues accurately and surgically remove tumors without compromising healthy tissues. However, one of the inherent challenges in the field is to develop imaging agents that are specific and sensitive for the tumor cells, particularly occult lesions that would not have been identified by usual techniques. While indocyanine green (ICG), a FDA approved near infrared (NIR) agent, has been used in image-guided surgeries for cancer, and it has been found to have significant limitations with respect to sensitivity and specificity, due to non-targeted nature of the molecule. Therefore, NIR agents that selectively label lung cancer tissues are currently under clinical development. These agents either target a receptor that overexpress on lung cancer cells or an enzyme or cell signaling pathway that uniquely present in lung cancer cells.



Real-time visualisation of malignant masses using cancer cell targeted-NIR agents will not only benefit to remove primary lung tumor masses with complete negative margins but also lymph nodes harboring metastatic tumor cells. Moreover, fluorescence imaging using these agents can aid in the surgical decision to conserve lung function by removing only the diseased tumor tissue rather than lobectomy or pneumonectomy.

Sumith A. Kularatne, PhD, is the Vice President of Research & Development at OTL. He has pioneer experience in drug designing on both small molecule ligands- and antibody-targeted drugs. Dr. Kularatne's scientific efforts have resulted in 6 drug candidate in human clinical trials with 3 different companies, over 50 US and foreign issued/pending patents and over 30 peer-reviewed publications. He has given multiple invited seminars/lectures in prestigious conferences as well as in multiple institutes and has received several

international and national awards including phase I and phase II NIH SBIR grant awards for over €2m. ■



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Drug development for cancer and inflammatory disease

Sumith A Kularatne, Vice President of Research and Development at On Target Laboratories shares the research strides he has made in drug development

"Men are haunted by the vastness of eternity. And so we ask ourselves: will our actions echo across the centuries? Will strangers hear our names long after we are gone and wonder who we were, how bravely we fought, how fiercely we loved?" – Odysseus (Troy).

Sumith A. Kularatne, Ph.D., is the Vice President of Research & Development at, On Target Laboratories, LLC (OTL), West Lafayette, IN (March 2012 – present). Dr. Kularatne is a world-class researcher and problem solver within the field of drug design and development for cancer and inflammatory disease. In fact, his distinctive and unparalleled approach to solve the problems associated with the diagnosis and treatment of cancer has been nothing short of unique and groundbreaking.

Dr. Kularatne says that "health holds a very important role in one's life, as President Thomas Jefferson said. Liberty is to the collective body, what health is to every individual body... Without health no pleasure can be tasted by man... without liberty, no happiness can be enjoyed by society".

Therefore, Dr. Kularatne uses his diverse set of skills, ranging from medicinal chemistry, organic chemistry, cancer biology, biochemistry, molecular biology, protein and antibody engineering, and animal model development for drug testing that



enables him to solve problems from a multidisciplinary approach and to discover better therapies with higher efficacy. Throughout his research career, Dr. Kularatne has been dedicated to developing targeted-imaging agents, diagnostic methods, and – therapeutic agents for cancers such as prostate, ovarian, lung, breast, and leukaemia and their metastatic disease and inflammatory diseases, such as rheumatoid arthritis and heart disease.

Research strides

Under his guidance, OTL has developed a strong pipeline for several types of cancer and inflammatory diseases. OTL38, a folate receptor (FR)-targeted near infrared (NIR) dye, has been proven safe in a phase I trial and effective in a completed phase II

clinical trial for ovarian cancer. A phase II trial for lung cancer and a phase III trial for ovarian cancer began in summer 2017. The same NIR dye has been conjugated to additional ligands targeting receptors on prostate (OTL78: PSMA-targeted NIR agent), colon (OTL338: CA-IX-targeted NIR agent), and pancreatic (OTL81: CCK2R-Targeted NIR agent) cancers. These ligands can also be conjugated to a photodynamic therapeutic (PDT) agent, giving surgeons the option to visualize and 'burn' targeted lesions using the same light source and camera. A lead folate- PDT compound (OTL228) has been identified with others to follow.

He pursued his postdoctoral studies in molecular biology and biomedicines with Peter G. Schultz, CEO and Professor of Chemistry at The Scripps

Research Institute (TSRI), San Diego, CA (Dec 2009-Feb 2012). Dr. Schultz was the founder and former director of GNF, and is the founding director of the California Institute for Biomedical Research (Calibr) La Jolla, CA. Dr. Kularatne's projects at TSRI focused on selective diminishing of primary tumor masses, metastatic cancers, and cancer stem cells using antibody drug conjugates (ADCs) or using bispecific antibodies (antibody-dependent cell-mediated cytotoxicity or ADCC).

“Innovation is a process that starts from coming up with a new idea to launching a new product in the market.” Dr Sumith A Kularatne.

Dr. Kularatne earned his Ph.D. in organic/medicinal chemistry from Purdue University, West Lafayette, IN (Dec 2005-Dec 2009), conducting research under the guidance of Philip S. Low, the Ralph C. Corley Distinguished Professor of Chemistry and Director of the Purdue Center for Drug Discovery at Purdue University. Dr. Low is also the co-founder and CSO of both Endocyte and On Target Laboratories. Dr. Kularatne's research at Purdue University concentrated on small molecule-targeted drugs for cancers and inflammatory diseases.

His scientific efforts have resulted in 6 drug candidate in human clinical trials with multiple companies, over 50 US and foreign issued/pending patents and over 30 peer-reviewed publications. He has given multiple invited seminars/lectures in prestigious conferences such as “Gordon Research Conference” on “Drug Carriers in Medicine & Biology”, as well as in national and international conferences, universities, and industries. Dr. Kularatne's scientific involvements have also led to several international

and national awards including, “SBIR Phase II Grant Award for Non-Small Cell Lung Cancer Research (2017)”, “Distinguished Partners in Hope Award for OTL for fueling innovation, and providing hope to lung cancer patients (2016)”, “Innovation Corps at NIH program for SBIR Award for Drug Development for Non-Small Cell Lung Cancer (2016)”, “SBIR Phase I Grant Award for Non-Small Cell Lung Cancer Research (2014)”, “AAPS Postdoctoral Fellow Award sponsored by Merck (2012) for CXCR4-targeted antibody drug conjugates for metastatic cancers”, “the Skaggs Postdoctoral Fellow Award (2010)”, “AAPS Graduate Student Award in Biotechnology, sponsored by Pfizer (2009) for PSMA-targeted drugs for prostate cancer, AAPS Graduate Student Symposium sponsored by Eli Lilly (2009) for PSMA-targeted drugs for prostate cancer, Delano Maggard, Jr. graduate research award (2005)”, ACS recognition Chemist of the year (2004), E. A. Talaty fellowship (2003) and the B. L. Paker Endowed fellowship (2002). He is an invited member of multiple honorary societies including Phi Kappa Phi (NSF), National Society of Collegiate Scholars, and Beta Phi Upsilon. He is also an invited peer reviewer for multiple scientific journals including Journal of Organic Chemistry, Molecular Pharmaceutics, Journal of Medical Case Reports, Nature Publishing group, and Drug Delivery.

Looking back on his 11 year career, Dr. Kularatne said that “I am fortunate and blessed to develop drugs that can possibly make a tremendous impact on human life, especially those who are suffering from cancer and their loved one”. He believes what Michael Jordan said “talent wins games, but teamwork and intelligence wins championships”. Dr. Kularatne stated that “I want to



emphasis that all the accomplishments I have been involved with were a team effort. I have always been around a great group of people committed to work in cohesion with one another. I have been guided by great leaders and mentors. I have great parents, family and friends who support me unconditionally. So, I feel I was prepared by mentors and family to accomplish great things as mentioned by Sun Tzu, The Art of War, 400 B.C. “Every battle is won before it is fought”.



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Organ donation – where next?

Fiona Loud, Policy Director at Kidney Care UK highlights the challenges of organ donation in England and how the country lags behind Wales and Scotland

The Scottish government has announced that they will bring forward legislation for a presumed consent system, 2 years after Wales did the same thing. This raises the question of whether England should also move forward in the same way.

In England, if a person has not registered their wish to donate organs after their death, there is no presumption of consent. Families will be approached to give consent, and knowing what their loved ones wishes were in life can make this decision much easier to support.

In Wales, since December 2015, where a person has given no indication, it is presumed that they have given consent (anyone who does not wish to donate their organs can opt-out by registering their decision). This is similar to the system that will be introduced in Scotland. Both countries held public consultations on consent, with 82% of Scottish respondents being in favour. The British Medical Association ran a UK public survey in 2017, with 66% supporting presumed consent¹. The government has never held a consultation on presumed consent in England.

Organ failure – the human toll

When kidneys fail there are 3 things that happen – dialysis, a transplant, or death. There are 6,400 on the transplant waiting list now (5233 awaiting kidneys)². At least 3 die waiting every day³. Dialysis is distressing and demanding with 4-5 hour sessions 3 days a week, along with dietary and fluid restrictions. People are often unable to continue to work, families and relationships are strained, and depression is common. It has been reported that levels of pain are equivalent to those from terminal cancer; patients are exhausted with aching bones, reduced mobility, and constant itching.

A transplant is transformational in restoring quality and quantity of life; we recognise the selfless generosity of organ donors, both living and deceased. We commend NHS Blood and Transplant for their achievements, with 50,000 people now alive with transplants in the UK. Kidney transplantation is also economically beneficial: maintaining a person's transplant is £5,000 pa compared with £30,800 pa on dialysis⁴.

Despite all the hard work there is still much more that could be done.

Opt-out

An opt-out system could result in more potential donors, provided the majority of the population support the adoption of such a system. However, this does not necessarily mean that the number of organs transplanted will increase to the same extent.

The Welsh and Scottish approach is called a soft opt-out system because the family will always be involved in all discussions about donation. They will need to be present to answer questions about health and lifestyle. They can also say if they knew the family member did not want to be an organ donor. This is why the 'donation conversation' is still so important. In the first year since the introduction of presumed consent in Wales, one quarter of transplants came from patients whose consent was deemed⁵.

Consent

About 63% of families provide authorisation for their loved one's organs to be transplanted. This figure has changed little over the last few years⁶. In the BAME (British, black, asian + minority ethnic) communities the consent rate is far lower, at 34%. The UK has one of the lowest rates of consent in Europe. The BAME population is about 10% of the population but 30% of the waiting list so there is a particular urgency to support organ donation in these communities.

NHSBT encourages donors to discuss their wishes with their families (as does Kidney Care UK) and aims to increase family authorisation to 80% by 2020.

Spain has one of the highest deceased organ donation rates in the world, at 43.4 donors per million people. The UK figure is about half this (21.6 pmp). Spain says it achieves this with a combination of fully engaged teams of staff who do not let any opportunities slip, adequate operating resources, and a culture where everyone expects organ donation to be usual, as well as a presumed consent regime⁷. The UK should aspire to similar standards. As improvements to the system of consent and family authorisation rates are likely to

result in more donations, NHS resources must be made available to ensure they are transplanted. This means trained surgeons and nursing staff plus theatre and bed capacity and access to necessary medications and other care for transplant recipients.

Summary

The recent changes in Wales and the decision made in Scotland to change were taken only after extensive consultation with the public. Kidney Care UK believes that people in England should have the same opportunity to express their views on improving the organ donation consent system. However, this must be accompanied by continued work to tackle family authorisation and the resources to carry out the additional transplants. It really is a matter of life and death. ■

- 1 <https://www.bma.org.uk/news/media-centre/press-releases/2017/february/bma-survey-shows-support-for-soft-opt-out-organ-donation-system-in-scotland>
- 2 <https://www.organdonation.nhs.uk/news-and-campaigns/news/more-than-50-000-people-now-alive-thanks-to-organ-donation-and-transplant/>
- 3 https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/4505/activity_report_2016_17.pdf fig 5.2 p 43
- 4 <https://www.england.nhs.uk/wp-content/uploads/2014/04/a07-renal-transpl-ad-0414.pdf>
- 5 <http://organdonationwales.org/News/first-anniversary?lang=en>
- 6 <https://www.organdonation.nhs.uk/news-and-campaigns/news/highest-number-of-organ-transplants-ever-across-uk-but-many-families-still-say-no-to-donation/>
- 7 <https://www.thelocal.es/20170111/how-spain-became-world-leader-at-organ-transplants>

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Is precision medicine for membranous nephropathy a dream?

Professor Pierre Ronco and Dr Hanna Debiec discuss the viability of precision medicine in treating patients with the rare disease membranous nephropathy

Membranous nephropathy (MN) is a rare disease that affects the kidney filter (glomerulus) and induces a massive loss of proteins in the urine. Considerable progress has occurred in the diagnosis and management of patients since the identification of the major antigens, recognised in the glomerulus by toxic antibodies circulating in the blood. Because the antigens are normally present in the glomerulus, one can conclude that MN is auto-immune in nature, and thanks to the recent advances in the disease pathogenesis, it can serve as a model for most organ-specific auto-immune diseases. The most prevalent antigen identified in 2009, the receptor of the phospholipase A2 (PLA2R1), is localised on the podocyte, a major cell of the glomerular filter where it serves as target for circulating antibodies.

Diagnosis of membranous nephropathy: Now possible with a simple serological test

Until recently, the diagnosis of MN required a kidney biopsy, an invasive diagnostic procedure with the risk of bleeding observed in less than 5% of patients. The development of assays of circulating anti-PLA2R1 antibodies and their transfer to clinical practice has been amazingly fast. The first immunofluorescence (IF) test used biochips coated with cells expressing the antigen, incubated with the patients' sera. The ELISA using the extracellular domain of human PLA2R1

coated to plastic wells enables a more quantitative and faster determination of anti-PLA2R antibodies, but it is a little bit less sensitive than IF. Detection of PLA2R1 antigen in immune deposits in biopsy specimens is also possible with the use of commercial antibody after a retrieval step to unmask PLA2R1 epitopes (domains of the antigen PLA2R that are recognised by the antibodies). These tests have ushered in a new era of precision medicine. Seventy to 80% of patients with MN have mounted an immune response against PLA2R1, which serves as a diagnostic signature since PLA2R1 antibodies are specific for this disease.

Monitoring patients with membranous nephropathy: Beyond proteinuria

For a long time, proteinuria was the only variable to follow disease activity. Now that specific antibodies have been identified, it has been shown that levels of these antibodies also predict outcome. High titers are correlated with a lower chance of spontaneous or treatment-induced remission, and a higher risk of the emergence of a nephrotic syndrome in non-nephrotic patients, and of renal function deterioration.

Furthermore, anti-PLA2R1 antibodies appear to be sensitive markers of treatment efficacy. Partial or complete depletion of anti-PLA2R antibodies precedes clinical remission, which is disappearance of proteinuria, by sev-

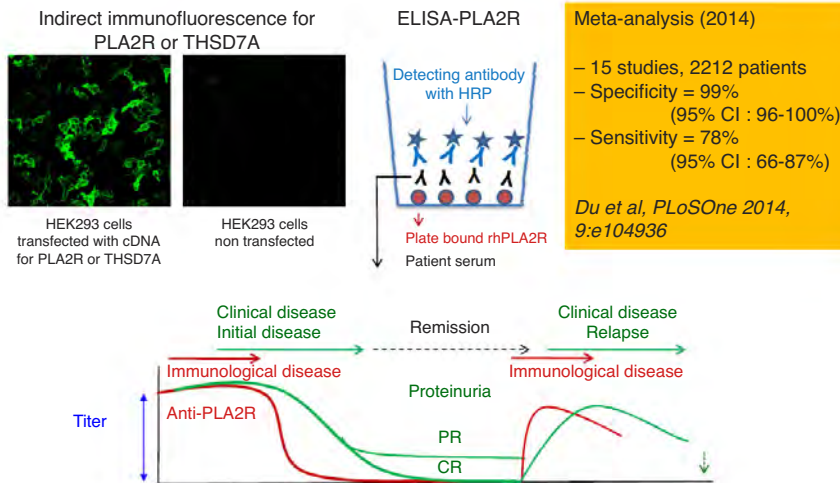
eral weeks or months, while re-emergence or an increase of these antibodies precedes by several weeks a renal relapse. The time lag of several months from immunological remission (depletion of antibodies) to renal remission is most likely accounted for by resorption of immune deposits and repair of the glomerulus. Even more, anti-PLA2R1 antibody titers at the end of therapy are predictive of later outcomes.

"Because the rate of remission (including partial remissions) does not exceed 70% with current immunosuppressive treatments, we hope that in future trials, close monitoring of anti-PLA2R1 antibody titer and epitope specificity as well as regulatory T-cells will allow a more personalised adaptation of treatment leading to increased rate of complete remission."

Toward a serology-based approach to treatment

Treatment of MN is controversial because of a high rate of spontaneous remission (up to 40%) and toxicity of immunosuppressive drugs that are used to treat patients with persisting nephrotic syndrome. Patients should not be overexposed to toxic medication if they don't need it. This is the reason why treatment is often delayed by 6 months to give the patients a chance to undergo spontaneous remission. We think that the international guidelines should be revised to include anti-PLA2R1 antibody in the

Serological tests for the diagnosis and monitoring of patients with membranous nephropathy



This picture shows the results of immunofluorescence test for the detection of anti-PLA2R1 antibodies (upper left) and those of a meta-analysis of >2,000 patients showing that anti-PLA2R1 antibodies are highly specific for MN and their sensitivity is close to 80% (upper right).

The scheme at the bottom shows that anti-PLA2R1 (in red) disappear before proteinuria (in green) and reappear before clinical relapse.

decision algorithm for patients with idiopathic MN. Measurement of anti-PLA2R1 antibodies may indeed obviate the need for a “wait and see” period of 6 months, and allow for more rapid treatment decisions. We recommend that antibodies are assessed every month in patients with a high level, and every two months in patients with low levels before starting immunosuppressive therapy to avoid unnecessary treatment in patients entering immunological remission (substantial decrease or disappearance of antibodies). This recommendation does not apply to patients with rapidly declining renal function, in whom a prompt initiation of immunosuppression is warranted.

If immunosuppression has been started, we recommend that antibodies be assessed every month during the first 6 months. Although the rate of antibody reduction varies among

studies, the general picture is that antibodies dramatically decrease during the first 3 months, and disappear over 6 to 9 months followed by remission of proteinuria over 12 to 24 months. Patients with a prompt and robust immunologic response may receive shorter than usual courses of immunosuppressive agents, whereas a conversion to an alternative therapy or a reinfusion of rituximab (for patients started on this drug which targets the B-lymphocytes involved in antibody production) should be considered in those who do not show a significant reduction in antibody titer at 6 months.

Toward more precision medicine: Lessons from molecular and cellular studies

There is more to come. Very recent studies by our group and a collaborating group in Nice suggest that diffusion of the immune response to several

domains of the PLA2R1 antigen (a phenomenon called epitope spreading) was associated with a lower rate of remission after 6 months in patients treated with rituximab. We also showed that a population of T-lymphocytes, the regulatory T-cells, involved in the control of auto-immunity, was decreased in patients with severe MN and that those who responded to rituximab had a lower percentage of regulatory T-lymphocytes at onset of treatment and an increased percentage of those cells as early as 8 days after starting treatment.

Because the rate of remission (including partial remissions) does not exceed 70% with current immunosuppressive treatments, we hope that in future trials, close monitoring of anti-PLA2R1 antibody titer and epitope specificity as well as regulatory T-cells will allow a more personalised adaptation of treatment leading to increased rate of complete remission.

Inserm

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The evolution of malaria drug development

David H Peyton at Portland State University outlines how research has discovered that heme is key to malaria drug development

The loss of the antimalarial drug chloroquine to drug resistance was among the most significant detriments to the antimalarial effort over the last half century. This is in part because chloroquine's target is not a protein – but rather heme, the by-product of haemoglobin digestion by the parasite. This made the evolution of resistance very slow – even in what must be regarded the worst and chaotic of circumstances. Even today's artemisinin combination therapies, that are the current standards of care, require a heme-targeting partner drug for the artemisinin. Many current malaria drug discovery projects are aimed at finding targets other than heme, but these often will usually lead to the evolution of drug resistance much quicker, rather than leading to a new heme-targeted drug.

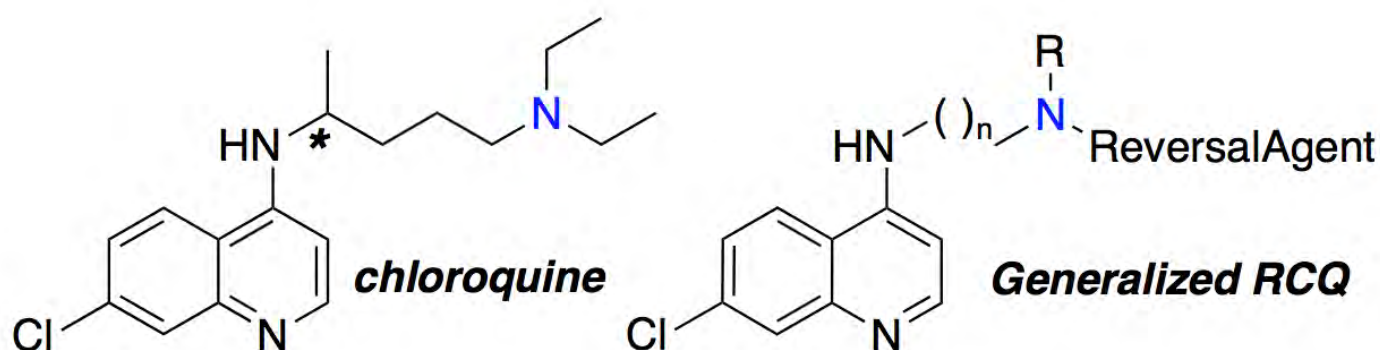
The goal of our work has been to provide a drug superior to what

chloroquine ever was, specifically by appending to the chloroquine structure another portion that inhibits Plasmodium falciparum chloroquine resistance transporter (PfCRT), the primary transporter whose mutation is responsible for the resistance to chloroquine and drugs like it. Exports of the drug from the parasite's digestive vacuole (DV) means that the drug can't build up to a sufficient concentration at the site of action to kill the parasite. The resulting hybrid drugs, including our lead molecule, were designed to be at least as potent and safe as chloroquine and could be less susceptible to the evolution of resistance. This is especially because it has been 'tuned' to have a shorter residence time in the blood at sub-therapeutic dose levels, and because they have never been available as a monotherapy in the regions of the world where malaria is found. Yet these new drugs would be fast-acting,

potent, and very reticent to develop drug resistance. We call these new drugs, reversed chloroquine drugs (RCQ drugs).

“Many current malaria drug discovery projects are aimed at finding targets other than heme, but these often will usually lead to the evolution of drug resistance much quicker, rather than leading to a new heme-targeted drug.”

We tried the approach with a prototype RCQ drug a few years ago and then refined the structures to make a more practical drug in terms of what might make an orally dose-able medicine. We studied the mechanism of action of the RCQ drugs, to make sure that they were still working like chloroquine did, and to show that they were not very susceptible to resistance, both against strains of malaria from patients and evolved in the laboratory. This all gave rise to our



Design of RCQ drugs: The Reversal Agent portion turns off the export of the drug via PfCRT



lead molecule but the time and effort between deciding on a molecule and getting approved for a Phase 1 safety study (first-in-humans) are large, especially for an academic (university) laboratory.

“The goal of our work has been to provide a drug superior to what chloroquine ever was, specifically by appending to the chloroquine structure another portion that inhibits *Plasmodium falciparum* chloroquine resistance transporter (PfCRT), the primary transporter whose mutation is responsible for the resistance to chloroquine and drugs like it.”

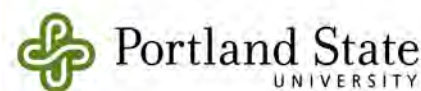
Laboratory tests conducted for malaria drug development

There are also extensive studies required to demonstrate the likelihood of safety (non-poisoning) and a lack of genotoxicity (e.g., not carcinogenic) that are needed before a Phase 1 study is approved by a governing body, such as the Food and Drug Administration (FDA) in the U.S. These

studies must be done under good laboratory practice conditions, which are generally available only from Contract Research Organizations (CROs), and not in-house at the university. In fact, a university researcher generally doesn't even know what tests to do during this process, so consultants need to be hired. For these reasons, and others, I co-founded a start-up company, DesignMedix, Inc., which has the mission of discovering and developing drugs against infectious diseases, especially those which are evolving drug resistance. This began with malaria but now includes bacterial diseases.

We have therefore spent the last few years learning the process of bringing a candidate molecule from “Lead” to Phase 1 candidate. Last week we announced a contract with the National Institutes of Health/NIAID to carry out the Phase 1 first-in-human study. Of course, even a successful conclusion of this study will not be the end of this process: There will be at

least one Phase 2 study that will be needed to be successfully completed, and then it will need to be partnered with another drug (and so, likely, another company) before the Phase 3 study (or studies). The entire process, from the start of the Phase 1 study, will likely be at least another 5 or 6 years before bringing a drug to market. That is if all goes well.



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Mental health and medication: The importance of perspective

Peter Kinderman, from Mental Health Europe looks at mental health medication and how we need a new perspective on care

Mental health is full of controversy, and especially when it comes to the benefits and harms of medication. Recently, to publicise a BBC TV [programme](#) investigating possible links between antidepressant medication and homicides, the Times newspaper published an [interview](#) with the headline; “I was a dribbling, suicidal mess – until I kicked the kill pills”. The critical response on social media was rapid and interesting, with at least one mental health professional even [suggesting](#) that science could be playing a role in what was perceived to be a very negative account of medication.

Official guidance tends to steer a measured, and balanced course, with clinical [guidelines](#) such as that of the UK's National Institute for Health and Care Excellence (NICE) recommending the proportionate use of social interventions, psychological therapies, and – for some people – antidepressant medication.

But there are critiques of this balanced, perhaps establishment, view. The UK-based [Council for Evidence-Based Psychiatry](#) and the UK [All-Party Parliamentary Group for Prescribed Drug Dependence](#) have recently joined the [British Medical Association](#) in publicising a range of concerns, including the rapid increase in the rates of prescriptions for [anti-depressants](#), [anti-psychotics](#) and [stimulants for children](#), and the fact that these seem to be [related to social deprivation](#). These bodies are also concerned about the [lack of medical science](#) behind the rationale for their prescription and the lack of [sound evidence](#) for their effectiveness, and substantial evidence of harm, especially in the long term.

But things don't get any easier when we also consider the idea of ‘pill shaming’. Many people feel strongly that psychiatric medication is fundamental to their wellbeing, health, and physical safety. As [Mark Brown](#)

put it; “To those who do not experience it, depression is something metaphorical, a symptom of some broader social malady. Popular discussion of antidepressant use often has a grim, tutting, morally judgmental edge. In the world of mental health, we call it ‘pill shaming’; the overt act of casting doubt upon the decision or need for others to take medication for mental health reasons.”

Navigating our way with humanity and humility through these tensions is unfortunately made more difficult because of a blizzard of myths and half-truths. Despite absolutely [no evidence](#) for a ‘chemical imbalance’ theory of depression (and indeed high-profile repudiation of such an approach by leading lights in the psychiatric profession), we still see leading healthcare providers such as the Priory Group in the UK suggesting that their approach might; “[include medication to restore the chemical imbalance in your brain's limbic system](#)”.

Psychological therapies

In the field of psychosis, there are very similar dilemmas. Again, authoritative [clinical guidance](#) is balanced, recommending both medication and, again, social and psychological therapies. As with the care of people who are suffering from depression, [psychological approaches](#) offer a great deal of promise. Just as with our understanding of depression, a [genuinely biopsychosocial approach](#) to understanding the nature of experiences such as hearing voices and fears of threat and persecution is possible, although, of course, here too we have much more to learn.

Once again, the landscape is characterised by controversy. Shortly after the publication of a news item supportive of a psychosocial approach to psychotic experiences in the [New York Times](#), we saw a [response from a senior health professional](#) suggesting that



the material could have the effect of: “challenging the veracity of diagnoses and giving people who have symptoms of a mental disorder, license to doubt that they may have an illness and need treatment”.

The path ahead is complex. We should carefully evaluate and appraise the effectiveness of psychiatric drugs – their benefits and their harms, in the short and longer term. We should understand, of course, that our thoughts and emotions are products of biological brains, with all the [implications that follow](#). At Mental Health Europe, we believe we [must move away from](#) the disease model, which assumes that emotional distress is merely symptomatic of biological illness, to be treated as such.

Mental health policies

In part – as the [data on anti-depressant prescription](#) make clear – our mental health and psychological well-being are matters of social justice. As Dainius Pūras, [United Nations Special Rapporteur](#) says; “The crisis in mental health should be managed not as a crisis of individual conditions, but as a crisis of social obstacles which hinder individual rights. Mental health policies should address the ‘power imbalance’ rather than ‘chemical imbalance’... targeting social determinants and abandon the predominant medical model that seeks to cure individuals by targeting ‘disorders’”. Unfortunately, the ‘quick-fix’ of offering medication might, especially when we extrapolate this approach

from the individual to the wider community, lead our attention to drift away from the social determinants of mental health and psychological wellbeing and the difficult but necessary societal changes that follow.

This doesn’t mean that we abandon those we love, tutting moralistically and preparing our placards for another political demonstration, as we do little to help people who are suffering. As [Mark Brown](#) says; “Inequality, prejudice, violence, poor jobs, and poverty all influence depression. But it’s hard to change the world when you can’t get out of bed”. It means working in the very real world of front-line services. But when a supposedly therapeutic response is in danger of causing more harm than good, we have an ethical responsibility to question our practices... and our [assumptions](#).

Mental Health Europe is the largest European network organisation representing mental health service users, professionals and service providers across Europe. ■

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From disease orientation to health promotion

Lena Kuhn of Pfalzlinikum outlines the need to develop a health centre and encourage health promotion in the Donnersberg district

Supply shortages in rural regions, long waiting times for therapy places and the demographic change call for the development of new structures for the promotion of mental health. New supply models with multi-modal approaches and a networking of the service providers are required. For this reason, Pfalzlinikum Westpfalz-Klinikum have developed a concept for a common, cross-sectoral health centre according to the motto "Health needs diversity, participation and resilience". The aim is to build up newly networked offers, wisely use interfaces of somatic and psychiatric care and sustainable health promotion in rural areas. The population is to benefit from short distances due to direct networking and communication between hospitals, registered doctors, care providers and follow-up care facilities. Programmes for the prevention of mental disorders and the promotion of mental health are of major importance for the state of health of a population. Thus, Pfalzlinikum – service provider for mental health strengthens its role as a preventively operating, regional health service provider.

Survey as a basis for new offers

The conceptual development is, among others, based on an empirical study carried out by the author in the form of representative, qualitative expert interviews. Its aim was to determine the expectations and the demand for preventive mental health



offers expressed by experts and persons living in the Donnersberg District. During the empirical investigation, relevant stakeholders and important experts were identified with the objective to gather and use their knowledge. The persons to be interviewed were selected by so-called theoretical sampling, i.e. a random sample of people who are, according to the author's opinion, able to make qualified statements on the need.

Due to the exchange of ideas with the experts and stakeholders, the planning and the aims of the health centre and, thus, the intended change in perspective in the Donnersberg District could be communicated. The evaluation of the responses to the qualitative, guideline-based interviews has yielded valuable insights. On this basis, the health-center project group

can develop programmes and services tailored to the population's needs.

Significance of information

All interviewees emphasised the importance of public relations work, either as a measure of primary, secondary or tertiary prevention, in terms of provision and transfer of information. Independently from each other, the experts agree that it is necessary to better inform the population about health topics and existing offers – also for the purpose of reducing the psychological barrier for seeking help. To this end, for instance, events concerning health issues and mental disorders are particularly suitable. Furthermore, the experts' statements confirm the existing difficulty in providing medical care for people living in rural areas and, as assumed by the project group, the demand for mobile offers that

should be provided in addition to the offers in the premises of the health centre. It is for example possible to provide mobile day-care services.

The results of the survey also show that the focus is on offers for the elderly. Pfalzlinikum and Westpfalz-Klinikum plan, among others, to extend and bundle their geriatric and geronto-psychiatric areas, for instance by offering a joint geriatric outpatient department.

New focus on prevention

The interviewees' statements show that there is a great demand for the prevention of mental disorders and the promotion of mental health. For this reason, a major objective of the health centre is to convince the public of the necessity and meaningfulness of turning away from a care-orientated to a prevention-orientated perspective on mental health.

To ensure a successful implementation, the services of health promotion have to be tailored to people's worlds and daily life and health equity has to be promoted. The population has to participate in this process, and furthermore on an even-handed level. If the planned services of the health centre are actively used by the population, individual resilience, i.e. the individuals' ability to recover from crises, organisational resilience (e.g. in the company) and local resilience (population in the Donnersberg District) can be promoted and empowerment processes can be triggered.

The new thinking for healthcare (such as health centres), which aims to implement strategies to both promote mental health and prevent mental disorders, should be adopted in other regions. This is the only way to reduce the number of people suffering from mental disorders. Such models should

focus on people's health resources and on the stabilisation of their health and rather less on risk factors and hazards to health. The change in perspective from disease to health orientation shall prevent or delay mental disorders and have a positive impact on the course of diseases. A holistic and sustainable service preparation is, thus, required to cover the broad range of the population's needs.

With regard to the interview results, it would be possible to devise health centre offers aiming at the following targets:

- Support for the creation of health-promoting life worlds: The offers could support or enable people to create good working and living conditions and, in the case of problems, empower the persons concerned in dealing with their social environment and their resources and skills (empowerment approach).
- Support of health-related community actions: The offers could aim at the health promotion of the community, such as support of community activities, self-help programs and social networks for the promotion of self-determination and autonomy over one's own health issues.
- Personal capabilities: Due to public relations work on the part of the health centre and offers to strengthen social skills as well as the development of one's own personality people could be empowered for lifelong learning and get support to cope better with difficult phases in their lives and mental disorders.
- Sustainability: The offers of the health centre can make a contribution to the long-term preservation of the mental health and the skills and resources of the persons to be supported.

- Participation: By means of a health centre and its services it is possible to create structural pre-requisites to facilitate health promotion and the prevention of mental disorders at any age, in all situations and all areas of life with the participation of the individual, the family, civic engaged groups and the community.

Due to the selection of experts, a sufficient number of contact persons from different stakeholder groups were granted. In this way, the selection of the study population led to sufficient perspectives, and new findings could be gathered. The empirical examination gives information about further research possibilities which might build upon the results of this study. In future, the prevention approach has to be linked to the care approach to enable unbroken counselling and care of persons suffering from mental disorders or crises.



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Disease-associated myosteatorsis in people with cancer: Can it be treated?

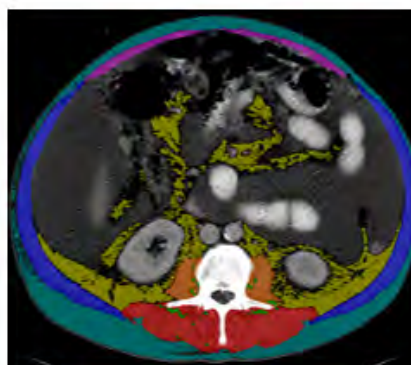
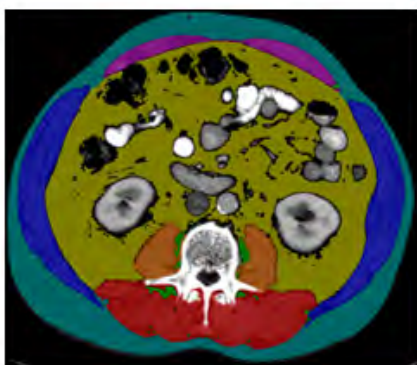
Pathological fat infiltration into muscle is a feature of disease-induced muscle loss that significantly associates with shorter survival in people with cancer. Fat is associated with skeletal muscles in the form of intra-myocellular lipid droplets within the cytoplasm of myocytes as well as intermuscular adipocytes. These lipid stores are thought to provide fuels for skeletal muscle contraction, however, excess deposition of triglycerides within cells and organs that normally contain only small amounts of fat (such as liver, pancreas, skeletal and cardiac muscle) is defined as steatorsis. Myosteatorsis (steatorsis of the muscle) is a pathological phenomenon reflecting an impairment of synthesis and elimination of triglyceride.

Myosteatorsis is revealed in vivo by computed tomography (CT) imaging as muscle with low radiodensity combined with presence of intermuscular adipose tissue. The evidence for a relationship between low muscle radiodensity and shorter survival in people with cancer is building. Loss of skeletal muscle mass appears to generally occur with accumulation of adipose tissue into muscle. We reported that patients undergoing treatment for lung cancer lost muscle mass and concurrently gained intermuscular adipose tissue during treatment for cancer, whereas patients who supplemented their daily intake with fish oil containing eicosapentaenoic acid and docosahexaenoic acid [EPA+DHA (2.2 g/day)] maintained or gained muscle

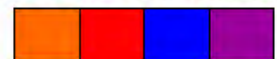


This slide shows a CT image from a cancer patient who underwent 16 weeks of first line platinum doublet chemotherapy for lung cancer. Only the intramuscular adipose tissue is shown in color

mass and experienced a decline in intermuscular adipose tissue over the same time period. This intervention also resulted in a greater response by the tumor to the drugs being used to



Skeletal Muscle

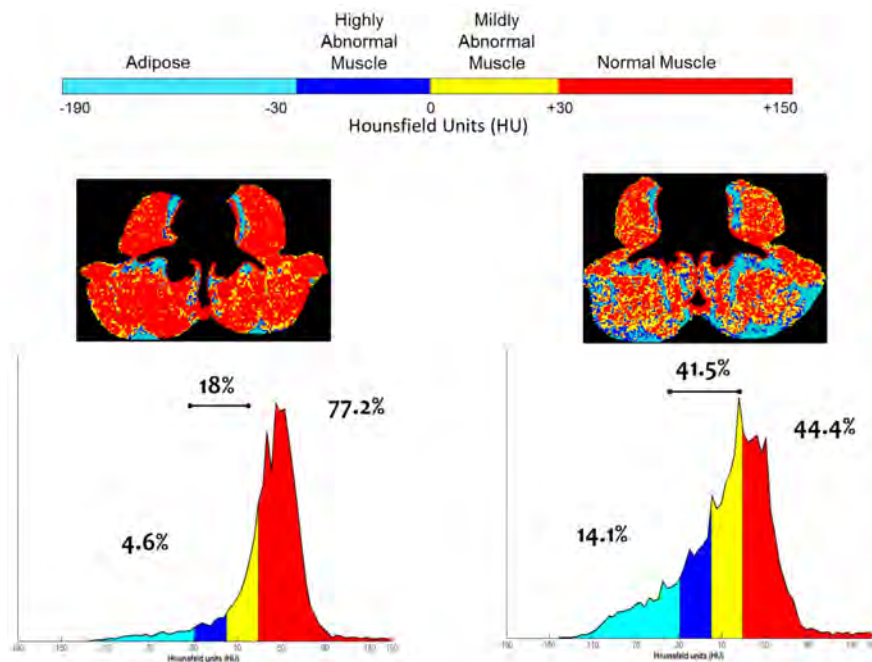


Adipose Tissue



To quantify different tissues for body composition analysis using computed tomography imaging, a bony landmark is used to consistently measure the same region of the body across patients. The 3rd lumbar vertebrae is an established landmark in body composition analysis that correlates with amount of whole body muscle and fat. Each tissue attenuates radiation in a specific way which is recognised by a software program to enable skeletal muscles and different types of adipose tissues to be identified. Each tissue of interest is then color coded (see legend). When more than one CT image exists in the patient record, tissue changes over the trajectory of the disease can be determined. This image presents 2 scans taken approx 6 months apart at the same region within the same patient. The marked decline in muscle and adipose tissue is evident, concurrent with deposition of adipose tissue into muscle

Illustration of Variation in Muscle Radiodensity



An illustration of annotated CT images, and accompanying histograms of radiation attenuation showing the percentages of total tissue cross-sectional area within the ranges of adipose tissue in paraspinal/psoas muscles is useful to understand the problem of myosteatosis. This illustration shows the percentages of total tissue cross-sectional area within the typical attenuation ranges determined for the respective tissues for 2 subjects. Subject 1 is a 63 year old male with muscle characteristics at the median values for male cancer patients with a diagnosis of solid tumor at our centre. For Subject 2 there is extensive macroscopic adipose tissue and less than half of the cross sectional area of his muscles falls within the normal attenuation range. Overall, Patient 1 has a greater proportion of fat and low attenuation muscle, than muscle with normal characteristics. Patient II is remarkable in several respects, including extensive visible fatty infiltration and extremely high proportion of total muscle area falling within a range of attenuation values generally recognized to be abnormally low (adapted from Aubrey et al 2014)

treat the cancer. Therefore there may be multiple benefits of dietary fish oil to the cancer patient undergoing treatment.

To explore these observations that cancer patients supplementing with EPA+DHA experience an improvement in myosteatosis, we established a pre-clinical model to enable intervention with EPA+DHA at various time points in the cancer trajectory. We used an rat model bearing the Ward colorectal tumor and treated in a manner that mimics standard clinical care for this disease in humans with respect to the types of drugs used and the toxicities they evoke. Using this model we have demonstrated that the results align with our human data suggesting an improvement in muscle condition concurrent with a better response by the tumor to the anti-cancer drugs.

Using this as the rationale for the next step of this line of questioning, we have planned a clinical trial upon which to test the biological efficacy of fish oil to reverse cancer- associated myosteatosis in a cancer population known to exhibit myosteatosis, verified by in vivo imaging of muscle features by CT scan. At the time of diagnosis and treatment planning, patients will be randomized and consented to consume EPA+DHA (2.2 g per day) until day of surgery (at least a 4 week period) or receive standard of care (no intervention). Muscle from the subjects will be collected at the time of surgery and prepared for analysis. Analysis of the muscle tissue will enable determination of differences in Triglyceride-fatty acid content (a hallmark of myosteatosis). We expect that this research will verify the tantalizing evidence we have in hand that

suggests an improvement in pathological features of myosteatosis by dietary EPA and DHA. If so demonstrated, this work will provide critical translational knowledge required to effectively plan treatment interventions that have significant potential to impact the lives of people diagnosed with cancer, a major cause of death globally.



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The Lamy report: Ensuring inspirational research

In a speech, EU Research Commissioner Carlos Moedas highlights the findings of the Lamy report and shares why it is necessary to reform the research system

Horizon 2020 has been hugely successful overall. We have got many things right: Supporting the very best new science, with the ERC as a European flagship; The simplest and most user-friendly programme in the EU; The decision to bring research and innovation together in a single programme.

So let's keep the things that have worked so well. Let's expand them.

The Lamy report also gives us a blueprint for what we need to change in the future. The 11 recommendations contained in the Report are ambitious, but they are essential.

“Richard Nixon was often criticised for setting a mission to cure cancer. As we all know, he failed. But I learnt something interesting about this at a recent conference in Norway. In fact, the scientific discoveries that were made as a result of this mission led the way to breakthroughs in other fields. Such as treatments for HIV.”

The first recommendation is as bold as it is simple: to double the budget.

There is plenty of evidence to support this. It would overcome the huge waste of top quality proposals that currently go unfunded. It would set the path for Member States to follow. The evidence is clear that we need both European funding and national funding for research and innovation. Also, an ambitious increase would demonstrate our commitment to cut the gap with the US and others. And to take leadership in investing in the future.

This first recommendation also builds on the European Parliament's opinion, authored by Soledad Cabezon

Ruiz, which recommends a budget of €120 billion for the next programme.

Just recently, the Commission published a reflection paper on the future of EU finances. In that paper, research and innovation is singled out as having exceptional European added value. So there is a clear case for an increase. But this will involve difficult choices. There are new priorities. Any budget increase must go hand-in-hand with reforms.

Reform is necessary

The remaining 10 recommendations in the Lamy report are precisely about the reforms that will be needed. Each of these recommendations merits a conference by itself. So I cannot go through all of them. But I would like to highlight 3 messages that cut across the recommendations. Messages that I believe will have profound impacts on the design of the next Framework Programme.

These are:

- Look at the whole picture;
- Focus on the person; and:
- Inspire Europe with mission-driven R&I.

The Lamy Group did not look at individual sectors or scientific disciplines. They did not look just at Horizon 2020. Instead, they looked at the whole system. I would urge us all to continue with this approach. It is the only way to break down the silos between disciplines, between policies, and between programmes. On this topic I often think of a story that Bertrand Piccard told me. I first spoke to him last year just before he made his incredible flight on the Solar Impulse. During that



EU Research Commissioner Carlos Moedas

first conversation he told me that when he wanted to build his plane, he went to every plane manufacturer. None of them agreed to partner with him. They said it was impossible. So eventually he went to a boat builder that agreed to do it. Because they didn't know that it was impossible. I think this is a great example of what can be achieved when researchers and innovators step outside their comfort zones and look at the whole picture.

As policy makers, we must also step outside of our comfort zones. For example, I very much welcome the fact that the Lamy group included education in their report and proposed some new ideas. Such as including more training activities in collaborative research projects. Or introducing incentives for university reforms. And capitalising on the education and training activities of the EIT Knowledge and Innovation Communities.

I also fully agree with the need to break down the silos between the Framework Programme and Structural

Funds. This is very important to really integrate the EU13 Member States in the global knowledge economy.

The Seal of Excellence I introduced with Commissioner Cretu has been a success. But its implementation is hampered by having different rules between the current programmes. So let's get to work on how to change this.

We also need to break down the silos between regulation and innovation. For example, the Lamy group suggest that improvements are needed to State Aid rules. They urge more policy experimentation, such as what we have done with the Innovation Deals.

This is the systemic approach that we need.

The second cross-cutting message I take from the report is the focus on the individual. One of the breakthroughs of the European Research Council was to address the individual scientist. To allow her to follow her dreams.

So I very much welcome the clear recommendation in the Lamy report to develop a European Innovation Council that focuses on the innovator. We spend a lot of time discussing the size of the company, or the sector, or the maturity. And focusing on the individual innovator will be a new approach which can bring a lot of value.

Inspirational research

I will be asking the new Group of Innovators to take forward this recommendation from the Lamy report. And help us turn it into a reality.

This brings me to the third cross-cutting message. Let's make European research and innovation inspirational. This is our future and it should be inspiring and exciting for European citizens.

I believe the recommendation to adopt a mission-driven approach in the next Framework Programme is the right

way forward. To engage people. Make them part of the process. And proud to be European. Mark Zuckerberg talked about feeling part of something bigger in a recent speech. He was referring to a well-known story about John F Kennedy. The President visited the NASA space centre and saw a janitor carrying a broom. He walked over and asked what he was doing. And the janitor responded:

“Mr. President, I’m helping put a man on the moon.”

That’s the kind of purpose I’m referring to. That sense that we are part of something bigger than ourselves. I would like us all to think seriously about a mission-driven approach. To bring together our best ideas. To reach out in a way to citizens in a way that we have never done before.

It is not my role to define missions. This needs a collective process. But I would like to highlight some of the points made in the Lamy report about missions:

They must capture the public imagination. Achieving a 1% increase in the efficiency of a hydraulic pump may be exciting for an engineer like me. It may have important environmental impacts. But it will not capture the public imagination.

Missions should be interdisciplinary, inter-sectoral and international. So I would encourage everyone to think beyond the limits of their sectors and disciplines. Where it does not only make sense, but is essential, to work together. To build European and global partnerships.

To go beyond what is currently possible. If we play it safe, and set missions that we all know are possible, then we will achieve all of our missions. But no one will be inspired. And the projects are unlikely to generate any new breakthroughs.

Richard Nixon was often criticised for setting a mission to cure cancer. As we all know, he failed. But I learnt something interesting about this at a recent conference

in Norway. In fact, the scientific discoveries that were made as a result of this mission led the way to breakthroughs in other fields. Such as treatments for HIV.

Thinking big leads us to great things.

The serious discussion on FP9 has started. Building also on the excellent report from the European Parliament. This is part of the wider debate on the Future of Europe. It is central to the reflection on the future of EU finances.

“The Lamy report also gives us a blueprint for what we need to change in the future. The 11 recommendations contained in the Report are ambitious, but they are essential.”

On the Commission side, we will be using all of these inputs to develop a proposal for FP9 that I aim to present around the summer of 2018. The Horizon 2020 Work Programme this autumn will be a stepping stone towards the changes to come. Including a pilot phase for the European Innovation Council. It is clear to me that Europe needs research and innovation. And research and innovation needs Europe.

We all want an R&I programme that matches that ambition of the report from Mr Lamy and the High Level Group. The 11 recommendations contained in this report will help us deliver an FP9 that is fit for the future. And we can achieve it.

This is an edited version of a speech which can be found [here](#). ■

Carlos Moedas

Commissioner for Research, Science, and Innovation

European Union

https://ec.europa.eu/commission/commissioners/2014-2019/moedas_en

www.twitter.com/Moedas



Innovative nanocapsules for skin care

Due to the unique properties achieved at nanoscale, nanotechnology has attracted an exponential interest, being the focus of numerous studies, developments and marketing actions in a full range of applications. Nanotechnologies and nano-enabled materials are already being used in several industries such as textile, pharmaceutical and cosmetic. Although the nanomaterials may bring many advances and benefits to society and the environment, it also poses new challenges and impacts in health, environment and safety, etc., thus being a thematic that needs to be handled in a responsible way.

Within this context, the project 'SKHINCAPS – Skin Healthcare by Innovative NanoCAPsules' is a research and innovation project funded by the European Union, under the Horizon 2020 research and innovation programme (grant agreement No 685909). It aims to develop the know-how and processes to manufacture novel, sustainable, safe, cost-effective and highly stable nanocapsules containing, at their core, different encapsulated active principles, for their incorporation into 'smart' skin care products such as textiles and cosmetics (creams, lotions).

The SKHINCAPS nanocapsules will be used to produce different demonstrator products for skin healthcare applications:

- First layer garments containing nano-encapsulated phase-change materials (PCMs) for thermal management and skin comfort;





- Anti-ageing creams containing a cocktail of nano-encapsulated vitamins and antioxidants to improve skin anti-ageing effect;
- Antimicrobial lotions and textiles containing nano-encapsulated natural essential oils to prevent or mitigate bacterial infections on end-users skin.

The project consortium comprises 8 partners from 5 different EU Member States, including 4 European research organisations – CENTI (PT, coordinator), UPC (ES), IVW (DE), VTT (FI) – and 4 industrial partners – Bionanoplus (ES), Devan-Micropolis (PT), TELIC (ES), Pro-Active (BE). The industrial partners involved in the project are all SMEs being key players in the value chain of high-tech textiles and cosmetics: a nanomaterials producer, a textile chemistry producer and distributor, a cosmetic formulator and a consulting company.

By combining the specific expertise fields, SKHINCAPS intends to bring the innovative technologies needed to increase the commercial potential of smart technical textiles and cosmetics, to improve the European competitiveness and create a new growth engine for economic development, and above all, enhance individual wellbeing and life quality, thus contributing to healthcare costs control. Furthermore, the project also intends to reduce the environmental impact related to the manufacturing process and the use of the novel nanomaterials.

Everyone has the right to show their full potential to the world



At present, more than 1 billion people in the world live with one or more disabilities or multiple health problems, seeing the possibilities of their interaction in society depleted.

At Tech4Freedom we believe that each person has the right to provide his or her full potential to the world, regardless each one's strengths or singularities.

Today, we have proven that special needs can be treated at the mainstream level but with the acuteness of a singularity equivalent. Society must provide each person with customisable tools that match their uniqueness, and offer them the key they need to unlock their full potential.

We provide people with tools to achieve their goals and dreams.

The Box One4All functionalities.

Implementing accessibility technologies that are already, and continue to be, developed is a worthy and equitable solution to addressing the still unfulfilled promise of humanity – to give each person his or her opportunity to meet their goals and dreams.

Additionally, by creating technological devices adhering to Smart Accessibility principles, we provide broad benefits to all of society, not just those who directly benefit from these solutions.

Caring each person's specific
Health & Singular needs
with one device

www.tech4freedom.net



Smart Accessibility, Unlocking Potential.

Imagine a world, where one billion people add all their talent to society?

Let's drive the World to be a better place.

We work hard to make it happen, setting an example with our actions.

Through our technology we prove that catering to all singular needs is the better way to provide both:

- Social welfare to those who wish to give their best to society.
- Economic prosperity to society as a whole.

The impact such tools have for individuals, their families, and society at large are undeniable. We are able to provide opportunity and dignity to those who deserve it most. Solutions have been created for people to achieve greater autonomy in their daily life.

T4F providing autonomy to blind people.

But we go much further in the worldwide health-tech sector. With the objective of empowering people with disabilities who can also coexist with health problems that require constant monitoring, such as hypertension, diabetes, or injury risk in the elderly.



Those who say it can't be done are usually interrupted by others doing it.

Joel A. Barker

T4F's mission is to improve people's lives by better meeting their specific health needs.

In this context, T4F is strengthened as the first vertical integration platform, which is already launching a device for universal use.

T4F has made it possible for technology to be the best ally to achieve a more inclusive society, creating social welfare and economic prosperity for all.

www.tech4freedom.net

Interesting Links:

["Tech4Freedom among the 13 most innovative companies at Mobile World Congress 2017"](#) (Mashable).

["The European Commission invests in Tech4Freedom"](#).

["Tech4Freedom recognized with the Alan Turing award for social commitment 2016"](#).

["Middle East welcomes Tech4Freedom"](#).

Investigating the application of biocatalysis for industry

Cristina Otero from the Biocatalysis and Bioenergy Group, outlines how the laboratory is applying the biocatalysis for food, cosmetics, and renewable energy

The Biocatalysis and Bioenergy Group (BBG) is a research group that belongs to the Institute of Catalysis and Petrochemistry, which is part of the Spanish Council for Scientific Research (CSIC). The Institute is one of the research centres included in the field of chemistry and chemical technologies. The group leader is Dr Otero. They investigate the application of biocatalysts to develop selective industrial processes in different areas: functional foods, nutraceuticals, sustainable chemistry, biomedicine, pharmaceutical, cosmetics, biodiesel, fine chemicals, etc.

BBG works in the design of new selective biocatalytic processes in both batch and continuous reactors. Since 1987, the group has exploited the advantages of bioprocesses in water and organic solvents (activity, selectivity, specificity, etc). BBG investigates the synthesis of compounds used as food additives or emulsifiers: mono-, di- and triacylglycerides, and fatty acid esters of monosaccharides, polyols, amines, alpha-hydroxyacids, biodiesel and phospholipids. BBG is involved in projects for the development of energy products and bioactive compounds from algae biomass.



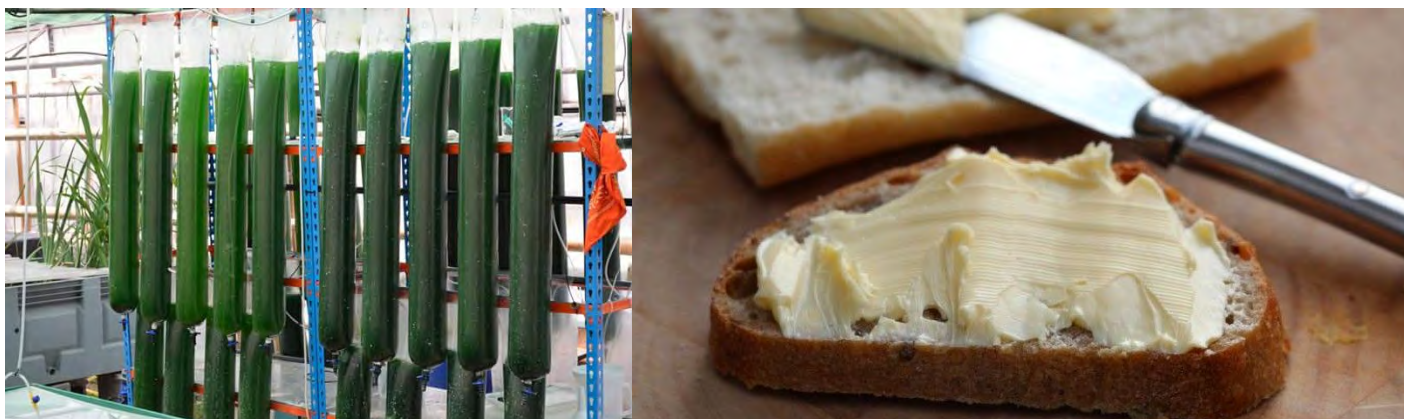
Cristina Otero

BBG has developed new extraction methods for algae biocomponents by enzyme-assisted protocols. BBG also carries out a complete chemical and functional characterisation of the different extracted biocomponents of algae biomass.

“BBG has developed a process of synthesis of biodiesel from sunflower oil. The process optimisation involves the design of new catalysts more efficient in the alcoholysis reaction, the reactor design and determination of optimal operational conditions.”

The group has wide experience in most of the techniques that are relevant in the field of biocatalysis: a methodology for the immobilisation/stabilisation of enzymes, reaction and reactor engineering. The chemical characterisation of products and the progress of the





Important products studied by BBG laboratory, from left to right: microalgae and spirulina cultivation for obtention of bioactive products via advanced enzyme assisted extraction methods of biomass biocomponents; fats free of trans-fatty acids obtained via enzymatic transesterification between a fat and an oil

enzymatic reactions are followed by TLC, HPLC, gas-liquid chromatography, NMR and others.

“BBG works in the design of new selective biocatalytic processes in both batch and continuous reactors. Since 1987, the group has exploited the advantages of bioprocesses in water and organic solvents (activity, selectivity, specificity, etc).”

Integration and collaboration of research

The laboratory of BBG is integrated into the network of laboratories of Madrid+D, running analysis of FAME, glycerides, and biodiesel according to directives EN ISO 9001. Determination

of FAMES, oxidative stability, oil composition in terms of mono-, di- and triacylglycerol, free fatty acids, water content, density, viscosity, solid fat content, etc are carried out.

BBG group has established fruitful collaborations with the Dept. Chem. Eng. of Wisconsin Univ., the Technological Institute of Veracruz (Mexico) and Korea University, and has participated in different international programs (NATO, European Union, Royal Soc. Of UK, Korean KOSEF, Romanian Academy of Sciences, etc). BBG liberates national and international scientific consortia for evaluation and demonstration of functional properties of new oil formulations for patients with obesity, metabolic syndrome, diabetes, cholesterol, hypertension and cancer, and for pregnant women, breastfeeding mothers and senior citizens.

BBG has developed a process of synthesis of biodiesel from sunflower oil. The process optimisation involves the design of new catalysts more efficient in the alcoholysis reaction, the reactor design and determination of optimal operational conditions. BBG also organises monographic courses

about synthesis and characterisation of biodiesel, methods of characterisation of materials, enzymes, applied biocatalysis, biotransformations, lipids and phospholipids.

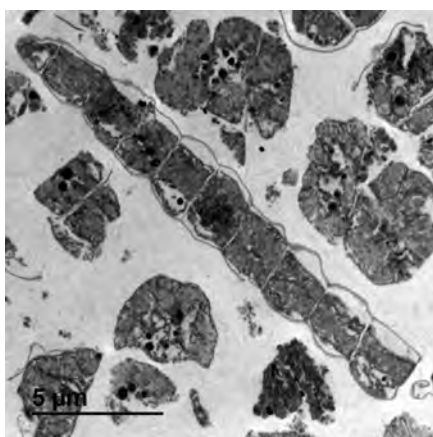


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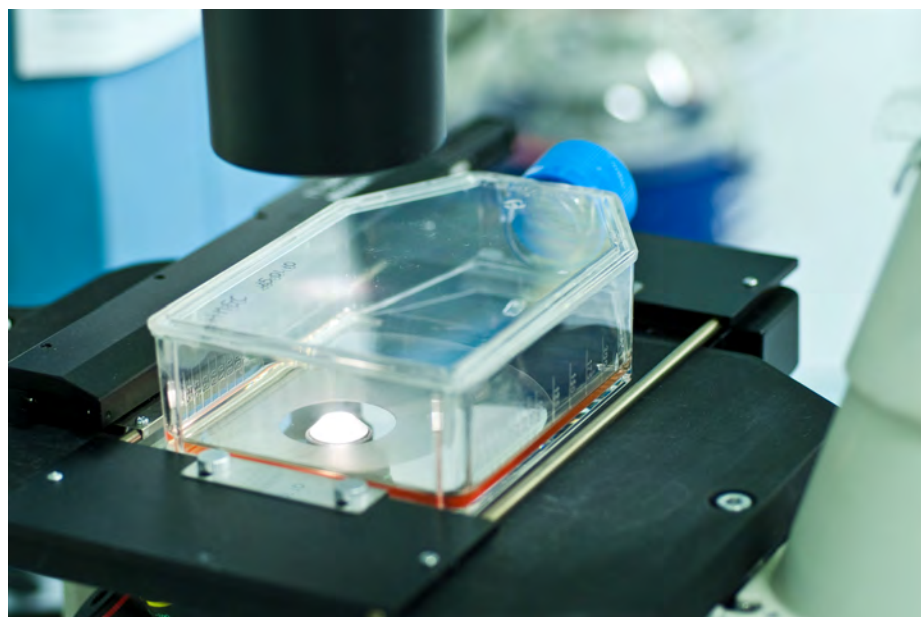
A micrograph of spirulina biomass

Understanding the adverse outcome pathway concept

Alberto Mantovani, Istituto Superiore di Sanità looks at how the adverse outcome pathway concept is the long way from molecular to adversity

Adverse outcome pathways (AOPs) describe the chain of events from the first interaction of any chemical with a molecular target (molecular initiating event = MIE) to an adverse outcome (AO) which can have an effect on regulatory toxicity testing, as well as causing health disorders in humans or animals. This approach only started in 2010 with the seminal paper by Ankley, Bennett, Erickson et al on 'Adverse outcome pathways: a conceptual framework to support ecotoxicology research and risk assessment' published in *Environmental Toxicology and Chemistry*; yet to date over 200 AOPs have been established, concerning both human health and ecotoxicology.

AOPs are not toxicity mechanisms but 'chemically agnostic'. AOPs simply depict the long, sometimes complex process from a molecular event (such as the interaction with a receptor or the inhibition of an enzyme) through to the perturbed function at cell and tissue level, leading finally to an appreciable disturbance of the organism's function and/or structure, which represents the AO. How do we build this path from molecule to organism? AOPs aims to provide a formal and consistent way of building such a path in accordance with a set of quality criteria. MIE and AO are sequentially linked by a series of biologically plausible and essential key events (KEs). Most importantly, the relationship between sequential KEs (KERs) has to



be concordant with dose response and temporality. In practice, an upstream KE (e.g., at a cellular level) must occur before and must require a stimulus of lower intensity as compared to a downstream (e.g. at tissue level) KE. Chemicals enter this scheme as toxicological (and in some cases, pharmacological) studies *in vitro* or *in vivo* and are used to provide the necessary 'empirical evidence', by characterising the relevant KE and KERs.

The ambition of the AOPs conceptual framework is to build a new paradigm of toxicological testing, based on the keywords 'relevance' and 'predictivity'. When the framework is implemented, any chemical triggering in upstream molecular/cellular events with sufficient intensity is flagged as a chemical able to perturb adversely a physiological pathway, and therefore induce a

certain kind of toxicity. The current research on AOP development aims at assessing the plausibility that a chemical with a mechanism 'X' (e.g., aromatase inhibition, leading to impaired oestrogen biosynthesis) is involved in the induction of the AO 'Y' (e.g., female infertility). As a positive side-effect, AOP development can identify new measurable markers and/or assays for possible inclusion in the toxicological testing strategies for chemicals. This is of special relevance because not all AO are currently reliably predicted by the parameters used in standard toxicity tests. For instance, the European Food Safety Authority (EFSA) has recently (2017) used the adverse outcome pathway approach to identify potentially relevant markers for 2 important human AO, such as Parkinson's disease and childhood leukaemia. Albeit of public health

relevance, these AOs may not be adequately captured by the endpoints currently assessed in toxicological tests.

AOP impact may go beyond toxicity tests. There is a great need to integrate valuable epidemiological studies into human risk assessment. Indeed, AOPs may support the development of predictive biomarkers to be used in human studies. Most importantly, AOPs may help to reduce a major uncertainty in environmental epidemiology, the 'biological plausibility' issue. The exposure to the chemical 'X' is associated with the increased frequency of the AO 'Y' (e.g., cleft lips in newborns): does scientific evidence support a causal association? In other words, is exposure to chemicals eliciting certain MIE or early KE plausibly linked to the observed increased risk of the adverse outcome 'Y'? Actually, the interests of the EFSA toward AOPs for Parkinson's disease and childhood leukaemias have been initially triggered by their observed epidemiological associations with pesticide exposures.

Many currently developed AOPs are often burdened by uncertainties and defined as 'putative' AOPs. Nonetheless, even a putative not compliant with the quite stringent quality requirements, can be used, at least as an issue deserving attention and points out what uncertainties should be dealt with.

The role of endocrine disrupting chemicals (EDCs)

One of the 'hot' topics in current toxicological sciences is the assessment of endocrine disrupters or endocrine disrupting chemicals (EDCs), i.e. the diverse ensemble of substances that induce adverse effects in humans, farm animals, and/or wildlife by altering the endocrine system function.

Endocrine disruption concerns the effects of chemicals on the broadest and most complex signalling system of the organism. Since this system is continuously stimulated both endogenously (hormones) but also by the environment, MIEs (e.g., interaction with the ERalpha nuclear receptor) continuously occur and it is unlikely that MIEs lead to adversity in a straightforward way. Thus, the relationship between the MIE and the early KEs clearly leading to adversity is a 'black box' of definite scientific interest: one example is the relationship, still not completely clear, between the MIE 'binding to aryl hydrocarbon receptor (ArH)' and several AOs (from cancer to reproductive disturbances) which are induced by ArH-binders such as dioxins.

AOPs of endocrine disruption is modulated by a number of factors. A single MIE/upstream KE may lead to different AO depending on sex, life stage, and concurrent levels of endogenous hormones. A typical example is the inhibited production of thyroid hormones, which may lead to impaired neurobehavioral development and growth in unborn babies and small children, to increased risk of goitres and possible secondary development of thyroid tumours in adults as well as to impaired reproductive capacity in women of childbearing age. Moreover, the AOPs related to thyroid hormone reduction are also modulated by iodine status: low iodine status alone may trigger the AOPs, but it may also facilitate (i.e., lower the threshold for a KER to occur) the AOP when it is triggered by a chemical.

AOPs can provide main leap forward in toxicity testing in terms of efficiency, relevance, and ability to predict adverse effects. It is a tool that (finally!) can connect, in a formalised, transpar-

ent, and quality-controlled way, mechanistic information and apical endpoints of classical toxicity testing. In this development phase, however, there is the risk of 'drowning in complexity' or making a lot of work which is not really fit for purpose. Therefore, both the general criteria and the definition of specific AOPs are under the close scrutiny of the OECD, which has implemented a programme on AOPs since 2012 as a major component of the updating of chemical testing strategies. In the European Union, the Joint Research Centre, has launched in 2014, a Knowledge-Base on AOPs, working in close collaboration with the OECD. Last but not least, the European research is also making a major effort: EU-ToxRisk is a project funded by the Horizon 2020 programme, led by Bob van de Water of Leiden University (NL) and involving 39 partners throughout the EU as well as Switzerland and the US. EU-ToxRisk is conceived as 'An Integrated European 'Flagship' Programme Driving Mechanism-based Toxicity Testing and Risk Assessment for the 21st century': obviously, the development of AOP-based approaches is a pivotal point for the ambitious project's work programme.



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Metrology enabling high temperature erosion testing

Louise Crocker and Tony Fry from the National Physical Laboratory looks at the role of metrology in developing new materials with improved resistance

The efficiency and service life of high-value industrial components can be critically impacted by solid particle erosion, particularly at high temperatures (HTSPE). Developing new materials with improved resistance to HTSPE can lead to major improvements in the efficiency of plant and aero-engines. The development and/or implementation of new materials and coatings has been hampered by the lack of traceable measurement in HTSPE testing, the assessment of the erosion resistance of materials and surface treatments has to date been largely empirical and non-standardised. The erosion rate is calculated through measurement of the rate of change in mass or volume as a function of the mass of erodent particles. To achieve this within conventional

HTSPE testing the sample is cooled periodically during the test, removed from the apparatus and mass change and/or the volume of the erosion scar measured. The sample is then reinserted into the apparatus, heated and the test can proceed. This leads to misalignment errors in repositioning the sample, thermal cycling, and long test times due to heating and cooling.

“Further developmental and validation work on the measurement methods described is progressing with the aim to provide the industry with a traceable HTSPE test through the NPL Measurement Services by early 2018.”

METROSION initiative

A European initiative – METROSION – was instigated to enable a step change in the monitoring and control of HTSPE testing providing traceable measurements and improved tests. As part of this project, the National Physical Laboratory (NPL), the UK’s National Measurement Institute, developed a new HTSPE facility extending the speed and temperature range which can be measured and incorporating in situ measurements, the first time this has been implemented worldwide. Within the project 3 novel in situ measurement systems have been designed, built and validated to measure the mass and volume change of the sample and the particle velocity and velocity distribution. This is the first time all 3 measurements can be made during the test and at high tempera-

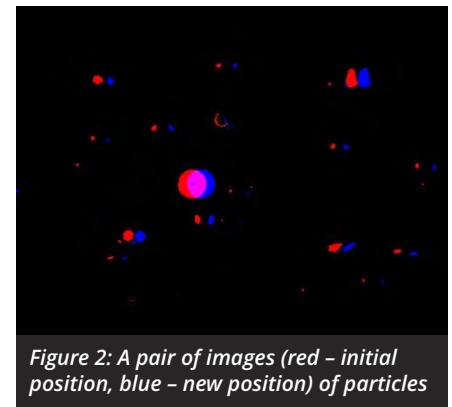


Figure 2: A pair of images (red – initial position, blue – new position) of particles

ture, greatly reducing the uncertainties relating to specimen positioning and decreasing the time needed to generate the erosion curves.

To perform the in situ mass measurement the rig has been designed to include a precision balance. A method of diverting the gas flow has been implemented which allows the mass to be measured between erosion intervals. Whilst the gas stream is diverted, a laser triangulation system developed at NPL can be used to scan the surface of the sample and measure the geometry of the erosion scar and thus calculate the volume change of the sample surface. It currently takes approximately 30 minutes to acquire the images required to generate a height map with the necessary resolution for precise volume change measurement, see Figure 1. These in situ measurements have enabled an HTSPE test to be conducted in as little time as 2 hours for purely mass change measurements and ~6 hours for both mass and volume change

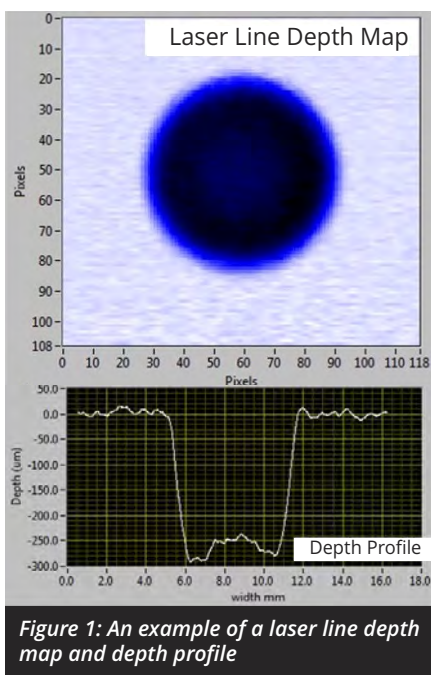
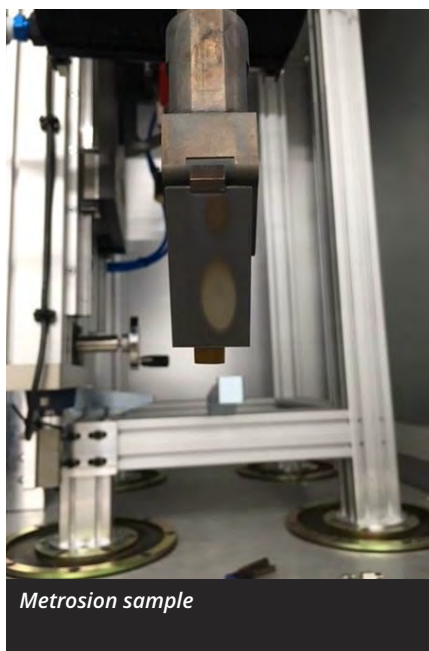


Figure 1: An example of a laser line depth map and depth profile

measurements. Conventionally this would have taken ~3 days of effort.

To be able to relate laboratory results to actual operating conditions, erosion tests should be conducted using representative particle velocities to reduce uncertainty in measured erosion rates and to account for any mechanism changes as a function of velocity and temperature. To realise the measurement of velocity and velocity distribution as a function of particle size, an in situ optical method was developed at the Technical University of Denmark (DTU), which enables high-speed particle image velocimetry to be conducted at high temperature, in a cost effective manner. The new method uses pulsed background lighting and high-speed image capture of moving particles which allow imaging and measurement of fast moving particles, see Figure 2. The velocity of each particle is calculated from a displacement of the centre of mass. Integration of this sensor to existing test rigs is possible and provides, for the first time, full measurement of the particle velocity distribution as a function of particle size across the gas stream.

Whilst this method is capable of providing size and 2D shape information as well as velocity measurements, to fully understand the erosion process, a more detailed method of particle sizing is required. The erosive particles can be characterised in terms of their



Metrosion sample

geometry and size, using a range of different measurement techniques, such as laser light scattering. PTB, Germany's National Metrology Institute, has developed, as part of this project, a method to describe the shape of the particles using mathematical descriptors based on X-ray computed tomography measurements of the particle geometry. These descriptors can be used with the in situ velocity measurements to generate velocity models for predicting the distribution of particle velocities as a function of their size, geometry and aspect ratios. This can be used in erosion models to provide more realistic predictions of damage accumulation and relate the HTSPE test results to real world conditions.

Further developmental and validation work on the measurement methods

described is progressing with the aim to provide the industry with a traceable HTSPE test through the NPL Measurement Services by early 2018. Further details on the Metrosion project can be obtained from NPL project [website](#).

“A European initiative – METROSION – was instigated to enable a step change in the monitoring and control of HTSPE testing providing traceable measurements and improved tests.”



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Internationalisation of education, science and research in Germany

The Federal Ministry of Education and Research details how their Internationalisation Strategy aims to help meet global challenges by working together

International cooperation in education, science and research is more important today than ever before: National research and innovation systems need to be open if they are to remain competitive. We can only make effective use of our knowledge and the existing potential for innovation if we work together in transnational exchanges. At the same time, we also need international cooperation to respond to the global problems of our time. The most pressing challenges facing humanity, such as climate change or food security, do not stop at national borders. Sustainable solutions can only be found if the countries of the world join forces.

Against this backdrop, the German Federal Government adopted the “Strategy for the Internationalisation of Education, Science and Research” in February 2017. This Strategy is aimed at strengthening Germany as a location for research and innovation and empowering Germany to assume responsibility at the global level.

A well connected Europe for research

Germany is already well connected internationally: The number of foreign researchers at German higher education institutions soared by about 84 % between 2006 and 2014. Germany is also an attractive destination for students from abroad: It ranks fifth in the list of the most popular host countries worldwide, behind the US, the UK, Australia and France. 320,000 foreign students were studying at German higher education institutions in 2015. This number is set to rise to 350,000 by 2020.

By the same token, more and more German researchers and students are going abroad and an increasing number of academic publications from Germany – around 50% – are now being written in cross-border cooperation. Germany’s Federal Government wants to

continue to actively shape this development: Foreign students and researchers who have studied and taught in Germany and Germans who have studied and taught in other countries are bridge builders for the future.

The Federal Government already carved out its first comprehensive strategic framework for international cooperation in science and research in 2008. The new Internationalisation Strategy, which was introduced in 2017, follows up on this while taking new trends and challenges into account. These include current migratory movements, the digital revolution, the development of the European Research Area (ERA) and the formation of new centres for innovation outside of the established science locations.

Germany is open to the World

With its Internationalisation Strategy, the Federal Government is sending a strong message that Germany is open to the world and taking a clear stance against the isolationist tendencies that have become apparent in a number of places. Rising budgetary allocations show that Germany is doing more than merely paying lip service to international cooperation: The Federal Ministry of Education and Research has increased its annual funding for international cooperation from €567m in 2009 to over €800m in 2015.

The Internationalisation Strategy defines 5 key objectives: Strengthening excellence through worldwide cooperation: The Federal Government is taking measures to further consolidate Germany’s position as an attractive destination for students and researchers. At the same time, they are continuing to remove barriers to the international mobility of scientists. Europe will remain a central point of reference in all of these efforts.

Developing Germany’s strength in innovation on the



international stage: As a location for high-tech activities, it is essential for Germany to be an integrated part of global knowledge flows and value chains. That is why the Federal Government is funding international networking activities, particularly those involving small and medium-sized enterprises. They are also working towards enhancing the central framework conditions for cooperation, for example with regard to intellectual property rights.

Internationalising vocational training and qualification: The Federal Government is taking action to further strengthen cooperation with industrialised and emerging countries in vocational education and training (VET), foster the mobility of apprentices and facilitate the recognition of qualifications gained abroad. Fighting youth unemployment in Europe continues to be a major objective.

Working with emerging and developing countries to shape the global knowledge-based society: A large number of these countries are developing into up-and-coming locations for science and are becoming increasingly relevant partners for cooperation. The Federal Government is expanding existing collaboration schemes and setting up new partnerships with these countries. The digital revolution offers significant opportunities for providing broader access to knowledge in this context.

Overcoming global challenges together: Education and research are creating the knowledge required for evidence-based policy-making and the development of sustainable solutions to global challenges. The govern-

ment is stepping up its efforts to improve networking among relevant stakeholders at the European and international level.

“International cooperation: networked and innovative” is the guiding principle of this strategy: Stronger coordination on the part of stakeholders will improve the coherence of the measures taken and the resulting synergy effects will enhance the quality and impact of international cooperation.

In a globalised world, internationalising education, science and research is key to protecting the quality of life and health and prosperity in the long term. The Federal Government is responding to this challenge with its Internationalisation Strategy, which provides a framework for Germany’s development as an open, sustainable and responsible location for science and innovation.

Download the English version of the Internationalisation Strategy at:

<https://www.bmbf.de/en/internationalization-strategy-2209.html> .

Federal Ministry of Education and Research – Germany
<https://www.bmbf.de/en/index.html>
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Biomedical research: crossing discipline borders

Biomedical research crosses borders of disciplines to help shape new imaging approaches, as scientists from Technical University of Munich explain

Roughly 6 years ago, we, a couple of researchers at the Technical University of Munich (TUM), Germany, envisioned a new form of doctoral training together with our partner in industry (GE Global Research). We saw the still prevalent silo approach of education and at times the lack of understanding amongst the different specialisms and sectors.

Bridging over these borders became our common motivator. Our first step was to analyse the status quo and define the room for improvement. We wanted to attract young talent to come and research in Europe. Our high set aim was to nurture and develop a new generation of early stage researchers (ESRs) by enabling them to:

- Become excellent researchers in an interdisciplinary setting, perform cutting edge science, acquire T-shaped education (combining depth in one specialisation with the skill to collaborate across disciplines)^{1,2}
- Increase awareness as responsible leaders by applying ethics in good scientific practice and clinical studies, reflect critically, be aware of diversity and respect other research fields, communicate with public & peers, bridge cultural differences
- Grow their scientific skills as knowledge distributors, work with others

and expand their own potential as well as enable others to use their potential by supervising master's students

- Become creative thinkers and develop their own ideas, think outside the box
- Stay focused as entrepreneurs, be realistic in planning be pragmatic
- Progress in self-management by utilising the provided broad toolkit for personal effectiveness, time management and prioritisation.

Adopting the approach of design thinking, which focuses on the solution itself and is human-centred, seemed to be the way to tackle the task. So, who did we see as our target group? Naturally, there were many. Our early stage researchers, their potential future employers and collaborators in academia and industry unless they would found their own start-ups, in the biomedical research context also patients and physicians, and the public that should benefit from the research and the training of the young BERTI ESRs.

Keeping this in mind, together with our 19 partners from 8 countries, we set out and created a unique and encompassing research and training schedule. Adapting it to changing needs was a challenge, but due to the immense flexibility of our training partners, we managed it very well.

Which scientific and socio-economic challenges did we set out to master?

Our topics circle around the interdisciplinary and intersectoral topic of biomedical research. We research Magnetic Resonance Imaging (MRI), with special focus on neuro, cardio and thermometry (cancer treatment), x-ray tensor tomography, optoacoustic imaging, and have some research aspects in the field of healthcare robotics. BERTI covers the whole aspects from very established techniques with high TRL levels³ to ground breaking new imaging approaches.

Starting with the established MRI, the new aspects we have been working on may be subsumed under "MR Plug and Play", this implies reducing the required time to take an MR Image, increasing the patient comfort by reducing the noise, and improving the information content by making the MRI quantitative. For a physician, these developments translate into getting their images faster and with significantly increased information, content, and quality, the patient does not have to stay in the MRI 'tube' for as long and for the hospital that it can allow for scanning of more people in a given time frame. Last but not least costs can be saved. Further, we work on making the MRI silent. Meaning that more patient groups, e.g. children or people suffering from neurological disorders, can benefit from the possibilities MRI offers. This philosophy has

Image: Miguel Molina Romero



also been adapted for cardiac MR, where we scan the moving organ without any external intervention, focussing on detection of the motion of the heart muscle itself but also of the aortic blood flow.

Being an inherently versatile imaging method, MRI can also be combined with heating devices, which come into play for tumour treatment. To this end, “thermometry”, which is the term for controlled heating of cancer tissue under constant MR-based temperature control, has been a further aspect of the research within BERTI, which has the potential of directly leading to improved outcomes of chemotherapy at reduced patient discomfort.

Multispectral Optoacoustic Tomography (MSOT) is a novel imaging methodology, which resolves optical contrast deep inside tissues at ultrasound resolution, thus offering high-resolution optical imaging and true molecular information. To obtain this molecular information, the quantification of the optoacoustic signals is important in characterising tissue chromophores or administered agents and/or nanoparticles. With this novel technology,

in vivo information, such as tissue oxygenation levels may be obtained in real time, which opens a direct window into tumour metabolisms, vital and essential information for physicians, pharmaceutical industry and patients.

Another innovative imaging modality, X-ray Tensor Tomography (XTT) allows unparalleled insights into tissue orientation and structures that are typically below the spatial resolution of a conventional imaging system. The structure orientation is deduced indirectly by reconstructing the scattering profile at every location within the measured sample. In biological and clinical applications, this technique has proven to give unique contrast also in soft tissue, like the human breast, enabling to enhance the diagnostic information of X-ray mammography, for instance for detection of breast cancer, significantly.

Healthcare robotics such as double-arm manipulator systems for transurethral resection for urinary bladder tumours represented a further focus research area of BERTI. For complicated and delicate anatomical structures like the urinary system, visualisation and the ability to reach obstructed areas is key.

Has BERTI been successful?

The achieved scientific outcomes are outstanding and would not have been possible in a different setting. The exchange across borders was essential. Not only did we work with partners from 8 countries, but also our 14 young talents (40% female) came from 9 different nations. Of the 3 BERTI researchers who have already completed the programme, all were recruited instantly: one for academia at Kings College London, UK, one for a medium size, and, one for a globally operating company based in Germany.

1 B Allenby. Rethinking engineering education, Proc Sustainable Systems and Technology, 2011

2 N Donofrio, C Sanchez, J Spohrer. Collaborative innovation and service systems. Holistic Engineering Education, 243-269. Springer New York, 2010

3 The European Commission. Horizon 2020: Work Programme 2016-2017, Annexe G: Technology readiness levels (TRL)



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Research on Egyptian and Nubian settlement archaeology

Julia Budka, Professor of Egyptian Archaeology, LMU Munich, outlines the need for further research addressing living conditions of Egyptian and Nubian towns

The European Research Council project AcrossBorders, concentrates on settlement patterns in Egypt and Upper Nubia in the 2nd Millennium BC: various interactions and mutual influences are attested for these regions which are situated across ancient (Pharaonic Egypt and Kingdom of Kush) and modern (Egypt and Sudan) borders with diverse environmental and cultural preconditions. Much progress has been made in Egyptian and Nubian settlement archaeology in recent years, but further research addressing general aspects of living conditions and the specific coexistence of Egyptians and Nubians is required. Of chief interest are the architecture and structure of the Egyptian towns established in Upper Nubia during the New Kingdom, their social stratification, the local relations of Nubians and Egyptians, and the specific material culture.

“Much progress has been made in Egyptian and Nubian settlement archaeology in recent years, but further research addressing general aspects of living conditions and the specific coexistence of Egyptians and Nubians is required.”

The international age of the New Kingdom in Pharaonic Egypt (c. 1539-1077 BCE) resulted in the foundation of several Egyptian towns and settlements in the area known today as Upper Nubia in Sudan. Some of these are well preserved and offer the unique chance to



Sai Island, SAVI, Martin Fera 2015, 300.000 faces reduced model

explore domestic life in an ancient Egyptian settlement outside of Egypt proper. The most promising example of such ‘colonial sites’ is the exceptionally well-preserved town on Sai Island because of its long occupation period and its attested history as an important site of the African Kingdom of Kerma. Prior to the New Kingdom, Sai was the northernmost stronghold of the Kerma Kingdom with a significant strategic role, well attested by archaeological remains.

The AcrossBorders project has conducted archaeological fieldwork on Sai Island in Sudan and Elephantine in Egypt from 2013 until 2017.

Archaeological excavations in the New Kingdom town and cemetery of Sai were complemented with kite aerial photography, structure from motion

approaches, terrestrial 3D laser scans, geoarchaeological surveys, micromorphological soil sampling and various archaeometric analyses of diverse materials. Human remains, animal bones, botanical material, soil, plaster, sandstone, and all kinds of objects are currently being assessed by the general question: can Sai be evaluated as an Egyptian microcosm, despite its location outside of Egypt and its specific topographical, environmental and cultural situation? How did the local Kerma Nubians react to foreign influences and how did the Egyptians present themselves outside of Egypt?

These research questions were tackled not only by field work on Sai, but also by a close comparison with the contemporaneous town of Elephantine in Egypt. In cooperation with the Swiss Institute in Cairo, directed by Cornelius



von Pilgrim, AcrossBorders has studied the material culture from 18th Dynasty buildings on this important site at the southern border of Egypt. Of particular interest was the common appearance of both Nubian and Egyptian cooking wares, providing close parallels for the situation on Sai Island.

“Combining research questions on the micro-level with the macro-level promises new information about cities and households in Ancient Egypt and Nubia with a focus on the development and situation during the Late Bronze Age.”

The AcrossBorders conference

Preliminary answers to the main research questions and the most recent results of the AcrossBorders project will be presented and discussed at an upcoming international conference in Munich, to be held from 1–3 September 2017 and hosted by Ludwig-Maximilians-University. It is the closing event of the AcrossBorders

project, bringing together not only all major cooperation partners but also renowned experts in the field like Manfred Bietak, Charles Bonnet and Neal Spencer among many others. The conference focuses on 1) individual households of selected sites in Egypt and Nubia (for example Tell el-Daba, Amarna, Elephantine, Amara West, Sesebi, Tombos, Kerma). Here, architectural studies as well as analyses of material culture, in particular of ceramics, will be presented, featuring up-to-date applications of archaeometry. In addition to this micro approach, introducing micro histories of individual sites according to recent archaeological field work incorporating interdisciplinary methods, the event also discusses 2) general patterns and regional developments – thus, the macrocosm of New Kingdom Nubia.

Combining research questions on the micro-level with the macro-level promises new information about cities

and households in Ancient Egypt and Nubia with a focus on the development and situation during the Late Bronze Age. The AcrossBorders conference will also represent a case study for the current status of modern Egyptian settlement archaeology which is characterised by a strong interdisciplinary focus. The rich potential of well-preserved but still not completely explored sites in modern Sudan, especially as a direct comparison for already excavated sites located in Egypt, will be highlighted. The expected outcome of the conference is, therefore, to build up future communication and collaborative research between settlement sites throughout Egypt and Sudan.



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Achieving excellence in Dutch science

Open Access Government's, MF Warrender outlines how the Ministry of Education, Culture and Science in the Netherlands is driving excellence in Dutch science

The Dutch government prides itself in its renowned excellence in research and funding, spending more than €4.5 billion on science every year. This funding primarily consists of grants for research centres, universities, international organisations such as CERN, research in specific fields, and programmes to encourage individual scientists, such as the Spinoza Prize: the highest award in Dutch science. These measures ensure that the Netherlands remains at the top of its game in areas of science and research, addressing the challenges facing both society and industry. The government has also been providing additional funding for basic research since 2014, with it rising to €75m in 2017 and plans for a further increase to €150m on a structural basis.

“The ministry also focuses on strengthening links with other countries within the EU in areas of science and research, but also culture.”

The Ministry of Education, Culture and Science is responsible for this drive for a knowledgeable, skilled and cultured country, and has been headed by Minister for Education, Culture and Science, Jet Bussemaker since November 2012. She has played a large role in determining the main aims for the government's new science policy: Science Strategy 2025. The 3 aims in order for Dutch science to sustain a leading international role will be:

- World class Dutch science (through matching European grants, introducing the national science agenda and renewing infrastructure).
- Stronger links with society and industry (by making closer ties between science and industry, encouraging competition and start-ups, open access to research, and ensuring better cooperation between public authorities and science).
- Using science as a breeding ground for talent (by providing challenges for talented scientists, increasing the number of PhD researchers, and improving policies on gender equality to maximise talent from female researchers).

The Rembrandt Treaty

The Ministry also focuses on strengthening links with other countries within the EU in areas of science and research, as well as culture. The most recent example of this is the signing of the Rembrandt Treaty by both France and The Netherlands. It is a pact between Bussemaker and her French counterpart, Fleur Pellerin, which agrees for Rembrandt's twin portraits of Maerten Soolmans and Oopjen Coppit to be restored and exhibited in the Netherlands for the first time ever.

Bussemaker comments on the importance of this treaty to Dutch cultural heritage, illustrating how countries can come together to support one another in many different areas. She states that it is “more than just a transaction. Our joint responsibility for these unique paintings will unite the Netherlands and France for very many years to come, in the best tradition of European cultural co-operation.”

In a speech, she highlights the importance of a European partnership, and how “culture, as we experience today once again, brings different worlds together.” This paves the way for the intertwining of national and European identities in wider areas such as science, research, and education.

Attracting students to study in the Netherlands

It is clear to see that Bussemaker and the Dutch government are not afraid to take action in these areas. In July last year, the Minister proposed a Bill to



Jet Bussemaker, Netherlands Minister for Education, Culture and Science

make studying abroad much more attractive to both students from the Netherlands and students wanting to study there from other countries. It will enable universities and HBO institutions to reduce or even waive tuition fees for students who are following a combined course of study at an institution in the Netherlands, as well as an institute abroad. This will increase the capacity for collaborations with young scientists all over the world, benefitting the Netherlands in areas such as research and innovation.

In addition to the government's annual funding in these areas, science receives about €7 billion from various sources such as charities, businesses, as well as EU funds such as tight links to the Horizon 2020 funding programme. Co-operation between countries is vital in terms of excellent science and research, especially regarding programmes such as Horizon 2020, which is expected to make such a huge impact on European

research and innovation projects. Dutch Science will continue to excel in these sectors as long as the ministry continues pursuing close relationships with neighbouring countries and using its governments funding to drive projects forward. ■

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Understanding the characterisation of sustainable materials

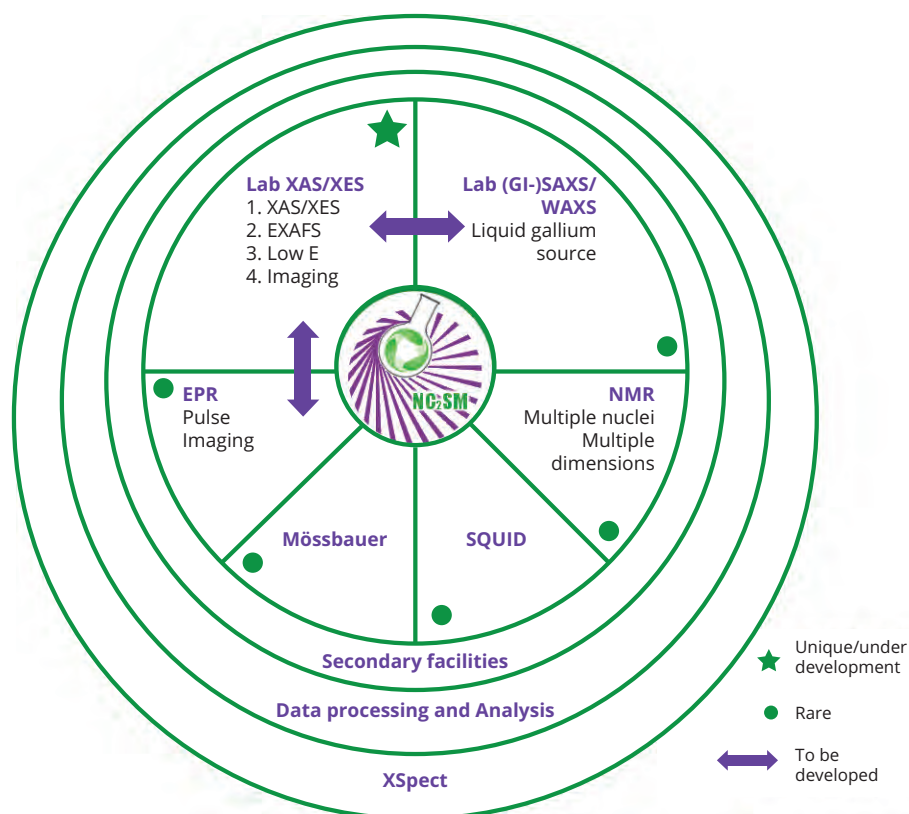
Moniek Tromp, Van t Hoff Institute for Molecular Sciences, Sustainable Materials
Characterisation sheds light on sustainable materials and their benefits

An integrated expertise characterisation centre providing a full set of advanced characterisation methods, some of which unique to the world, will enable sustainable materials scientists to characterise their materials and processes in all detail; using all eyes and ears to make pictures and movies of molecules and materials in action. This allows the rational design of novel materials and processes, which meet today's societal challenges, i.e. clean, requiring limited energy and using cheap and abundant resources.

Important ace of sustainability

Sustainability is important to accommodate the growth of the world's population and its future demand of resources for water, food and energy at a higher average standard of life. This requires a significant change of today's practice, including the minimisation of the manufacturing footprint of a material, but also the sustainable gains of its use during the life cycle and clever reuse of the material or its components. Integral sustainability must become a driver for new energy technologies, to produce durable systems to convert, produce and store clean energy.

Resources for energy (fossil origin) and raw materials (rare elements) are depleting and this requires a transition to sustainable energy production as well as the reduction, replacement, or recycling of rare elements and the



further development of bio-based materials. The transition to a sustainable society will likely have a tremendous impact. While initial efforts are aimed at reducing the footprint by making existing technologies more efficient, the final goal is a (circular) society based on truly sustainable resources for energy and materials. In this transition to a sustainable society, advanced materials will play a crucial role; a sustainable society cannot be realised without the corresponding materials that enable it. These materials will have in common: less non-renewable energy use and less greenhouse gas emission during the

synthesis, construction, processing, packaging, transportation usage, recycling, and reuse.

Materials science

Materials Science is the discipline that engages with the design, synthesis, structure, dynamics and performance of materials. It is a multidisciplinary field that includes physics, chemistry, biology, and engineering, and studies materials in a broad range of length scales from the atomic scale, through nano and micro, all the way up to the macro scale. In order to replace scarce raw materials, the functionality of materials needs to be understood

much better, i.e. at all levels and in all its details. Further development and increased availability of the characterisation toolbox for this is a prerequisite in this domain.

Proper understanding not only means characterisation of the geometrical structure, from atomic to molecule and agglomerate /particle scale, but also the electronic structure. The latter determines, for a large part, the properties and reactivity of materials, but is also typically difficult to pinpoint, requiring a multitude of different and non-standard characterisation techniques. A radically different approach towards materials characterisation is thus required.

Most laboratories active in a specific materials research area specialise and invest in one characterisation technique only, which is most important or best available to them, and have experts in that one technique only. The problem with most techniques is that they only provide partial characterisation of the material under investigation. Combining several measurements of the same sample, under identical conditions, often leads to much more information than just the sum of individual data. Current challenges in sustainable materials, as described above, require detailed characterisation on multiple levels which can only be achieved with multiple techniques, i.e. 'all the eyes and ears one can have'. Groups or laboratories generally do not have the possibilities (staff, finances and expertise) to offer, develop and/or execute all of these well. In addition to that, important X-ray techniques, allowing characterisation from atomic (Angstroms) up to inter-molecular

information (micrometer) are typically performed at synchrotrons, with high oversubscription rates, severely limiting the accessibility. A radically different approach to materials characterisation is therefore crucial to ensure one can meet the materials science challenges we are facing today.

"Sustainability is important to accommodate the growth of the world's population and its future demand of resources for water, food and energy at a higher average standard of life."

National Characterisation Centre for Sustainable Materials

To unravel the novel chemistry displayed by these feedstocks and materials as well as their differing reactivity requires multiple advanced techniques, in an integrated approach. We are therefore in the process of setting up a National Characterisation Centre for Sustainable Materials (NC2SM) in which we bring important non-standard techniques together in one place, as well as develop novel and combined ones, by making x-ray absorption, emission, and scattering techniques available in the laboratory. Having access to all techniques in one place, thus making it possible to collect all necessary data in an unequivocal manner on the same sample under identical (operando) conditions, is key to fundamental materials understanding and subsequent rational design and development.

The suite of techniques will give detailed structural as well as electronic information on the broad range of materials, at different time and length scales, from all different parts of the material/molecule. All techniques have

their individual strengths and limitations, and only a combination of all can provide a full picture and movie of the sample and its reactivity. Moreover, the integrated centre will therefore not just act as a place to obtain data, but also as a sounding board and discussion platform for materials scientists, spectroscopists and theoreticians, which will catalyse novel and exciting science and advances in all fields.

Overview of the facility, including embedding with full laboratory and computational facilities as well as data processing and analysis. Moreover, a commercial service for data acquisition and analysis will be set-up (XSpect).



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The peer review process: is there room for improvement?

Professor Stan Gielen, President of NWO discusses whether changes are needed to the peer review process and how these can be implemented successfully

In the Netherlands, as in many other countries, peer review has been the standard procedure for selecting the best research proposals for decades. But, in recent decades, the system has come under pressure for various reasons. First of all, the fierce international competition for research excellence has triggered researchers to write more proposals. This has led to an increase in the number of research proposals in most countries, whereas the funding has not increased by the same amount. Consequently, more and more academics write and evaluate proposals that have very little chance of being awarded funding. In several research grant competitions, the Netherlands Organisation for Scientific Research (NWO) has experienced a misbalance between a large amount of time spent in writing and evaluating research proposals and the relatively few proposals that will be funded.

Many scientists spend lots of time preparing their own research proposals and being involved in the peer review process of their colleagues. We have to achieve a more acceptable balance between available budgets – which will always be limited – the success rates, and the time spent on funding acquisition. Another aspect is that over the years, peer review has proven to be an academically effective route to selecting proposals with the highest scientific impact. However, to predict societal impact – an important criterion for funding – it has proven to be a less useful selection method. So we should definitely redefine how we prepare and evaluate research proposals.

Investigating alternative methods

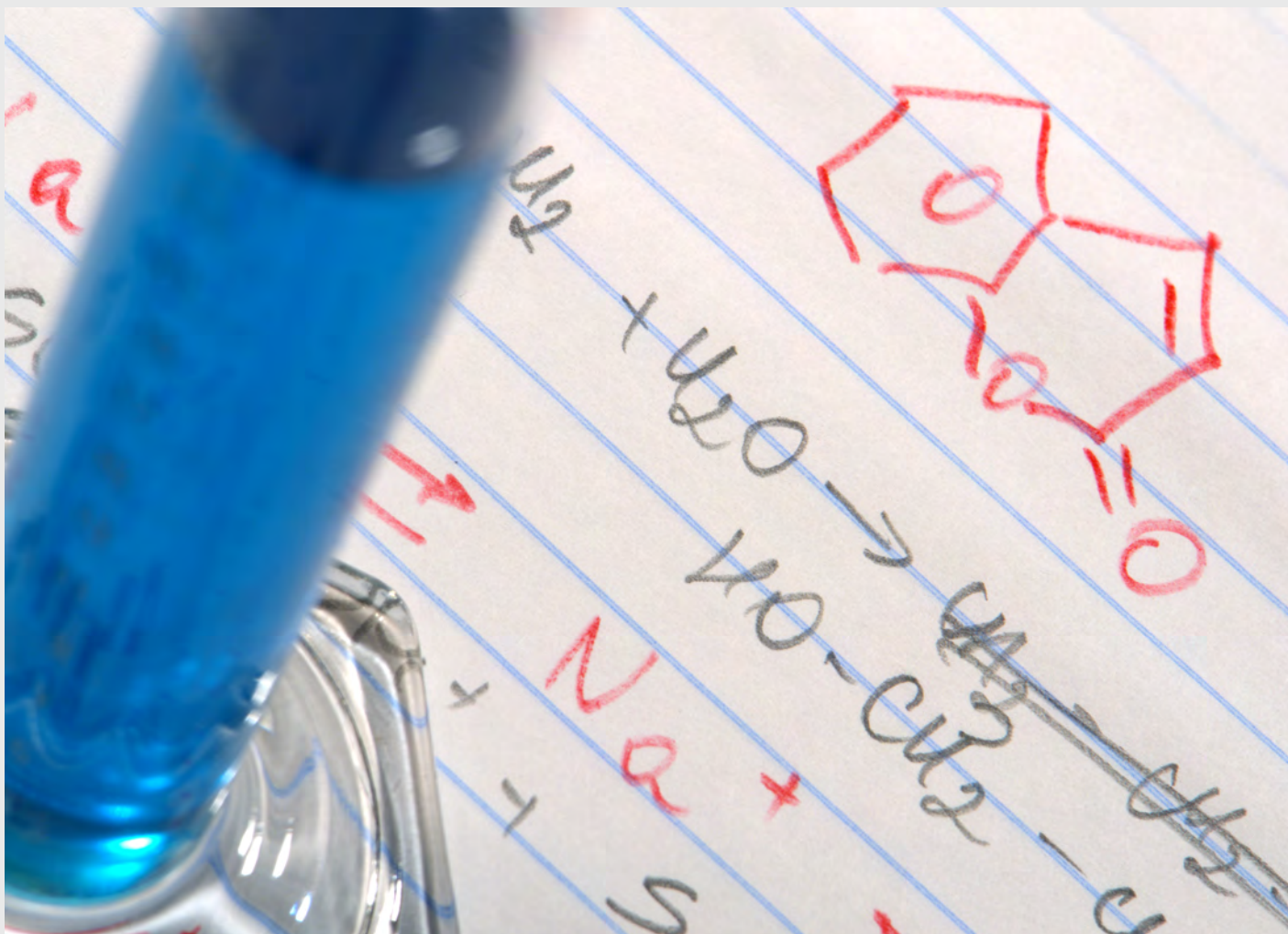
Based on these observations, the Dutch Minister of Education, Culture, & Science recently asked NWO to consider alternative methods for evaluating proposals and to explore alternative evaluation strategies. This is why NWO has organised a series of conferences in

2017 dedicated to discussing the consequences of the high application pressure on the peer review procedure, considering what potential adjustments to the peer review process are needed, and investigating which alternative review methods could be used.

“The conferences were a great success, and many researchers appreciated the opportunity to share their experiences and explain their ideas. It became clear that many research councils worldwide are facing the same problems as NWO in the Netherlands regarding a high number of applications and success rates.”

NWO started off with a national conference on 4 April 2017 in Amsterdam. For this conference, we invited scientists based in the Netherlands as well as managers from universities and from NWO’s partners and policy makers to discuss possible improvements to how we allocate funds for research. Subsequently, on 21 May 2017 during an internal conference, employees of NWO explored the possibilities of mitigating application pressure due to a large number of proposals. On 29 and 30 June we invited delegates from research councils and granting organisations around the world, but also researchers and peer reviewers, to an international conference.

With this international conference – which was attended by representatives from 20 countries – NWO aimed to jointly discuss various topics regarding application pressure, applicant workload, and the cost and efficacy of peer review in its current form. Are there any alternatives we could take into consideration? How can we implement them? Building on our joint experiences: how can we solve the problems we have come to identify and how can we work together to improve the peer review system? Is the solution to be found in



alternative methods of evaluating research proposals? If so, which methods are the most appropriate?

“Many scientists spend lots of time preparing their own research proposals and being involved in the peer review process of their colleagues.”

The conferences were a great success, and many researchers appreciated the opportunity to share their experiences and explain their ideas. It became clear that many research councils worldwide are facing the same problems as NWO in the Netherlands regarding a high number of applications and success rates. Ideas for alternatives within the peer review system and experiments with new evaluation methods were discussed. With the input gathered during the conferences, NWO will make a proposal to the Dutch Minister of Education, Culture, and Science by the autumn. Since this will be an ongoing challenge for us and for most research councils, we will simultaneously investigate how to build

a strong international network where research council members and other stakeholders can continue sharing their ideas and lessons learned. This will ensure that the issue remains high on the agenda so that we can keep working on further improvements to our methods of evaluation. ■

Professor Stan Gielen
President

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Tackling gender imbalance in the research ecosystem

The gender imbalance in the research ecosystem is something that must be addressed.
Stephan Kuster, Acting Director of Science Europe discusses

Talent, curiosity, resilience, dedication, passion, integrity, and intellectual capacity are just some of the attributes associated with a successful career in scientific research. They are not the purview of one part of humanity over another, however, and they certainly are not distributed unevenly among genders. So why then is ‘being a man’ one of the most consistent predictors for a successful career in research?

Any imbalance between genders, in terms of success in research, has to be attributed either to failings in the selection process within the research system, or to factors outside the system that affect the career choices women make. Based on vast amounts of available evidence and scholarly literature on the subject, a combination of both of these factors is responsible for this imbalance.

Both issues within and outside of the research system must be addressed if we wish to achieve gender equality. We should not only do this because we consider it a basic human or social right, or because it is one of the sustainable development goals; we should also do it for the sake of scientific research and for our capacity to innovate. Plain and simple, excluding a large part of talented, passionate, dedicated, and intellectually capable individuals from the career rungs on the scientific ladder is bad for research.

Addressing the imbalance

Through Science Europe, research funding organisations and top research performing organisations across Europe work together to address issues within the institutions that structure the research system. The Science Europe ‘Practical Guide to Improving



'scissors' curve indicates, the gender gap widens dramatically at both higher and later career stages.

If, as a funding organisation, you realise that success rates for funding applications submitted by men are higher than those for women, then your selection process is most likely affected by unconscious bias. Funding decisions tend to be made by groups of fellow researchers in peer-review panels, and there are some simple ways to help them to be more aware of potential bias in their deliberations. Training, for example, can be very useful.

Finally, numerous causes for the men-women imbalance in research can be attributed to the fact that women frequently take on a bigger share of the care-related responsibilities within the family. National legislation provisions such as maternity, paternity, and parental leave vary strongly across European countries. Research organisations can help by providing additional and more tailor-made support to help minimise the impact on the careers of promising women researchers through specific measures and additional funding.

Skewed gender balance in scientific research careers is a well-documented issue. It is not for a lack of evidence, nor for a lack of political momentum, that the problem is such a persistent one. Real practical changes and support to researchers that research organisations can introduce are necessary to bring about the change in our culture that is required to achieve true gender equality at all stages of a researcher's career.

1 <http://scieur.org/gender-guide>



Stephan Kuster
Acting Director

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Research Equality in Research Organisations¹ has been in high demand since its publication in February of this year as a key resource that addresses gender inequality. The guide provides tips and best practice examples from research organisations in 3 key areas: monitoring of gender data, addressing unconscious bias, and providing support measures through grant management.

The first thing you need to have in order to address a problem is data. All research organisations collect data on their own operations such as the funding they allocate, and the researchers they recruit or promote. Making sure that these data are always collected in a gender-disaggregated way, and broken down by scientific field and career stage, is crucial to the ability to monitor gender balance issues. As the famous

imec start-up incubation for digital entrepreneurs

For those looking to kick-start their tech business, this imec start-up incubation programme offers support with coaching, facilities and funding

Imec.istart is an imec business incubation programme that supports tech start-ups with coaching, facilities and funding. The programme has been recognised by UBI Global as one of the world's best University Business Accelerators.

Imec is the world-leading research and development and innovation hub in nanoelectronics and digital technologies. As a trusted partner for companies, start-ups and academia, imec brings together brilliant minds from all over the world in a creative and stimulating environment. By leveraging a world-class infrastructure, as well as local and global ecosystem of diverse partners across a multitude of industries, imec accelerates progress towards a connected, sustainable future.

Imec start-up incubation takes off

As part of its activities, imec has created a leading business incubation programme, imec.istart, to support young tech start-ups in developing their business. Getting a tech start-up off the ground requires skills, resources and the right technology. Turning it into a success is an even bigger challenge. The imec.istart programme offers entrepreneurs and start-ups in-depth coaching, facilities and support services, as well as a safe and stimulating environment to develop and grow their business.

The goal of an imec.istart incubation project is to assess the feasibility of its (digital) business idea, create a start-up to drive commercialisation and prepare the (commercial) launch of its first product(s). The programme is open to any entrepreneurs (be it from the imec research community, other academic researchers, external entrepreneurs or students) who wish to engage in the commercialisation of a technology-driven innovation or project.

“Entrepreneurs from anywhere around the globe are welcome to join the growing community of 120 successful imec.istart start-ups...”

The imec.istart programme combines pre-seed funding, coaching and mentoring, and other types of support (e.g. housing, software deals, marketing and communications support). The coaching and mentoring aspect focuses on access to market, technology, finance and talent. Additionally, imec.istart (often together with industry partners) offers market-specific support. The following figure depicts the overall imec.istart offering.

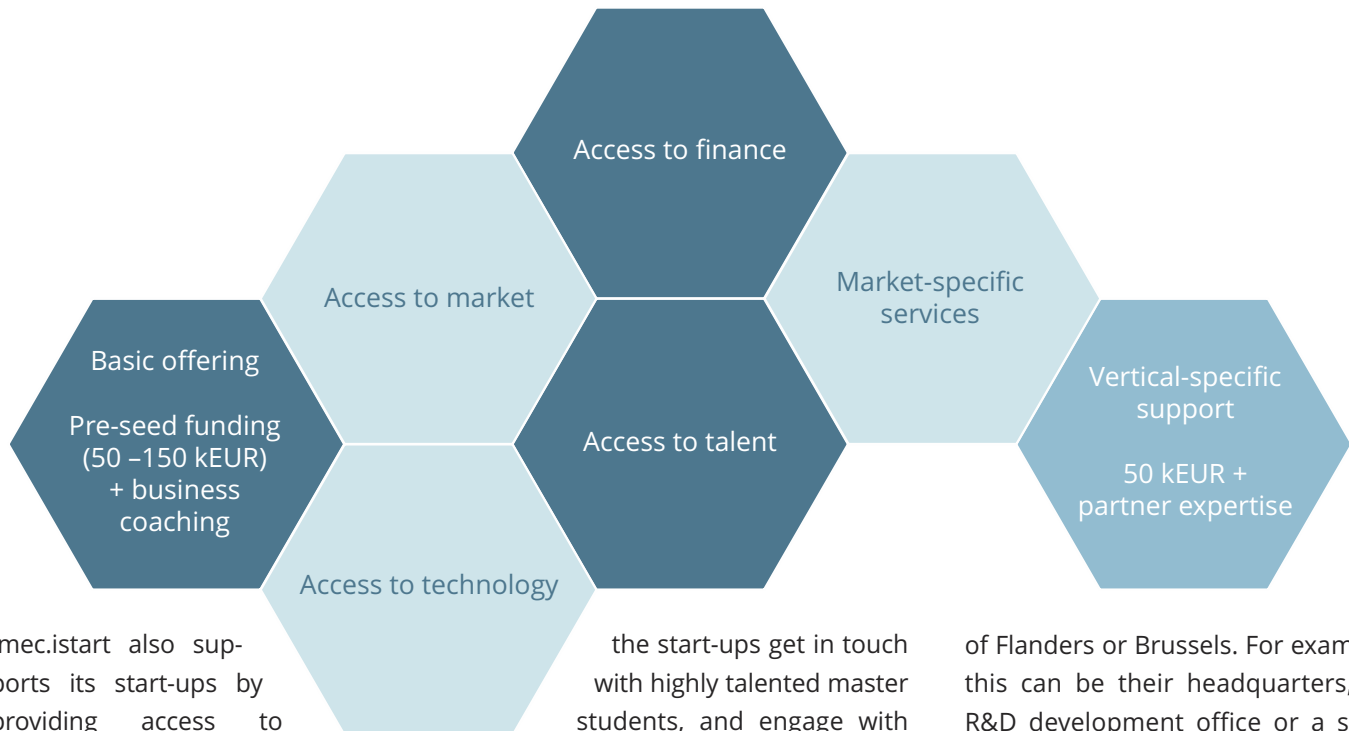
The basic offering of imec.istart consists of pre-seed funding of €50,000 (under certain conditions extendable up to €150,000), complemented with a substantial package of coaching and mentoring by experienced imec Innovation Managers and external industry experts. These coaches and

mentors advise the start-ups for an intensive 12- to 18-month period on all aspects of their business. Industry experts are used to cover specific topics, such as B2B sales, branding, legal matters related to fundraising, or intellectual property rights in start-ups. Additionally, the start-ups can count on marketing and communications support, housing, and additional perks and benefits provided by imec.istart partners (including software deals from amongst others Amazon, Google, Microsoft, Hubspot, Github, and many others).

This little start-up went to market

One of the 4 focus domains of the imec.istart programme is access to market. The programme helps start-ups prepare for the market launch of their first product(s), by challenging their business model, by helping them shape their pricing strategy or by suggesting the most optimal go-to-market strategy for their specific product(s). Imec's local and international network also provides invaluable introductions to help find reference customers or commercial partners.

Being primarily a research organisation combining the strengths of over 3,500 researchers, imec has a vast amount of innovative technologies in its portfolio. One of imec.istart's missions is to help its start-ups use these technologies by lowering the adoption barriers.



Imec.istart also supports its start-ups by providing access to finance, as most start-ups need additional funding to achieve growth. The imec.istart coaches advise the start-ups in developing a sound business and financial plan, help them practice their pitching skills and provide them with access to local and international investors. Different reports and benchmarks (including the 2015 benchmark by UBI Global and the Europe Scale-Up Report 2016 by Omar Mohout) have positioned imec.istart as one of Europe's most successful programmes in terms of creating scale-ups (i.e. start-ups that attract at least 1 million EUR in follow-up funding). Twice a year, imec organises an Investor Day to draw attention to some of its most promising start-ups.

Matching start-ups with mentors

Last but not least, the imec.istart programme aims at reinforcing start-up teams. In the first place, it helps the founders develop additional skills and acquire new knowledge through coaching, expert advice and workshops. Secondly, imec.istart has teamed up with partners that can help

the start-ups get in touch with highly talented master students, and engage with those as interns, freelancers and/or (future) employees. Last but not least, through its entrepreneur-in-residence programme, imec.istart matches start-ups with experienced entrepreneurs to join their teams.

For certain industries, mainly those in which imec.istart already has a few start-ups in its portfolio, market-specific services have been developed by imec and its vertical partners. In the healthcare industry, for example, additional workshops and experts are available to cover CE certification and/or FDA approval of digital innovations. In the media and entertainment industry, imec's partners open up their production systems or provide datasets to experiment with. Additionally, in this vertical, imec's partners can top imec's pre-seed investment with another €50,000.

Entrepreneurs from anywhere around the globe are welcome to join the growing community of 120 successful imec.istart start-ups, as long as they're willing to establish a substantial part of their business in the Belgian region

of Flanders or Brussels. For example, this can be their headquarters, an R&D development office or a sales office for Western Europe. Imec.istart has 3 application calls per year (in January, May and September).

More information can be found on [imec's website](http://imec.be/istart).



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Health research, from molecules to patients, at DCU

Director of Research Support Dr Ana M Terres notes the importance of health research and the strides being achieved by researchers at Dublin City University

Health is one of the cornerstones of the research and innovation activity at Dublin City University. Even in the absence of a medical school, health related publications represent a quarter of the overall university journal article output, and nearly 5% of the overall national output according to Scopus data. The activity is encompassed into 4 broad domains: Health technologies, molecular and biological mechanisms of health and disease, health and wellbeing interventions, and health service and systems research.

Health Technologies Research

From molecular neurotherapeutics for pain to pharmaceutical bioprocessing improvements, through to connected health interventions and sensor web technologies, the range of healthcare innovations for a healthy society developed at DCU is fairly comprehensive.

DCU hosts the first Irish Fraunhofer Project Centre for Embedded BioAnalytical Systems, in which 'Lab on a chip technologies' have a wide range of applications including the development of point of care diagnostic devices to enable personalised healthcare. An initial investment of €5M co-founded by Science Foundation Ireland and Fraunhofer, and led by Prof. Jens Ducree, will focus on applied solutions that can readily translate to the market place. DCU has an established track record for the application of smart molecules

and materials as sensors for health applications (Prof. Robert Forster, Tia Keyes, Dermot Diamond, Richard Kennedy, etc), much of which will represent the basic science pipeline which will complement the more applied research and innovation activities at the Fraunhofer project centre.

At the DCU International Centre for Neurotherapeutics, Prof. Oliver Dolly is developing the next generation of biotherapeutics to treat chronic pain. His approach involves molecularly engineered modifications of the botulinum toxin which actively inhibits neuro exocytosis of neurotransmitters involved in the transmission of pain. These potent molecules have been proven to have prolonged relief of neuropathic pain in rodents and will be tested in clinical trials in the very near future.

Other novel approaches to health improvements at DCU, to name a few, include the development of plasma technologies for hospital acquired infections and the development of stem cell therapies for ocular disease. Biomarker discovery and biopharmaceuticals production is also a strong research area at the DCU National Institute of Cellular Biotechnology, where one of the strands lead by Prof. Martin Clynes and Dr Paula Meleady focuses on improving the production of protein based biopharmaceuticals in bioreactors in order to lead to more

efficient and cheaper processes and, in turn, greater accessibility for patients.

DCU bio-mechanical engineering expertise also contributes to advances in health research. Examples include Prof. Nicholas Dunne's research, which focuses on the development of biomaterials for drug delivery as well as biomaterials for orthopaedic applications. Or, Prof. Owen Clarken's work on hydrogel based composite materials for the treatment of vascular diseases, including cerebral aneurysms and other cardiovascular conditions.

Molecular and biological mechanisms of health and disease

A significant body of work focuses on immunomodulation and the regulatory immune responses associated with a number of health conditions. Prof. Sandra O'Neill's work studies the immune response to worm parasites and aims to discover potential vaccine candidates to protect against helminth infections. The immune response associated with infection by the influenza virus is the focus of Prof. Patricia Johnston while Prof. Christine Loscher's research concentrates on the impact of nutritional compounds and food in the immune system, in order to understand the molecular mechanisms of actions with a view of using these natural products to modulate inflammation in a number of immune-mediated diseases.

Prof. Anne Parle-McDermot's research focuses on the understanding of folate nutrition for human health. By using a combination of genetics, genomics, biochemistry, and cell biology the group aims to understand the importance of folate from pregnancy to ageing with a view to help prevention, diagnosis, and the treatment of common conditions associated with folate deficiency.

The molecular and biological mechanisms of cardiovascular disease, diabetes, and associated conditions are also the focus of much activity. Prof. Paul Cahil aims to find novel targets for therapeutic applications for CVD by focusing on specific intracellular signalling pathways in the endothelial cells. Prof. Phil Cummins is involved in a US-Ireland partnership which brings together a unique set of expertise to develop a gene therapy for diabetic retinopathy, a widespread complication of diabetes.

Disease prevention, Health and wellbeing

Research within this theme is mainly carried out in the Schools of Health and Human Performance (SHHP), Nursing and Human Sciences (SNHS), and Biotechnology.

Much of the research at the SHHP focuses on the understanding of the mechanisms by which exercise can be used to prevent disease and improve life expectancy and recovery in patients suffering from chronic illnesses, such as cancer, CVC, or diabetes. Prof. Kieran Moran leads an EU funded collaborative project that aims to provide individual technology enabled exercise pro-

grammes to promote cardiac rehabilitation. This is done through the provision of an internet-enabled sensor-based local exercise platform which allows participation in the programme from the comfort of their own home. Prof. Ronan Murphy's team is trying to unravel how genetics, diet, and exercise can be used to manage chronic illness, while Prof. Donal O'Gorman's research focus is on the impact of exercise on the regulation of energy metabolism in the body, key information to understand how diabetes may be prevented and alternatively treated.

Since 2006, and based on this vast expertise, the university runs MedEx Wellness, a novel community-based chronic illness rehabilitation programme which is one of the largest programmes of its kind in Europe. Located in the University Sports facilities, it offers medically supervised exercise classes and educational workshops on nutrition to patients with a range of chronic illnesses.

Research in the SNHS spans many areas of health and well-being, including children's public health (Prof. Anthony Staines), dementia and positive ageing (Prof. Kate Irving), mental health (Profs. Evelyn Gordon and Liam MacGabhann) and behavioural neuroscience (Profs. Teresa Burke, Lorraine Boran and Sinead Smyth), nutrition and exercise (Prof. Mary Rose Sweeney), health and sexuality (Prof. Mel Duffy), ethical issues and health care (Profs. Donal O'Mathuna and Bert gordijn), and living well with illness and disability (Profs. Pamela Gallagher, Veronica Lambert and Gemma Kiernan).

Between 2014 and 2017 nearly 7% of nursing related publications from DCU were in the top 1% most cited publications worldwide, vs a national average of 1.9%.

Health Systems and health service research

Health Systems research at the SNHS, lead by Prof. Anthony Staines, Anne Matthews, and Pamela Hussey, centres around a variety of topics, such as eHealth, with a view to support integrated health and social care, health workforce planning and intelligence, as well as evidence based practice. At DCU Business School, Prof. Regina Connolly has significant expertise in healthcare technology impact assessment, as well as in eHealth Business model development, and is the lead investigator in several Ambient Healthcare Technology research projects.



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NSERC: Advancing science and technology in Canada

Open Access Government's M F Warrender highlights the work being undertaken by NSERC to pioneer scientific advancement in Canada

Science and technology are now driving forces within discovery and innovation sectors all over the world, with countries constantly matching and surpassing one another's technological advances. This has established a fast moving and cutting-edge platform for new innovations everywhere, and therefore constantly shaping the world we live in. Canada is one of these many countries on the brink of an exciting, dynamic, and prosperous future, as it refines its vision and further develops its Natural Sciences and Engineering Research Council (NSERC). The goal is to ensure that Canada can continue producing major discoveries and building upon the foundations of economic growth within a rapidly changing world.

The NSERC was formed in May 1978, and is an agency that provides grants for research in natural sciences and engineering. It is governed by a council composed of the President along with up to 18 members appointed from both private and public sectors. In June 2014, B. Mario Pinto was appointed the president of NSERC, and one year on from his election, he spoke of the NSERC's achievements, primary aims, and future plans. He stated: "NSERC creates value for Canada by investing in scientific inquiry and discovery research. This is at the core of NSERC's mandate. In doing so, we have established the powerful brain trust needed to fuel this country's knowledge-based economy." He also illustrated in detail the 5 clear goals that will be pur-

sued through his launch of NSERC 2020: a “strategic plan” to promote science and technology as the primary enablers in pushing Canada forward.

Key strategies for 2020

The 5 strategies established to push NSERC to where it wants to be in 2020 are:

- 1. Foster a science and engineering culture in Canada** (in order to make science and engineering mainstream, thus increasing interest, awareness, and appreciation of science as a way of experiencing, understanding and enriching the world).
- 2. Launch the new generation** (in order to enable early-career scientists to launch independent research careers).
- 3. Build a diversified and competitive research base** (to stimulate breakthrough research, and connect expertise across populations, institutions and sectors).
- 4. Strengthen the dynamic between discovery and innovation** (deepening interactions between its own partnerships).
- 5. Go Global** (in order to increase international research endeavours through the solidifying of Canada’s access to global scientific and engineering knowledge).

Thus far, the NSERC has built many strong partnerships across the research and innovation ecosystem in Canada, embracing and connecting the private sector, universities, colleges, government led research labs, training partners, and other non-governmental players. Students, in particular, play a vital role in fuelling research and discovery, and the NSERC provides many with industry experience and business skills, benefitting both the students and the industries themselves. It is important to note that 1 in 3 companies’ hire a student trained under NSERC partnership programs in Canada, and there have also been efforts to work with the research and development sectors of other countries worldwide. Most recently, as part of NSERC 2020 in

May this year at the 6th Annual Meeting of the Global Research Council, President Pinto finalised changes to strengthen collaborative research and training ties for students, with President of the German Research Foundation, Dr. Peter Strohschneider. This will create opportunities for student exchanges between Canada and Germany, maintaining a strong working relationship between the 2 countries. In Canada, 10,000 students trained each year in industrial settings, and increasing the levels of collaboration with other countries will without a doubt widen these students’ future opportunities.

Boosting Canadian research

Presently, countries all over the world are both competing and working together to maintain a prominent presence within this ever-growing sector. Through the NSERC, Canada is able to boost private sector research and development, and also focus on small and medium sized enterprises (SMEs), which, more often than not, have difficulty in making the transition into growth companies, and therefore use partnerships through the NSERC to scale up. Today, 97% of companies that have used NSERC’s partnership programmes would recommend them to others, and NSERC 2020 will continue to further improvements through its set of goals. However, its aims are perhaps best summed up by the president himself: “It seeks to maximize the efficacy and extend the reach of existing tools, while also taking advantage of new modalities. With the new strategic plan, NSERC 2020, we can contribute to positive change.” ■

M F Warrender

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The development of low-permeability hydrocarbon resources

Professor and NSERC/Chevron Industrial Research Chair, David W. Eaton, talks about the need to ensure hydrocarbon resources are developed responsibly

Fossil-fuel supply chains have been radically altered by unprecedented development of low-permeability hydrocarbon resources (LPHRs), especially North American shale gas, tight oil and, more recently, liquid-rich shale plays. Access to these vast low-permeability hydrocarbon energy resources has been driven by new technologies, primarily massive, multi-stage hydraulic fracturing and long-reach horizontal drilling. While there are opponents and proponents of the development of LPHRs, it is generally much less controversial in jurisdictions that have a legacy of oil and gas activities. Even so, the deployment of these disruptive technologies has, to a large extent, outpaced the advancement of fundamental scientific understanding of underlying physical processes as well as the capacity of agencies to implement science-informed regulations.

How can economic, environmental and social considerations be brought to bear on these complex issues? The concept of responsible development entails a holistic approach in which environmental, economic and social considerations are integrated, based on transparent, science-informed regulations that inspire public confidence. This article applies this philosophy to key aspects of scientific research and training of highly qualified personnel that are essential for responsible development of LPHRs, within a framework that embodies the need to

reduce environmental impacts, as well as resource intensity.

Improved efficiency

Commercial extraction of LPHRs is enabled by the drilling of horizontal wellbores that are completed in multiple stages using massive (typically water-based) hydraulic-fracture stimulation treatments. Current practice in the unconventional oil and gas industry uses a 'factory' design philosophy with uniform spacing of stages along the wellbore, and is trending toward increasing the number of fracture stages along with increasing the net injected volume. Further, horizontal laterals are being placed closer together in the horizontal plane, and vertically in the development of "stacked" LPHR plays. This trend places enormous stress on resource utilisation, including water use, as well as energy required for resource extraction. Research is currently underway to support the development of enhanced fracture-design and surveillance technologies, based on new geophysical, well-test, and geochemical imaging techniques combined with laboratory measurements of reservoir properties, displacement phenomena, and modelling through digital core analysis. The goal of this research is to develop a more efficient approach that combines reservoir ('sweet spot') targeting with improved fracture surveillance and numerical simulation methods, such that less intensive but more effective hydraulic fracturing stimulation can be achieved.

Environmental impacts

Natural gas derived from LPHRs is sometimes promoted as a cleaner fuel that could enable a smoother economic transition away from coal towards renewables. The effectiveness of this strategy, however, depends upon the amount of methane emitted into the atmosphere ('fugitive emissions') from resource extraction processes and delivery to the customer. Intensive use of hydraulic fracturing for LPHR development has also generated public concerns regarding the potential contamination of surface waters and groundwater's and soils. These concerns arise from the potential for groundwater contamination due to fugitive gases that escape from the wellbore and/or contamination from flow back fluids containing saline formation waters and chemicals used during hydraulic fracturing.

A significant impediment to informed public debate is a general lack of quantitative data, including baseline groundwater data. Furthermore, knowledge is lacking concerning effective and scientifically defensible approaches for accurate assessment of potential environmental impacts on shallow freshwater resources and the atmosphere associated with the development of LPHRs. Together with improved extraction efficiency, the acquisition of new data and development of improvement regional and local monitoring technologies are topics of ongoing collaborative research.



Induced seismicity

Earthquakes induced by activities linked to LPHR development have galvanised public attention. Despite vigorous research since the 1960's on the topic of injection-induced earthquakes, fundamental questions remain unanswered. For scenarios, other than hydraulic fracturing, the basic triggering mechanism of injection-induced seismicity is thought to be a pore-pressure increase within a diffusively expanding region. Fault activation by hydraulic fracturing is more complex and even a basic understanding of the phenomenology requires improved knowledge of fracture and fault characteristics over a wide range of spatial and temporal scales. The challenge is exacerbated by the subtle expression of potentially active faults using existing imaging techniques. Finding science-informed solutions is an urgent priority for industry and regulators.

In Canada and elsewhere, regulations are largely based on ad hoc traffic light protocols (TLPs), which mandate operational changes (or complete shutdown) in response to uncertain

observed parameters, such as computed magnitude and proximity of the event to the injection site. Provisions for TLPs have been developed by combining current industry best practice with trial-and-error; arguably, such an approach is not conducive to scientific innovation – or fostering of public confidence in the regulatory framework. Underlying this is the issue of how to mitigate and to manage risks of induced seismicity from hydraulic fracturing. Solutions will demand a departure from a business-as-usual approach to academic research.

Collaboration and interdisciplinary training

There are several common cross-cutting issues that need to be addressed in order to achieve the goal of responsible development of LPHRs. First, the development of improved scientific understanding needed to inform industry practices and regulatory frameworks, and to deal with complex associated socioeconomic issues, will require an open dialogue and extensive cross-sector collaboration between

academia, industry and government. Moreover, the next generation of leaders who are critically needed to implement the global energy transition must draw from exceptionally broad interdisciplinary understanding of the relevant issues. Timely progress means that these leaders must possess both a depth of expertise developed within traditional science and engineering disciplines, together with a complementary breadth of experience working with business, legal and social-science paradigms.

Reducing the impact of fossil-fuel extraction

A fundamental transformation of global energy systems is essential in order to achieve the ambitious goals of the 2015 Paris Agreement on climate change. Global energy demand is increasing; even with aggressive deployment of renewables, fossil fuels will continue to provide a major contribution to global energy supply over the coming decades. There is therefore an urgent need to reduce greenhouse-gas emissions and other environmental impacts of fossil-fuel extraction.



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Measuring the impact of science and research in Ontario

Minister Reza Moridi explains how Ontario is bridging the divide between ideas and application when it comes to science and research

On Earth Day this year, more than 1.3 million people in 600 cities around the world marched to celebrate science and support its public funding. It was remarkable to witness these events because people don't usually get excited about science.

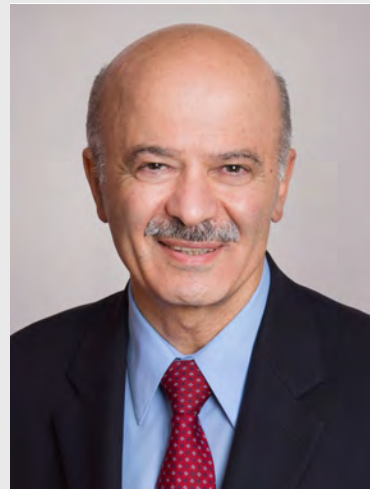
But citizens are increasingly worried that the global progress we have made in combatting the negative impacts of climate change will be destroyed in short order by a recent wave that rejects science as fact and advocates for a rollback in funding of scientific research. Science is under attack.

As an elected official in Canada's largest province, and as a scientist, I am deeply concerned with this trend. Governments have a responsibility to act in the best interest of their constituents by tackling the key challenges that impact everyday lives. Most importantly, this includes our health and the environment; but it also includes the economy, which bridges the divide between fundamental scientific ideas and their practical application.

Ontario is a haven for scientists. That's because we provide them with an environment in which they are free to push the boundaries of innovation. We support the full cycle of research – from the seeds of discovery to commercialisation and global market access.

Global leader

Ontario understands that a knowledge-based economy is the key to health and prosperity, and that scientific innovation and economic growth are closely linked. That is why the provincial government works hard to attract the best and brightest innovators and researchers from around the world, keep home-grown talent here and seize opportunities for global leadership.



Reza Moridi, Minister of Research, Innovation and Science

To build sustainable economic and social prosperity, Ontario has made strategic investments in:

- Supporting world-class research and scientists at Ontario's leading-edge institutions;
- Building and strengthening an entrepreneurial ecosystem to accelerate the start, growth and success of Ontario's innovative companies;
- Catalysing a stronger returns-based risk capital industry to support the growth and retention of Ontario's innovative firms, and;
- Ensuring that youth have the skills needed to excel in the modern economy.

Our combined investments have been mobilising and preparing Ontario researchers, entrepreneurs and firms to succeed, compete and create the jobs of the future.

We are making headway. The measured impact of Ontario research is well above the world average. With Ontario comprising nearly half of the research enterprise

in Canada, the nation ranks sixth in the world in quality and impact of research. As well, Ontario incubators/accelerators are ranked among the top in the world.

We are also in the process of hiring a Chief Scientist to help the government work smarter and better by relying on evidence and research, feeding the world's best ideas into government policies and programs. The Chief Scientist will formulate a long-term vision and strategic research agenda for Ontario that will help address future challenges and advance the scientific frontiers in Canada and around the world.

Collaborative approach

Ontario's universities, colleges, academic hospitals and research institutes are vital partners with government in ensuring the province remains at the forefront of the global knowledge-based economy. Ensuring that these facilities have modern infrastructure and consistent, predictable funding for research operations is the best way to facilitate the collaboration of businesses and researchers in critical economic sectors. Ontario's flagship research funding program, the [Ontario Research Fund](#) has 2 streams:

Research Excellence, which funds total direct and indirect research operational costs, with an emphasis on projects of significant impact to Ontario.

Research Infrastructure, which makes investments in cutting-edge research facilities and equipment.

Since 2003, the Ontario Research Fund has leveraged over \$3.8 billion in funding and helped create more than 103,000 training opportunities.

We also support scientists through the [Early Researcher Awards](#) program, which helps promising recently appointed Ontario scientists build their research teams. This world-leading, multidisciplinary program is investing in, generating and attracting a workforce with first-rate skills in science, engineering, creative arts, business and entrepreneurship.

Since the program's inception in 2005, Ontario has given 978 Early Researcher Awards to the province's leading early career researchers, invested approximately \$136 million in award recipients and leveraged over \$48 million in private and public sector partnerships.

This year, our support will help research initiatives such as:

- Improving brain flow and function after cardiac arrest;
- Developing cost-effective ways to recover metals and reduce the environmental impact of mine waste; and
- Evaluating the impact of social media technology on mental health awareness.

Since receiving his Early Researcher Award, Dr. Jason Fish, Scientist at the University Health Network's Toronto General Hospital Research Institute, has rapidly established himself as an emerging world leader in understanding how inflammation leads to heart disease. This research has established an entirely new paradigm in how cells communicate within the cardiovascular system. Dr. Fish continues to leverage his award to attract external funding, train research talents and translate the knowledge gained from his research to the clinic and marketplace.

I invite you to visit the [Ontario Ministry of Research and Innovation](#) website for more details on the work we are doing to sharpen our competitive edge.

By fostering scientific discoveries, including new technologies, treatments and cures for illnesses, Ontario is mobilising and preparing our researchers, entrepreneurs and firms to succeed, compete and create the jobs of the future. ■

Reza Moridi

Minister of Research, Innovation and Science

Ministry of Research, Innovation and Science – Ontario

www.ontario.ca/page/ministry-research-innovation-and-science

[www.twitter.com/OntInnovation](https://twitter.com/OntInnovation)

Focusing on high quality research in Sweden

Open Access Government's MF Warrender shares how Education Minister Helene Hellmark Knutsson is ensuring high quality research in Sweden occurs

The Ministry of Education and Research in Sweden has a staff of 200 who work together in areas such as education, research, and youth policy. The government's most recent plan for strengthening its innovative capacity in these areas is highlighted in last year's presentation of the research policy bill: "Collaborating for knowledge – for society's challenges and strengthened competitiveness." The bill presents the government's view on the direction of research policy for the following decade, focusing in particular on measures in 2017-2020. Some of the main goals of the bill include basic appropriations to higher education institutions; initiatives in research linked to global societal challenges and increased resources to strengthen Sweden's innovative capacity.

Helene Hellmark Knutsson, has been the Minister for Higher Education and Research in the Swedish government since October 2014, and stressed the bill's significant focus should be high-quality research, and long-term conditions for researchers, rather than pressure for quick results. She states that the primary aim of research policy is for Sweden to be one of the world's foremost research and innovation countries, as well as a "leading knowledge nation" where high-quality research, higher education and innovation leads to society's development and welfare, the business sector's competitiveness and responds to the societal challenges we face, both in Sweden and around the world.

Knowledge nation

The proposed autumn budget will ensure Sweden's status as a knowledge nation, with the government announcing an increase in the appropriations for research and innovation of over SEK 3 billion until 2020. With this budget, the bill plans to safeguard free research, prioritise research in areas such as climate, health and life sciences and digitalisation, and also

increase research quality within schools through practically-based research. Furthermore, by increasing and distributing basic appropriations, the Swedish Research Council will enable higher education institutions to play a larger part in being responsible for the long-term responsibility of research.

"The Ministry of Education and Research also maintains its prominence in the area of space, with the Research Bill containing a large section which deals with space activity. There are several exciting projects underway in the field of space, in both Sweden and Europe, where a few processes are ongoing that will be of major significance to Swedish and European space activities in the future."

Hellmark Knutsson is quoted on the overall importance of education and research. She said: "Knowledge is the foundation of positive societal change and our primary means of competing internationally. Sweden must compete on the basis of knowledge and skills – not low wages."

Gender equality

The bill also aims to fuel the government's plans to strengthen gender equality – a difficult but vital target to achieve within research. To work towards the objective, a number of measures are being carried out; for example, creating new and more ambitious recruitment targets for professors. This stress on gender equality and the underrepresentation of women in leadership positions within academia is reinforced through a speech made recently by Hellmark Knutsson at the 5th European Women Rectors Conference in May. She speaks of raising awareness of this gender gap, making reference to Sweden as having "the world's first feminist government," and stresses that "the goal of gender equality policy is a very high prior-



ity, with lots of work to be done.” The share of female professors today in Sweden is only 27%, despite the fact that more women than men attend and graduate from higher education. This needs to improve drastically. One way of doing this is Sweden’s strategy of gender mainstreaming, which is absolutely crucial to make a change. The strategy is a way of ensuring that all policy making has a gender equality perspective and analysis, and is a policy that lies at the heart of their work. The minister ends her speech with the inspiring words: “Let us do that and continue to fight the inequality within academia today. The world needs more science and science needs more women.”

Space research

The Ministry of Education and Research also maintains its prominence in the area of space, with the Research Bill containing a large section which deals with space activity. There are several exciting projects underway in this field, in both Sweden and Europe, where a few processes are ongoing that will be of major significance to Swedish and European space activities in the future.

It is important to remember the value of research into space activities and how vital these developments and innovations from the space sector can be to many other areas. Deeper interdisciplinary cooperation will increase with a deeper focus on space, as it often inspires an interest in technology and science among young people, engendering them to enter the world of education in the areas of engineering or research. ■

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A roadmap of graphene on SiC

Rositsa Yakimova, of the Department of Physics, Chemistry and Biology (IFM) highlights the strides being made in graphene research

Since the beginning of the new millennium, the properties of graphene stand at the forefront of the fundamental physics and device-oriented research. Although physicists had predicted the unique properties of this material half a century ago, its existence has been questioned or even denied until its demonstration by mechanical exfoliation of highly oriented pyrolytic graphite. Being an electron-rich pi system, graphene possesses unprecedentedly large carrier mobility. This gave promises of tremendous outperforming of the traditional Si-based electronic devices. While graphene physics has enjoyed numerous discoveries made on exfoliated graphene as a unique free-standing 2D material, the demands for practical applications have shifted the focus over the years. Currently scientists are mainly exploring graphene diversity, including a wide class of low dimensional graphene-related materials (quantum dots, nanoribbons, heterostructures, conductive paints, composites) possessing tunable and narrowly specific properties enabling definite applications. In spite of the increased availability and quality of the varying-sized/shaped graphene, further progress towards electronic components and systems requires integration with different substrates. To this context, epitaxial graphene on SiC that can be formed on semi-insulating (SI) and conductive substrates has appeared on the 2D materials scene as a non-

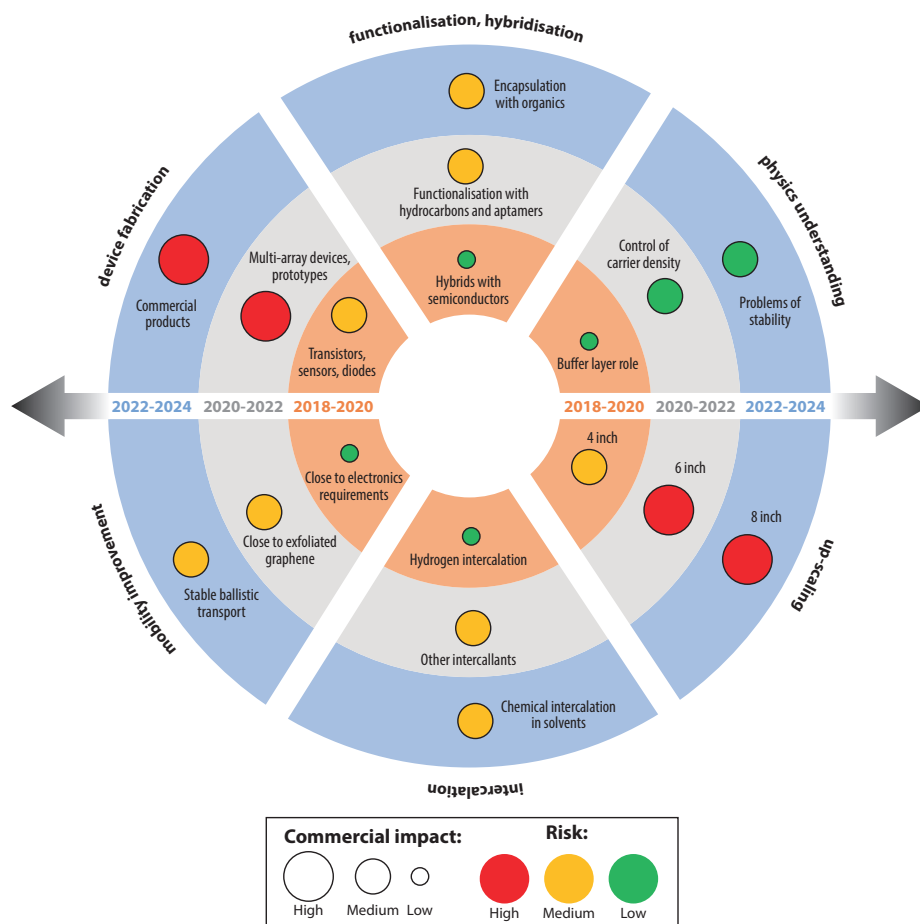


Fig.1 The roadmap of future development scenarios in studies and commercialization of epitaxial graphene on SiC. Varying-sized empty circles designate the expected commercial impact as a result of the achievement of interim goals. Varying-colored circles correspond to estimated risks related to technological challenges.

alternative multifunctional product offering a unique complementary combination of self-assembled graphene layers with a SiC template.

Silicon carbide sublimation

In recent years, the experimental and theoretical studies of Si sublimation from the topmost layers of SiC, and rearrangement of the remaining

carbon atoms under specific temperature and pressure settings elucidated the conditions to grow well-ordered epitaxial graphene. During the past decade, Si sublimation technique realised via thermal decomposition of SiC has developed from a facile graphitisation technique to a scale-up production of large-area high-quality monolayer graphene

along with the advancements of highly-precise characterisation methods and corresponding theory. A breakthrough was made in 2008 when large area (mm scale) monolayer graphene on SiC was produced, as has been published by the research group at Linköping University (graphene being processed in the laboratory headed by Prof. Rositsa Yakimova). The most outstanding results concerning the epitaxial graphene are related to the demonstration and application of the unique half-integer quantum Hall effect (QHE) with an unprecedented robustness and precision (2010). In 2015 for the first time measurements of the QHE with part-per-billion (ppb)-accuracy was demonstrated in a small table-top cryogen-free pulse-tube system. "Both the longitudinal resistivity R_{xx} and the contact resistance R_c were well within the limits set by the guidelines for primary resistive metrology" said collaborators from NPL, UK who built up the system [R. Yakimova et al. Operation of graphene quantum Hall resistance standard in a cryogen-free table-top system – 2D Mater. 2 (2015) 035015]. The design and the technical features of the system are easy-to-use and do not require particular experimental skills or laboratory infrastructure, thus significantly advancing production and utilisation of primary quantum standards for precision electrical metrology. Such achievements have been possible only due to the unique properties of the epitaxial graphene on SiC.

Profound studies of graphene on SiC have boosted the discovery of many

new physics effects, e.g. magnetic quantum ratchet effect, extremely unusual nature of the carriers, non-trivial magneto-electronic properties, interface-related phenomena, and so on. Furthermore, graphene on SiC allows easy patterning which is used to process, in fact, new materials that is graphene nanoribbons possessing the potential for digital device manufacturing. All these phenomena being graphene on SiC hallmarks are prerequisites for controllable and exclusive manipulation of the graphene/SiC interface towards the design of different high-performance magnetic and electronic devices. In 2011 the first commercial unit in Europe for graphene on SiC production, Graphensic AB was founded by R. Yakimova and co-workers as a spin off company from LiU, with the aim to link the fundamental research and industrialisation of 2D materials. One of the steps undertaken towards large scale graphene production is the construction of a growth equipment for epitaxial graphene on 100 mm SiC wafers and the development of a technological process.

A roadmap for advancement

Despite the large progress that has been made towards graphene globalisation, a roadmap to further advance the epitaxial graphene research is still needed to enable the transition from crude device prototypes to the customer needs. Bearing in mind the already existing concepts and focusing on novel ideas, herein we are proposing a framework for future investigations addressing commercialisation challenges of the epitaxial

graphene grown on SiC substrates by their thermal decomposition.

According to our vision efforts should be dedicated to physics understanding, carrier mobility improvement, intercalation, functionalisation, device fabrication, and up-scaling. The roadmap shown in Fig. 1 covers a 6 year period and includes the mentioned development areas which are expected to have the highest impact on graphene commercialisation. In each area of interest 3 evolution stages with increasing demands are presumed. The roadmap is also accounting for eventual risk factors which may lead to a time delay in a realistic perspective.

We believe that the knowledge of state of the art of graphene on SiC should reach the policy makers in Europe and must be considered with a priority in funding distribution for the next 10 years.

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Supporting basic research in Switzerland

Basic research is a key area that the Swiss National Science Foundation (SNSF) promotes and funds, as Open Access Government's Ciara Ruane outlines

The Swiss National Science Foundation (SNSF) primarily supports basic research: i.e., research that is not tied to a specific institution or industry, but seeks to improve knowledge overall. The SNSF describes the projects they fund as ‘use-inspired’, which means research that aims to provide practical solutions to problems.

Use-Inspired Basic Research (UIBR) differs from standard basic research in a number of ways. The SNSF defines it as dual-purpose, with an aim to “solve or illuminate one or several practical problems, as well as advancing science”. Applications marked UIBR face a more selective process and are less likely to be successful than others. Last year this approach was

evaluated by an independent consulting firm called Technopolis, focusing on their definition of UIBR. The report stated that the introduction of the UIBR category in 2011 had allowed the SNSF to broaden the scope of their research and did not require an overhaul. However, it recommended that the category be defined ‘more clearly’. They also stated that the reduced success rate of UIBR applications could be attributed to the complexity of the dual-purpose approach. It also suggested more diverse selection panels and a greater emphasis on the ‘broader impact’ criteria outlined under UIBR.

Encouraging young people into research

The SNSF places a great deal of emphasis on encour-

aging young people to pursue careers in research and development. They outlined a [2013-2016 action plan](#) to best achieve this. They emphasise a 'career friendly' approach, removing obstacles and restrictions that make it difficult for young people to secure a permanent role below the level of a professorship. The aim outlined was to increase doctoral student salaries by 7%, increase the potential for promotion, and provide support for doctorate students with families. The '120% model' is aimed at those who have childcare obligations impacting their work, and allows them to work reduced hours with the chance to apply for childcare funding.

“The SNSF places a great deal of emphasis on encouraging young people to pursue careers in research and development.”

The SNFS has different funding programmes available for researchers at different stages of their career. [They have a guide](#) on which programme is best suited to the individual, detailing the level of study, the nature of the test, and what resources are required. The overall aim is to provide complete flexibility for applicants, allowing people in a multitude of different circumstances to pursue a career in research and development. They also have international study schemes available, through partnerships with countries in Asia and Eastern Europe. They hope this allows young researchers the opportunity to study in a new environment and build an international network for Switzerland within the scientific community.

Ethical practices

The SNFS makes a strong point of reinforcing ethical practices. In 2014 they published a document detailing their use of [animal testing](#). The SNFS follows the guidelines laid out by relevant authorities and does not get personally involved with decisions on the ethics of animal testing in individual research projects. The report states that animal testing makes up for a small part of the research process, and currently there is no effective alternative available for most experiments. However, they state that animal suffering “must be kept to a min-

imum”, and researchers often use alternative models such as cell structures. They state that they welcome debate on the issue, but distance themselves from ‘misinformation’.

Gender equality

The SNFS takes a firm stance in favour of gender equality. Their [statement on the issue](#) outlines a ‘gender neutral’ atmosphere they hope to create, with a zero-tolerance policy towards any form of prejudice. They have a number of legislative actions aimed to enforce this goal. They have a gender equality grant, specifically targeted at young women researchers, a ‘non-discriminatory pay system’, work-at-home options to balance family life, and carries out regular evaluations to ensure equality is being maintained. These efforts are ongoing, and the SNFS places responsibility on the highest levels of the organisation. This goes alongside their aim of encouraging all young researchers and creating a more forward-thinking research community. ■

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Declining fish stocks: complex pathways of toxic chemical impact

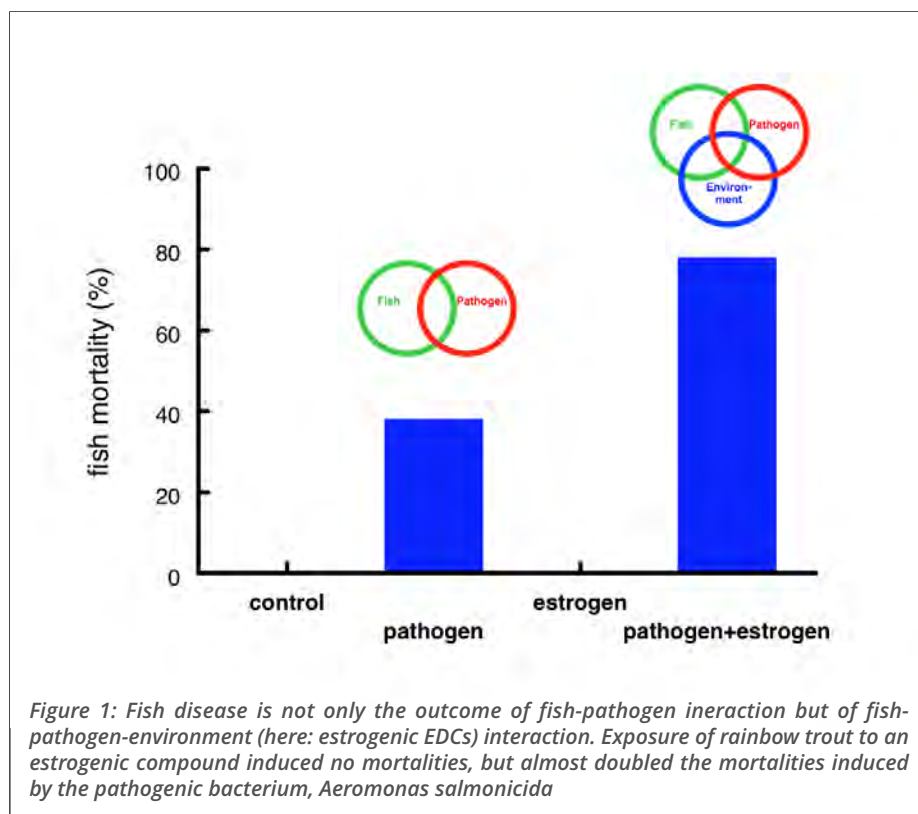
Profesor Helmut Segner at the Centre for Fish and Wildlife Health discusses the possible role of chemical pollution in the decline of freshwater fish stocks

Freshwater fish stocks are experiencing a worldwide decline. In fact, during the twentieth century, freshwater fishes had the highest extinction rate among vertebrates. In order to take action against the drastic loss of fish diversity, it needs an understanding of the causative factors.

One factor that has been associated with decline in fish stocks is the chemical pollution of freshwaters. Catastrophic events, such as acute fish kills, as well as the extinction of many fish species during the 1950s and 1960s in European and Northern American freshwaters, created concern on the possible adverse consequences of toxicant release into the aquatic environment. Many of the adverse effects observed were caused by “macro pollutants”, which were found at high concentrations ($\mu\text{g/L}$ to mg/L) in freshwaters.

“Diseases are a key factor in controlling fish population abundance, but this mechanism can get dysfunctional in combination with anthropogenic stressors such as toxic chemicals or global warming.”

Measures such as chemical regulations and improved wastewater treatment technologies have led to a substantial reduction of freshwater pollution by macro pollutants. However, with this the issues caused by “micro pollutants” (ng/liter to low mg/liter) became evident. Micro pollutants include

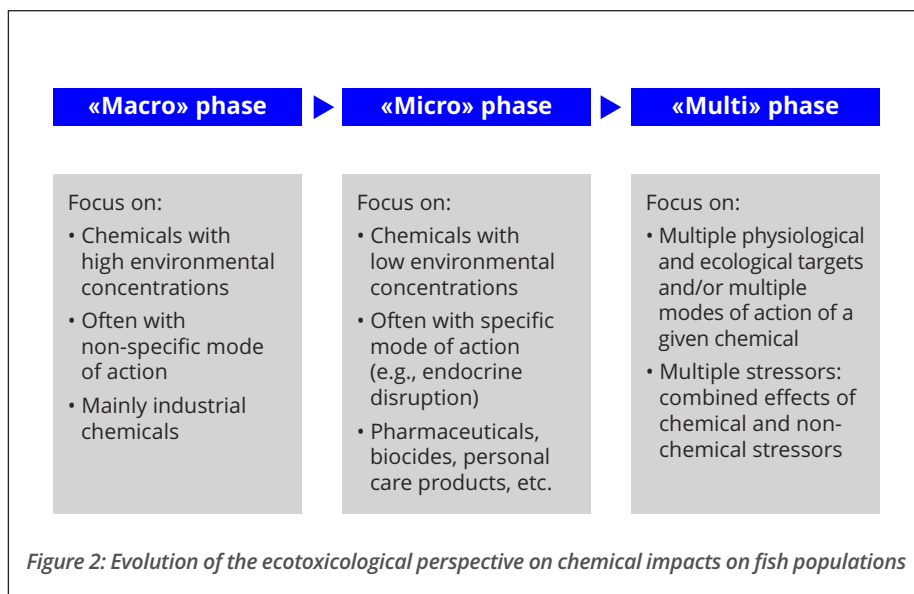


substances such as pharmaceuticals which are biologically active at (very) low concentrations, and can affect fitness traits such as reproduction or behaviour, which are critical for population recruitment. An example to the case are endocrine-disrupting compounds (EDCs). Attention to EDCs was sparked by numerous observations on developmental abnormalities and reproductive dysfunctions in fish and in other wildlife species which were caused by the interference of the EDCs with endogenous hormone metabolism or action. Particularly estrogen-active compounds such as 17β -estradiol (E2) or the contraceptive pill component, ethinylestradiol (EE2),

which are excreted via urine and reach the aquatic environments via sewage treatment plants, were found to disrupt sexual differentiation and reproductive fitness of fishes. A compelling study on the impact of estrogen-active compounds on fish populations was conducted in Canada where a whole lake was contaminated with EE2 (at approximately 5 ng/L), leading to recruitment failure and extinction of the fathead minnow (*Pimephales pimephales*) population.

The fish immune system

While the majority of research and regulatory actions on EDCs focused on their effects on reproduction, hormones



have multifaceted actions and regulate a broad variety of biological functions, and thus may impact fish stock populations through a variety of physiological pathways and life history traits. One potential target system of estrogenic EDCs that our group has been focusing on recently is the immune system. An immunomodulatory role of estrogens is well documented in mammals. Our research also revealed that in fish, immune pathways and functions are under estrogen regulation. This leads to two key questions: first, what are the relative sensitivities of the reproductive and immune systems of fish to estrogenic EDCs? In previous studies, our group could show that, for instance, EE2 disturbs the sexual development and reproduction of fish at the environmentally realistic concentrations of 1-2 ng/L. Such low concentrations appear to be immunodisruptive as well. This means that an exposure scenario that would induce reproductive disturbances of fish would simultaneously interfere with immune functions. This leads to the second question: are there adverse consequences of an estrogen-induced disturbance of the

fish immune functions? Adverse effects of estrogen exposure become evident not necessarily in the resting immune system, but after a challenge with infectious pathogens as an additional stressor. In their environment, fish are constantly exposed to pathogens. Under favorable conditions, the fish immune system is able to fight (most of) these agents to prevent disease. However, under unfavorable conditions, for instance, under co-exposure to estrogenic EDCs, the fish may become susceptible to the infectious agent and disease develops. In fact, we could demonstrate that fish exposed to estrogenic EDCs show a higher infection prevalence, stronger disease intensity and elevated disease-related mortalities after pathogen exposure when compared to non-exposed fish (see Figure 1). The conclusion from this is that estrogenic EDCs may impact fish stocks not only via impaired reproduction, but also via enhanced pathogen susceptibility.

The example of the estrogenic EDCs illustrates that to understand the role of chemical contaminants in the

continuing decline of freshwater fish stocks, we have to consider on the one hand the “multi-target” toxicity of chemicals, that is their ability to impact a variety of fitness-relevant functions, and, on the other hand, potential “multiple stressor” effects, that is the combined effects of toxic chemicals with other environmental stressors. Diseases are a key factor in controlling fish population abundance, but this mechanism can get dysfunctional in combination with anthropogenic stressors such as toxic chemicals or global warming. Clearly, for understanding the reasons of the decline of freshwater fish stocks, we have to go beyond linear cause-effect thinking and/or the isolated consideration of single factors, but we have to go “multi” (Figure 2).

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The evolution of *Staphylococcus aureus*

Head of the Genomic Research Laboratory François shares insight into *Staphylococcus aureus* and how the bacteria has evolved over the years

Introduction

Staphylococcus aureus is a frequent bacterial colonizer of our skin, present in 20-30% of the general population without causing any clinical manifestation. However, it is also capable of causing a wide spectrum of diseases in humans ranging from benign skin infections, to severe diseases such as food poisoning, endocarditis, osteomyelitis or septicaemia. *S. aureus* is also frequently reported in veterinary clinics causing important problems in milk-producing ruminants. The versatility of this pathogen could be explained by different adaptive strategies and virulence properties. For instance *S. aureus* is capable of surviving various environmental conditions including acidic, oxidative, high temperature variations, as well as in nutrient-limited medium. In addition, *S. aureus* shows a particular capacity to resist to the presence of chemicals including antibiotics or antiseptic molecules. Some of the properties required to resist to these different conditions are intrinsic to the bacterium but others require adaptation and are linked to genomic evolution. Our purpose will be to evaluate the different strategies used by *S. aureus* to evolve and adapt its genome composition and content following environmental conditions and selective pressure.

Bugs evolve by fair means or foul

S. aureus is a common bacterium able to multiply and survive independently,



thus *S. aureus* is not an obligatory parasite. In the laboratory, in rich medium and in optimal conditions, *S. aureus* population density doubles every 30 minutes. It means that all the bacterial compounds or molecules could be duplicated in 30 minutes to generate a daughter cell “identical” to its mother. This phenomenon requires billions of enzymatic and chemical reactions in a limited time span. Even if protection mechanisms exist at various levels to avoid accumulation of errors, each replicative process could engender punctual errors. In the case of *S. aureus* the genome is composed of approximately 2.8 million nucleotides containing 2800 genes. Even if the process of chromosome replication is tightly controlled errors appear yielding to punctual mutation¹. This type of mutation appears more frequently in non-coding sequences but could also

yield to the modification of the sequence of a protein with unpredictable consequences. To illustrate this evolution process, different groups observed emergence of spontaneous mutations in metabolic pathways yielding to optimization of the utilization of carbon source present in the growth medium. Another example is the mutation of a single base at specific location among the 2.8 million bases of the chromosome that triggers resistance against specific classes of antibiotics such as quinolone or mupirocin. Note that the presence of the antimicrobial in the medium contributes to increase the emergence of such an event.

In the environment, bacteria from various species are in close contact and could exchange information, nutrients and genetic material. Bacterial death results in cellular envelop disruption

and release of bacterial chromosomes. These nucleic acids could be integrated by bacterium yielding to the acquisition of new genes. This process is named natural transformation. Considering bacterial populations, numerous mobile genetic elements could contribute to genome evolution. Plasmids, transposons or bacteriophages represent efficient processes for the acquisition of new genomic features. In *S. aureus*, plasmids are frequently observed in clinical strains and encode generally for antimicrobial resistance determinants. *S. aureus* is also able to produce a plethora of toxins contributing to its virulence such as a toxic shock syndrome toxin, Penton Valentin leucocidin, exfoliatin toxins A and B, and more than 20 enterotoxins which are generally acquired through integration of genetic elements (e.g. lysogen bacteriophages).

Examples of bacterial evolution

Exposition of bacterium to stress or selective conditions contributes generally to the selection of resistant organisms. The most famous example was the introduction of the methicillin (a semi-synthetic penicillin resistant to β -lactamases) in human medicine in 1960. Only 6 months later, the isolation of the first methicillin resistant *S. aureus* (MRSA) was reported. The resistance was acquired through the integration of a large genomic element containing the methicillin resistance determinant as well as other resistance genes, yielding to multi-resistant strains of *S. aureus* which are difficult to eradicate. An interesting example of evolution has been reported recently in the veterinary clinic. *S. aureus* strains infecting poultry showed increased capacity to grow at 42°C and to alter avian cells reflecting a “human-to-poultry host transition”.

My group is also active in this domain of adaptation of animal *S. aureus* strains to the human clinics. Originally detected exclusively in pig farmers in Europe, *S. aureus* belonging to the CC398 lineage has become a worldwide threat associated with livestock, their human contacts and food products. During collaboration work with Doctor Nathalie van Der Mee-Marquet (University Hospital of Tours, France), who performed an active bloodstream surveillance program since 2000, we observed constant increase in the prevalence of ST398 in patients living in animal-free environments; from 0% in 2007 to 15% of *S. aureus* isolates responsible for severe infections in 2015. Basically, this surveillance program allowed us to identify: i) ancestral ST398 strain only able to colonise animals, ii) pre-evolved ST398 strains able to infect animals, iii) evolved strains infecting or colonizing humans and iv) ST398 isolates infecting humans even without contact with animals. Important efforts were deployed using whole genome sequencing approach on these different populations of isolates. Analysis of the genomes of these isolates showed that each population contained specific bacteriophage content. Whereas the ancestral isolate associated with animals are devoid of bacteriophage, emerging clades are characterized by the presence of ϕ 3 prophage variants that encode two immune-modulating proteins, altering or prevent chemotaxis, phagocytosis and killing of *S. aureus* by human neutrophils. Recently, we mobilized prophages from virulent strains and introduced them in ancestral non-human pathogenic isolate. Our experiments clearly showed new features, potentially mediating the virulence of the bacterium, accompanying acquisition of bacteriophages. In vitro experiments showed that strains

containing prophages have increased capacity to interact with human extracellular matrix proteins and increased ability to penetrate into the cytoplasm of non-phagocytic cells. Even if *S. aureus* is not recognized as an intracellular bacterium, this capacity allows the bacterium to survive in a protected niche, hidden from cellular or humoral defences. In addition, in an experimental model of infectious endocarditis, we showed that ST398 isolates containing bacteriophages were more prone to infect cardiac tissue and to multiply within cardiac vegetations, yielding to more severe infection than the prophage-free parental strains. Phages serve as a driving force in bacterial pathogenesis, contributing both to the evolution of bacterial hosts through gene transfer, and to bacterial pathogenesis at the time of infection. Temperate bacteriophages play an important role in the pathogenicity and cellular tropism of *S. aureus*.

¹ Punctual mutation: error during chromosome replication consisting in the integration of an erroneous bases in the newly synthesized DNA strand compared to the template strand.



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The France Europe 2020 strategy will develop strong research

Open Access Government's MF Warrender explains how the France Europe 2020 strategy will help researchers respond to the societal challenges of the future

The Ministry of Higher Education, Research, and Innovation (Ministère de l'Enseignement supérieur, de la Recherche, et de l'Innovation, MESRI) oversees university-level education and research in France. This sector is vital to driving innovation and research in France, and its continued success in these areas. The French research policy itself is conducted by the MENESR (Ministère de l'Éducation Nationale, de l'Enseignement Supérieur et de la Recherche). Research activities are carried out either in higher education institutions or research organisations (public research) or in enterprises (private research). A total of 575,300 people work in this sector, including 266,221 researchers.

As of 2017, Frédérique Vidal has been the Minister of this department and most recently has helped launch the priority research programme combatting climate change: Make Our Planet Great Again, alongside the General Commissioner for Investment, Louis Schweitzer. This was a response to the decision from the United States to withdraw from the Paris Agreement last June. Vidal will commit to a focus on high-level scientists, encouraging them to apply – be it experienced researchers or young people with high levels of potential. The total funding will amount to €60m over a period of 5 years, benefitting 50 researchers. The areas that this funding will help the scientists prioritise are:

- The science of the climate;
- Observation and understanding of the Earth;
- Energy transition science and technology.

France's research universities, equipment and scientists are among the best at an international level, all of which will be involved in this new programme. According to Vidal, 'Make Our Planet Great Again' will also

strengthen the research potential of labs hosting these scientists all over France.

The country believes that access to science will greatly benefit economic growth and sustainable development, as do many other European countries.

This has encouraged the Ministry to push forward with innovation plans in recent years. For the first time, France introduced 'A new deal for innovation' presented on 5 November 2013. This plan has 3 main priorities: to stimulate a culture of innovation in higher education, to encourage exchanges between public and private laboratories, and to set priorities that are internationally coherent. It is important to remember that innovation is multifaceted, and that there is no single process of innovation. In order for France to maintain its relevance in the innovation sector, it must remain informed of the many different factors driving innovation, for example, market needs, economic criteria, and technological advances etc.

France Europe 2020

The launch of 'France Europe 2020' will be doing just this, as it promotes France's participation in the Horizon 2020 European Programme, and will in total allocate €12bn to this cause, with €4.1bn going towards the actions carried out by the MESRI including:

- €150m will be invested in the development and dissemination of key technologies in support of reindustrialisation;
- €400m on translational health research;
- €50m on space;
- €50m on intensive computing.



The France Europe 2020 strategic agenda hopes to enable French research, in all its diversity, to provide better responses to the ever changing major scientific, technological, economic, and societal challenges of the decades to come.

Another endeavour by France to boost initiatives in terms of science and innovation is by financing 3 actions under EUREKA: support for cooperative projects carried out by companies, the EUROSTARS programme, and the so-called 'clusters' strategic initiative. EUREKA aims to coordinate efforts of governments, research institutes and commercial companies concerning innovation, and supports innovative international projects to strengthen Europe's competitiveness. It follows a bottom-up approach to research and development funding – allowing companies to initiate projects themselves. France has agreed to support these projects as part of its 3 actions under EUREKA, however, to be certified, projects must include independent partners from at least 2 member countries, and also be aimed at technological innovation leading to a marketable product, process or service. Since 2008, French projects were predominantly funded by OSEO, which is now known as Bpifrance. The second of the 3 actions that France has become

involved with is the EUROSTARS programme – which is aimed at research and development performing SMEs. France moving behind this programme will greatly benefit the country's role within the innovation sector. Finally, France also plays a big role in developing EUREKA Clusters: strategic initiatives proposed and led by industry, developing generic technologies of key importance for European competitiveness.

All of these initiatives and partnerships overtly display France's enthusiasm within the research and innovation sectors, and if this continues into the future, there will be a significant positive socio-economic impact on France itself. ■

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Improving access to research data

French National Institute for Research in Agriculture (INRA) explores the importance of ensuring research data is easy to access in the agriculture field

Facilitating the access to public data has always been an important endeavour in life science.

The variety of data and sources has been growing even since the empirical sciences have arisen¹, questioning the communities on their best practices for data sharing and re-use. In addition to this ancient but still existing problem, the evolution of technologies used to generate data have added the challenges of their exponential volumes and speed of production. Nowadays, big data questions the agility and the sustainability of the data management systems that emerged in the 90's, essentially based on a backbone of international archives. The whole community is working towards a new model with the help of international organisations or consortia, such as the [Research Data Alliance](#) or the [Global open data for Agriculture and Nutrition](#). The necessity to enable a more distributed model for data management has emerged, to be combined with higher efforts for standardization at different levels and supported by an ecosystem of infrastructures, institutions, consortia of researchers and/or private companies, organisations².

Unit of Research in Genomic-Info (URGI)

The Unit of Research in Genomic-Info (URGI) at the French National Institute for Research in Agriculture (INRA) is a very active player in the plant community initiatives, towards enhancing access to data in plant biology. The



story started 15 years ago with the development of a centralised information system, [GnpIS](#)³, aiming at storing, integrating and giving access to different type of data on different crops and pathogens: genetic resources, genetic and physical maps, genomes and their annotations, polymorphisms, phenotypes, GWAS. More recently, URGI contributed to 2 initiatives, the TransPLANT infrastructure (FP7 EU program, n°283496) and the Wheat Information System (WheatIS) of the [Global Wheat Initiative](#), that allowed us to build the vision and a proof of concept for a federated information system for research in plant biology and breeding. The shared vision of the 2 projects was that information systems sharing the same global semantics should be able to program-

matically expose the description of their content to a unique web portal that could be used by researchers and breeders to search data. The technical bricks of this vision were built by the [TransPLANT](#) project and 2 demonstrations of the concept were implemented, one involving 9 European databases and the [other involving 12 international databases](#). The challenges that are now ahead are (i) to improve the technical system to facilitate its maintenance (e.g. make it possible for one node of the federation to update its software versions without affecting the whole system) and (ii) to allow increasingly user-friendly searches (e.g. be able to retrieve with "yield" query, anything in relation with yield but not necessarily associated to the yield world in the data set). These 2

challenges are currently endeavoured by the partners of the [ELIXIR](#) European infrastructure (Excelerate H2020 EU project, n°676559) and also specifically by the French node of ELIXIR for [some aspects](#).

URGI and its ELIXIR partners have also been very much involved in the development of another technical brick that enabled improvements of such federation of databases: an international standard web service called the [Breeding API](#). The current version allows programmatic standard retrievals of data about the genetic material and of phenotyping data and is being implemented in relevant ELIXIR nodes.

In parallel to these “technical” proofs of concept, INRA has used the WheatIS project to develop with the wheat community of researchers and breeders a set of guidelines for making their data [findable, accessible, interoperable and re-usable](#) and meet the best the standards for open data. These guidelines are available on the WheatIS portal and have been implemented in a central file repository accessible from the same portal that was developed by URGi to complement the existing databases. These 2 resources help the data producers to describe the purpose and the content of a dataset in a way which is understandable by any new user. The European community of plant data managers, together with specialists of data standardisation and the data producers (e.g. partners of EMPHASIS, the European Infrastructure for Plant Phenotyping) have also worked very actively to develop

and improve a standard for phenotyping data that did not exist before: Minimal Information About Plant Phenotyping Experiment ([MIAPPE](#)). This standard was presented for discussion to the international community of plant scientists and adopted. Recently, a mechanism of governance has been set up at the initiative of ELIXIR to regulate its future evolutions. The plant science community is now working on transferring the tools and knowhow gained through the WheatIS and TransPLANT/ELIXIR experiences to all crop communities through actions of communication⁴ or training and implementation of good practices in biology driven projects.

An important part of the work achieved by plant biologists, however still relies on central archives and knowledge databases maintained for instance by EMBL or the NCBI. These resources are invaluable and ELIXIR is currently working on how to better identify additional core resources and what could be their sustainable business model.

Finally, it has to be stressed that the building of such an ecosystem of information systems to the benefit of the final user requires a lot of effort in community building, within and between several communities: the data producers across crops, the data managers, the developers and the specialists of standards, ontologies and semantics.

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Maintaining high quality innovation in Denmark

Open Access Government's Ciara Ruane explores how Denmark has excelled in research and innovation when compared to other European member states

Denmark has maintained its status as the second most innovative EU country, beaten only by Sweden. Through attracting researchers, providing good HR, and creating environments that are highly supportive of innovation, the nation has maintained its status as a top EU Innovation Scoreboard for 3 years running. However, the EU as a whole remains behind global competitors such as South Korea and Japan, putting high hopes on its ongoing Horizon 2020 programme.

The Danish Minister for Higher Education and Science, Søren Pind, [sent a position paper](#) to EU member states outlining Danish interests in relation to the next framework for research and innovation in June. In the paper he emphasised the importance of synergy and collaboration between institutes of higher learning, businesses, research organisations, and international institutes. This position was further highlighted in a speech he delivered at the Confederation of Danish Industry in May, where he emphasised the potential benefits of innovations created through higher learning and businesses, with the knowledge of how to make the best use of them.

Global research power

The Minister's position paper highlighted not just the interests of Denmark, but the need for the EU to remain a global research power. [Section 10 of the document outlined](#) the need for international cooperation. Pind urged the EU to explore the possibility of collaboration between countries within the EU, as well as countries outside. In section 8, he encouraged taking steps towards the Open Science Agenda. This agenda aims to work towards open European data clouds, including third country participants such as the USA and Australia. Through open digital transfer of information and networking, this programme hopes to create an

environment of global innovation. Denmark's support of this is mirrored by their support of Joint Research Centres and the European Innovation Council.

'Elite' researchers

Under Horizon 2020 Denmark has secured DKK 4.2 billion in research funding. Horizon 2020 aims to provide funding for research projects across the EU with minimal red tape, encouraging innovators to seek funding for new ideas. Denmark's funding covers [976 projects](#), which Pind believes is a 'testament to the fact that Danish researchers and companies are among the absolute elite'. The DANRO (Danish Research Office in Brussels) collaborates with the EU to ensure Danish research interests are considered and supports researchers. They primarily work with Universities throughout the country and other research centres, and function as a part of the Danish Agency for Science and the Danish Ministry for Science and Higher Education. These collaborative organisations are seemingly a central part of The Minister's ideas for Denmark's future in research. ■



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Hitting new targets for new antibiotics

Assistant Professor Clare Kirkpatrick shares insight into the development of new antibiotics for the opportunistic human pathogen, *Pseudomonas aeruginosa*

From time to time, the same sensationalist phrases about the problem of antibiotic resistance appear in the news headlines: for example “ticking time bomb,” “antibiotic apocalypse,” “global threat,” “return to the dark ages of medicine” and so on. But the headline writers do have a point: many bacteria with a significant disease burden in humans are developing resistance to many drugs in clinical use and antibiotic resistance genes are spreading. Meanwhile, the number of existing molecules that have anti-bacterial activity, and the number of bacterial macromolecules (structural proteins, cell wall components, enzymes) which are targeted by these molecules, remains low. As the development of new antibiotics is unlikely to ever be a source of significant revenue for drug companies, very little industrial resources have been focused on it and the rate at which new antibiotics come to the clinic is very low. Discovery of new pathways within bacteria that could provide a source of new drug targets, as well as new molecules (or alternatively, existing antibiotics in novel combinations) that interfere with them, is a challenge that can more easily be met in an academic setting without the requirement to generate profits for shareholders.

Pseudomonas aeruginosa

I am currently establishing my research group at the Department of Biochem-

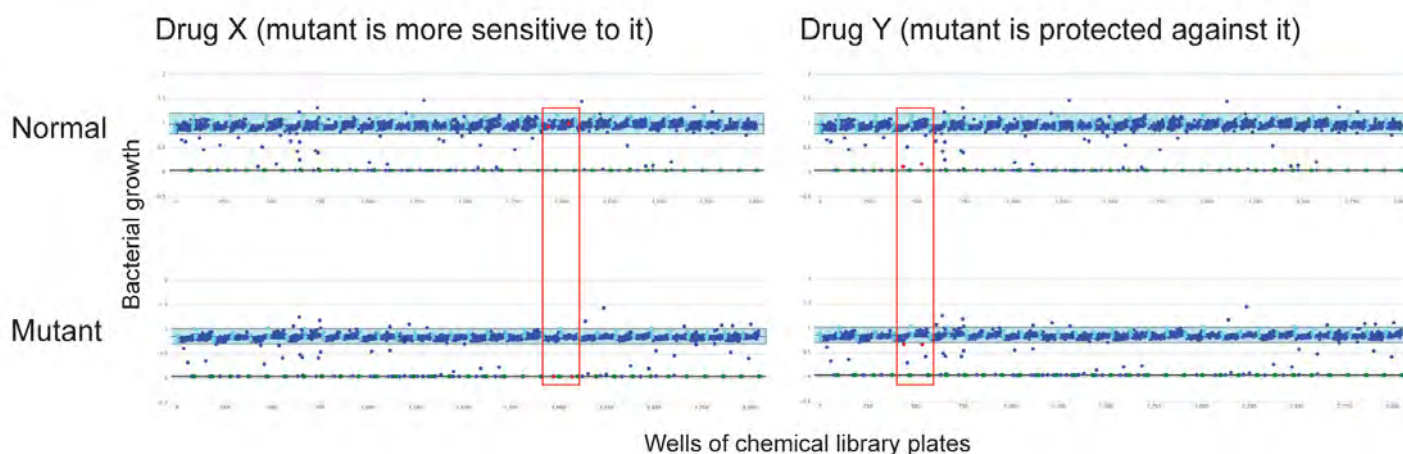
istry and Molecular Biology, University of Southern Denmark, with the aim of studying cell cycle and motility control in the opportunistic human pathogen, *Pseudomonas aeruginosa*. We focus particularly on how the factors controlling cell division and motility (bacterial movement) interact with each other and their potential as eventual drug targets. *Pseudomonas aeruginosa* is highly versatile in terms of the environments it can colonise, and can establish acute or chronic infections in burn wounds, skin ulcers implanted medical devices like catheters or pacemakers and the lungs of cystic fibrosis patients. It is also highly naturally resistant to many classes of antibiotics because it possesses multiple defence mechanisms against them. New drugs active against this species are therefore needed urgently. Indeed, carbapenem-resistant *Pseudomonas aeruginosa* was named by the World Health Organization in February 2017 at the top of the “Priority 1: Critical” category of the WHO Priority Pathogens List of bacterial species for which new drugs ought to be developed as a matter of urgency.

The ability of *Pseudomonas aeruginosa* to establish infections fundamentally depends on its ability to move around, in liquid or on surfaces, to find the best possible niche to proliferate. This movement is dependent on the flagellum, a corkscrew-like structure that protrudes from one end of the cell

and works like a propeller to enable the cells to swim, and thread-like strands of protein called pili that extend and retract, allowing the cells to pull themselves along on surfaces. Both these structures are also necessary for the first stages of forming a biofilm, where the cells attach themselves to the surface they are going to colonise. The flagella and pili are always located at the ends of the rod-shaped *Pseudomonas* cell and this location is vital for them to function correctly. Mutants which produce flagella or pili out of the sides of the cell can no longer move properly and are therefore at a disadvantage for establishing a biofilm or colonising an infection site. Production of flagella and pili in the correct place is co-ordinated with the cell cycle and the environment that the cells are in, but the mechanisms that control it are not fully understood. In order to shed some light on this subject, my group is investigating the roles and interactions of the protein factors that control the location of flagella and pili using a chemical genetic approach.

Bacterial Chemical genetics

Bacterial Chemical genetics is a relatively new research field in which drugs, chemicals, or other small molecules are tested against bacteria, not necessarily to see whether they have antibiotic activity or not, but to see which (if any) processes in the cell they interact with. This can be discov-



An example of chemical-genetic screening data showing the response of one of our mutants of interest to two different drugs, here denoted X and Y, relative to the non-mutant bacteria. Every dark blue dot corresponds to a reading of cell growth in the presence of one of the chemical collection compounds, while the light blue and green dots are the negative and positive control conditions, respectively. Most of the compounds cluster with the negative controls because they do not affect cell growth, while a few are just as effective antibiotics as the positive control. Two different drugs are highlighted in red because of their different effects on the mutant strain, which is more sensitive to drug X but protected against drug Y, relative to the normal bacteria

ered by comparing the response of a normal, non-mutant strain and a mutant that is lacking one of the genes involved in the process of interest, to a collection of drugs or small molecules and identifying ones where the mutant responds differently (either by growing better in the presence of the drug, or worse) to the non-mutant strain. Both these responses indicate that the drug interacts with the process of interest, and can be followed up by using that drug in other experiments to find out what exactly it is interacting with. Work from several other laboratories has shown that this approach can identify missing enzymes in metabolic pathways or previously unknown factors involved in, for example, cell wall synthesis.

My group's objective is to use the same approach to identify previously unknown factors involved in the control of flagella and pili positioning and function in *Pseudomonas* and to

define what potential these factors have as drug targets. Our preliminary data on screening a panel of five *Pseudomonas* mutant strains lacking known control factors involved in this process against a 1280-compound chemical collection has identified 4 drugs with differential effects against one or some of the mutant strains (two examples are shown in the figure) and we are currently investigating their mode of action and the reason for the mutant-specific effects on growth. We were very surprised to see that in a few cases, instead of the mutations causing increased sensitivity to one of the compounds, they appeared to protect against it, despite the gene in question having no apparent relationship to the known function of the drug. Since this could indicate a previously unknown potential mechanism for antibiotic resistance, this interaction is a priority for my group's short-term future work. In the long term, we hope to characterise how

factors controlling *Pseudomonas* flagella/pili positioning and function are coordinated into a regulatory network and to understand which nodes in the network are the most critical for the cell's ability to cause disease (and which could, therefore, be the best targets for novel antimicrobial compounds).

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Photonic nanostructures and the electron microscope

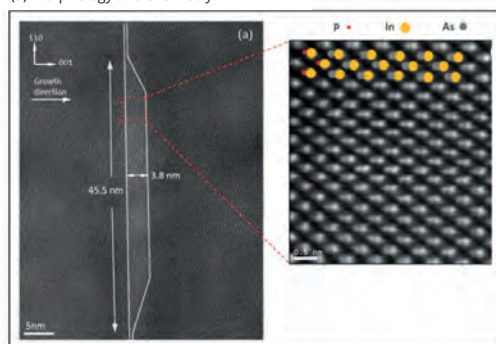
Shima Kadkhodazadeh, researcher at DTU Cen talks about the role of electron microscopy in developments in photonic nanostructures

Humanity has always been fascinated by light and its interaction with matter, manifested by the ageless desirability of precious stones. Today, nanostructures exploiting optical phenomena are prevalent in fields ranging from telecommunications to solar cells, catalysis, biological sensing and medical diagnostics. A key requirement for future progress in these technologies is obtaining a better understanding of the structure – functionality relationship of their constituent components on the nanometre scale. This calls for characterisation methods that are capable of probing structure and properties with nanometre spatial resolution and beyond. A powerful tool for nanoscale characterisation is Transmission Electron Microscopy (TEM). Today's aberration-corrected TEMs can routinely image structures with atomic resolution. In aberration-corrected scanning TEM (STEM) electrons can be focussed into a probe below 1 Å in diameter, allowing both imaging and chemical analysis to be carried out with atomic resolution. Other characteristics such as strain, polarity and electric field strengths can also be measured in today's TEMs, all of which influence the optical performance of structures.

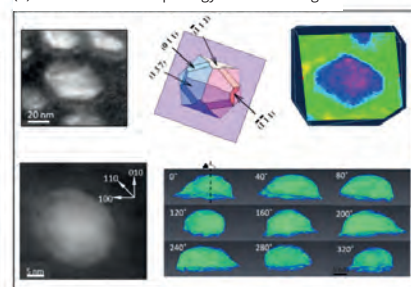
Our studies of photonic nanostructures have included III/V semiconductor quantum dots. Low dimensional semiconductor structures are of interest in a number of fields, due to their

III/V semiconductor quantum dots:

(a) Morphology and chemistry



(b) 3-dimensional morphology vs. embedding



(c) Strain

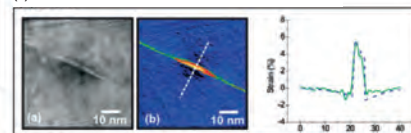


Figure 1: (a) Atomic resolution STEM image of an InAs/InP quantum dot in cross-sectional view. The position of different atomic species can be directly detected in the image and the dimensions and profile of the quantum dot can be accurately measured¹. (b) Electron tomography analysis of InAs/InGaAsP quantum dots before and after embedding in InGaAsP matrix, revealing the morphological changes undergone as the result². (c) Electron holography measurement of strain in InAs/InP quantum dots³

characteristics that differ from those of the bulk, and which can be manipulated by controlling their structure and chemistry. Quantum dots have dimensions so small that quantum mechanical effects result in the quantisation of their electronic density of states in 3 dimensions. The exact configuration of the electronic states and subsequently, the optical properties of the quantum dots, are largely determined by their structure and chemistry. Thus, a significant step in optimising their performance and synthesis is understanding their subtleties on the nanometre or even atomic scale. Our studies have included atomic resolution imaging to determine the morphology and chemical distribution¹, 3-dimensional reconstruction of morphology², and strain measurement³ (Figure 1). The

results have contributed to tailoring the synthesis process for fabricating structures with desired optical properties, and formulating more accurate theoretical models to predict the properties of such structures.

TEM capabilities

A very unique capability in TEM is the possibility of probing optical properties with sub-nanometre resolution. While light-based methods are the obvious choice for optical characterisation, they are limited to spatial resolutions on the order of tens of nanometres at best. Traditionally, the energy resolution attainable in TEM was insufficient to access the energy ranges relevant for optical excitations. However, continuous advances in instrumentation have bridged this hurdle and improved the energy

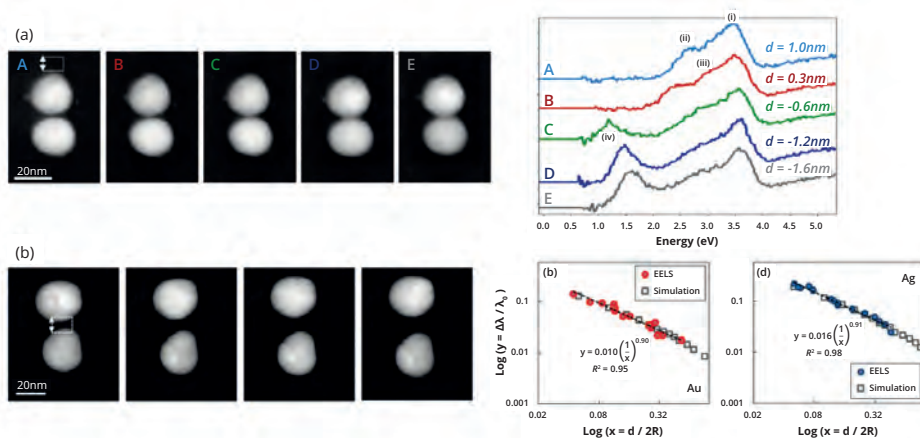


Figure 2: (a) Electron energy-loss spectra probing the surface plasmon resonances in silver dimer nanoparticles at separation distances (d) below 1 nm, revealing the evolution of surface plasmons resonances in a non-classical regime. (b) Electron energy-loss measurement of the surface plasmon resonance wavelength for gold and silver dimers as a function of separation distance. Establishing an accurate scaling of the surface plasmon resonance with distance is highly important for nanometrology applications

resolution of state-of-the-art TEMs to values comparable to optical techniques. Another focus of our TEM studies of photonic nanostructures has been metallic nanostructures for plasmonic applications. Plasmonics is an emerging field in which metallic structures are used to guide light or to enhance interactions between light and materials placed in their vicinity. This is due to the ability of these nanostructures to support surface plasmon resonances in the optical range of the electromagnetic spectrum.

Our studies have included probing the evolution of the surface plasmon resonances in gold and silver nanoparticles as a function of particle size⁴ and separation distance between particles^{5,6}, including sub-nanometre separations (Figure 2). The results have provided novel insight into the characteristics of plasmonic nanostructures, otherwise unreachable by optical methods, as well as testing and validating new theoretical descriptions concerned

with the plasmonic properties of low dimensional metallic structures.

“A key requirement for future progress in these technologies is obtaining a better understanding of the structure – functionality relationship of their constituent components on the nanometre scale.”

These examples highlight how improvements in the spatial and energy resolutions of modern TEMs contribute to bridging the gap in our knowledge of the structure – functionality relationship in photonic nanostructures. A step forward in this quest entails in-situ TEM probing of nanostructures under working conditions. In-situ methods in TEM are rapidly expanding, and currently include heating/cooling, electrical biasing, light injection and detection, and gas/liquid environment. Future efforts in this field will focus on combining these tools with TEM measurements of morphology, crystal structure,

chemistry, strain, electric field, etc., to “shed better light” on the structure – functionality link in photonic nanostructures.

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Highlighting the key Italian research priorities

Open Access Government's Ciara Ruane details research funded by the Italian Ministry of Education, Universities and Research and their key priorities

The Italian Ministry of Education, Universities, and Research (MIUR) works to implement international policies and standards in science, education, and innovation. Funding offered by the Ministry covers 3 categories: basic research, projects of relevant national interest (PRIN), and industrial research.

Basic research, as outlined by the Ministry, covers research that is not linked to specific industry. For example, climate and biodiversity research is driven by the 'curiosity' of the researcher, with the broader aim of improving society in the future or advancing science. The basic research fund backs up the creation of public and private networks, both in Italy and internationally. A priority for the funding is to encourage participation in European initiatives: promoting a collective use of people and resources available within the EU. The dual goal of strengthening science and research in Italy, and collaborating with other EU Member States is mirrored in other areas of the MIUR. The ministry also supports Eurostars 2, a research and development programme that funds projects run by participants from 2 or more EU Member States. Ideas are submitted through the MIUR and managed by Eureka, an international network of research and development.

PRIN covers research of 'national interest'. This funding aims to reinforce the ideas of collaboration and peer review within Italy, and specifically targets research taking place in institutes of learning. The MIUR is part of the Inter-Ministerial Committee for Economic Planning (CIPE) which includes the Ministry of Foreign Affairs and the Ministry of Labour and Social Policy. Industrial research funded through the MIUR covers projects related to industry and infrastructure, again with the intention of economic growth within the country itself.

Image: © Ministero Istruzione



The Minister for Education, University and Research, Valeria Fedeli

The Ministry's position on pan-EU projects

The MIUR's position as a collaborating member of pan-EU projects and programmes is an essential component of its existence. The Minister for Education, University and Research, Valeria Fedeli has spoken about the need to foster these relationships. In July of this year she spoke about Italy being selected to host the 2020 science forum in Trieste. She said that Italy has always 'worked as a team', and that the city is perfectly situated as a meeting point for several other states. She also reasserted the government's desire to continue investing in universities, calling them 'essential' for the development of the country.

Fedeli has also spoken recently about the concepts of global citizenship and the future of the EU. In a speech at the 'Erasmus and the Future of Europe Conference', which took place in Florence earlier this year, she praised the European values of peace, collaboration, and multiculturalism, and the need to protect these qualities for future generations. The speech focussed on the chance given to Italian students to study in other EU countries, and for foreign students to study in Italy. Minister Fedeli said that the programme improves employment and on



a personal level, increases confidence and helps to teach students important skills for life and work. She also praised the Erasmus free movement program for reinforcing a sense of community among EU countries and fostering academic links between them.

“PRIN covers research of ‘national interest’. This funding aims to reinforce the ideas of collaboration and peer review within Italy, and specifically targets research taking place in institutes of learning.”

Global citizenships role in education

At a conference taking place at the University of Bologna, the Minister spoke about global citizenship to an audience of politicians from in and outside of the EU. She outlined the need to solidify ideas of global citizenship through legislation, especially in regards to its role in education. She stated that they must take ‘concrete’ action to ensure an atmosphere of global collaboration, and to end racial and gender based discrimination.

She also believes that there would be ‘no answer’ to questions of gender based violence without countries

across the globe working together to address inherent societal problems. In her speech, Fedeli emphasised the importance of looking to the attitudes of younger generations as an example of forward-thinking community and cultural exchange. In reference to the history of the Bologna University she said ‘knowledge has no boundaries’, and emphasised the role universities have to play in forging a global identity. ■

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The “PEGASO – Fit for Future” project

Giuseppe Andreoni and Maria Renata Guarneri discuss how the PEGASO project is promoting sustainable behaviours geared towards achieving healthy lifestyles

Challenging teenagers in the context of their own areas of interest, PEGASO Fit 4 Future aims to promote sustainable behaviours geared towards achieving healthy lifestyles. The goals of the PEGASO project were achieved by implementing innovative mobile solutions for prevention in healthcare, thanks to the development of a multi-dimensional and cross-disciplinary ICT system. This included game mechanics to influence behaviours, with the hopes of fighting and preventing obesity in the younger population, encouraging them to become co-producers of their wellness, and take an active role in improving it.

PEGASO leverages a modular behaviour change platform targeted at teenagers. When it comes to preventing obesity and related comorbidities, smartphones are thought of as a central agent for behaviour change. Additional sensors could be used along with a modular approach. The platform is designed to deliver a positive message and act as a tool dedicated to improving teenager's lifestyles according to 4 dimensions:

- Movement, i.e. adopting an active lifestyle. Increasing sedentariness together with unhealthy eating habits in our everyday life are producing negative effects on the health of the younger generations. Particularly in terms of increased body weight and potential development of metabolic diseases;

- Play, i.e. enjoyable continuous engagement and, therefore, compliance;
- Eat, i.e. tasty but balanced nutrition;
- Share, i.e. a social approach.

The project has developed an educational platform able to motivate people through games and group challenges – virtual and real – with a social approach where people influence each other. It has an ecosystem of coordinated mobile apps, a virtual community, an educational game, and wearable devices to monitor physiological parameters.

Mobile platform

PEGASO is based on a mobile platform in which the smartphone is the converging technology, i.e. the first and key sensor system. The mobile device also acts as a communication gateway towards the other sensors. In addition, with a modular approach, wearable sensors can be added to the system, according to the users' preferences:

- A bracelet that monitors physical activities, called WWAT (Waterproof Wearable Activity Tracker). Sensors embedded in the bracelet give more precise measurements than the phone and can be worn 24/7.
- A WES (Wearable Electronic System). A smart garment that monitors fitness/sports activities. It is expected that while people will not want to

wear complex sensor systems every day, they might be willing to put on additional sensors when performing specific activities oriented at improving their level of fitness.

The Feedback System of the PEGASO system is the Companion. The PEGASO Health Companion represents the guidance system and is the main interface between the user and the PEGASO system. The PEGASO Health Companion is a personal digital 'friend', acting as a daily life-guide for coaching, caring for, and empowering teenagers in their activities toward healthy habits. Main attributes of the PEGASO Companion are:

- Digital: The Companion exists in the smartphone;
- Personal: The Companion is customised to the single user;
- Friend: The Companion would establish an effective relationship with the user;
- Daily-life guide: The Companion accompanies the users (coaching, caring, and empowering) during their daily activities toward healthy habits: supporting behaviour change to promote healthy lifestyles is the main goal of the Companion and PEGASO project in general, with a special focus on obesity prevention.

The Companion is an ecosystem of different elements, apps, and services.

In the PEGASO vision for teenagers, the Companion wants to be a compass to guide towards a healthy lifestyle. From the user perspective, the Companion is structured as follows:

The Companion is the main app that represents the entry point for the user inside the PEGASO universe. A set of other apps are integrated into the Companion. Different apps in support of the development of awareness and motivation towards healthy behaviour are accessed via the Companion:

- eDiary, to record food consumption;
- Challenges, to set goals against the system or among friends;
- Dashboard, providing an overview of current achievements;
- PEGASO City, linked to gamification and city marketplace;
- Mobile Serious game, a key component to providing education and motivation;
- Report app, linking PEGASO to a healthcare system.

Through an innovative and multi-dimensional PEGASO virtual individual Model, a conceptual framework of basic relations between the individual's status and behaviours in different domains, which are considered to dynamically concur to health, have been built.

This allowed us to set up an efficient user feedback system: The PEGASO Behaviour Recognition is the core of the reasoning system aimed at the identification of behaviours and matching them with target behaviours.

The scoring system is based on 3 levels:

- A short-term analysis;
- A long-term analysis;
- An overall risk analysis.

Gaming system

The gaming approach in PEGASO wants to exploit social connectivity (share) and engagement (play). The overall gaming system in PEGASO is managed via the Companion and is based on a 3-fold approach:

1. The PEGASO game: a 3D serious game aimed at increasing nutritional awareness and promoting physical activity – motivational component.
2. The PEGASO gamified approach: linking 'real world activity' with online & gaming applications – social component.
3. The PEGASO minigames: addressing specific aspects of healthy behaviour – educational component.

The PEGASO minigames are small games with very specific goals; they can be completed in a short time span and provide information in a playful manner. The main goal is to develop awareness and encourage healthy behaviour, developing intrinsic (autonomous) motivation. Education and awareness are important triggers for developing autonomous motivation. Minigames have been embedded within the PEGASO serious game: examples include SCAVENGING, i.e. to collect as much food as possible and match the food icons belonging to the same nutritional category, or RESEARCH, i.e. to match a single food

item, collected through the scavenging mini-game, to a recipe requirement (Fig. 6). Stand-alone minigames have also been developed to be played as separate elements for education and entertainment.

400 students (aged 13-17) in 4 European pilot sites tested the PEGASO System: Lombardy in Italy, Catalunya in Spain, and England and Scotland in the United Kingdom participated in this phase. The evaluation approach was mainly dedicated to the system and technology acceptance, usability, and long-term use. These factors are also a secondary assessment of motivation and engagement. The reliability in assessing teenager's lifestyles and their changes (with the focus on the eating habits and on physical activities) and related efficacy on the sensors' network system was investigated too. The subjective assessment was adapted for awareness.



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Large frame ring lasers and their role in earthquake research

Dr Angela Di Virgilio, of the INFN Sezione di Pisa shares insight into the GINGER project and the importance of large frame ring lasers in earth science

Catastrophes such as earthquakes are the end point of processes that have started much earlier. Previsions are based on models, and reliable measurements are necessary to validate models. In principle, very sensitive instruments could record how small changes are evolving. This is not an easy task since very high sensitivity, long-term stability, high duty cycle, large dynamical range and fast response are required all together. Especially long-term stability, which is difficult to obtain with very high sensitivity instruments.

Large frame ring lasers fulfil all the above requirements. Ring lasers in general measure absolute angular rotation rates and smaller devices are widely used for navigation. At present a few large frame ring lasers are operating, mainly in Europe, the Gross ring G at the geodetic observatory of Wettzell, ROMY array for geophysics near Munich, and GINGERINO inside the underground laboratory of Gran Sasso in Italy. They are directly attached to the surface of the Earth and routinely detect very small signals down and below pico-radians per second. Being inertial sensors they measure the Earth's rotation rate and any variations with very high precision. GINGER is a project designed for fundamental science, to measure the Lense-Thirring effect of general relativity on Earth.

This measurement is very challenging. In the last 7 years, a group of scientists

in Italy have developed models for the deep comprehension of the instrument, and very carefully identified the key specifications to design the experimental apparatus. Tools and a suitable strategy to detect the tiniest signals have been investigated. GINGER has been designed for fundamental physics, but being attached to the Earth it would be able to detect the tiny signals of the Earth, like the geodynamic of the crust, local earth deformations, non-volcanic tremor (NVT), and slow earthquakes. It is very ambitious, as are most of the experiments in fundamental physics, but it has all the characteristics to operate as a geophysical observatory and to monitor variations of the Earth's rotation rate.

Last but not least the apparatus is rather small, and several apparatus could be distributed on top of the Earth's surface, the confrontation between different stations will be very meaningful. GINGERINO is the prototype built inside the underground laboratory of the Gran Sasso, and has tens of pico-rad/s sensitivity, but at the same time, it has recorded a strong signal of the nearby earthquake of Visso (M6.9), a million times larger than its floor sensitivity.

Pioneering research

GINGERINO has shown us the advantage of being in an underground location. It runs unattended for months, the natural thermal stability of the cave and the isolation from environ-

mental perturbations guarantees high duty cycle and a fast response. Gyroscope based on ring lasers is now a mature technique and it could be at the base of a geoscience and fundamental physics observatory.

The high sensitivity ring laser community is a very small one, it is highly interdisciplinary and it brings together theorists of general relativity, experts in laser and optics, metrology, geodesy and Earth science.

Dr Angela D. V. Di Virgilio is the leader of the research group in Italy, She has proposed the GINGER project, and in the past, she has actively participated in the pioneering work to develop the gravitational wave antennas.



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The COSMOS project: a first progress report

Professor Nicola Vittorio of Università degli Studi di Roma 'Tor Vergata' reviews the first 6 months of the COSMOS project and how it is progressing

At the end of June 2017, the Italian Space Agency formally reviewed the COSMOS project 6 months after the kick-off meeting. Although the project is still in its beginning phase, the main lines of development were clearly defined. The organisation of the project nation-wide requires careful management activity. A series of meetings open to all the Italian Cosmic Microwave Background (CMB) community were organised to present and to discuss the activities foreseen in the various project nodes.

“Inflation is a theory of the very first instants of the Universe, and as such it took place at very high energies, much higher than what can be presently tested in ground-based laboratories. This makes inflation a privileged window into very high-energy physics and offers the possibility of testing various aspects of fundamental physics.”

The COSMOS project has 11 nodes: Università di Roma 'Tor Vergata' (coor-

minating node), Università di Milano, Università di Milano-Bicocca, Scuola Internazionale di Studi Superiori Avanzati (SISSA), Università di Padova, Università di Ferrara, Università di Genova, Università di Roma 'Sapienza', Istituto Nazionale di Fisica Nucleare (INFN-Pisa), Istituto Nazionale di Astrofisica (INAF-Trieste and INAF-Bologna). Each node has the responsibility of coordinating its activity at the national level, as well as monitoring the implementation and delivery of the products. A common effort was devoted to incentivise the interactions and the collaborations among people belonging to different institutions. The first meeting of this series was held in Bologna the 20th of January 2017. A final meeting devoted to presenting the main findings of each of the nodes after 6 months of activity was organised in Bologna the 26th of May 2017. In parallel to all these activities, a lot of discussion have been dedicated to defining an Italian roadmap for the next decade of CMB experiments. The idea is to arrive at a final document as

soon as it will be clearer how to position the Italian CMB community in the international scenario and, in any case, by the end of the project in December 2019.

Effective international coordination

The strong and effective coordination at the Italian level provided by the ASI/COSMOS project has made it easier to interface with other internationally coordinated activities concerning CMB experiments. In fact, a lot of effort has been dedicated to the realisation of ground-based and balloon-borne experiments, as well as to the proposal of the ESA/CORE space mission. At the European level, there is the attempt to coordinate a joint effort for the realisation of a ground-based CMB research infrastructure. A proposal has been submitted to the EU in the framework of Horizon 2020 under the 'Excellent Science' pillar for the program part relative to 'European Research Infrastructures'. While still waiting for the referee report, a meeting 'Towards the

Table 1

| Project @ Atacama Desert, Chile (5200m) | Leading institution(s) | Year |
|---|-------------------------|--------|
| ACTPol (Atacama Cosmology Telescope – Polarization) | Princeton University | 2014– |
| POLARBEAR (POLARization of Background microwave Radiation) | U.C.Berkeley | 2012– |
| Simons Array | | Future |
| CLASS (Cosmology Large-Angular Scale Surveyor) | John Hopkins University | Future |
| ABS (Atacama B-mode Search) | Princeton University | 2011 |

Table 2

| Project @ South Pole, Antarctica (2800m) | Leading institution(s) | Year |
|---|--|--------|
| SPTpol (South Pole Telescope – Polarization) | University of Chicago | 2012– |
| BICEP2 (Background Imaging of Cosmic Extragalactic Polarization) | Caltech, Cardiff, U. Chicago, Harvard, JPL, CEA Grenoble, U. Minnesota, Stanford | 2014– |
| KECK (Keck Array) | | 2010– |
| Bicep/Keck program | | Future |

Table 3

| Project @ different sites | Leading institution(s) | Year | Observing site |
|---|----------------------------------|---------------|-------------------------------------|
| QUIJOTE (Q U I JOint Tenerife) | IAC | 2012– | Teide Observatory, Tenerife (2400m) |
| LSPE/STRIP (Large Scale Polarization Experiment) | Univ. Milano | Future (2018) | |
| GroundBIRD | | Future (2018) | |
| QUBIC (QU Bolometric Interferometer for Cosmology) | Univ. Paris 7 | Future (2019) | Alto Chorillo, Argentina (5000m) |
| C-BASS (C-Band All-Sky Survey) | Oxford, Manchester, Caltech, JPL | 2015– | OVRO, Ca, & South Africa |
| B-Machine COFE (Background Emission Anisotropy Scanning Telescope) | U.C. Santa Barbara | 2002– | White Mountain (3800m) & Balloon |

European Coordination of the CMB programme' will be held in Villa Finaly in Florence next September. It is worth mentioning that the CMB polarisation observations from the ground have been implemented by several research groups, with a clear tendency to concentrate the activities in few high-quality sites, with excellent atmosphere and already existing infrastructures. Running and planning experiments from the Atacama Desert in Chile, from the South Pole, and from other sites are presented in table 1, 2 and 3, respectively.

All these efforts from the ground, together with those from stratospheric balloons and satellites, aim to detect the so-called B-modes in the polarisation of the CMB photons. Infla-

tion is a theory of the very first instants of the Universe, and as such it took place at very high energies, much higher than what can be presently tested in ground-based laboratories. This makes inflation a privileged window into very high-energy physics and offers the possibility of testing various aspects of fundamental physics. Inflation makes a crucial prediction, namely the generation of a stochastic background of primordial gravitational waves. This background imprints a unique CMB polarisation pattern, the B-modes, whose detection is considered a smoking gun of the inflationary paradigm. Although still now very elusive, the B-modes therefore constitute the frontier of research in cosmology to better understand the very early universe and very high-energy physics.



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Prioritising investment for research in Norway

Open Access Government outlines how research in Norway is tackling key challenges and details the Ministry for Education and Research's long-term plan

Norway's Minister for Education and Research, Torbjørn Røe Isaksen believes that times of economic and political uncertainty require a greater investment in innovation. He called investment in research and development "the smartest thing we can do," to ensure a more stable future, and believes Norway offers unique opportunities for innovation, saying: "Our strengths are largely related to the country's geography, economic specialisation patterns and institutional characteristics."

The Ministry for Education and Research in Norway has set out a [long-term plan](#) for improving research throughout the country. Their focus points include solving 'major challenges' to society, increasing competitiveness, and developing 'high-quality' research groups. They view the improvement of research as an essential part of the plan to strengthen the economy, especially in the face of uncertainty and recent economic issues and with Norway's 'high cost of living'. For the government, these improvements come from public investments. They have pledged, from 2015-2018, to invest kr 400m in research infrastructure, add 500 new recruitment positions, and increase the number of allocations available for schemes such as Horizon 2020.

Prioritising research in Norway

The Ministry has also given a list of priorities for problems that researchers must tackle to ensure the future of the country. These include:

- The oceans;
- Climate change;
- The public sector;

- Enabling technological advancement;
- Creating 'world class' research groups.

The Ministry also plans to create a new building for life science and chemistry at the University of Oslo, and upgrade the Ocean Space Centre in Trondheim. In the '[Research in Norway](#)' brochure, Isaksen praised Norway's 'strong tradition' of ocean and energy innovation, saying: "The exploitation of natural resources has had a profound impact on our innovation and research profile....More recently, special priority is given to research related to renewable energy, and carbon capture and storage." The brochure singles out Norway as a leading nation when it comes to petroleum and hydropower efficiency. However, while petroleum in particular is a large part of the Norwegian economy, the Ministry is also looking towards renewable energy. Three new energy research centres, established in 2011, currently receive kr 9m every year for 5 years.

In 2015 the Ministry published a [consultation paper](#) proposing amendments to the Research Ethics Act. This covers day-to-day research practices as well as specific cases relating to the prevention of misconduct. The paper found that many institutions establish their own procedures, with the same 'core ideas'. The paper suggested that recent cases show there is a need to clarify research ethics rules. New proposed guidelines again emphasise the responsibility of individual researchers to ensure ethical practices, but suggests this system of self-monitoring must be regulated and monitored by the Ministry.

The Ministry also strives for diversity in research. For them this begins with education, from kindergarten through to university, establishing more placement



opportunities for vocational research positions and boosting the amount of time spent on science and maths in classrooms.

Norway's ambition to become a world leader in research and innovation goes hand-in-hand with their policy of international collaboration on projects. Their strategy for cooperation with the EU and Horizon 2020 lists their priorities for participation, including the improvement of social welfare, economic development, and the international success and recognition of Norwegian research. They wish to increase their share of EU contribution, which is relatively low compared to other member states. They are looking to receive 2% of Horizon 2020 funds, which is ambitious, but they believe it is possible given Norway's contributions and the quality of their research.

The Ministry's ambitions mirror a spirit of both collaboration and personal growth that is prevalent throughout Europe. Programmes such as Horizon 2020 and Erasmus encourage and fund international research

cooperation, at educational levels, as well as in laboratories and established institutions. Minister Isaksen has said that research is 'international in nature', and that international research must become an integral part of Norwegian innovations. Norway is also not alone in being forward thinking and ambitious, desiring to boost its own economy and ready themselves to face the challenges of the future, in particular climate change and the current landscape of political uncertainty. ■

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Augmenting the performance of future structural components

Professors Jan Torgersen and Filippo Berto highlight how new technologies are helping to develop the next generation structural components

In the midst of continuous digitalisation of manufacturing processes, modern short product life cycles and the ever-growing need for high performance, for example the requirement to fabricate stiff and low weight products within only few simple production steps, we face stringent requirements on both time and sophistication of modern structural design and property prediction. For digital production and advanced components of the future, conventional design methods, structural evaluation routines and production techniques fail to fulfil necessary requirements for structural complexity, the complexity requirement to boost modern products to the next performance level. The autonomous production in the ambit of the 4th industrial revolution paired with the need for parts that challenge today's production constraints necessitates the use of enabling technologies such as additive manufacturing (AM). These technologies allow the direct conversion of digital designs into physical products within one production step and completely autonomous avoiding setup time and the use of tools. This digital workflow prompts a product development process and structural property prediction without physical testing, only utilising advanced simulation-based methods for both, structural optimisation and failure prevention.

The Additive Manufacturing dilemma

With AM, however, a significant prob-



Figure 1: High stiffness and low weight titanium upright for high performance race car fabricated by AM, courtesy of Jørgen Eliassen, Revolve NTNU Trondheim

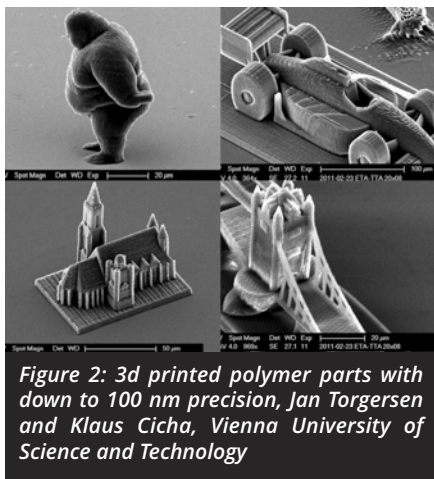
lem arises. In conventional manufacturing technologies, one utilises a given material with defined and well-known material properties and removes material to obtain the desired geometry. In contrast, the material properties in AM evolve during the fabrication process. Geometry and material properties are closely related, every change in the geometry will change the way the AM machine performs its building routine, affecting the toolpath and ultimately the properties of the resulting solid. Parts are no longer isotropic, in some cases not fully dense, surfaces are rough and there is a high chance of inclusions, impurities and in homogeneities, all related to the underlying manufacturing strategy, which, in turn, is dependent on the input geometry.

We face a dilemma; on the one hand, we possess a technology that is undoubtedly of high potential and can fulfil the needs of modern digital man-

ufacturing, enabling unprecedented complex designs in an economic fashion. On the other hand, we cannot guarantee that respective parts will withstand complex loading scenarios because of the still poor and/or poorly known material properties as well as the insufficiently accurate failure criteria allowing their prediction.

In our research, we tackle both aspects of this dilemma. Utilising modern AM, we aim to create digital material designs fulfilling stringent requirements of aerospace, automotive and biomedical applications. We employ the latest topology optimisation routines and develop them further for better usability and better interaction with the AM manufacturing process chain. Specifically, we work on improving the interfaces between the topology optimisation routine and its compatibility to solid modelling. This will enable easy downstream processing. Further, we aim to optimise the tessellation routines, streamlining the entire development process and allowing a smooth transition between the individual steps of the process.

Further, we aim to optimise support structures. These are necessary for attaching AM parts to the building platform to ensure dimensional accuracy. We consider these support elements as part of our optimisation routine maximising speed and minimising failure already happening in the building process.



Quality assurance

We further develop a sound experimental and theoretical understanding of the fatigue and fracture behaviour of these advanced geometric complex components. To date, this assessment and the quality assurance of AM components is not accurate as microstructural features as well as the specific mechanical/cracking behaviour of AM materials cannot be modelled effectively due to their complex microstructural configuration. For complex AM components, no specific design criteria are in place considering stress concentration phenomena arising from geometrical discontinuities/features. Additionally, no fatigue data generated by testing such geometrical discontinuous AM metals can be found in the technical literature. We therefore, aim to fill this knowledge gap allowing future applicants to take full advantage of the unique features of AM, which is key to integrate this promising technology in everyday manufacturing. Drawing from extensive expertise in the development of modern fatigue assessment criteria, our group aims to contribute to the fundamental understanding of the mechanical/cracking behaviour of AM materials subjected to fatigue loading as well as the integration of this knowledge in an innovative design methodology. The key feature of this unifying approach is the

consideration of microstructural features (such as porosity, grain shape, defect morphology, etc.) of the material near crack initiation locations.

Due to the geometric complexity of AM advanced components (see Figure 1) and materials related structures naturally have large surface to volume ratios. Large areas are exposed to and interact with the surrounding, which is even further enhanced through the typically rough surfaces AM many parts exhibit. This can be beneficial, as for example in biomedical applications, where cells tend to easily attach to the porous and rough structure of AM fabricated implants. However, this exposure can also lead to detrimental effects such as corrosion, environmental induced embrittlement or wear through friction. Independent from the intended use of the part, the ability to tailor surface characteristics and surface material properties of advanced geometric complex components will allow for the ultimate design freedom. Our group combines AM with thin film deposition reaping these technologies' advantages while bypassing their limitations. We aim to equip parts with mechanical and electrical properties that are conventionally not achievable, not in costs nor in performance. This way, we aim to introduce key surface properties ranging from corrosion to scratch resistance, hydrophobicity all the way to enhanced flow characteristics. These performances shall rise from a geometric and material optimisation across multiple length scales, from nano to macro (see Figure 2).

In summary, our group works on the forefront of three emerging technologies, simulation-based design and property prediction, additive manufacturing and thin film deposition. All fields together will enable novel digital

materials and designs, their direct conversion into physical parts as well as the guarantee of their compliance through properly defined and tailored failure criterions. This interdisciplinary and integrative research will streamline the digital manufacturing workflow all the way from the idea to the final product and will enable designers and engineers to better transform their ideas into reality.

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Why apprenticeships are a vital part of our industry

There has never been a more exciting time for apprenticeships in the UK. Here Clair Prosser at BSRIA explains more about the recent Apprenticeship Levy

When the Apprenticeship Levy came into force in April this year for all employers who are turning over more than £3 million a year, apprehensions still existed over whether the scheme will be able to supply the “first-rate” training that both industry and apprentices need.

Julia Evans, Chief Executive, BSRIA, said: “The Apprenticeship Levy has gone ‘live’. BSRIA welcomes the government’s emphasis on increasing investment in apprenticeships and the industry is ready to stimulate more training and apprenticeships. However, quality is essential over quantity per se and BSRIA is keen to see long-term success for the scheme.

“What is paramount is how important it is to close the industry skills gap. Apprenticeships provide the backbone for a career in engineering for many employees and no compromises should be made regarding them.

“In essence: the levy must meet industry and apprenticeship needs.

“BSRIA is leading by example and looking forward to welcoming apprentices; junior apprentices are to be placed in the engineering divisions and in the marketing department. BSRIA is also exploring the possibility of a higher apprenticeship which will ultimately result in a BA (Hons) award. It’s a great time for employers to be investing in their people.”

Industry concerns:

- Some firms face paying for the levy but are unable to access new or updated training standards, or have no approved providers available locally.
- A lack of accessible information for employers about the government’s list of approved providers and their quality of training.

- The government should give employers longer than 24 months to spend their levy vouchers, if current issues remain unresolved in the first year.
- Ineffective careers guidance in schools about available apprenticeship options.
- Moving forward: the government should consider a more flexible skills levy, to not only support apprentices, but also retraining for adults.

Over 900 construction firms are to be charged the levy, which will help fund the government’s target of creating 3 million apprenticeships by 2020.

Back in March – BSRIA celebrated National Apprenticeship Week (NAW 2017) which brought together employers and apprentices from across England to celebrate the success of apprenticeships.

Julia Evans, Chief Executive, BSRIA, said: “With the proposed government housing targets of between 225,000 to 275,000 (or more) new homes per year that will be needed to keep up with population growth and years of under-supply, which could translate into almost one million new homes built by 2020, construction and engineering apprentices are crucial.

“Indeed, apprenticeships are essential for up-and-coming builders to get into the workplace: we hope this week can highlight the importance of such vital trades.

“We need to change the image of our industry and make it a more attractive career proposition. The government can certainly help the industry to communicate better to make engineering more exciting. Maybe we need to move the focus away from one of being a ‘construction industry’ to one focused on ‘the built environment’.”



Undeniably, one of the major threats to the government's infrastructure plans is the skills shortage in construction. The need to stem the skills gap and attract more people into construction careers is more essential than ever since Brexit, as many of BSRIA's members – and the wider industry – rely on skilled workers from Europe.

An apprenticeship can take you anywhere and young people, engineers and entrepreneurs alike can rise to the top through traineeships and apprenticeships."

So the memo is clear: apprenticeships can help industry to plug the fissure within engineering and, ergo, the wider construction industry!

The spirit of NAW 2017 fits in well with BSRIA's current INSPIRE project which is working with local schools, national and local politicians and the media to promote STEM and change its perceptions.

National Apprenticeship Week 2017 – ran from 6th to 10th March 2017.

National Apprenticeship Week is co-ordinated by the National Apprenticeship Service and is designed to celebrate apprenticeships and the positive impact they have on individuals, businesses and the wider economy.

The 10th National Apprenticeship Week brought together employers and apprentices from across England to celebrate the success of apprenticeships over the last decade and will seek to encourage even more people to choose apprenticeships as a fast-track to a great career. ■

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Creating a highly skilled workforce for the future

Ontario's Ministry of Education shares why a highly skilled workforce is vital for progression and how this is being encouraged in the province

Building the Workforce of Tomorrow: A Shared Responsibility is the final report of the Premier of Ontario's Highly Skilled Workforce (HSW) Expert Panel. The report contains the Panel's final recommendations on developing a strategy to help the province's current and future workforce gain the skills needed to adapt to the demands of a changing economy.

The Province has since developed a Highly Skilled Workforce Strategy based on these recommendations. The Strategy includes specific direction for both the kindergarten to Grade 12 and postsecondary education systems in Ontario to support these changes.

What strategies are in place to ensure this happens and students are supported?

We've already made significant progress since the HSW Strategy was released. Moving forward, a new emphasis on global competencies and experiential learning will permeate the education system at all levels.

In addition to the HSW Strategy noted above, Ontario launched *Achieving Excellence: A Renewed Vision for Education in Ontario* in 2014. It focuses on what Ontarians view as essential outcomes for children and students through 4 goals: achieving excellence, ensuring equity, promoting well-being, and enhancing public confidence.

All of these elements are also present in Building the Workforce of Tomorrow: A Shared Responsibility, and have been carefully integrated into the implementation work of the HSW strategy. Similarly, the HSW strategy involves and builds on the existing work of a number of Ontario ministries, including the Ministries of Advanced Education and Skills Development, Education, Citizenship and Immigration, Economic Development and Growth, Infrastructure, and Indigenous Relations and Reconciliation.

How important is it for education to prepare students for the jobs of tomorrow?

Our government is working hard to give Ontario students the chance to develop strengths, interests and goals during their school experience – through programmes, such as Cooperative Education, Dual Credits, and Specialist High Skills Majors (SHSM). Starting in September, more than 50,000 students will be enrolled in almost 1,900 SHSM programmes. This represents 2,000 additional students and 108 new programmes for the 2017-18 school year. This is an innovative, high demand programme that lets high school students focus on a career path that matches their skills and interests while meeting the requirements of their high school diploma.

We are looking at ways we can expand experiential learning to provide all students from kindergarten to grade 12 with a broader range of learning opportunities outside of school that are connected to the community. These opportunities and the province's education and career/life planning programme are outlined in Creating Pathways to Success Kindergarten- Grade 12, which helps students to successfully make the transition to their post secondary destination.

Can you explain a bit about the career studies pilots and how they will enable this process?

Reviewing the guidance and career education curriculum on a priority basis is a key recommendation of the HSW report to ensure that it introduces students to a variety of learning pathways and opportunities.

The career studies pilots are in progress now until the end of this school year, as a part of the current grade 10 career studies course. The educators participating were provided with topics for the 4 modules on digital

literacy, career life planning, financial literacy and entrepreneurship, which they will customise for delivery with their students. Once the projects are complete, teachers will provide their final observations, about the impact of the project, the effect on student achievement and engagement, and artefacts of student learning. As these pilots are currently underway, it's important for us to review the data collected once they are completed to inform next steps.

This past November, Minister Hunter announced that financial literacy will be integrated into the careers studies course. Since 2011, we have invested more than \$3 million in financial literacy resources and professional learning opportunities for teachers to enhance financial literacy among Ontario's elementary and secondary students.

How will these be monitored?

Ontario's Achieving Excellence: A Renewed Vision for Education in Ontario includes a plan to monitor and evaluate our progress. Each of the renewed goals is accompanied by a "plan of action," as well as measures by which we will assess our progress toward each goal.

A variety of data and results from both internal and external sources contribute to knowing and understanding how our students are progressing towards the goals we've set out. Standardised tests, and assessments through EQAO, TIMMS and PISA provide a variety of evidence that inform our next steps. All of these contribute data that tell us how our students are doing in relation to the goals we've set out.

For instance, we launched our Renewed Math Strategy in the fall of 2016, based on solid evidence pointing to the need to improve student achievement in math. We are evaluating this strategy, as well as the results, to ensure that it is having the desired outcomes for student achievement. ■

Ontario Ministry of Education
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Non-Indigenous individuals' responsibilities within higher education contexts

Dawn Zinga, from the Department of Child and Youth Studies at Brock University explore the responsibilities of non-Indigenous individuals within higher education settings and the inequalities that exist

As a non-Indigenous scholar working in the area of Indigenous education, I spend a lot of my time thinking about my own role in perpetuating inequality within higher education and answering questions posed by non-Indigenous faculty, staff, and students. These questions usually fall into two broad categories. The first category consists of questions about why I am raising an issue or why something is important, while the second category tends to focus on questions about what individuals can do now, so that they know about the inequities that exist. These two categories of questions point to some interesting aspects about the responsibilities of non-Indigenous individuals' within higher education settings. One of the first responsibilities is to become educated about the realities of Indigenous peoples and related the systems of inequality. The second responsibility that I will focus on is what to do with the knowledge that you gain when you become educated.

Starting with myself, I am a several-generations-removed immigrant to the ancestral lands on which I reside and I have experienced a position of some privilege in the mainstream structures of society, such as education, health services, and other governmental systems. While I grew up in a blue-collar home and experienced



the discrimination that can be associated with class and being a girl, I was afforded many privileges and rarely had cause to question that I belonged in the classrooms that I occupied. I frequently saw myself and my life experiences reflected in the classroom and my experiences within society. From a young age, I had a questioning mind and often challenged teachers about why some voices and some life experiences were not represented in the curriculum or were represented in very narrow and proscribed ways. Through my own search for knowledge and the generous teachings of my Indigenous colleagues, I became aware of the systems of racism and inequity experienced by individuals who are

minoritised by the mainstream systems of privilege and discrimination that continue to be reinforced throughout society and particularly within systems of education. In my role as a university professor, I am also responsible for exposing undergraduate and graduate students to these systems of inequity and to challenge their taken-for-granted assumptions.

Some of my students resist any challenges to their understanding of society and the status quo and remain facing the first responsibility of education. Other students engage in the teaching but sink into guilt and seem paralysed by the immensity and



complexity of the issues they have just learned exist. The second responsibility of what to do with the knowledge once you have learned it is easier to address than the resistance to learning that the world does not necessarily operate in a way that you thought that it did, and that with or without your knowledge, you have occupied a position of power and privilege. The first thing for non-Indigenous individuals to realise is that guilt is an emotion that will not be helpful. It must be experienced but in the end we are not responsible for the actions of those who preceded us, but we are responsible for how we address the legacy

that was left behind. Essentially, non-Indigenous individuals must focus on how to act on the knowledge that has been gained.

Non-Indigenous individuals have a choice. They can choose to close their eyes to uncomfortable realities and continue on perpetuating them or they can choose to use their individual voices to make a difference. Using one's voice can be as simple as speaking up when an inequality is being perpetuated, or challenging a policy that negates other people's experiences or lived realities. It can be exposing others to knowledge they

may not be aware of or supporting someone when that person's viewpoint is being shut down as invalid or irrelevant. Sometimes it can be listening to another perspective and being open to being challenged and educated about how your own actions or lack of action may have reinforced inequalities or alienated Indigenous individuals.

Addressing these two responsibilities within educational contexts can lead to educational settings in which Indigenous students and other Indigenous individuals feel welcome and accepted. It can open up important spaces to talk about ways of moving forward together towards positive change that does not reproduce or perpetuate systems of inequality. While I have focused on higher education contexts, this can also be extended to other educational contexts. Making a choice to address these responsibilities daily is a choice to move beyond resistance and guilt to positive action and strong relationships that can help us all negotiate a new future of education for all students.

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Why you can't brand a university

Ian Allison, Strategic Creative Director, Instinctif Partners talks about creating an effective university brand and how traditional methods have changed

Traditional, linear models of branding don't stack-up for universities. You can't brand a university – you engage its constituencies in a forensic process of discovery, insight, co-creation, testing and validation. This journey is non-linear, elective and challenging to measure.

University brands are unique. They need to function as corporate brands, service brands, employer brands and product brands. They are complex not only because of the socio-economic and geo-political landscape, but also the range of stakeholders, and the fact that universities seldom deliver one service or product.

“A strong, differentiated, trusted brand is now of great strategic significance for a university. It's essential to cut through the noise of the competition, and a brand that is 'owned' by its community will enjoy the benefits of (global) promotion through trusted social and professional networks.”

Why the old way no longer works

Brand traditionalists will tell you that if you don't manage your reputation, your audiences will manage it for you. But there has been a paradigm shift in recent years: brands now have participants not audiences – the relationship dynamic has changed.

This shift has been driven by a number of factors including the exponential growth and integration of communication technologies into our lives; our rapidly expanding (and global) social networks, and brands' own data-driven CRM and marketing in pursuit of ever-closer personalisation. This is only set to expand further with brands now looking to exploit artificial intelligence, augmented and virtual reality.

We have also become far more sophisticated in our understanding of how we're being marketed to, and who we're giving our data to, leaning towards our trusted, personal networks for information, advice and validation. The age of broadcast became the age of conversation; social media has enabled us all to create, edit and share instantly and brands have encouraged this participation.

The divide between brands and real-life has become fuzzy. Brands always aimed to be part of our lives, but they expect it to be on their terms – however, brands are now what consumers tell each other they are.

So what does this mean for universities?

Universities are competing harder than ever before to recruit students, attract and retain the best staff, maintain and improve their service and product, and secure funding for research and innovation. Potential staff, students and funding are internationally mobile which makes attraction and retention an on-going challenge.

In addition to meeting educational criteria for entry, students now have to pay fees. They also believe that a university's brand can attach itself to their future careers. As a result, like consumers, they are highly specific about their choices and can be vocal about their experiences, for example via the National Student Survey (NSS scores) – one of many criteria (e.g. the impact of research, the quality of teaching and even how up-to-date and integrated their tech is) against which universities are now judged.

Staff can be equally vocal, researchers have international reputations, and partners hold important local, national and international relationships.



A strong, differentiated, trusted brand is now of great strategic significance for a university. It's essential to cut through the noise of the competition, and a brand that is 'owned' by its community will enjoy the benefits of (global) promotion through trusted social and professional networks.

“Universities are competing harder than ever before to recruit students, attract and retain the best staff, maintain and improve service and product, and secure funding for research and innovation. Potential staff, students and funding are internationally mobile which makes attraction and retention an on-going challenge.”

Brand engagement is essential

A university is a rich community – and finely balanced ecosystem – of students, academics, teachers, professional services staff and key external partners. They all have a vested interest, and a stake, in the university's success.

Brand engagement is therefore essential to success – this means harnessing co-creation and deep collaboration, and being agile, not dogmatically linear, in your approach. Effective university branding is created with its constituencies, not done to an institution.

If you would like to hear more, get in touch with Sarah Harrison Sarah.Harrison@instinctif.com . ■

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Protecting nature: an ambitious action plan

Karmenu Vella, EU Commissioner for Environment, Maritime Affairs and Fisheries details how protecting nature, people and the economy is a priority in Europe

Protecting nature has always been a hot button issue in the United Kingdom. So it came as no surprise, when I was asked to review the state of EU nature legislation, to see massive support emanating from the UK. More than 105,000 people, the second highest turnout in the EU, replied to the Fitness Check consultation, with an enormous majority supporting the existing framework.

That framework has been in place for 25 years, with the Birds and Habitats Directives combining to form the [Natura 2000 network](#), the largest coordinated network of biodiversity-rich protected areas in the world.

You may ask what is Natura 2000? Well instead of that name, think of the most iconic nature spot in your country or region. You can be almost 100% sure that it is a designated Natura 2000 site. If you are not sure, you can even check on our own [Natura 2000 viewer](#).

This vast network is something the EU can be proud of, but there is no doubt that it could perform much better. Our comprehensive review showed that while the principles are sound and the goals are still valid, we need real change on the ground. Protecting the ecosystems of today requires a more modern approach, more suited to the 21st century. That's the idea behind the new Action Plan – ensuring that the Directives fully deliver their potential, with a triple benefit for nature, for citizens, and for the EU economy.

The improvements will centre around managing protected areas more efficiently, improving the connections between nature protection and socio-economic activities, and engaging more closely with young people, stakeholders, and national authorities.

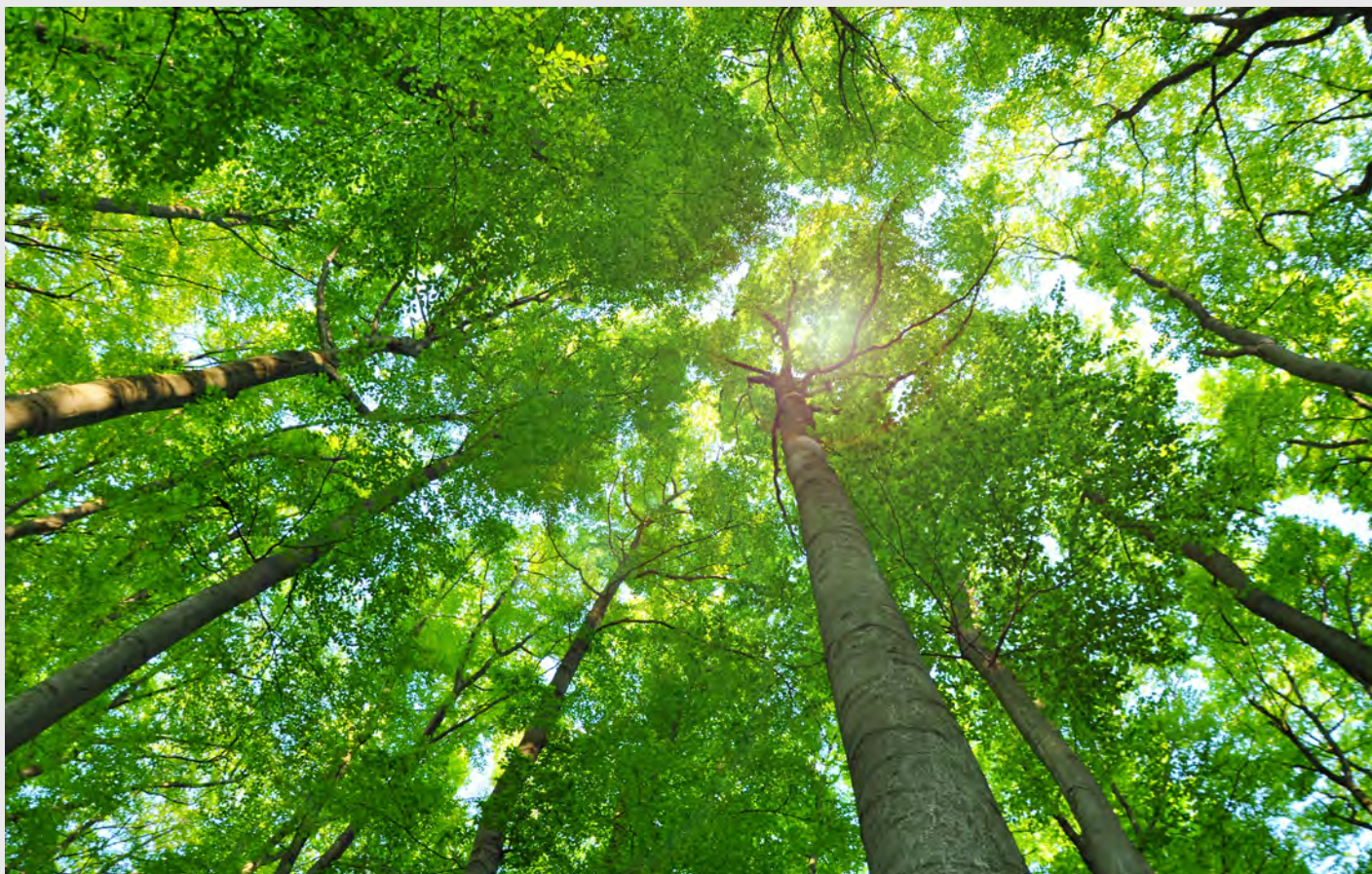


Karmenu Vella

Protecting nature starts with improving knowledge

It starts with improving guidance and knowledge. We will begin by promoting smarter participatory approaches that strive to involve landowners and users in the implementation process. We will also develop on-site permit procedures, species protection and new guidance on topics like wind energy, hydropower and aquaculture. The Action Plan will explore ways to integrate ecosystem services into the heart of decision-making processes. Better public access to data necessary for implementing the Directives (like satellite imagery from the Copernicus programme) will also help.

A second priority is to build political ownership and strengthen compliance. This isn't just about the UK, it's about encouraging all Member States to take ownership of the network, and to ensure that the necessary conservation measures are in place for all Natura 2000 sites. We want stronger collaboration with national and regional authorities, landowners, civil society and other



stakeholders, as this is the best way to safeguard local biodiversity and encourage economic activities in harmony with nature protection.

We also need more investment in Natura 2000, and more efficient uptake of EU funding. Over the next 3 years of the [LIFE programme](#), the Commission is proposing to allocate an additional €60 million to Natura 2000 and biodiversity projects. Apart from that measure, our goal is to stimulate and encourage private investment in nature projects [Natural Capital Financing Facility](#), a financing partnership between the Commission and the European Investment Bank providing tailored loans and investments.

The last priority is communication. The Natura 2000 network covers a million square kilometres, but a large majority of citizens have never heard of it. That needs to be remedied. So we are stepping up outreach activities, supporting knowledge exchange through a joint platform with the Committee of the Regions, and involving young people through initiatives like the European Solidarity Corps volunteering programme. We have also proclaimed 21 May as the European

Natura 2000 Day in order to raise awareness around Europe.

The success of the Plan will depend on building a strong culture of collaboration and trust. That means reaching out to citizens, local, regional and national authorities, to industry, business and civil society.

This Action Plan isn't about fencing off nature. Quite the opposite – it's about finding ways to live in harmony with nature, where society and industry continue to develop, but while treading more softly on the Earth. You can sum it up with one simple thought – the only sustainable path to a more competitive economy is the one that embraces the protection of nature. In 2017, I can't think of a better path. ■

Karmenu Vella

Commissioner for Environment, Maritime Affairs and Fisheries

European Commission

https://ec.europa.eu/commission/commissioners/2014-2019/vella_en

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Harmonising the bio-based economy policies

Standardisation can accelerate bio-based economy growth. Here, Suzan van Kruchten, Standardisation Consultant, NEN explains

Bio-based products represent an important part of the bio-economy, which is seen as a major source of economic growth and employment for Europe in the 21st century. Standardisation can accelerate bio-economy growth as several projects of NEN, The Netherlands Standardization Institute, show!

Standards

Standards, being voluntary agreements between stakeholders, are a powerful tool to support the uptake of the bio-economy! Standards will support the growth of the bio-based products market by increasing transparency, reducing technical barriers for trade and boosting customer confidence.

In 2011, the European Commission requested the development of horizontal standards for bio-based products. Serving as the acting secretary of the European Technical Committee CEN/TC 411 bio-based products, NEN has helped developing these standards. Some examples:

- Common terminology (EN 16575)
- Methods for determining bio-based content (EN 16587-1)
- Sustainability Aspects (EN 16751)
- Life Cycle Assessment (EN 16760)
- Declaration tools for B2B (EN 16848) and B2C (EN 16935).

Standards are developed through a multi-stakeholder consensus process between private companies, govern-

ment and civil society organisations. Therefore, with standardisation you can count on broad societal support!

Pre- and co-normative research

Another aspect, where NEN has proved its value for the bio-based economy by building knowledge, is the execution of pre- and co-normative research for bio-based products. This means setting up test methods, validating these methods and establishing test method standards. NEN has led several pre- and co-normative projects, like the projects "Open-Bio" and "STAR4BBI".

Certification

Certificates enable companies to demonstrate that they comply with standards. Certification schemes specify the rules for the certification process. NEN has established two of these certification schemes relevant for the bio-economy:

- **Better Biomass:** is used by organisations to demonstrate that the biomass they produce, process, trade or use meets well established international sustainability criteria.
- **Bio-based content:** is used to specify and validate the amount of biomass in a bio-based product, based on the European standard EN 16785-1:2015 "Bio-based products – Bio-based content – Part 1: Determination of the bio-based content using the radiocarbon analysis and elemental analysis". This standard provides a

method of determining the bio-based content of solid, liquid and gaseous products using the radiocarbon analysis and elemental analyses.

Communication

Additionally, NEN is involved in dissemination and engaging relevant stakeholders. InnProBio (Forum for Bio-Based Innovation in Public Procurement) is an example where public procurers are informed and encouraged to engage in the bio-economy. The project develops tools for purchasers, facilitates the creation of buyers groups, and increases awareness in order to lower the barriers to purchasing bio-based products.

More information

Want more details on our work for the bio-economy? Please visit our website www.biobasedeconomy.eu



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NEN

Assessing climate change in the Arctic

Norwegian Polar Institute's Director Jan-Gunnar Winther highlights the challenges associated with climate change in the Arctic and its global impact

It is a fact that no region of the planet is experiencing more dramatic climate change than the Arctic. In recent years, this has resulted in melting glaciers, rapid ecosystem changes, diminishing sea ice, and changes in the atmospheric circulation and ocean properties. Ocean temperatures are increasing due to global warming. The Arctic is undergoing changes unknown to have occurred during the last 1,450 years (Intergovernmental Panel on Climate Change (IPCC), 2013). Climate models project that the most pronounced warming in the future will happen in the Arctic. In a business-as-usual scenario for greenhouse gas emissions, temperatures may increase by 8 to 10 degrees Celsius. Even in IPCC's most aggressive scenario for cutting greenhouse gas emissions, the Arctic will warm with several degrees and in turn fundamentally change this region as we know it today.

Global impact

The Earth's regions are connected by circulation in the atmospheric, ocean, climate and weather patterns. Arctic climate change therefore has profound global consequences and affects global conditions such as sea level rise, ocean acidification, permafrost thawing (which releases potent greenhouse gases) and changing weather patterns, such as the monsoon. Arctic climate change is therefore arguably relevant to the weather and climate in regions distantly located from the Arctic.



Photo: Allison Bailey/Norwegian Polar Institute

The lipid-rich zooplankton Calanus Glacialis is an important source of nutrition for seabirds and fish in the Arctic

Although the development is disturbing, climate change also provides some advantages. Increased biomass production in the northern waters – not at least in the highly productive Barents Sea – may become an important resource for the world's ever-increasing need for food and proteins. Furthermore, the Arctic's special role in global change makes it a potential laboratory for developing new green technology and new solutions that may be utilised in a global context, under the idea that: What works in the Arctic will work elsewhere.

The opportunities in an Arctic with much less summertime sea ice are numerous. New shipping lanes, increased commercial fishing, new

bioprospecting activities and harvesting marine ingredients for bio-production (including organisms at lower trophic levels in the food web and at greater depths,) are among the main gains from the situation. Oil, gas and minerals are other resources that may be possible to exploit increasingly further north in the near future.

A call for knowledge

However, today's rapidly changing climate and the major ecosystem changes that go with it, impose a fundamental challenge for management: the system is highly dynamic with large seasonal changes. We must avoid making decisions and investments for the future based on yesterday's situation. This calls for a



Photo: Jon Aars/Norwegian Polar Institute

Female polar bear between ice floes in the Barents Sea

continuously updated knowledge base and sophisticated earth system models to project future changes.

Also, we experience a northward expansion of marine species from the south. The fishing fleet has recently taken advantage of this development and fishing grounds are relocated northwards into the shelves of the Arctic Ocean, especially in the North Atlantic region.

This raises the question whether we may experience commercially viable fisheries in the Arctic Ocean in the future. The area of the Arctic Ocean beyond 200 nautical miles of Canada, Denmark/Greenland, Norway, Russia and the U.S is 2.8 million square kilometers. Up to now, scientists have documented an increase in zooplankton biomass over some areas of the continental shelf. However, scientists raise doubts about whether the same

will happen over deep water in the central Arctic Ocean. An important limiting factor for increased production is available nutrients, which are much lower in abundance in deep water than over the shelves.

When the Arctic marine systems become warmer, expanding pelagic fish stocks will likely migrate into the Arctic Ocean to utilise the short peaks in production there, but will likely retreat to the more productive shelves when the peaks decline. Thus, most of the fisheries in the Arctic Ocean may be confined to the shelves. As a precautionary action to avoid illegal, unreported and unregulated fishing (IUU) in areas beyond national jurisdiction, the 5 Arctic coastal states signed an agreement in July 2015 where they agree to not fish in this area. Furthermore, a scientific research and monitoring programme was established in order to obtain more knowledge in support for future management. The longer-term goal is that other countries also commit to withstand from IUU-fishing in this area.



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The EU Action Plan against wildlife trafficking

Much has already been achieved when it comes to wildlife trafficking, but the hard part is still to come, says Colman O'Criodain and Emilie van der Henst

It is already a year since the Environment Council agreed Council conclusions endorsing the European Commission's Action Plan against wildlife trafficking. Since then, as Commissioner Vella reported in this journal in February, the Commission has already achieved a great deal. Virtually all of the measures they proposed to strengthen the Convention on International Trade in Endangered Species of wild fauna and flora (CITES CoP17) were adopted at the 17th meeting of the Conference of the Parties in Johannesburg last October. These included increased protection for all pangolins and certain species of sharks, precious timbers, parrots and reptiles, as well as measures to address corruption in international wildlife trade, and to tighten the rules on trade in hunting trophies.

Since Commissioner Vella's article appeared, the European Commission has also published guidelines on the interpretation of its rules governing ivory trade. These effectively ban the re-export of all ivory for commercial purposes, even if the ivory originated before the CITES trade ban entered into effect. They also clarify existing rules for the trade of antique ivory.

What remains to be done?

Well, for a start some NGOs are lamenting the fact that the EU has not opted for a complete ban on domestic ivory trade. They point to the US market rules enacted last year. However, while these were announced as a ban, in fact they allowed for a range of exemptions, making them very similar to the highly restrictive rules



The penalties for offences under the EU wildlife trade laws vary enormously among Member States. Despite the fact that the EU has endorsed the rhetoric that wildlife crime is organised crime, and that it requires an organised criminological response, the maximum sentences applicable in many Member States do not reflect this. The UN Convention against Transnational Organised Crime (UNTOC) is an essential tool in securing international cooperation in fighting transboundary crime. But in order for it to be invoked, the alleged offence must carry a maximum applicable sentence of more than four years. However, approximately half of Member States do not have maximum penalties on their statute books that meet this threshold.

Another respect in which Member State commitment is crucial is in the resources they allocate to their enforcement of wildlife laws. This is much harder to measure. However, there is a lot of anecdotal evidence from customs and other staff suggesting that, at least in some Member States, wildlife crime is not adequately resourced. One would have hoped that the Member States would have used the opportunity of the June 2016 Council Conclusions to make a collective commitment to allocate more resources to the problem. Sadly, this did not happen.

What's the verdict overall?

The EU wildlife trade Regulations are certainly among the strictest and the best drafted in the world. And, by and large the Union has been a force for good in the wider CITES arena, especially at CITES COP17, which followed on the publication of the action plan. The plan has contributed to making CITES more effective. But unless the Member States play their part it will not realise its full potential. ■

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the EU has had in place for the last 20 years. Therefore, WWF is not among the NGOs calling for a domestic ban. While we have no objection to tighter rules if these are supported by evidence, we note that the CITES-mandated Elephant Trade Information System (ETIS) does not identify the EU as a significant destination for illegal ivory. Therefore, we support the EU's approach of a stakeholder consultation on the need or otherwise for tighter rules. In the meantime, we would prefer to see the EU address matters of more urgent concern.

By the EU we mean the collective entity of the EU institutions and the Member States. In this regard, it is the Member States we are most concerned about. EU wildlife trade law devolves the issuance of relevant permits to the individual Member States. In line with EU norms, responsibility for legislation setting out offences and penalties, and the enforcement of such legislation, also lies with the Member States.

EU Zoos Directive drives conservation, education and research

European Association of Zoos and Aquaria's David Williams-Mitchell shares insight into the EU Zoos Directive and explains the impact of it on the sector

The European Commission (EC), as part of its drive to increase the effectiveness of EU legislation, is currently carrying out Regulatory Fitness and Performance Programmes (REFIT) on Directives and Regulations. For environmental concerns, the EC has already carried out a REFIT evaluation on the Birds and Habitats Directives, which were retained in full, partly thanks to the lobbying of groups such as the European Association of Zoos and Aquaria (EAZA), and is currently carrying out a REFIT on the key European legislation regulating zoos – the Zoos Directive 1999/22/EC.

Member States, driven by the views of their citizens, have expressed concern that the EU is trying to do too much. In response, the European Commission is looking at its policies to confirm that they are still following the subsidiarity principle and to examine their value to the EU. As a result, the impulse to review these laws and assess their suitability for the canon of European Law should be welcomed; however, the Commission should be wary of rejecting some laws, notably ones that encourage those they regulate to lead the world in their sectors. One such law is the EU Zoos Directive.

EU Zoos Directive

The EU Zoos Directive was enacted in 1992, and regulates the activities of cultural institutions that hold animal collections for public display. Before the directive, attitudes towards animal

husbandry and the role of zoos differed quite widely across Member States; national legislation, if it existed at all, was equally varied. It would not be insulting to our Members to say that the requirements of the Zoos Directive have revolutionised their approach to operating their institutions, and they are now global leaders in the field.

The requirements of the directive are quite simple in essence: it requires zoos and aquariums to practice good husbandry of their animals, and contribute to conservation, research and education. A zoo operating under the directive cannot be a collection of mismatched animals living in substandard conditions for the amusement of visitors; neither can it just concentrate on good husbandry and accommodation. It must seek actively to preserve biodiversity both locally and globally, conduct zoological research that assists in the conservation mission, and sensitise the public to the natural world in order to foster a sense of care and engagement.

EAZA was founded in part to allow zoos to collaborate on these missions in order to not only meet the directive's requirements, but to go beyond them; the Association now comprises over 350 zoos and aquariums across Europe and the Middle East. We believe that working together as a pan-European network has a multiplying effect that allows even the smallest of zoological

institutions to make a greater contribution than would otherwise be possible; our faith in the ability of our Members to make this contribution relies on a measure of compatibility between our institutions wherever they may be. It would be impossible, for example, to run successful breeding programmes without the sure knowledge that every zoo and aquarium in our network holds to the same high standards of scientifically based operation.

EAZA, admittedly, requires its members to go beyond the requirements of the Zoos Directive. As such, the directive should be seen as the entry level standard for zoos in Europe, not the end state. This does not mean that the directive does not have value. Indeed, its value lies in the generality of the mission it describes: it is not sufficient for a zoo to concentrate on the totality of its efforts on one particular activity at the expense of others. A zoo with wonderful education programmes loses credibility if it has substandard accommodation for its animals or no conservation programmes. The directive's baseline also provides the starting point for zoos that wish to meet EAZA's Standards – moving to our requirement is easier for zoos that already meet those of the directive, as it means that much of the groundwork for EAZA Membership has already been done.

It is worth noting too, that the Zoos Directive is only one part of a larger



Legislation encourages the zoo conservation of animal biodiversity in all its forms

regulatory framework that ensures sustainable and socially profitable operation of zoos. European Ex situ Programmes (EEPs), the EAZA administered population management programmes for conservation of species and education of the public, were implemented back in 1985 to complement the terms of the Convention on the International Trade in Endangered Species (CITES). From that time, zoos in the EEP network committed to building sustainable ex situ populations of species. The programmes hold the animals in common, meaning that for over 400 species of wild animals, there is no sale or purchase of animals in our network – removing any profit motive from the breeding of these animals, and helping to dissuade wider trade in these species. Another part of the framework is the Convention on Biological Diversity, an international treaty that requires signatory states to, among other activities, work to preserve biodiversity and educate the public on its value. These

states have, as a matter of necessity, outsourced many of these obligations to zoos, aquariums, botanical gardens and science centres.

In short, the Zoos Directive is one of several parts of a system that not only requires zoos to fulfil certain conditions, but also encourages them to go well beyond them. EAZA zoos and aquariums, for example, contributed more than €25m to field conservation projects from 2014-2016, and our conservation education standards are world leading. With this in mind, and in full understanding of the motives of the European Commission in streamlining EU law, EAZA believes that removing the directive from EU law would be a mistake, and encourages the Commission to retain it in full; it's a great starting point for zoos to make a real difference to biodiversity, zoology and education, and we support it fully.

The EAZA Position Statement on the Zoos Directive REFIT can be found

[here](#). For more information on EAZA activities please contact the EAZA EU Policy Manager, Daniel Nuijten daniel.nuijten@eaza.net.



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Good marine health remains a challenge due to climate change

Climate change and marine health are intrinsically linked. Open Access Government's Ciara Ruane explains how the National Science Foundation supports both

Marine health is an essential part of the war against climate change. The US National Science Foundation (NSF) highlight it as a key issue, of both economic and environmental significance. The NSF's Division of Ocean Sciences (OCE) promotes collaboration between scientific and educational fields to tackle these challenges head on. Through research support and funding, the OCE provides knowledge which is critical to addressing some of the most pressing environmental challenges involving earth processes. Ocean research looks to the future, with a focus on expanding weather forecasting abilities to predict weather years in advance. Oceans are a key factor in innovations such as these.

"The greater metabolic strain required in these environments creates a greater need for oxygen, which is lacking. The study revealed that these changes cause animals to migrate away from the equator."

The NSF hopes that the need for more accurate weather predictions in the face of climate change will mean more funding for ocean research. They also believe that physical oceanographers have made an 'enthusiastic' start on the issue, giving hope for big advancements in the field over the next decade. However, they also name global climate prediction 'one of the most difficult' problems scientists in the field of ocean study have faced.

The average lifespan only sees a few incarnations of the oceanic climate system, meaning it is extremely difficult to gather extensive data on the subject. The NSF is currently running a funding programme for the Center for Ocean-Land-Atmosphere studies. This awards grant funding to "1) basic research on pre-

dictability on intraseasonal, seasonal, interannual, and decadal timescales; 2) evaluation of the predictability, skill, and fidelity of US national climate models; and 3) contributions to the development of next generation seamless prediction systems."

The grant aims to work towards developing more accurate models of climate prediction and boost knowledge of Earth's oceans through community integration and education as well as the funding of scientific research.

Mapping

Another goal for the NSF is ocean observation and mapping. Innovations like the TOPEX/POSEIDON satellite mission allow for a level of ocean observation accuracy within the centimetre. Ocean floor mapping is essential for scientists to understand much of how the world works. Continental shift, ocean currents and 'ecological niches' can all be explored and discovered through the technique. However, advancements still must be made. The current technology utilises sound waves to create images of what lies under the sea.

Sound wave technology is mainly used by ships to create localised maps, and allows for enormous detail compared to previous mapping techniques. In recent years new submarine formations, volcanoes, hot springs, and trenches have been uncovered. In 2014 the NSF published an article about new discoveries made with satellite data. Authors of that study said that 80% of the ocean floor at the time was still unmapped. The most recent and advanced image of the ocean's geography, made with data from a NASA satellite, can capture 'any feature larger than 5km'. This map was made by detecting gravitational anomalies. This is a fairly recent advancement from sonar technology, and represents a potential new path for geographical surveying.



“Ocean floor mapping – is essential to scientists to understand much of how the world works. Continental shift, ocean currents and ‘ecological niches’ can all be explored and discovered through technique. However, advancements still must be made. The current technology utilises sound waves to create images of what lies under the wave.”

Warming waters

Scientists fear that oceans becoming warmer and less oxygen-rich in the face of climate change presents a challenge for marine wildlife. In 2015 the NSF outlined a study on the effect these changes would have on Atlantic rock crabs. Irwin Forseth, of the National Science Foundation’s Division of Integrative Organismal Systems, said of the study: “Understanding connections such as this is essential to allow us to predict the effects of environmental changes on the distribution and diversity of marine life.”

The greater metabolic strain required in these environments creates a greater need for oxygen, which is lacking. The study revealed that these changes cause animals to migrate away from the equator. Cod numbers are also threatened by these changes, with their population already in decline. This obviously has indications for feeding earth’s population, but would also create disturbances in the marine ecosystems and food chains. Further monitoring of such changes will be essential to adapt to the effects of a changing climate and prevent the worst of it. ■

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Polar vortices and their interactions

What are polar vortices, and how do they influence the rest of the atmosphere and climate system? Johns Hopkins University's Professor Waugh explains

Polar vortices are planetary-scale systems comprised of rapid west-east flow that circumnavigates the pole in middle or high latitudes. These vortices influence not only the Polar Regions where they exist, but their influence also extends into the tropics and down to the surface, as well as into the oceans. As a result, polar vortices play an important, but often underappreciated, role in Earth's climate and weather.

In each hemisphere there are 2 distinct polar vortices in Earth's atmosphere: one in the troposphere (lowest 10-15km of the atmosphere) and one in the stratosphere (10-50km). These 2 polar vortices differ not only in their vertical extent but also in their latitudinal scale and seasonality: The tropospheric polar vortex is larger than in the stratosphere and it exists all year, whereas the stratospheric polar vortex exists only from fall to spring. The existence of 2 distinct polar vortices with different characteristics, and impacts on the rest of the atmosphere, has led to some confusion in the press and social media.

Stratospheric vortices

The most pronounced influence of stratospheric vortices in Earth's climate system is their role in stratospheric ozone depletion. Very low temperatures occur within these vortices, and this is a necessary requirement for the chemical processing that leads to the destruction of ozone by chlorine and

bromine species. Furthermore, vortex air is largely isolated from surrounding air, containing ozone depletion within Polar Regions. The formation of the Antarctic ozone hole but not an equivalent Arctic ozone hole occurs because the Antarctic vortex is less disturbed and colder than its Arctic counterpart.

"Polar vortices are not exclusively a feature of Earth's atmosphere, and there are polar vortices in the atmospheres of Mars, Venus, Saturn, and Saturn's moon Titan. Many similarities exist among these polar vortices, including strong winds circumnavigating a cold winter pole, and the occurrence of unique chemical processes within the vortices (ozone depletion on Earth, and formation of CO₂ clouds on Mars and HCN clouds on Titan)."

The influence of stratospheric polar vortex is not confined to the stratosphere. The strengthening of the Antarctic polar vortex over the last few decades due to ozone depletion, has contributed to a southward shift in the Southern hemisphere tropospheric circulation as well as changes in the Southern Oceans. Stratospheric vortex – surface connections also occur in the Northern hemisphere, with a disturbed, weak Arctic stratospheric vortex linked with an increased likelihood of the movement of cold tropospheric air from Arctic into middle latitudes (so called cold-air outbreaks).

The connection with cold-air outbreaks is more direct for the tropospheric polar vortex. During cold-air outbreaks there are generally planetary-scale distortions of edge of the tropospheric vortex, where part of the vortex is displaced further equatorward than normal, while at other longitudes the edge is further poleward. Anomalously cold surface air occurs in regions of equatorward displacement of the vortex edge. The cold-air outbreak over the United States in January 2014 that gained a lot of media attention is a classic example of this tropospheric vortex – cold surface air connection.

While much progress has been made in recent years on polar vortex – surface connections, there remain many areas where a greater understanding is required, for both climate and extreme weather. My research group and collaborators are currently exploring some of these issues, including the relative contribution of each vortex on surface extreme weak events, and the impact of the Antarctic stratospheric vortex on the ocean circulation.

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formation of CO₂ clouds on Mars and HCN clouds on Titan). There are, however some very distinctive differences. For example, Mars polar vortices have an annular structure, Saturn's Northern polar vortex has a persistent hexagonal shape, and Venus' Southern vortex experiences dramatic changes in its internal structure and shape.

“The connection with cold-air outbreaks is more direct for the tropospheric polar vortex. During cold-air outbreaks there are generally planetary-scale distortions of edge of the tropospheric vortex, where part of the vortex is displaced further equatorward than normal, while at other longitudes the edge is further poleward.”

Martian polar vortices

My group and collaborators have been examining the structure of Martian

polar vortices. The persistence of Mars' annular polar vortices is surprising as classical fluid dynamical theory would suggest it would be unstable. It turns out that the existence and persistence of the Martian polar vortices is related to another distinctive feature of Mars' atmosphere: the condensation of the predominant atmospheric gas species (CO₂) that occurs inside the polar vortices. The latent heat release associated with this condensation modified the stratification and leads to the formation of the annular structure, and also suppresses the growth of instabilities. An open question is whether this also facilitates mixing of dust and trace gases across the vortex edge. This, and other transport issues, is a current avenue of research. As is the structure, dynamics and chemical processes of other polar vortices. The range of planetary vortices across the

Solar System allows us to determine the commonalities of polar vortices in general, and to improve scientific understanding of the role they play in regulating a planet's atmospheric compositions and climate.



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Sweden must continue to push climate reform

Climate reform is a necessity to safeguard the future of the planet. Open Access Government's Ciara Ruane explains what Sweden is doing to ensure this

The Swedish government introduced their climate policy framework in June this year, which contained new climate goals, a climate act and plans for a climate policy council. This is said to be the most important climate reform in Sweden's history.

Domestically, Sweden is aiming to eliminate its greenhouse gas emissions by 2045. The ultimate aim is to achieve 'negative emissions', meaning CO₂ produced will be absorbed by the eco system faster than it is produced. The Ministry of the Environment and Energy in Sweden has advocated for the bonus-malus system, a proposal that, if passed, would see high emission vehicles charged a higher tax for the first 3 years of their use. She says the Bill would make it 'easy' to make the right choice when buying a new vehicle, and make sure increased vehicle sales are going in the 'right direction'.

As well as reducing greenhouse gases, Sweden are supporting the need to reduce pollution on land and in our oceans. The Minister for the Environment in Sweden, Karolina Skog [appeared at the UN Ocean Conference](#) in New York, and pledged her support to the UN's marine environment work. Speaking about Sweden joining the Clean Seas Campaign, Skog said, "We have a collective responsibility to act, and to act now. We need to turn the tide on plastic waste, protect biodiversity and keep the oceans rich and clean. It's an investment in our own survival." One aim she has highlighted is the need to ban 'entirely unnecessary' micro plastics in cosmetics, which can find their way into the oceans and prove harmful to marine animals.

Launched in January 2017, the Clean Seas Campaign aims to raise global awareness of the need to reduce marine litter. In joining the campaign, Sweden will provide SEK9 million in support, as well as a further SEK 5

million being invested to support UN Environment in its efforts to tackle pollution from land-based sources.

Gender equality and climate reform

Much has already been said on the link between gender inequality and climate change. With both the causes and effects of global warming it seems women are widely absent from decision making at every level, and suffer most as a result of climate based disasters. Women are glaringly absent from the boards of energy companies climate groups, despite the fact they are statistically more likely to 'believe' in climate change.

"As the minister responsible for urban development, I have a vision of sustainable cities for everyone, and to get there we need to tackle several challenges at the same time."

In a recent shocking development, Donald Trump pulled out of the Paris Climate accord, a widely criticised move that he reasoned would help remove restrictions from businesses. Isabella Lövin of the Swedish Ministry for the Environment released a statement condemning Trump's decision shortly afterward. She reaffirmed Sweden's commitment to the environment and to becoming fossil-free, and highlighted the negative effect the US pulling out would have on the 'world's poorest'.

The Swedish parliament recently voted against a law that would require listed companies to fulfil a gender quota on their governing boards or face a fine. On their parliamentary website it was stated that corporate equality should be achieved 'through other means than legislation'. Many believe that the key to achieving gender parity in high and low decision making lies in both socialisation and high-level subconscious bias. There are a number of independent female-led organisations campaigning for the environment, and a



handful of groups and networks connecting women in the field. On a governmental level, politicians and experts have spoken out against this disparity.

“Domestically, Sweden is aiming to eliminate its greenhouse gas emissions by 2045. The ultimate aim is to achieve ‘negative emissions’, meaning CO₂ produced will be absorbed by the eco system faster than it is produced.”

Swedish Minister Karolina Skog spoke about environmental equality at the November 2016 [Climate Change conference](#) in Marrakech, saying: “Social inclusion, gender equality and access to good quality public transport are keys in the work on urban development.”

This talk on sustainable cities came as a result of Goal 11, outlined by the UN, which proposes a set of achievements that must be reached to ensure urban development is sustainable. Target 11.7 states that by 2030 they will ‘provide universal access to safe, inclusive and accessible, green and public spaces, particularly for women and children, older persons and persons

with disabilities,’ which they aim to achieve through setting a proportionate area of green space to city space and monitoring the ration of population growth and land use.

Skog added: “As the minister responsible for urban development, I have a vision of sustainable cities for everyone, and to get there we need to tackle several challenges at the same time.” ■

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Wood: reducing the impacts from harsh weather

Herje Boström, CEO of Sioo Wood Protection AB in Sweden highlights the benefits of protection systems to reduce the impact that weather has on wood

Although wood is an incredibly versatile and beautiful material it does suffer from some problems. For exterior applications in Use Classes 3.1 and 3.2 (EN 335 Part 2) wood in exposed conditions will weather to give a silvery-grey driftwood appearance. However, when wood is sheltered (such as under overhanging eaves) then the wood will retain its original colour. This leads to a very unsightly appearance with uneven weathering, examples of which are not hard to find. The weathering of wood has been researched for over 100 years, and although we understand very well why it happens and what causes it, there has never been a solution developed. Wood is composed of three structural polymers: cellulose, hemicelluloses and lignin. It is the lignin that is the Achilles heel where wood weathering is concerned. Lignin is a crosslinked phenolic polymer that imparts a brown colour to wood and is the 'glue' that holds wood cells together and gives wood its stiffness. However, lignin also strongly absorbs ultraviolet light which causes the breaking of chemical bonds and leads to fragmentation of the lignin polymer. These lignin fragments are then washed out by rain, where they become food for staining microorganisms, leading to the familiar grey appearance. Because the lignin is no longer present, the cell walls at the surface become loose and can be washed away in the rain. Although this is not a problem with uncoated



wood, it most certainly is an issue for clear coated wood because the coating no longer adheres to the wood surface, meaning regular and expensive maintenance is required.

Conventional wood coatings

Conventional wood coatings rely on adhesion to the wood surface for their integrity. Over time, the movement of the wood under the coating due to the effects of wetting and drying result in localised failure of the coating, usually at the earlywood/latewood boundary. Once this happens, liquid water is able to penetrate below the surface of the coating, which is then forced off due to hydrostatic pressure. The only remedy is to sand back to good material and re-coat. The only way to stop this from happening is to use more flexible coatings, but this is not feasible

because the coating would then be tacky and pick up dirt very rapidly in service. Conventional paints and varnishes also use carbon-based chemistry, and carbon-based compounds are susceptible to UV degradation when exposed to sunlight. Clear coatings suffer from the additional problem that the wood underneath is susceptible to UV degradation, and failure can also occur because the surface layers of the wood start to lose their structural integrity as the lignin (which binds the wood cells together) degrades. Putting UV stabilisers and filters in the coatings may slow down this degradation to some extent, but it is the wood that is the Achilles heel in the clear-coating system.

The Sioo:x Wood Protection System is different; it is not a coating, but an



envelope. The protection system has two components; the first (the wood protector) penetrates the wood where it gradually forms an inert glassy polymer, by reaction with atmospheric carbon dioxide. The second component (the surface protector) acts to seal and protect the first application until it is fully cured, but it also forms an inert water-resistant envelope which penetrates the wood and gradually creates a grey surface appearance. It does not stop the lignin from degrading, but it takes the same role by keeping the wood cells glued together, essentially using the strength of glass. The Sioo:x polymers that form in the wood have silicon-oxygen bonds (the same as in glass) and are completely UV stable.

Sioo:x is a patented (WO2007111556) water-based 2-part wood surface treatment process that was developed in Sweden over 15 years ago.

The wood protector undergoes a chemical reaction with atmospheric carbon dioxide to deposit insoluble silica particles into the wood. The surface protector prevents leaching of the wood protector until it is fully cured. It is the evenness of the silvery-grey appearance that is one of the most attractive features of the product. The product works best when there is good penetration of the wood material: rough sawn surfaces are always preferred and planed surfaces must be sanded to break through the machining glaze. Curing is accelerated with higher temperatures, but applying in direct sunlight is best avoided since rapid drying of the water-based product will limit diffusion into the wood. Application in damp, cold conditions is also to be avoided since curing is slowed down and there is a risk that the wood protector will be leached out before curing has occurred. For these reasons a factory-

applied finish by a Sioo:x accredited treater is always the best option. The treatment can be applied using brushing or spraying and good penetration is the key to good performance.



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The US National Park Service and the environment

Open Access Government's Ciara Ruane explores the role of the US National Park Service and explains how it protects the environment across the US

The US National Park Service (NPS) works to preserve the landscape and biodiversity of protected areas of the United States. A government organisation, the NPS collaborates with native tribes, universities, local government, and communities to restore and protect urban and rural environments, as well as educating the public.

The NPS aims to preserve the biodiversity of US National Parks through careful monitoring of ecosystems, the regulation of climate and air quality, and preventing development on National Park sites. In an ever-developing world, the task of preserving ancient wildlands can become increasingly difficult. A single invading species or a decline in an existing one could alter the entire ecosystem of an area, meaning crucial preservation efforts must be made. The NPS states that the preservation of nature is important 'for its own sake', for the benefit of human life through the food and medicine biodiversity offers, and for the enjoyment of future generations.

Public engagement

Each year the NPS holds a 'bioblitz', challenging citizens to identify as many plant and animal species in their area as they can, creating an informal census of flora and fauna. This works through an app – iNaturalist – which allows people to track and record plant and animal species in their local area and share it into their online database. This aims to create an ongoing public engagement with nature and encourage a mind-set of research and discovery. Even if the public are unable to identify the species themselves, it is still recorded and can be identified by scientists. NPSpecies is an online database of all known species across US National Parks. It lists the species and information about them and offers the chance to submit potentially undiscovered specimens into their records.

The need to foster a public involvement in nature is heavily emphasised by the NPS. Through volunteer work and educational programmes, the NPS aims to get as many people as possible involved with the natural world in their region, including urban areas which may not have easy access to it. On an official level, the NPS monitors not just the species themselves but other factors, which may affect their numbers. Recording water temperatures, weather, and other long-term changes allows them to predict future changes in ecosystems, as well as protect against potentially damaging events.

“In January, the NPS released its strategy for fighting the effects of climate change on ‘cultural resources’, specifically targeting landmarks, as well as culturally or historically significant areas. Acting Director Michael Reynolds called climate change “the biggest challenge the National Park Service has ever faced”, and identified the need to preserve American history as a priority for the service.”

Collaboration

The NPS also collaborates with other organisations, non-profit, governmental, and local, to share resources and expand research knowledge. Institutes such as the University of Maryland and the University of Wyoming work with the NPS, who provide job opportunities and internships for students whilst benefitting from their research and resources. Collaborative research stations provide a unique look into local ecosystems, as well as offering grants. The UW-NPS (University of Wyoming, National Park Service) Research Station funds around 12 projects a year, with this year's priorities including monitoring wildlife species and assessing the effects of climate change on biodiversity.

During this year the NPS is running several projects to



View of El Capitan and the Merced River in Yosemite National Park in California, United States

protect specific species, many which include public involvement. A planned excavation of sea turtle nests by biologists in August and September in North Carolina will be open to the public, who will have the opportunity to watch biologists collect eggs, count eggshells and dig up nests, as well as be educated on the species. 2017 is also an important year in terms of fighting potentially damaging legislation from a climate-sceptic US administration.

“The NPS aims to preserve the biodiversity of US National Parks through careful monitoring of ecosystems, the regulation of climate and air quality, and preventing development on National Park sites. In an ever-developing world, the task of preserving ancient wildland s can become increasingly difficult.”

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the need to preserve American history as a priority for the service. The strategy names 4 ‘pillars’ of fighting climate change; science, adaptation, mitigation, and communication. There is an emphasis on education and public awareness, as well as collaboration with institutions and partners. The overall aim is to use significant sites to study how climate change was adapted to in the past and to preserve history for the sake of the future. ■

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Some essentials on coexisting with carnivores

Coexisting with carnivores can be a challenge, but their value makes it worthwhile

The well-being of many human communities depends on healthy forests and grasslands. Those ecosystems can be degraded by over-browsing and over-grazing by large herbivores – moose, deer, elk, gazelles and so forth. That overconsumption is far less likely to occur when large herbivores are limited by healthy populations of large carnivore – wolves, lions, lynx, wolverine, bears, etc. Moreover, ecosystems with healthy populations of large carnivores tend to have greater levels of overall biodiversity. In a nutshell, and at risk of glossing over details, the conservation community has concluded that large carnivores have great ecological value.

Nevertheless, human communities often find it difficult to live near populations of large carnivores. Difficulties arise in three ways. First, carnivores kill domestic livestock, which provide for the well-being of some humans. Carnivores do not kill for malice; they do so because their well-being depends on it. Moreover, carnivores would naturally prey on wild animals. In many cases, however, the wild prey have been displaced by domestic livestock.

Second, carnivores kill wild prey that are also hunted by humans for subsistence or recreation. In this way, large carnivores are treated as competition to be eliminated.

Third, some species of large carnivores, on some occasions, threaten



and take human lives. Important examples include human-eating lions in portions of Africa and human-eating tigers in portions of south Asia.

While these three elements of conflict are real, they are also frequently and grossly exaggerated. In the United States, for example, the impacts of wolves on livestock and hunting are very small and wolves do not pose a threat to human safety¹. Yet, these concerns are important fuel for wolf persecution.

Under threat

Genuine and perceived threats lead to humans killing carnivores at high rates through illegal poaching and legal culling and hunting. The result of all this killing is that two-thirds of the world's

carnivore species are threatened with extinction and most places do not have their native complement of carnivores. The end point of treating this conflict – as humanity has thus far – is irreversible extinction and gross mistreatment of carnivores that manage to persist. An important element of this conflict concerns the received and oft-repeated motivation offered for why carnivores should be treated better: because they are ultimately of value to humans. The genuine wellbeing of humans is an important reason to conserve, but it is not the only one and alone it is inadequate.

European colonists and their descendants drove various large carnivores to extinction over a substantial portion of eastern North America. Britain

drove its large carnivores – wolves, lynx and brown bears – to extinction centuries ago. It is difficult to mount a case that the wellbeing of those humans is worse as a result of those extinctions. When an object (think, carnivores) is valued only for its utility, its utility may go unrecognised, be outweighed by costs of maintaining it, or replaced by a substitute. This is not a denial of carnivores' utility, but acknowledgement of the risk in valuing something only for its utility. As such, nature's utility is an (important, but) insufficient motivation for conservation.

“Genuine and perceived threats lead to humans killing carnivores at high rates through illegal poaching and legal culling and hunting. The result of all this killing is that two-thirds of the world's carnivore species are threatened with extinction and most places do not have their native compliment of carnivores.”

Conserving carnivores

What if, carnivores are valuable, not only for advancing human wellbeing, but also because they have a value in their own right? What if, we have an obligation to treat carnivores fairly and with at least some concern for their wellbeing? The response to those questions begins with the supposition that humans possess this kind of value and are entitled to this kind of treatment because we have interests (e.g., to avoid pain and to flourish). It follows that any entity with such interests would also possess this kind of value. Because all vertebrate organisms possess those interests, they also possess this kind of value and deserve this kind of treatment. The force and universality of this reasoning is indicated by the principle of

ethical consistency, i.e., treat others as you would consent to be treated in the same position. Most human cultures are undergird by some variant of this principle (e.g., golden rule). This intrinsic value of at least some non-human portions of nature is widely acknowledged – reflected by sociological evidence and many instances of laws and policies. Ethicists encapsulate these ideas by saying that carnivores (and many other forms of life) possess intrinsic value².

Future success in carnivore conservation will depend, in part, on better understanding ideas that will foster effective and fair mitigation and adjudication of conflict, especially:

- The extent to which conservation can be achieved through protected areas and land-sparing, opposed to land sharing³;
- Mechanisms of socioeconomic behavior that adversely impact carnivores. Some elements may be underappreciated (e.g., wealth inequality,⁴) and other elements may be favorable to conservation (e.g., tendency to increasingly embrace nature's intrinsic value with increasing economic development,⁵);
- How to subsidise coexistence by compensating those adversely affected by living with carnivores. The challenge is tailoring compensation in ways that are fair and effective, yet do not foster, e.g., perverse incentives, additionality, or leakage⁶;
- How to best juxtapose the values of conservation and social justice in a manner that genuinely honors the intrinsic value of carnivores without being misanthropic⁷.

Conservation is no longer limited by ecological knowledge about carnivores' ecological value or needs. Increasingly, the limiting factor is effective application of knowledge rising from the synthesis of social sciences, social justice and conservation.

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Meeting sustainable development goals must be a priority

European Economic and Social Committee's Luca Jahier calls for the EU to become a world leader when it comes to meeting sustainable development goals

On 22-23 May, the Various Interests' Group of the EESC organised a high-level conference on the 2030 Agenda and how to move from declarations to concrete action.

To make the UN 2030 Agenda a reality, we must have the courage to imagine a new world. We must have the ambition to put opportunities and goals before problems. We must have the creativity and determination to transform a vision into a positive European narrative for a flourishing sustainable development union. We must have the foresight and discipline to protect what is beautiful and fragile in our world and prepare for the future.

It is very easy to relegate discussions on sustainable development to experts and academics. But this would

be a major mistake. For the debates surrounding sustainable development are profoundly political and they must take centre-stage in our political reflections on the future of the EU, on the future of Member States and of our global relations. To my great regret, the EU has not demonstrated that it has assimilated and embraced the opportunities for a paradigm shift provided by the 2030 Agenda. Unfortunately, the Agenda is quite absent from the 5 scenarios in the European Commission (EC) White Paper on the Future of Europe. Even the Rome Declaration and last years' Communication on a 'Sustainable European Future' provide only partial and half-hearted commitments. In my opinion, this could be an immense missed opportunity. It also contradicts the EU's commitments to the UN Climate Change Paris Agreement.



Luca JAHIER, President of the Various Interests' Group

Prioritising sustainability in the EU

It is now time for the EU to take the political decision to make the 2030 Agenda a central pillar to the future direction and identity of the EU. It is crucial that we make sustainable development a horizontal European priority and that we strengthen the governance of the SDGs. We must take the global leadership and align the Agenda with the EU's longer-term 2050 sustainable development strategy. For to be credible, the EU has to deliver the 2030 Agenda and lead by example. This will involve building an overarching European Strategy for sustainable development. This strategy should abandon silos and embrace a holistic, coordinated and systematic approach. It should mainstream sustainable development across all EU programmes, policies and financial instruments. As a first step, we need an inter-institutional agreement on sustainable development between the Commission, the Council and European Parliament. Indeed, I would call on the EC to present a new scenario on the Future of Europe, which would put centre stage a sustainable democratic Union.

For 30 years after the definition of the concept of sustainable development our common future is very much under threat. At precisely the time when others turn away from their commitments, it is imperative that the EU maintains the momentum, accelerating, investing in and embracing change. Now is the time for long-time engagement, to make the transition to an inclusive, equitable, resilient, low-carbon, circular and collaborative economy. Now is the time for political leadership, to rethink our growth models and improve well-being. To balance economic prosperity with innovation, social inclusion, democratic participation and

environmental sustainability, all within our planetary boundaries. We must have the conviction and boldness to defend the universal, indivisible and mutually reinforcing dimensions of the 2030 Agenda.

Hence, it is crucial for us to build on our European values and safeguard the exercise of human, economic, social and cultural rights. However, we can only design and deliver this new world, by working transparently in partnership with a maximum number of social and economic actors from a wide spectrum of civil society organisations (CSOs). It is civil society which will drive change, with bottom-up initiatives which respect the opinions and rights of local people. Moreover, we can only embark on this new world by making sustainable development financially accessible to all citizens, by transforming perceptions, attitudes, developing a new attractive narrative and ultimately, by creating a sustainable culture among Europeans.

This will be the basis for re-installing hope and trust in our democratic systems. The UN 2030 Agenda for Sustainable Development will become our European Social Contract of the 21st Century. ■

Full recommendations:

<http://www.eesc.europa.eu/?i=portal.en.events-and-activities-agenda-2030-recommendations>



European Economic and Social Committee

Luca Jahier

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The Smart City Charter and the missing link to climate resilience

Prof Dr Daniela Jacob, Climate Service Centre Germany, highlights the Smart City Charter and what it means for the future of cities

Cities are confronted with many challenges in relation to urbanisation, natural hazards, climate change and their interactions. Cities are not only contributing to climate change, they will also be affected by expected climate change impacts such as urban floods after heavy rain events or heat stress. The concentration of people, assets, critical infrastructure and economic activities exacerbates the potential of natural hazards and extreme weather events. This is why cities need to adapt on time to enhance protection. The relevance of mitigation and adaptation efforts is also highlighted in the Global Risks Report 2017. Four environmental risks – extreme weather events, natural disasters, failure of climate change mitigation and adaptation, as well as man-made environmental disasters – were ranked both high-risk and high-likelihood, with extreme weather events emerging as the single most prominent global risk.

The Smart City Charter

At the same time, cities and regions all over the world are increasingly trying to become smarter, because smart cities are committed to sustainable and integrated urban developments to enable long-term economic growth. Recently the Smart City Charter has been presented and published by the German Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety (BMUB) aiming to outline the standard model for a smart, future-oriented city. According



to that a smart city is – among others – climate-neutral, resource-efficient, responsive and sensitive. A missing point, however, is climate-resilience. The Smart City Charter is also intended as a basis for discussions on the future of cities in the digital age and aims to extend the public scope of these discussions. We herewith like to sensitise and highlight the need to broaden the view to risk perception and resilience as a whole by paying more attention to systemic risks regarding critical infrastructure.

Due to the fact that cities' stability and prosperity rely on vast networks of infrastructure which provide essential services, urban critical infrastructure needs to be smarter, too. This will be reached in a way that they are more intelligent and interconnected in order to integrate multiple information, as well as new information and commu-

nication technologies to manage city's assets. However, the interactions between interconnected critical infrastructure elements work smart in normal operation and everyday use. But, what happens to smartness during longer periods of dysfunctioning that are mostly not considered? Will smart city infrastructure elements still be smart and resilient when they are exposed to external shocks like natural disasters, climate change impacts, terrorist attacks or human failure? Or will smart cities finally be even more vulnerable due to their multiple dependencies?

Critical infrastructure element

In general, critical infrastructure describes assets that are essential to maintain vital societal functions. Therefore, failures or functional impairments can have immediate and high impacts on several sectors as

well as to the whole society. Furthermore, interactions between critical infrastructure elements – in particular in different sectors such as energy supply, communication, information technology, water supply, wastewater treatment, transportation, and emergency services – have become a growing phenomenon. Individual elements can be vulnerable against one or more impacts and can have the function of an interface that connects different infrastructure networks, enabling the transfer of disorders across multiple infrastructure sectors and elements.

Critical infrastructure is exposed to various kinds of threats. There are man-made or technical (terrorism, sabotage, software failures etc.) and natural threats. The latter differ from geological (mass movements, earthquakes etc.) to hydro-meteorological hazards (climate change impacts). Whereby in particular climate change induced extreme weather events have a high potential to act as a trigger for cascading effects. The effect generates a sequence of events in human subsystems that result in physical, social and/or economic disruption. Thus, an initial impact can trigger other incidents that lead to consequences with significant magnitude.

With respect to smart cities, the ongoing interlinking of infrastructure elements is leading both to opportunities for innovation, but also complex, specific and rather novel risks. Furthermore, the economic value of physical infrastructure networks in cities increases with its scope. For instance regarding information and communication technology, the more people a network connects, the more useful it becomes. For supply infrastructures

like energy and water, the connection of more people is in theory often expected to lead to more flexibility for the operation, a higher intrinsic resilience of the network and leverage necessary economies of scale.

However, as different infrastructure networks become more interdependent, there is also a growing – and currently often still underrated – scope for systemic failures to cascade across different networks and affect society in multiple ways.

As an example the relations and interactions between the water supply and energy sector show, that a malfunction within the energy supply chain – starting from the power production over distribution and transformation stations to power lines – can affect water supply in a broad sense. Pumps, control elements, water treatment and recently digital communication do not work without electricity. Finally this leads to a breakdown of the water works. The outage of the water supply even considered separately has a further impact on other public facilities such as health care. With respect to waste water treatment, the missing water supply starts a second cascading step, because the malfunction of sewerage system elements, like sewerage treatment plants, has a further impact on other public facilities too.

To reduce the vulnerability to climate impact, cities need to focus on the whole system including the complex interactions of non-climatic and climatic drivers, as well as all critical infrastructure elements. Local councils are key actors when it comes to the implementation of adaptation measures. Thereby, increasing a cities resilience to climate change impacts is

highly context specific, due to its geographical location, structure, institutions, inhabitants, available information and operational capability. Therefore there is a need to understand risks and resilience jointly by paying more attention to systemic risks regarding critical infrastructure and cascading effects.

As a result of new threads for digital-based infrastructure elements, it must be guaranteed that all sub-systems remain functional in case of disruptions. Technical – most suitable analogue – redundancies must be provided for the core components of the critical infrastructure.

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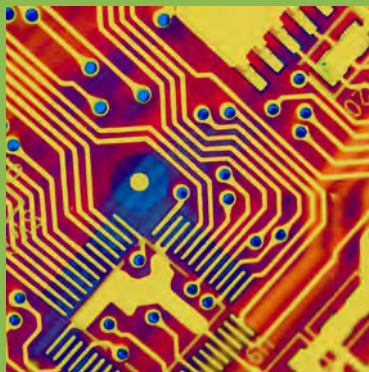
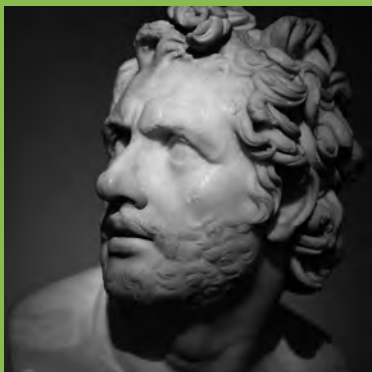
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Fighting food insecurity through global cooperation

Eradicating food insecurity remains a global challenge. In a speech, EU Agriculture Commissioner Phil Hogan highlights why working in partnership is vital

The goal of eradicating global hunger has never been as high on the international policy agenda as it is today.

This fact is to be welcomed, because there is no region of the planet that has not been affected by hunger and its crushing effect on human wellbeing and society. We know that developing sustainable food security and fighting hunger go hand in hand.

In Europe, the CAP (Common Agriculture Policy) was established to fight food insecurity in post-war Europe, and it has served our continent well for the past 60 years. Today, the policy has a far more global outlook and it is more closely aligned to other important EU policies, such as development and regional cooperation.

Working in cooperation with our global partners, there is a clear realisation that agriculture is critical for economic development, prosperity and food security in all regions of the world.

This is particularly true in Africa, where 300 million young people will reach employment age in the next 15 years. These citizens are already born, and two-thirds of them come from rural areas. Urgent action is needed to end rural poverty and provide jobs and prospects for these young people – who hold the continent's future wellbeing in the palm of their hands.

Supporting a rural economy

Agriculture and rural development is the chief focus of EU development assistance. More than 60 partner countries have agriculture or the rural economy as a focal sector.

The EU is ready to invest up to €8.8 billion in the 2014-2020 period drive this agenda, with a focus on small

scale farmers and on preparing the most vulnerable to better cope with food crisis.

Our support also goes to the development of value chains and in providing smallholder farmers with better access to local, national and regional markets.

As farming remains largely a private sector activity, the private sector and responsible agribusiness investments have a major role to play.

“Responsible investment in the rural and agricultural economy; value chains and integrated markets; the sustainable management of natural resources: these are all key factors for economic growth, job creation and development in African countries.”

Global agriculture has to meet a triple challenge: to raise farm incomes, to boost productivity to feed a global population of 9 billion in 2050, and to do so in a way that conserves resources for future production needs.

Bearing this fact in mind, it is fair to say we are now at a policy crossroads.

Sustainable goals

Agriculture is the heart of Sustainable Development Goal 2: ending hunger and extreme poverty by 2030. 60% of developing economy populations rely on agriculture, this is particularly acute among the very poor, with up to 80% relying on farming.

The SDGs recognise that agriculture plays a substantial role in any truly sustainable future, given that it is intrinsically linked to issues such as jobs, food, air, climate change, water, soil and biodiversity.



EU Agriculture Commissioner Phil Hogan

In the EU, we have been streamlining our policy work to ensure a more coherent approach across all our policies in this regard, including our agriculture and rural development policies.

But we can and will do even more.

Common Agricultural Policy

The CAP is currently going through a modernisation and simplification process which will maximise its contribution to meeting the targets of the Sustainable Development Goals.

We've just finished a major public consultation on the future of the CAP that will feed into a Commission Communication later this year.

Developing partnerships

It is my hope that 2017 will be a defining year for European agriculture and its contribution to food security and sustainability both at home and abroad.

2017 is also a defining year for the partnership between Europe and Africa.

The 5th Africa-EU Summit in November 2017 can give fresh impetus to this partnership.

Together with the AU Commissioner, Mrs. Josefa Sacko, we organised an EU-AU ministerial conference on the theme of "Making Sustainable Agriculture a Future for youth in Africa". Our aim was to build up political engagement and agree desirable concrete outcomes for the summit.

"Global agriculture has to meet a triple challenge: to raise farm incomes, to boost productivity to feed a global population of 9 billion in 2050, and to do so in a way that conserves resources for future production needs."

To fuel the growth of Africa's economy, investments are needed. Neither Official Development Aid nor Remittances can provide sufficient resources. Private investment is required – indeed it is already the biggest source of development funding.

Responsible investment in the rural and agricultural economy; value chains and integrated markets; the

sustainable management of natural resources: these are all key factors for economic growth, job creation and development in African countries.

They should be accompanied by a better focus on research and innovation with Information and Communication Technology and digitisation as important enablers.

A further key to growth is generating increased value added for African products, coupled with better access to higher-value international markets. Young African agri-entrepreneurs need quality products to sell, better production methods to grow them, and access to good markets upon which to sell them.

“Agriculture is the heart of Sustainable Development Goal 2: ending hunger and extreme poverty by 2030. 60% of developing economy populations rely on agriculture, this is particularly acute among the very poor, with up to 80% relying on farming.”

EU trade policy and our partnership agreements give guaranteed access to EU markets and stability for investments.

We are consolidating the relationship with Farmers' Organisations and agribusiness to include them in policy dialogues under the Economic Partnership Agreements.

To accelerate this process, new impetus is needed for research and innovation to drive sustainable agricultural productivity. The focus should clearly be on: sustainable food and nutrition security; resource-use efficiency; and climate-smart agriculture. We have to strengthen the link between research, farmers and the industry.

External Investment Plan

The EU's proposed External Investment Plan (EIP) will introduce a landmark shift in how the EU works in partnership with Africa countries. It provides a comprehensive framework for a massive mobilisation of private investment.

The purpose of the Commission's 2016 proposal on the External Investment Plan is to support investment, strengthen partnerships, promote a new model of private sector participation, contribute to the achievement of the Sustainable Development Goals and address the root causes of migration in Africa and the European Neighbourhood.

The EIP is there to strengthen socio-economically important sectors, and so agriculture is of primary importance as a target of the EIP.

The farming and agri-food business communities have a key role to play, while governments and public sector must promote a stable, responsible and inclusive business environment.

The goal is to set in motion a virtuous cycle of investment, which will drive both food security and economic growth, which in turn will help to erase hunger.

This is an edited version of a speech by the Commissioner at the Panel discussion on “Zero Hunger: Regional Commitments to Eradicate Hunger, Food Insecurity and Malnutrition”, in Rome last month and can be found [here](#). ■

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Precision phenotyping for efficient animal agriculture

MoSAR, INRA's Research Director, Nicolas Friggens, explores the role of precision phenotyping in agriculture and explains how it is driving animal research

The advent of affordable automated technologies in livestock farming has already had a substantial positive impact on animal, and farmer well-being. However, this is the tip of the iceberg with respect to the potential benefits of these precision livestock technologies. We are on the cusp of a revolution in livestock farming.

In modern animal agriculture, there is an increasing focus on efficiency and resilience. Greater efficiency of food production is needed to feed the planet, and in the context of animal agriculture, this means more efficient conversion of non-available feedstuffs (grass, processing industry bi-products, etc.) into human edible proteins. In order to ensure that the resulting efficiency gains are sustainable, strong demands are placed on the resilience of animals because these poorer feedstuffs are of variable quality and frequently associated with variable (grazing) environments. Both resilience and efficiency impact on farm viability, but if one considers the abilities an animal needs to thrive in an alpine grazing system or in an intensive system, it is clear that the relative importance of resilience and efficiency differs depending upon the prevailing conditions in the local production environment.

The problem is that resilience and efficiency are difficult to measure in research farms and, at present, well-



nigh impossible to measure under commercial conditions. This drastically limits the ability of farmers to manage their livestock for an optimal balance of resilience and efficiency, and for animal breeders to select for resilience and efficiency. However, precision livestock technologies can overcome these constraints, and new projects to capitalise on this potential breakthrough are being initiated.

Precision livestock technologies

Until very recently precision livestock technologies have been directed at monitoring specific events such as the onset of disease or the detection of heat, often using single technologies (e.g. accelerometers). Although this has resulted in very useful on-farm

tools it has tended to neglect the potential of these technologies for precision phenotyping, i.e. achieving a radically improved description of the animals' capabilities, at low cost. Imagine if all the dairy farms that already have accelerometers, and other technologies, for monitoring could also use them to characterise resilience and efficiency. We have already shown that frequent, automated weighing of animals (e.g. when they come to feeders or to be milked) can be used to calculate key components of efficiency such as energy balance¹. Accelerometer measures of activity and automated measures of body temperature, both available commercially, provide further components of efficiency. Given this, it

seems clear that large-scale phenotyping of animal efficiency is within reach. Similar arguments can be put forward with respect to phenotyping resilience, although in this case the key feature that needs to be captured is the variability in the time-series of measurements, which reveals the animal's dynamic pattern of response and recovery when faced with an environmental perturbation². Again, the use of precision livestock technologies is key because they readily provide the high frequency of measures needed to capture these resilience features.

There are of course, significant issues that need to be resolved in making the step change from monitoring to phenotyping. Data integration and signal processing from multiple technologies that may be recording with different frequencies and different levels of reliability is statistically challenging even if advances in machine learning and similar methods hold great promise. Then there is the biological interpretation of such measures. Almost all measures that are made on animals reflect different biological processes; an observed dip in growth rate may be due to the animal being ill or it may be due to a change in social behavior, or a number of other biological causes. This is where the use of multiple technologies measuring different aspects of animal biology is important (if the animal with the dip in growth also has an elevated temperature, or better still an elevated immune indicator, then it is likely a health event). However, this is far less straightforward for complex phenotypes such as resilience and

efficiency. A recent EU Horizon 2020 project called GenTORE is tackling the issue of developing large-scale phenotyping of resilience and efficiency in both dairy and beef cattle.

“In modern animal agriculture, there is an increasing focus on efficiency and resilience. Greater efficiency of food production is needed to feed the planet, and in the context of animal agriculture, this means more efficient conversion of non-available feedstuffs (grass, processing industry bi-products, etc.) into human edible proteins.”

GenTORE³ is also fully engaged in building the tools needed to make the use of precision phenotypes operational in tailored farm management systems, taking advantage of the opportunities provided by genomic selection. Because of its enhanced precision, genomic selection is well-suited to making progress on complex traits such as resilience and efficiency. Accordingly, GenTORE will develop genomic selection for these traits across a broad range of breeds, including cross-breeds. It will provide tools for assessing local production environments, which in combination with the precision livestock approach and genomic selection, will allow farmers to tailor their breeding management⁴ to achieve an optimal balance between resilience and efficiency. Projects like this one, and others across the range of farm animal species, will make a significant contribution to meeting the needs for sustainable efficiency and enhanced farm resilience in a diversity-rich livestock sector.

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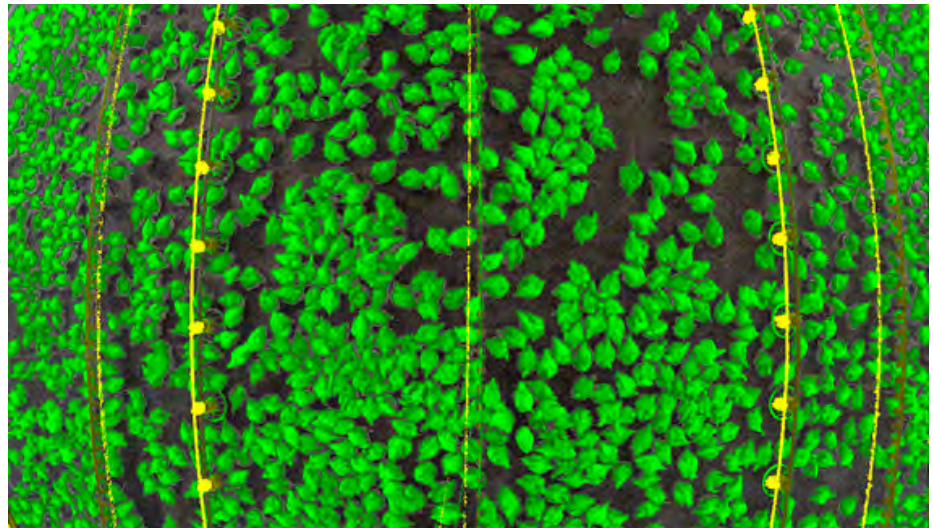
Solving challenges through precision livestock farming

Daniel Berckmans, Catholic University of Leuven asks if precision livestock farming could help to monitor health and environmental impacts of farming

These days over 60 billion animals are slaughtered every year for food production. The worldwide demand for animal products is expected to increase 75% by 2050. How will we monitor and manage the health, welfare, efficiency of production, and environmental impact of all these animals? Precision livestock farming is at least one answer to be considered.

Producing more animal products (meat, eggs, milk) while reducing environmental impact and guaranteeing high animal health and welfare is a serious challenge to be solved. It is crucial to improving efficiency and producing more animal products with less feed intake, less manure, and fewer emissions from the livestock sector. We estimate that we have not reached the genetic potential of existing animal species and this has to change. The increasing demand for animal products comes alongside a reduced number of livestock farmers which leads to bigger herds. The farmer has less time per individual animal and that is where precision livestock monitoring (PLF) can help.

Precision livestock farming aims to deliver a management system for livestock through continuous automated real-time monitoring of production/reproduction, health, welfare of livestock, and environmental impact. The system allows for the monitoring of livestock 24 hours a day and 7 days a week. This is realised by using



Problems monitor in broiler house by real-time image analysis

cameras, microphones, and sensors around or attached to the animals. The advantage of real-time image and sound analysis is that the animals are not touched and one camera or microphone can monitor many individual animals. These sensing technologies are combined with smart algorithms for immediate signal processing. Not all the raw data of 25 images per second and 20,000 sound samples is sent higher up, relevant information is sent higher up using Internet of Things. At the higher level this information can be combined using big data analysis with other information which is not available at an animal level such as genetic information, prices of feed, energy, and animal products to take management decisions.

Precision livestock farming technology solutions

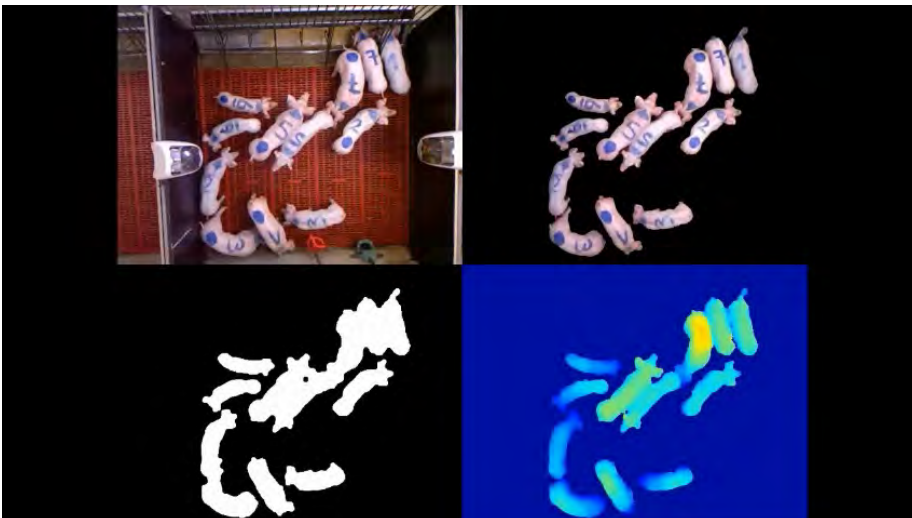
It has been shown that this technology

can provide several solutions already such as:

- Early warnings for infections in fattening pigs through real-time sound analysis. This allows the farmer to take immediate action to the sick animal(s) and prevent spread to other animals, thereby reducing the need for antibiotics;
- Monitor the first sign of lameness in milking cows and give a list of cows to be inspected due to potential lameness problems;
- Give an alarm for more than 95% of all experienced problems (light, climate, feeder line, drinking line, etc.) in broiler houses;
- Detect unacceptable aggression in fattening pigs through real-time image analysis;



Cow lameness monitor by real-time image analysis



Pig aggression monitor by real-time image analysis

- Monitor real feed intake of broilers, being the most costly process input to be optimised with precision feeding;
- Monitor accurately the water intake of pigs as an indicator for health problems.

Today the technology is at the level of being implemented in commercial farms as demonstrated in the EU-PLF project where 20 farmers all over Europe used the technology on their farms for milking cows, fattening pigs, and broilers. The advantage is that early warnings can be given to the

farmer for immediate actions to help him manage the health, welfare, and production efficiency of the process. The PLF technology is a tool to help farmers but will never replace them since the process is far too complex. The farmer's management remains the most important factor deciding on the efficiency of the livestock processes. PLF might give him tangible advantages (less labour, more efficiency, less production loss or risks, more profit) but also non-tangible advantages (less time to be spent, peace of mind, different lifestyle etc.) that are not less important.

We are confident that this technology will help the world to produce enough animal products with healthy and happier animals that should get a life worth living while helping to feed the world.

“Precision livestock farming aims to deliver a management system for livestock through continuous automated real-time monitoring of production/reproduction, health, welfare of livestock, and environmental impact.”



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Green Paper: Providing a roadmap for food and agriculture

Federal Minister of Food and Agriculture, Christian Schmidt, outlines how the Green Paper process is helping to build bridges between farmers and consumers

Healthy food and nutrition is a very immediate and personal part of our lives, and it is our agricultural sector that lays the foundation for this. Our agricultural, horticultural, viticultural and forestry sectors also shape our homeland and landscapes. Since time immemorial, three aspects food agriculture and homeland have been inextricably linked. However, our post-industrial, globalised societies, which rely heavily on the division of labour, have led to many people losing sight of this natural connection.

Whereas, fifty years ago, most people had farmers in their families or among their friends, many consumers today have lost all personal links with farming. This is also the reason why farmers and the food they produce no longer enjoy the appreciation they deserve.

Whereas in the past, and well into the 20th century, the main issue was whether enough food could be

produced for everyone, contemporary social and political debate now sometimes even questions whether we need a productive agricultural sector at all. This attitude often goes hand in hand with pronounced criticism of globalisation. The aim of using our agricultural production in Europe, a region that boasts excellent land for agriculture, to help feed the world is often fundamentally contested. Some even suggest that agriculture should focus only on protecting nature and conserving biodiversity.

This idea adopts a one-sided, idealistic view, dispensing with the connection between life, economic activity and conservation which is the basis of the concept of sustainability. Although such ideas are not by any means representative of how the majority view the farming sector today, they do cause great uncertainty among people working in the farming, forestry and food sectors.

In an open society, and in light of the current challenges we face from a growing world population, climate change and changing values, it is natural and necessary to discuss and question how things have been done in the past. Some sections of the population focus intensively on their diet and food. They consider diet and food to be a lifestyle issue, and indeed often an issue of identity. Our farmers' work is regarded sceptically by many members of the public and, increasingly, it is being questioned whether "grow or go" can really be the solution for all regions. To stabilise support for their profession, our farmers face the challenge of meeting society's new and different expectations of farming. We discuss the ways and means of how we eat, how we treat our animals, how we manage water, air and soil, and how we can make our homeland an attractive place to live.

Green Paper process

At my initiative, representatives from agriculture, civil society, the church, industry, academia, research and politics have joined together with the objective of talking with each other rather than about each other. We have listened to each other in an open, fair and equal dialogue. The discussions were sometimes very heated, involving as they did some diametrically opposed standpoints. We have jointly identified challenges which we must face. We have developed ideas from which we are deriving viable solutions. My political work is guided by the concepts of personal accountability, self-determination and voluntary commitment rather than patronage by the state and statutory regulation. I called this dialogue the Green Paper process, as the Green Paper on Food, Nutrition, Agriculture and Rural Areas offers direction and is a guiding vision for our policy delivery. This process is helping us to build bridges between farmers and consumers.

The Green Paper maps out paths to potential solutions; we intend to cooperate with all stakeholders and strike out along these paths. We intend in this way to anchor the food and agricultural sectors where they belong: at the centre of society - with secure prospects for the future.

In order to provide good prospects for the future, we need to know in what direction we want to develop the European Union's Common Agricultural Policy (CAP) after 2020. We will continue to need a strong and financially well-equipped CAP that should be based on



Image: © Michael Gottschalk
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Christian Schmidt,
Federal Minister of Food
and Agriculture

two solid pillars. The EU agricultural budget must not be used as a quarry to stop up financing gaps in other EU policy areas after Brexit. The cost of Brexit must not be borne by agriculture and rural areas. We must at any rate use CAP funds in a more targeted manner. Direct payments should support family farms and livestock farms that are particularly affected by society's demands regarding animal husbandry. We must focus support more on active farmers with strong roots in the regions and not on non-agricultural investors whose main occupation is the production of spectacles or furniture.

The Green Paper also identifies prospects for rural regions. Our aim is for our rural areas to be workshops for the future and to provide ideas for the development of our society. We will gear the support instruments more closely to address demographic change and support weaker economic areas. This includes ensuring good medical care throughout the country, optimising mobility structures, strengthening local amenities, and also promoting voluntary work. Creating equivalent living conditions is a guiding principle of our political engagement for rural areas.

We aim to enable people to have safe and healthy food, to increase people's appreciation of food, to create the framework for an economically viable agricultural sector with strong regional roots, to improve animal welfare, to ensure sustainability and to establish rural areas as workshops of the future. The Green Paper is our road map to achieve these aims. ■

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Honey bee health: managing and reducing the risks

Managing the health of the honey bee is integral to the agriculture sector. Here Elke Genersch from the Institute for Bee Research explains further

In recent years there has been growing awareness of the relevance of insect pollination for the preservation of intact ecosystems and biodiversity but also for a profitable agriculture. By now it is widely accepted that the observed declines in the richness of species, as well as the numbers per species of pollinating insects are of concern to human society as a whole. Among the threatened pollinators are “bees” in general, meaning solitary bees like carpenter bees and mason bees, as well as eusocial bees like stingless bees, bumblebees, and the honey bee. Most of the global honey bee population is managed by humans (beekeepers) in order to harvest honey and other bee products. These managed bee colonies are also versatily used in agriculture to increase yield and the quality of many crops and fruit. Therefore, honey bees have a good lobby comprising both the beekeeping and the agricultural sector. Therefore, the increasing problems with honey bee health and colony losses in recent years received the attraction it deserved, and thus also helped the case of the other pollinators at risk.

The fact is that in contrast to many other bee species honey bees are not facing a global population decline. Quite the contrary: The number of managed honey bee colonies has been steadily increasing over the last 60 years at a global scale. However, it's also a fact that we are confronted



with a forever growing gap between pollination demand in agriculture and pollinator supply, because the increase in the number of managed honey bee colonies did not and still does not keep up with the increase in cultured crops and fruit, depending on insect pollination. It's also fact that there are soaring problems with honey bee health and with colony losses in particular, due to diminishing honey bee health which exacerbate the dire situation caused by insufficient pollinator supply. Therefore, honey bee health – or the other side of the medal: honey bee diseases – are at the core of the problem of pollinator shortage and improving honey bee health by developing sustainable measures against honey bee diseases will solve a big part of this pressing problem.

Understanding honey bee diseases

Although considerable knowledge has been acquired to date about bee diseases we are still far from understanding these diseases and the causative pathogens. This situation has to be changed. We urgently have to acquire a level of knowledge and understanding of honey bee diseases comparable to the one we have with human infectious diseases. Only then will we be able to save the bees. In 1906, hence, more than a century ago, the US American bee scientist George F. White already noted: “In order to combat a disease to the best advantage it is clear that its cause must be known, as well as the means by which the infection is transmitted and the environmental conditions which are favorable for the breaking out of an epidemic.”

This notion is still valid and its content is quite trivial: If you want to combat a disease you first need to identify the causative agent and then you have to unravel its weapons, its strategy, and its tricks. That's exactly what we at the Institute for Bee research are doing in the field of the infectious diseases of honey bees. In order to cover the entity of honey bee pathogens, i.e., viruses, bacteria, fungi, and metazoan parasites, with our research, we chose to work on model pathogens for each class. Thus we are working on:

- Deformed wings virus (DWV), causing i.e. crippled wings, as the name suggests;
- The bacterium *Paenibacillus larvae* which infects and kills only the honey bee brood resulting in the notifiable epizootic American Foul-brood (AFB);
- The fungi *Nosema apis* and *Nosema ceranae* which belong to the microsporidia and cause an adult bee diseases called nosemosis which is characterised by dysentery and sometimes results in death of individuals or entire colonies;
- The ectoparasitic mite *Varroa destructor* which parasitises both pupal and adult stages of the honey bee and became established as a biological vector of DWV.

Our work on DWV and *V. destructor* considerably contributed to understanding the triangular relationship between DWV as a viral pathogen, *V. destructor* as mite vector of DWV, and honey bees as a host. Our work was

seminal to realise the relevance of the mite as biological virus vector and to recognise that the symptoms of what was called varroosis and originally considered mite inflicted, were actually due to the activity and virulence of mite transmitted DWV infections.

“Although considerable knowledge has been acquired to date about bee diseases we are still far from understanding these diseases and the causative pathogens. This situation has to be changed.”

Our work on *P. larvae* started more than 10 years ago by correctly classifying this bacterial pathogen and by demonstrating that differentially virulent genotypes of the etiological agent of AFB circulate in the global honey bee population. Meanwhile we are deciphering the molecular aspects of the pathogenesis of AFB by identifying and functionally characterising virulence factors of *P. larvae*. Prerequisites for this work are, that we succeeded (i) in obtaining high quality genome data of different *P. larvae* genotypes, which enabled us to perform comparative genomic analyses and (ii) in establishing protocols for the genetic manipulation of this fastidious bacterium. Our understanding of the pathogenic strategies of *P. larvae* progressed in such a way over the last decade that we expect to be able to develop alternative diagnostic and control strategies for this detrimental brood disease, based on our results quite soon in the future.

With *N. apis* and *N. ceranae* we started to work only recently. But we already achieved a lot. We established a cell

culture model for these fungal parasites which constitutes the first cell culture model ever for a honey bee pathogen. Based on this model, we developed a medium throughput screening assay for substances inhibiting the growth of this parasite. This assay revolutionised the screening for anti-nosemosis drugs and already resulted in the identification of 2 substances inhibiting *Nosema* spp. proliferation in cell culture.

Despite all these achievements in the field of molecular bee pathogen research, we still have a long way to go to provide sufficient knowledge on bee pathogens which might ultimately save the bees and also help other pollinators. But we are eager to continue and we are curious of what our future research will unravel.



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Supporting healthy forests across America

Open Access Government highlights the role of forests within biodiversity and how the USDA supports agroforestry in America

Forests are said to play one of the most important roles in biodiversity. They cover 31% of the world's surface, with the US and Canada being 2 of the 5 countries with the biggest forest areas worldwide. As well as playing a role in the environment, forests also provide more than 10% of the GDP in many poorer countries and the forestry sector is estimated to provide formal employment for 10 million people. In order to protect our forests and reduce deforestation, which occurs in many countries, sustainable forest management is key.

To ensure the protection of forests and its wildlife, the Food and Agriculture Organization of the United Nations (FAO) works to improve knowledge on sustainable forest and wildlife management. It also supports the development of policies and practices to improve the capacity of forests, conserve biodiversity, as well as sustain wildlife populations.

According to the FAO report, '[State of the World's Forests 2016](#)', forests play key roles in water cycle soil conservation, carbon sequestration and habitat protection, as well as their sustainable management being crucial for sustainable agriculture and food security.

USDA and agroforestry

The US Department of Agriculture (USDA) also plays a role in developing healthy forests. Agroforestry is a process that combines both agriculture and forest technologies in order to create more integrated, diverse, productive, and sustainable land-use systems.

[The USDA Agroforestry Strategic Framework](#) aims to provide new direction on how USDA agencies, partners and landowners can together significantly expand agroforestry to balance agricultural production with natural resource conservation.

USDA states that the key concept in agroforestry is 'working trees – putting the right tree in the right place, for the right purpose'.

Through their strategic framework, the US agroforestry community is provided with an opportunity to positively influence the long-term health and sustainability of all lands for future generations.

Supporting forests using farming techniques

There are a number of farming techniques that utilise and support forests. These are intended to make the best use of available, land, especially in rural areas, and work alongside nature without clearing areas of forest or disturbing habitats or natural processes.

"Farming systems must adapt in order to both meet increasing demands and maintain the environment at a time when it is at risk."

[Silvopasture](#) is the practice of grazing livestock in fields with trees. This provides the animals with shelter and shade and allows them to use the same area for producing wood. This lowers stress in animals and provides a dual income for farmers, as well as preserving natural habitats and reducing the risk of wildfires.

[Agrocropping](#) involves planting trees or shrubs in rows to provide alleys in which to plant crops for fruit, vegetables, herbs, and biofuels. Again, it allows for a dual use of land and is more environmentally friendly than normal farming practices. It also allows for a better use of nutrients within the same space, as the plants and trees selected can make the best use of the soil environment and complement each other's development.

[Forest farming](#) is a specialised practice that uses the protection of forest canopies to produce valuable



crops such as shitake mushrooms and other speciality ingredients. This also allows for additional income through timber production and provides a chance for more specific products like hazelnuts and maple syrup to be produced.

The USDA supports scientific research into agroforestry, with the intention of improving the cost-effectiveness and produce yield for farmers. They aim to educate farmers and allow for more opportunities for agroforestry, leading a global support for sustainable farming.

Agriculture can often pose a threat to biodiversity, with areas of land being cleared and repurposed, and natural food chains being disturbed. Agroforestry techniques provide a method of maintaining biodiversity, but the USDA has a number of directives for achieving this. In the face of climate change and ever-increasing demands for food, maintaining the natural environment is becoming a more difficult and essential task.

The USDA's mission statement seeks to improve the relationship between agriculture and the natural environment. Their suggestions for ensuring the protection of biodiversity include:

- Assessments to identify at-risk species and environments;
- Ensuring genetic diversity to increase resilience of wildlife;
- Identifying patterns of growth and decline, as well as changes in behaviour;
- Integrating climate protection into agriculture practice.

Farming systems must adapt in order to both meet increasing demands and maintain the environment at a time when it is at risk. The USDA is taking a systematic, ongoing approach to making environmental protection an essential part of farming. ■

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Recognising the important role of biodiversity

Pamela S. Soltis, Director, University of Florida Biodiversity Institute, reveals the key work being done in the US to respond to the 'biodiversity crisis'

Biodiversity refers to the extraordinary variation of life on Earth. While it is widely accepted that natural biological diversity is fundamental to a healthy, sustainable planet and that its loss has a negative impact on human well-being (e.g., see *Science* magazine, July 2014), the connections between biodiversity, ecosystem function, and services that contribute to human well-being – from the flow of fresh water to pollination of crops – are less well understood. Ecological economists note the effect of invasive species (more than \$120bn annually in the US alone) and have begun to quantify the economic benefit of ecosystem services, but less is known about the impact of lost ecosystem services on other aspects of both environmental and human well-being. Global responses to societal problems arising from both loss and alterations of biodiversity suffer from insufficient information and inadequate policies for sustainable use of natural resources, in part due to the slow rate at which biodiversity data are gathered and the difficulty in accessing the information once it is available. Consequently, much of the diversity of our planet is likely to disappear before it can be discovered and understood. This 'Biodiversity Crisis' – that is, the loss of biodiversity and its attendant consequences – creates both the necessity and the opportunity for a new type of response.



Why biodiversity matters

Recognising the important role of biodiversity in the biological and sociological health of the planet, the U.N. declared 2010 the 'Year of Biodiversity' to focus attention on the accelerating loss of biodiversity in the face of human population growth, landscape modification, and climate change. In 2011, the US President's Council of Advisors on Science and Technology called for improved accounting of ecosystem services and greater protection of environmental capital, citing the need for further biodiversity science and application of informatics to enhance our understanding of ecosystem services and develop

appropriate policy to protect them. More recently, the International Platform on Biodiversity and Ecosystem Services (IPBES), which has 118 member nations and is modelled after the Intergovernmental Panel on Climate Change (IPCC), has begun assessing the scientific and social knowledge of Earth's biological diversity and how environmental change will impact ecosystems and human societies. Like IPCC, the IPBES does not conduct primary research but assesses knowledge and attempts to influence policies aimed at protecting ecosystems and pursuing sustainable economic growth. The recent establishment in the US of NEON

(the National Ecological Observatory Network) is beginning to provide extensive environmental data and baseline ecological monitoring at select sites across the country, with fully operating data streams from all sites later this year. Current and future assessment targets include impacts of declines in pollinator populations on food production, invasive species, and habitat degradation, all topics that threaten food security in the coming century and are relevant to agencies such as the US Department of Agriculture (USDA), which governs not only food production but also forestry in the US. Despite increased awareness, more integrated, accessible science and technology platforms are needed to leverage novel planetary data, models, and tools to create and link knowledge to policy.

The University of Florida (UF) Biodiversity Institute

The University of Florida (UF) Biodiversity Institute was launched in 2016 to bring together scientists, social scientists, and policy experts to address critical societal issues of the 21st century related to biodiversity: invasive species, emerging pathogens, climate change, and food security, to name a few. This interdisciplinary Institute is accelerating synthetic research on biological diversity to serve stakeholders in Florida (a biodiversity hotspot) and globally through efforts to understand and manage biodiversity, develop relevant conservation, educational, and outreach programs, and shape policy to protect and enhance environmental capital.

The Mission of the UF Biodiversity Institute is to conduct high-quality research and develop programs to

advance 3 primary goals: (1) Initiate and lead large-scale, collaborative biological surveys to document and monitor biodiversity on a global scale; (2) Conduct collaborative and interdisciplinary research on biodiversity, with an emphasis on the use of Big Data; and (3) Translate biodiversity science to solve major societal problems.

“Recognising the important role of biodiversity in the biological and sociological health of the planet, the U.N. declared 2010 the ‘Year of Biodiversity’ to focus attention on the accelerating loss of biodiversity in the face of human population growth, landscape modification, and climate change.”

The UF Biodiversity Institute is exploring the world’s past and present biodiversity at all levels of biological organisation, from molecules to ecosystems, and the relationship of biodiversity to climate change and to healthy and sustainable natural and human environments. Institute scientists conduct synthetic research using data from all relevant sources to address fundamental problems in biodiversity science and solve pressing societal problems. Newly synthesised knowledge from the Institute is available to individuals and organisations seeking validated biodiversity information.

The UF Biodiversity Institute has already established strong links to data science, informatics, computer science, and engineering, as well as to specialists in environmental law, agricultural economics, climate science, land use, and human population growth. The Institute benefits from strong ties to iDigBio, the US national coordinating centre for digitisation of

biodiversity collections – that is, the integrated database that shares biodiversity data for the nation’s natural history specimens. iDigBio currently serves over 105 million specimen records, representing approximately 300 million of the estimated 1-2 billion specimens in US collections. This growing resource is driving innovations in management, analysis, and interpretation of biodiversity data, both in the US and globally, with a promise to address problems ranging from food security to invasive species to response of species to climate change.

In an upcoming series of articles, we will focus on the role of the UF Biodiversity Institute in applying data science and informatics to biodiversity-centered problems, the resources of iDigBio, the need for innovative training programs for students and practitioners to take advantage of ongoing developments in data availability and use, and case studies of how biodiversity scientists are addressing societal problems such as food security.



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Cohesion policy offers support for low income member states

Policy must be tailored to help low-income regions catch up. Corina Crețu, Commissioner for Regional Policy, explains how cohesion policy ensures growth

In June 2015 I launched an initiative to examine the factors that hold back growth and investment in certain regions in the EU. It distinguished between two groups of regions: "low growth regions" which are characterised by a persistent lack of growth over the last decade or more (mostly in Europe's South), and "low income regions" whose GDP is on the rise, but which remain very poor (mostly on the eastern part of the EU).

"Cohesion policy supports programmes to strengthen institutional capacity and improve the efficiency, transparency and accountability of public administrations, as well as promote e-government, reduce regulatory red tape, modernise public procurement, support anti-corruption measures and support judicial reform."

There are several reasons why some regions have not yet reached the expected rate of growth and income. In the south of Europe unemployment is rife, particularly among the young. In the East the process of catching up with EU living standards has slowed down, and disparities within countries have increased. Investment has also declined in these regions due to the crisis, by as much as 40% in southern regions.

All low-income regions have lost population since 2000 (in some regions by more than 20%) primarily due to net migration. This meant an out-migration of young qualified workers ('brain-drain') and a limited capacity to attract talent from other regions, which is likely to limit their growth prospects. Public and private investment dropped in these regions, especially in low-growth regions.

What is very clear is that the answer to each region's problems needs to be tailor-made.

For some, it will require investments in infrastructure – this is the case for the regions in the eastern part of the EU. This should help unlock their economic potential, which is currently held back, by an insufficient or inadequate road network. Therefore, completion of the Trans-European Network is a priority.

Others, in particular the southern regions, need investments in human capital, skills and innovation, with particular attention to the insertion of university graduates into the labour market, avoiding common problems of mismatch between educational supply and labour demand.

Creating links

Another important factor is to create stronger links between cities and their surrounding areas. These regions continue to urbanise either through faster population growth in cities in low-growth regions or through population reductions outside cities in low-income regions. Generating more spill overs from these successful cities (which function as economic engines) would be beneficial.

The quality of institutions and regional administrative capacity are also an essential criterion to boost economic growth. Cohesion policy supports programmes to strengthen institutional capacity and improve the efficiency, transparency and accountability of public administrations, as well as promote e-government, reduce regulatory red tape, modernise public procurement, support anti-corruption measures and support judicial reform.

In addition, these regions will create more and better jobs if they find their niches, by building on their assets and on what they can do best. This is the concept of "smart specialisation", which we have developed in the



Corina Crețu, Commissioner for Regional Policy

Cohesion policy

Cohesion policy plays an important role in low-growth and low-income regions and accounts for a very high share of their public investment in most of them. The 2007-2013 cohesion policy has produced strong results in practice, helping small and medium-sized enterprises develop and create jobs, helping people acquire skills, develop transport, social infrastructure, helping to achieve greater energy efficiency and protect the environment. Moving to the next level of economic development cannot be accomplished by a one-size-fits-all policy, but will require regionally differentiated investments and policy responses.

It is clear that comprehensive and well-timed development strategies are therefore needed not only to address some of the basic problems of lagging regions, but also to enhance their capacity – and, as a consequence, that of the entire Union – to adopt new technology, retain and attract talent, generate and stimulate new investments, and, last but not least, make the most of the economic potential across all of the EU.

Helping the regions of Europe still struggling with low growth and small incomes to thrive remains a challenge. It requires a sustained and concerted effort across many fields, at EU, national and regional level.

European cohesion policy holds one of the keys to addressing this challenge, by providing investment, savoir-faire and by guiding these regions towards finding their own solutions to development. ■

Corina Crețu **Commissioner for Regional Policy**

European Commission

https://ec.europa.eu/commission/commissioners/2014-2019/cretu_en

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EU. Smart specialisation requires improving regions' innovation systems, along with a stronger partnership between businesses and higher education institutions. The active involvement of all regional actors – universities and schools, employment organisations and trade unions, SMEs, investors, national and regional administrations – is crucial for focussing on the activities that can put regions on a growth path.

Romania and Poland are the first countries to pilot this initiative with 2 regions each, respectively the North-West and the North-East, and Swietokrzyskie and Podkarpackie. Based on the results of the pilot projects, this model of cooperation of EU, national and regional actors will then be transferred to other European regions facing similar challenges.

Can diversity in cities create social cohesion?

Dr Gideon Bolt, Assistant Professor at the Faculty of Geosciences – Utrecht University highlights research into the importance of diversity in cities

Since Louis Wirth's classical essay *Urbanism as a way of life*, a central tenet in urban studies is that there is a negative link between heterogeneity and social cohesion. As our present-day, cities are even more diverse than in the era of Wirth, there seems to be not much room left for optimism about the social fabric of the city. Hyper-diversification might lead to more social exclusion as individuals increasingly segregate themselves from others belonging to a different class, ethnicity or lifestyle (Fincher et al., 2014). This complicates the creation of feelings of belonging and community, as people are generally inclined to connect to similar others which might make urban groups prefer to live side-by-side without socially integrating with each other. Putnam (2007), who primarily focused on ethnic diversity, reported negative effects on social outcomes, like trust, social networks and political efficacy. However, his findings have been refuted on methodological grounds (Abascal & Baldassarri, 2015).

Moreover, qualitative studies show that living amidst diversity does not necessarily lead to social withdrawal and that residents in diverse neighbourhoods are often open, or at least civil, towards other cultures (Wessendorf, 2014). Noble (2009), for example, describes the ways in which difference is perceived in unproblematic ways on a daily basis as 'unpanicked multiculturalism', contrasting it

with the 'panicked multiculturalism' that is common in today's debates on multiculturalism and mainly focuses on conflicts and tensions between different ethnic groups.

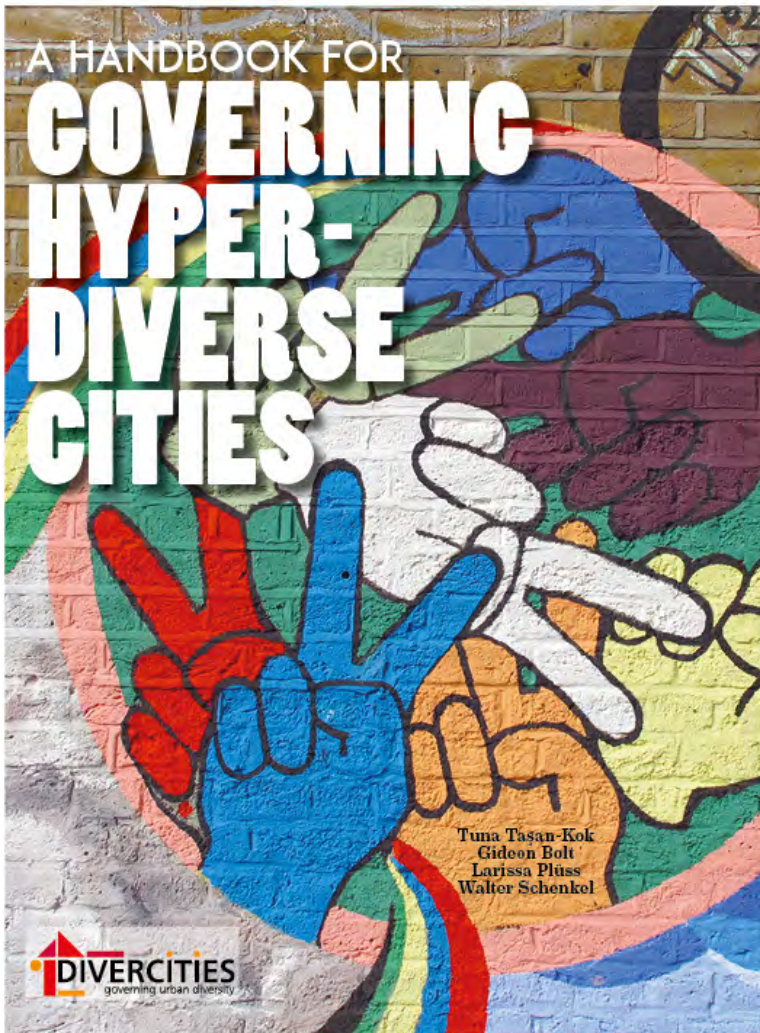
The benefits of diversity

Noble's observation is corroborated by the DIVERCITIES research project which aimed at examining the ways in which Europe can benefit from diversity. The research for this project was undertaken in 11 EU cities: Antwerp, Athens, Budapest, Copenhagen, Leipzig, London, Milan, Paris, Rotterdam, Tallinn, Warsaw; and 3 non-EU cities: Istanbul, Toronto, and Zurich. Most residents of our diverse research areas take diversity more or less for granted. This is more apparent in places with a longer history of diversity (like Toronto and London) than in places with a short history of immigration (like Leipzig and Athens). We have also seen clear differences between young people and adults. Young people spend much more time in public spaces such as streets and plazas. There they meet and make friends with neighbourhood children from diverse social backgrounds. More often than adults, young people develop friendships across different boundaries and are less likely than adults to perceive ethnicity as the main social divider in the area. Instead, young people distinguish groups based on their school, sub-neighbourhood, or subculture. Even more than adults, they tend to see

diversity as an ordinary part of their everyday lived experience. If this reflects a generational effect (and not just an age effect), their general acceptance of diversity is a hopeful sign. If a new generation is more at ease with diversity and has more open and dynamic networks, social divisions may be broken down. Political discourses should adapt to this trend by reconsidering the use of old terms such as multiculturalism and assimilation. The 'ordinariness' of diversity could be highlighted in the public realm as a positive element of urban life (Maloutas & Souliotis, 2015).

Diversity and social cohesion

One of the points of departure of the DIVERCITIES project is that diversity does not necessarily have a positive or a negative effect on social cohesion. Policies should focus on creating the conditions which stimulate encounters that lead to bridges across (ethnic, religious, class and other) boundaries. The ways in which people do or do not interact in different places are related to 4 conditions which facilitate encounters: multifunctionality, connectedness, comfort, and sociability. By integrating different activities, places can successfully stimulate the intermingling of diverse audiences by allowing them to participate in shared activities which stimulate interaction and collaboration. Obviously, such places must be embedded in and connected to the local infrastructure. In addition, the spaces must have a



good image, be clean, and feel safe; these conditions will ensure that diverse groups would like to spend time there and feel relaxed enough to interact with others. Lastly, successful spaces of encounter encourage planned as well as spontaneous meetings by integrating the routes and routines of different groups.

Although we have come across many positive experiences of diversity in our research, we have also found people who have had negative experiences with local diversity. These may take various forms: crime associated with disadvantaged youth; residents who do not speak the language of the host society in public and semi-public spaces; and a lack of amenities for specific groups. Negative experiences

with diversity in the local area should not be addressed by attempts to reduce diversity there. Our research areas have an important function on the local housing market: the availability of affordable housing is one of the main motivations for low-income households and recent immigrants to settle in such neighbourhoods. Diminishing the number of affordable housing alternatives will diminish the housing possibilities for low-income households. Complaints about the neighbourhood are often not directly related to diversity but rather to livability issues which are sometimes associated with the population composition of the area. Making the public realm cleaner, safer, and more attractive helps to deal with many of the issues that are raised by residents.

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¹ This project has received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement No. 319970. SSH.2012.2.2.2-1; Governance of cohesion and diversity in urban contexts.



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Stability and instability in the Caucasus: social cohesion

A consortium coordinated by the University of St. Gallen looks at the Caucasus and the importance of social cohesion for stability in the region

The Caucasus is a region in the post-Soviet space, spanning from the Black Sea to the Caspian Sea, bordering Turkey and Iran. The region comprises the North Caucasus Federal Republics in Russia's South as well as Armenia, Azerbaijan, and Georgia. Inter-ethnic tension, stalled economic development, significant gaps in the socio-economic development of both urban and rural areas, as well as authoritarian patterns of rule put the stability of the Caucasus at risk.

The Caucasus belongs to the Eastern neighbourhood of the European Union. Armenia, Azerbaijan, and Georgia are 3 of the 6 states included in the European Union's Eastern Partnership programme. Frictions in the region bring Russia, Turkey, and Iran as regional powers on the scene and thus may easily amplify. It is therefore of crucial importance for policy-makers and academics alike to pay more attention to the developments in the region. Against this background ISSICEU, an EU-funded FP7 project, set out to study newly emerging and hardly considered sources of stability, and instability, that affect social cohesion in the Caucasus. A consortium of 8 universities and think tanks from Azerbaijan, Georgia, Russia, Turkey, Germany, and Switzerland have combined lenses of different disciplines; i.e. economics, political sciences, the study of religion, anthropology, sociology, and geography to pursue deductive and inductive research.

Social cohesion in the Caucasus

The 25 researchers have studied influences on social cohesion in the Caucasus from a wide range of perspectives. We have studied frictions between state and citizens in matters of socio-economic development and looked into which actors and mechanisms help to accommodate them. ISSICEU was also interested in civic participation discourse and practices prevailing in the Caucasus, and how societal players from Turkey and Iran influence them. In focus were also the origins and implications of economic dependencies and, finally, the foreign policy of Turkey and Iran towards the Caucasus. The project has undertaken empirical research in the South Caucasus states of Armenia, Azerbaijan, and Georgia and the North Caucasus republics of the Russian Federation Kabardino-Balkaria, Karachay-Cherkessia, Chechnya, and Dagestan. The region does not only share a common historical background and societal links through migration, but also the struggle with the authoritarian tendencies which mark their political regimes to a varying degree. ISSICEU also paid attention to the de facto states Abkhazia, South Ossetia, and Nagorno-Karabakh. These small entities with a population of 50.000 in South Ossetia. 240.000 in Abkhazia and 145.000 in Nagorno-Karabakh have emerged as de facto states from the violent conflicts in the early 1990s in which South Ossetia and Abkhazia claimed independence from Georgia, and Nagorno-Karabakh

from Azerbaijan. The conflicts lead to the deaths of several ten thousands, and left several hundreds of thousands with unsettled refuge. The de facto states are internationally not recognised but are relatively stable policies. Yet, the conflictual impact of their domestic politics on the region needs more attention.

The results of ISSICEU highlight that tensions over access to public goods and over the power to shape socio-economic development in villages and towns are on the rise in all entities studied. The recent economic crisis has fortified the socioeconomic pressure, particularly in rural and remote mountainous areas, and has limited the governments' capability to mitigate tensions with selective investments. The societies' lack governance mechanisms that efficiently mediate between people and the state. The dominant central rule undermines formal and informal societal bodies which could act as a mediator and avoid destabilising conflict. One lesson for the EU would be to strengthen efforts to foster de facto local self-governance and civil society.

However, civil society promotion needs to consider that government and societal actors often associate instability, not stability, with Non-governmental Organisations (NGO). These domestic actors, therefore, tend to meet international efforts to promote and stabilise a landscape of NGOs with great



North and South Caucasus, source: ISSICEU

scepticism. To avoid such scepticism NGOs should be supported in the context of sectoral cooperation where people can see how NGOs make a difference in the development of a respective sector, be it agriculture, energy, environment or social security. However, participation in NGOs are not common, while a vivid civic engagement in form of neighbourhood help is. It may build a basis for developing mechanisms of participation in decision-making and interaction with the state. The lesson for the EU is to broaden its perspective on civil society actors beyond the conventional focus on established organisational formats. Yet, this implies a better-informed knowledge about the situation on the ground.

Links between the North and South

The North and South of the Caucasus are linked by flows of people, cultural

values, trade, and capital. These links have a stabilising effect for the region but are weak and underdeveloped. They should be promoted through widening the focus of assistance projects from the South Caucasus to the entire region. Diaspora groups are crucial neighbourhood actors. Abkhaz, Armenian, Azerbaijani, or Georgian diaspora act in support of economic prosperity, but also tend to strengthen radical stances, e.g. on the secessionist conflicts.

The secessionist conflicts in the Caucasus are not frozen. Changing economic parameters in Azerbaijan and Armenia create uncertainty which increases the likeliness of military escalation in Nagorno-Karabakh. While Turkey cannot be directly involved in conflict mediation, it may still enhance regional security by balancing extreme foreign political positions through cooperation with different

parties in the region, for instance, in the framework of the trilateral security alliance with Georgia and Azerbaijan. After the lifting of the sanctions, Iran may contribute to stability through economic engagement. Without discarding non-negotiable norms and values, the EU might consider venues that allow for achieving mutual benefits from cooperating with both Turkey and Iran in the region.

A topical discussion is the South Caucasus countries' foreign trade orientation towards Russia or the EU. This orientation builds on geopolitical considerations than on a sound economic basis. Contradicting political and economic actions may have a destabilising effect. This should be considered in the EU's trade relations with the Caucasus. Overall, the findings of ISSICEU call for paying increasing attention to the societal conflicts in the region and for exploring alternative approaches to cooperation with the Caucasus.



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Varberg takes responsibility – again

For the coastal city of Varberg, Sweden, 2015 was the year when the community united in a joint effort to take responsibility for peace and human rights – just as they did at an international peace summit held there one hundred years before. The municipality has an active role to play and views the project as an extension of the work towards its vision of developing the city of Varberg as the Swedish West Coast's creative hotspot, with the help of local residents.

As the 100th anniversary of a significant peace summit approached, here in Varberg we chose a different way to celebrate. The result was the VARBERG CALLING for Peace project, with the aim of engaging and involving residents in actively working for peace and a sustainable society. The basic idea is to draw attention to the local and international history of peace, and in doing so combine the forces of Varberg's administrative bodies, organisations, civil society and local residents to increase awareness of the important perspectives that are vital for peace and a sustainable future. It is also important to encourage participation in order to highlight issues of democracy, human rights, cultural understanding and sustainable environment, and to examine them in greater detail. Also for there to be a legacy once the project has ended, which can be built on and will provide support for future development.

Photo: Mimmi Persson



Greater awareness of the age in which we are living and a common educational perspective on our history provide the conditions for future creativity, innovation and action. We believe that the big, universal human issues can unite many, both organisations and individuals.

Thinking globally and taking into consideration situation analysis and environmental and resource perspectives cannot be restricted to municipal or national borders. VARBERG CALLING for Peace is an opportunity, therefore, for Varberg municipality to take a forward-looking, general approach to sustainable development in a project that involves local residents. Engagement on humanitarian issues and the all-pervading problems we now face in the world around us may also increase interest in important issues at local level. The project therefore represents a step towards the realisation of Varberg's plan: Vision 2025 "Swedish West Coast's creative hotspot" and a sustainable future.

Christina Josefsson
Head of the Culture and Leisure department
The City of Varberg

Come to Varberg. Share our vision.

Inspiring people to create everyday peace



**VARBERG
CALLING
for Peace**

The city's local education centre, Campus Varberg, is today the largest vocational college in the Halland region and is one of Sweden's leading providers of vocational education. The core values at Campus Varberg include knowledge, innovation and creativity, and it was not long before it became involved in the VARBERG CALLING for Peace project.

At the college's events and management course a number of students are running their own projects as part of VARBERG CALLING for Peace. Here they tell us about the solid peace work they have done, which has given them valuable experiences.

"We are studying on a three-year events and management course and during February and March we studied a course in 'project-based development work'," explains Lina Rundbom, one of the students.

"During the course, we had the opportunity to choose from a number of assignments to work on and we five chose 'VARBERG CALLING'. We had to examine and communicate the questions 'What do you stand for?' and 'How can you get strangers to talk to one another?' to the general public."

The assignment came from the two process managers for VARBERG CALLING for Peace, Malin Bellman and Jon Liinason.

"They gave us some good advice before we started. 'Don't think – just do it and see what happens!' they said. So we did. We tried out our ideas on people using quick and easy prototype tests, with the results leading to new ideas."

One of the prototype tests involved leaving a bicycle in the entrance to the city's galleria. The girls left the bicycle "right in the way" and stood a few metres away to see how people reacted. Contrary to what you might expect, most people did not seem particularly irritated. It gave some people something to talk about as they wondered why the bicycle was there. Another was the mobile "everyday peace cycle café". Loaded up with coffee and pastries, the bicycle was pushed around to various parts of the city, offering coffee and cakes for free.

They asked the people they met how we can create everyday peace. Smile at someone you don't know, pick up litter, and hold open the door for someone were some of the suggestions.

"It really doesn't need to be any more difficult than that," says Lina. "Everyone can do something. The cool thing was seeing how our own positive energy clearly spread to those people we were talking to."

Annette Wenklo

varberg

varberg.se

The European Union: Challenges or lost opportunities

Kieran McCarthy, a member of the European Committee of the Regions, looks at the European Union and the positive activities that we should focus on

The financial crash, the refugee crisis and Brexit have created a myriad of concerns and challenges for the institutions of the European Union (EU). And, watching the news on television and reading newspapers, it seems that the EU is caught in a downward spiral.

But, on the ground and viewed from the EU's assembly for local and regional politicians, the European Committee of the Regions, the EU is engaged in many positive activities. These are positive narratives about the EU that we rarely hear. Across the EU, from north to south and from east to west, great work is being pursued with money from the European Structural Investment Funds, innovative work is being done by scientists thanks to the Horizon 2020 programme, inspiring projects are connecting people across borders, and the free movement of people, trade and capital is having positive effects.

The role of Cohesion Policy

We need to hear more about the opportunities that the EU offers. Take for example, the EU's support for regions, provided through its 'cohesion policy' and European Structural Investment Funds. We need to speak more about the value that these add, about how they support the EU's growth strategy (Europe 2020) and promote inclusiveness, about how they improve the quality of life in regions, and about how cities and regions are becoming lighthouses for research and development. Cohesion policy offers a means of improving our social and political context, it enhances research and economic development, and it encourages 'smart specialisation' so that regional entrepreneurial ecosystems emerge. We never hear that every €1 invested produces an average return of €2.75-€3 for that region or city.

Image: © EU / Laurie Dieffembacq



Kieran McCarthy, a member of the European CoR

When we talk about the EU and its Cohesion Policy, we need to talk more about solutions and resolutions not demolition or dilution, about re-invention not the status quo, about communication not isolation, about growth, about opportunity and about the next generation. We need to create more agile regions capable of facing globalisation full on.

A downward narrative does not help anyone. More communication and more outreach are needed – the positive stories of the EU need to be told more. Every institution has a responsibility, as do citizens. We are all the future of the EU, and local and regional authorities are critical to delivering its success.

Kieran McCarthy is an independent member of Cork City Council. ■

Kieran McCarthy

Member, European Alliance Group

European Committee of the Regions

<http://cor.europa.eu/en/Pages/home.aspx>

[www.twitter.com/EU_CoR](https://twitter.com/EU_CoR)

Smart cities are a driver for innovative solutions to urban challenges

Leading Construction, Energy and Projects lawyer, Jeremy Williams analyses smart cities and explains why they are vital for economic growth

In recent years, major cities across the globe have heartily embraced the smart city concept. But definitions of the term – and examples of the ways cities are becoming technologically ‘smart’ – vary widely. The terms used to describe smart cities also differ – cyberville, digital city, electronic communities, intelligent city, MESH city, teletopia and wired city being just a few.

But what exactly does it mean?

At its core, smart cities aim to gather information to create actions that create positive change in a community. This can vary from city to city, but often includes environmental factors like reducing pollution, utilising resources more cleverly, or enhancing the happiness of visitors and residents.

“It can be daunting and difficult for smaller cities to compare themselves against big name smart players like London, New York or Hong Kong, but, if their infrastructure and policies are becoming smarter, they need to vie for the recognition they deserve.”

Economic factors hugely influence what a city’s smart ambitions are. The needs of a city in a developing nation will, of course, be vastly different to those of an advanced city in a wealthy nation – like Tokyo or San Francisco.

So a smart initiative could be anything from wirelessly managing streetlights to lower energy costs, or using sensors to monitor water mains for leaks and air quality for high pollution. It could also be more complex – creating smart parking initiatives that track available parking spaces and vehicle movement to control traffic flow.

Ultimately what all smart city initiatives have in common is the desire to drive economic growth by

utilising technology to create smart outcomes. This, and the aim of improving the quality of life for the city’s inhabitants by promoting local development.

However, it’s important to remember that while the use of cutting edge technology is an important factor in categorising how smart a city is, it’s not the sole criteria. Perhaps more important are the citizen-driven smart initiatives. Things like increasing the accessibility of Wi-Fi in public spaces, for example, can be revolutionary for citizens of developing nations – while it’s often par for the course in the Western world. Smart cities aren’t just about delivering the most advanced technology – they’re about delivering what their citizens need to improve their wellbeing – as well as driving economic growth.

This broader focus has led to a benchmarking system that smart cities can be ranked against – and compared to one another. This has created competition to be recognised as the leading smart city and has led to a rapid growth in smart initiatives.

So, what’s the methodology for comparing smart cities?

To be considered smart, cities may have adopted and made technological strides to cover some (or all) of the following six principles:

1. Smart Economy

Such as innovative or dynamic funding platforms – this could be for example incentivising small businesses through loans or grants to develop innovative practices. On the opposite side of the spectrum, it could mean providing substantial funding for large developments.

2. Smart Environmental Practices

For example, schemes to strategically reduce landfill



Jeremy Williams

waste and create easy alternatives. This could also lead into smart energy initiatives such as remotely controlling utilities to use cleaner energy – and crucially – to do so more efficiently.

3. Smart Governance

An example of this could be city regions launching initiatives to advance health and wellbeing, like wellness centres.

4. Smart Living

Such as the introduction of Acts or Bills that encourage public bodies to improve the social, economic and environmental well-being of the city. This could mean, for example, legislation that encourages a public body to prioritise environmental impacts – such as using recyclable materials instead of new materials in construction and development projects.

5. Smart Mobility

For example, Metro schemes or methods of joined-up public transport. As an example, this could relate to smart roads which, depending on the traffic, could utilise the hard-shoulder on an access road into the city to substantially reduce bottle-necking and increasing the flow of the traffic.

6. Smart People

Such as ‘catapult centres’ that give the relevant industry leaders access to state of the art facilities allowing them to create new products. Such initiatives in major cities often include programmes aimed at current university students who may have innovative ideas while carrying out their studies. Those students may be given the opportunity to pitch their ideas, develop prototypes, and funded to implement the innovative ideas.

So, how can a city utilise these features to become recognised as ‘smart’?

In many cases, cities can miss out on being acknowledged as smart simply because of a lack of self-promotion. They may have many smart successes – but they need to shout loudly about them.

It can be daunting and difficult for smaller cities to compare themselves against big name smart players like London, New York or Hong Kong, but, if their infrastructure and policies are becoming smarter, they need to vie for the recognition they deserve.

It’s also important to have an overall, national vision. Pockets of good practice are not enough and can result in missed opportunities for real growth and a place on the smart city stage. By combining a mix of ambition and a willingness to challenge and change, cities across the globe can seize the opportunity to become recognised as innovative, forward thinking and, most of all, smart. ■

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Why you shouldn't ignore environmentally friendly construction

Reconomy's Richard Walker shares the value of environmentally friendly construction and why everyone should continue to push the green agenda

Did you know that the planet could reach its capacity in regards to its global consumption of oil within the next 2 decades? However, demand continually appears to rise as the global production of oil decreases. In light of this, the construction industry still requires most of its energy sources from oil-based fuels.

In the construction sector of the Western world, many businesses are reliant on cheap crude oil that can be used in processes that help to build with the machines that they use. Surprisingly, within the UK, 50% of all carbon emissions produced by machinery and production are accounted for by the construction industry.

There has been a shift in attitudes though, with increasing awareness that pollution is having a long-

term effect on the planet. For instance, this is evident in that by passing legislation, the UK government is now instructing firms to use green processes when constructing a new house or building. Post-construction, firms are also encouraged to incorporate green technologies within the build to benefit the environment once construction is complete.

With estimated revenues for eco-friendly construction amounting to \$245 billion across the US in the past year alone, it goes without saying that relevant companies in the UK should be considering this lucrative new opportunity within construction themselves.

To go about achieving this, Reconomy, a specialist in waste management solutions for recyclable materials and skips for hire, has answered the main questions

surrounding environmentally friendly construction in this handy guide...

Which eco-friendly construction techniques can I use?

Before you begin construction, consider these 3 points to ensure a structure that you're working on will be ecologically beneficial to the environment:

1. Establish whether materials have been locally sourced or if they're renewed; if they aren't, can they be recycled in the future?
2. During construction is any energy being wasted? Machines can often be overused during the production process, which leads to expendable energy that is wasted and can never be used again. Electric vehicles and machines with hybrid-engines should be used so that when a motor is being overworked – an electric engine can be engaged to cope with the load.
3. Finally, once building the structure is complete, is there any energy generated within it that is wasted?

Also, take note that both during and following the construction of roofing, recycled paper can be used for insulation. Insulation materials are often expensive. By using a cheaper and practical alternative, the cost of producing insulation for one roof will be minimised drastically by using already existing materials. Furthermore, timbers sourced from sustainably managed forests in the local area can also be used. As well as reclaimed wood, this is an alternative to chopping down trees that are used within construction.

How do I go about designing ecological structures?

There are numerous energy efficient practices and eco-friendly technologies that can be used when designing a proposed structure. These can include:

Solar energy panels. To generate electricity within a building, or domestically to power boilers and other electrical equipment, solar energy is fast become a cheaper alternative to other forms of domestic power.

Drainage systems and water filtration. With these systems in place, water can be re-used when biological waste is treated safely, which can then be recycled.

Rainwater can also be collected in specific drains and storage taps, as opposed to always relying on water from a tap.

Low-energy lighting. Accounting for an energy saving of 100%, low energy lighting lasts twice as long as a regular lightbulb.

Why will eco-friendly construction be beneficial to me and my business?

A total of 80% of a building's entire running costs can be associated to the operating and maintenance of the structure during its lifetime. Green initiatives reduce the total running costs of a building by one third, which amounts to around 53.3% of a building's running costs.

Consider the fact that the costs of artificial lighting can be brought down by factoring in daylight into the design of a building. The 'indoor environment quality' of a building can also be improved when daylight can shine through a building, which benefits the health of all of the occupants that are present in the building.

Once you begin constructing a building, think about using materials that are recyclable and long-lasting where possible. As a result, fewer new materials will be used within the structure, helping to reduce costs whilst less energy is consumed (from crude oils) in order to produce the structure. ■

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Supporting the urban Aboriginal population in Canada

Indigenous and Northern Affairs Canada explain how the organisation is working to better the lives of the urban Aboriginal population in Canada

Over the last 25 years, the urban Aboriginal population in Canada has been growing steadily. More than half of Indigenous peoples in Canada are believed to live in urban centres, which are considered to be an urban area having a population of at least 1,000 people and a population density of no fewer than 400 people per square kilometre.

Indigenous and Northern Affairs Canada works together to make the nation a better place for Indigenous and Northern Peoples communities. Supporting Indigenous Peoples (First Nations, Inuit and Metis), the department aims to: improve social well-being and economic prosperity, develop healthier, more sustainable communities and participate more fully in Canada's political, social and economic development – to the benefit of all Canadians.

Here the department answers *Open Access Government's* questions about how their programmes, including the new Urban Programming for Indigenous Peoples (UPIP) help to improve the lives of Indigenous and Northern Peoples communities.

How important is it to ensure that the lives of Indigenous people's in Canada are supported and improved? And how does the Minister work with communities to ensure this happens?

The Government of Canada believes it is vitally important to advance reconciliation with Indigenous Peoples through a renewed relationship based on recognition of rights, respect, co-operation and partnership as the foundation for transformative change.

The Government of Canada, through its last 2 budgets is making historic investments totaling \$11.8 billion for Indigenous peoples, in areas such as safe housing, clean drinking water, child and family services and

education, to address some of the root causes of poverty, ensure that Indigenous children receive the best start possible in life, and begin a renewed relationship with Indigenous communities. These investments are flowing to communities to help meet the needs of communities from coast to coast to coast.

The new Urban Programming for Indigenous Peoples (UPIP) prioritises improving the quality of life of First Nations, Inuit and Métis in urban centres.

We are also implementing the Truth and Reconciliation Commission's Calls to Action to redress the legacy of Indian Residential Schools and advance the process of reconciliation. To date, implementation of two-thirds of the Calls to Action under federal responsibility is underway. The Government of Canada is also working towards forging a new fiscal relationship that gives Indigenous communities sufficient, predictable and sustained funding.

How does the government support Indigenous peoples through programmes such as the new UPIP?

The new Urban Programming for Indigenous Peoples (UPIP) received Budget 2017 investments of \$118.5m over 5 years. Combined with funds previously allocated to the former Urban Aboriginal Strategy (UAS) programme, the government will provide \$53m each year to UPIP, beginning in 2017-2018.

What is UPIP designed to do and how will it help?

The Urban Programming for Indigenous Peoples supports organisations in urban areas that provide programmes and services for First Nations, Inuit and Métis. These centres are tailored to meet the needs of women, men, youth and families that live in particular



communities. For example, these organisations can offer navigator services (e.g. help navigating programs and services like health services and acquiring a driver's licence), land-based activities for youth, parenting programmes and other specific programs that help meet the needs of urban Indigenous peoples and support their transition to life in the city. The new programme will continue to support organisations in providing holistic and culturally-appropriate programmes and services to their clientele. Through UPIP, multi-year funding is now possible. Targeted funding to specific Indigenous groups is also a new benefit under the new programme.

Respecting language and culture are fundamental in giving all Indigenous people the best chance for success when living in or transitioning to an urban environment.

Why are programmes such as this crucial to help support people in more urban communities?

More than half of Indigenous peoples in Canada live in urban centres. Supporting First Nations, Inuit and Métis where they live is about improving quality of life and contributing to stronger economic growth in their communities, and in Canada. UPIP seeks to support

and build upon the existing network of Friendship Centres, which are working on the front-lines to address the numerous and often critical issues faced by Indigenous people in urban environments.

What is considered as an urban area? How much of the population does this include?

In the context of Urban Programming for Indigenous Peoples, an "urban centre" follows the Canadian census' definition of a "population centre": an urban area having a population of at least 1,000 people and a population density of no fewer than 400 people per square km. The Urban Programming for Indigenous Peoples applies mainly to large urban centres, but also to rural and northern areas that act as hubs for those living on reserves, or in smaller northern settlements. ■

Indigenous and Northern Affairs Canada
www.aadnc-aandc.gc.ca
[www.twitter.com/GCIIndigenous](https://twitter.com/GCIIndigenous)

Clean energy is vital for all of Europe

In a speech, Climate Action and Energy Commissioner, Miguel Arias Cañete, highlights the clean energy transition taking place across Europe

Firstly, I would just like to outline the pace of change that we have witnessed as the clean energy transition takes hold; Secondly, I would like to say a few words about the Paris Agreement; and thirdly, I would like to talk about our Commission proposals in the Clean Energy for All Europeans Package – and how things stand at the moment.

In reality, the level of investment and new projects is moving more quickly than the gathering of statistics. The key point is that renewable energy is now cost-competitive and frequently becoming more and more cheaper than fossil fuels. With 12,5 GW of gross additional wind capacity installed in 2016[1], wind has now overtaken coal as the second main source of energy in Europe (after gas) and the EU remains the second largest market for wind power (after China).

Figures for 2016 from the renewables agency, IRENA, show that the level of power capacity from renewables continues to increase, with a global increase of 9% last year, relative to 2015. In Europe, the level of growth in 2016 was around 5% and this is in good part because the EU is already doing more than others. Per capita, the EU has installed 4 times more renewable power than the rest of the world (0.8 kW/capita versus 0.2 kW/capita) – and twice as much as China (0.4 kW/capita).

In total, the renewables sector in Europe employs over 1 million people, attracts more investments than many other sectors, and has reduced our fossil fuels imports bill by €16 bn since 2005. On top of that, whereas in the past we used to see a clear link between energy consumption and GDP growth – with any rise in GDP only possible with an increase in energy consumption. In recent years we have managed to fully decouple these 2 elements. Whereas GDP grew by some 10% from 2005 to 2015, primary energy consumption decreased by

almost 11% in the same period. The signal is clear – cleaner energy and economic growth can go hand in hand. In short, this is not just a transition, we are truly undergoing a clean energy revolution. Our job as policymakers is to see how we can steer and accelerate this process most efficiently by creating the right regulatory and enabling framework.

This brings me nicely on to my second point – the most important global achievement – the ratification of the Paris Agreement. The Paris Agreement was a remarkable, perhaps unique exercise in collective responsibility to slow down global warming to well under 2 degrees; 195 parties working together to establish the most efficient vehicle for fighting climate change. Sealed by the EU ratification of the deal, the moment that this accord came into force was one of the most fulfilling moments of my political career. This is why, I will do whatever it takes to defend and implement it.

Of course, the EU deeply regrets the unilateral decision of President Trump to withdraw the USA from the Paris Agreement. In our response, we have made clear that the 29 articles of this accord are not up for renegotiation. The Agreement is ratified. It is fit for purpose. It is here to stay. I was touched by the stance taken by many cities around the world and the number of green-coloured town halls that were pictured on social media. Perhaps this is a good chance to acknowledge the role that can be played by cities and local authorities in this contest. A good instrument to make this happen is the Global Covenant of Mayors, which should become fully operational in the course of this year.

Such a single, global coalition of cities is important for a range of reasons, but I will mention only one: cities and regions can inspire each other and learn from each other's best practices. In other words: our cities



can team up with cities in other continents to jump over the fossil age.

As European Commissioner responsible also for Climate Action, I will work relentlessly to forge new partnerships around the world, from the world's biggest economies to the most vulnerable developing countries, supporting and helping them to adapt and mitigate climate change, a good example of this renewed partnership is China.

But first and foremost – and that brings me on to the third point I would like to cover – we, the EU, are putting in place our own ambitious domestic energy and climate change policies and setting the conditions right to steer the necessary investment in the clean energy transition thanks to the Clean Energy Package.

Clean energy for all

I see the Clean Energy for all Europeans package as the way of cementing the EU's Paris Agreement commitments into our rulebook.

The key here is creating the optimal conditions for energy transition, not only by setting the necessary regulatory framework, but also, by driving the necessary investments – both public and private – to support this transition. This time the commission took a different approach by going beyond regulation, and by developing, at the same time, the enabling instruments and support measures that would be needed to reduce greenhouse gas emissions by at least 40%, to achieve an energy efficiency target of 30% and to reach the level of at least 27% of renewable in our final energy consumption.

I would like to highlight a few elements, starting with Energy Efficiency, the most mature file, at least in Council. I would like to be clear: energy efficiency is not a slogan, it is one of the most cost effective ways to support the transition to a low carbon economy and a key policy to implement the Paris Agreement. Besides, it is also an effective way to create investment opportunities, growth and employment domestically.

According to our estimates, the 30% energy efficiency target will increase Europe's GDP of €70 billion, create about 400,000 new jobs – especially among SMEs – and reduce our gas imports by 12% by 2030.

Moreover, the binding nature of the target will provide additional certainty to the investors. Many industry representatives are fully in line with an ambitious binding target, to have more predictability. After the productive discussions that we had in Malta at the occasion of the informal Energy Council, I am happy to see more and more Member states moving in our direction.

But ambition is not only about the target, it is also about the requirement for Member States to make annual savings of 1.5%, foreseen by article 7. This is a core provision, since through it we achieve about half of all the savings of the directive.

How can we explain to our citizens that undergoing energy transition and combatting climate change is more important than ever, and yet we lower the existing requirements? This makes no sense. Of course, I recognise the need for more flexibility, notably as far as renewables are concerned, but this should not lead to the creation of loopholes in the legislation and should not be at the expenses of the level of ambition.

If that will be the case, I would rather be in favour of giving ourselves more time, to work out a better compromise. Another key point is the need to improve the energy performance of buildings, given that this accounts for 40% of Europe's energy consumption and 36% of CO₂ emissions.

Significantly accelerating the rate of building renovation has the potential to help more families move out of energy poverty, and to improve the quality of life for many – as well as stimulating jobs, in particular for local SMEs. In this context, our proposal for pre-cabling and charging points for electric vehicles in new and existing buildings – and the recent mobility package – should help to address one of the key bottlenecks holding back electric vehicle growth in Europe. On this specific issue, I regret that as far as charging points are concerned the

council compromise will reduce the level of ambition by more than 95% compared to the Commission original proposal. I look favourably at the work ongoing in the European Parliament and I hope that we will be able to bring back a certain level of ambition here.

“In total, the renewables sector in Europe employs over 1 million people, attracts more investments than many other sectors, and has reduced our fossil fuels imports bill by €16 billion since 2005. On top of that, whereas in the past we used to see a clear link between energy consumption and GDP growth – with any rise in GDP only possible with an increase in energy consumption.”

Also because by the end of the year we will adopt the post 2020 emission standards for cars and vans and, there, we are considering options to set a dedicated target for zero and/or low emission vehicles. And of course the availability of charging infrastructure is going to be essential for the penetration of these vehicles into the market.

I attach a lot of importance to two main elements: first, preserving the consistency between the different proposals of the Package and second, ensure that the legislation that we will adopt will be enforceable. ■

This is an edited version of a speech by the Commissioner that can be found here http://europa.eu/rapid/press-release_SPEECH-17-1721_en.htm

Miguel Arias Cañete

Commissioner for Climate Action and Energy

European Commission

www.ec.europa.eu/commission/commissioners/2014-2019/arias-canete_en

[www.twitter.com/MAC_europa](https://twitter.com/MAC_europa)

A SmartNet for a cleaner energy system

Ricerca sul Sistema Energetico's Gianluigi Migliavacca highlights how the EU-funded project SmartNet can help to manage the so-called 'energy transition'

Recently, the EU Sustainable Energy week in Brussels focused on what can be considered 'The' topic for this and the next decade: how to manage the so-called 'energy transition' – from traditional fossil fuel generation to greener energy systems, where electricity is generated from wind, water, sun, and other Renewable Energy Sources (RES).

One of the tricky points in the transition concerns the change of roles when it comes to managing the existing electricity network. Electricity is generated more and more at local/low voltage level and needs to be injected into the transmission/high-voltage level – while in the past it was exactly the opposite. How do we make this reversion possible and smooth?

In Europe, there is a sharp increase in reserve needs for coping with the variability introduced by a steadily increasing RES share in the generation. The big challenge is to extend the possibility of providing Ancillary Services (AS) (frequency and voltage control, congestion management, etc.) to entities connected to the distribution network. The legislative package proposed by the European Commission in November 2016, nicknamed the Clean Energy Package, assigns a role to Distribution System Operators (DSOs) for local congestion management but not for balancing, whose management would remain in the hands of the Transmission System



Operators (TSOs)¹. However, such a sharp decoupling risks leading to inefficient system operations.

SmartNet Project

All these issues are addressed by the SmartNet European [research project](#), under technical and administrative management by RSE², which aims to compare different TSO-DSO interaction schemes and different real-time market architectures with the goal of finding out which would deliver the best compromise between costs and benefits for the system. The objective is to develop an ad hoc simulation platform which models all 3 layers (physical network, market and ICT), analysing 3 national cases (Italy, Denmark, Spain). Subsequently, this simulation platform will be scaled to a full replica lab, where the performance of real controller devices will be tested.

SmartNet considers 5 possible coordination schemes characterized by different coordination patterns, roles and market design (Centralized AS market model, Local AS market model, Shared balancing Responsibility Model, Common TSO-DSO AS Market Model, Integrated Flexibility Market Model). Specificities, benefits, and attention points of these coordination schemes are analysed in this [report](#).

Reserve needs do increase and this justifies enabling Ancillary Service (AS) markets participation from flexible resources connected to distribution grids. AS market products have traditionally been designed for large transmission-connected generators. It is essential to propose a diversity of market products, while ensuring a sufficient level of liquidity to provide a level playing field to all flexibility service

providers (including distributed generation, storage and demand response). More can be found in [this report](#).

ICT architectures must be re-configured according to the changing service requirements of the different TSO-DSO coordination schemes. A more detailed description of the process and ICT architecture model in [this PDF](#).

“Electricity is generated more and more at local/low voltage level and needs to be injected into the transmission/high-voltage level – while in the past it was exactly the opposite. How do we make this reversion possible and smooth?”

Small and dispersed generation units need to be aggregated and connected, in order to participate in and profit from the AS market. Aggregators gather the flexibility of many DERs, and forward them, in the form of complex price-quantity bids, to the AS market. They play a key role in reducing the amount and complexity of the data passed to the market, such that near-real-time results can be obtained, while retaining a straightforward way to transform market results into the activation of [single DERs](#).

Additionally, the SmartNet project includes 3 physical pilots for testing specific technological solutions:

- Demonstrating technical feasibility and requirements in terms of communication processes for the monitoring of the (distribution) network and enabling the participation of DER to ancillary services (Italian Pilot);
 - Demonstrating the use of price signals to control the set-points of swimming pool heating systems in rental summer houses (Danish Pilot);
 - Demonstrating the prospects for the DSO of using the flexibility of mobile phone base stations to reduce congestion in distribution grids, and to help the TSO maintain system balance by fixing an exchange schedule at the TSO-DSO connection point (Spanish Pilot).
- In the final stage of the project, SmartNet will assess policy provisions necessary to enable needed TSO-DSO interaction and compare them with present national and European regulation. Whereas final regulatory recommendations will be possible only towards the end of the SmartNet project, a few preliminary considerations can already be highlighted:
- While it could be appropriate that TSOs retain a responsibility for the provision of balancing services, nonetheless they could have to share part of this responsibility with DSOs to the extent that the importance of the contributions to this service from entities connected to distribution will grow;
 - A balance has to be sought for between local optimality and the implementation of a harmonised pan-European design;
 - Smaller DSOs have to integrate their efforts in order to be fit for the new responsibilities;
 - Only if the architecture of real-time markets will be able to take fully into account the characteristics of the potential flexibility providers connected to distribution grids, it will be possible to obtain a significant participation on their side;
 - Aggregators must be able to provide a simplified interface towards the

market, hiding most details and complexities of the characteristics of the single flexibility providers. Aggregators must deliver flexibility providers efficient price signals to incentivise their participation;

- Viable business models must be available for all market participants, including DERs, aggregators and other customers;
- Network planning will also have to facilitate better utilisation of RES, while minimising infrastructure investments, or postponing investments so to reduce the risk of stranded assets. Technical optimality should be supported by a thorough cost-benefit analysis.

¹ EC (2016) Proposal for a DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL on common rules for the internal market in electricity – Art.32.

² Ricerca sul Sistema Energetico: <http://www.rse-web.it>



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Citizen participation in energy-related activities

ENTRUST is a H2020 project exploring human behaviour towards energy-related activities. University College Cork's Niall Dunphy explains

Energy has traditionally, and indeed it continues to be, framed almost exclusively as a commodity. From this perspective, citizens mainly occupy the role of passive – or occasionally as so-called ‘active’ – consumers whose only legitimate interaction with the energy system occurs through their purchasing choices and consumption practices. Other societal and environmental considerations are more often suppressed or superseded by this dominating paradigm. This ignores the fact that consumption represents only one component of the human interaction with the energy system. Such a limited view has led to poor policy decisions that have resulted in, for example, bottom-up resistance to energy infrastructure and the design of ineffective initiatives aimed at changing energy behaviour and practices.

Despite this, the energy system is currently undergoing a rapid transformation, reinforcing the need for a greater understanding of the human dimensions of energy. The EU has set targets to reduce greenhouse gas emissions by at least 40% from 1990 levels, and to have a minimum of 27% of energy produced by renewables, as well as a 27% improvement in energy efficiency. In order to achieve this transition to a low carbon future that is both efficient and effective, we need to re-evaluate the way in which energy is viewed at a personal and wider societal level.

Calls to move beyond the narrow view of energy as a commodity are growing apace and many policy makers are beginning to recognise the need to integrate the public as much as possible as active stakeholders in the energy system. The role citizens often play in strategic, energy-related infrastructural projects is usually consigned to passive participation with ‘community engagement’ on the part of those leading the project being rather perfunctory and non-committal. Community consultations invariably comprise of information meetings with developers where local people are told how the developers wish to proceed. The ENTRUST project is exploring how attitudes on participation can move to a more inclusive space where all stakeholders in the energy system can contribute to co-developing the transition to low-carbon configurations.

ENTRUST is meeting this challenge by adopting a number of key theories to inform our conceptual framework, most notably the idea of energy citizenship. The project is developing an in-depth understanding of people's awareness and perceptions of the energy system, their attitudes towards various energy technologies, and their energy consumption behaviours and practices. This analysis examines how socio-demographic factors (especially gender, age and socio-economic privilege) impact and shape these attitudes and practices. Building on this understanding, the

project also engages the public in the current energy transition and uses consensus decision-making tools – emerging from deliberative democracy theory – for creating public interest in European energy policy and innovation. The research team are currently implementing a suite of citizen jury-style engagements across 6 communities, to co-develop with participants their vision of the sustainable energy and low carbon future.

“The ENTRUST team have placed particular effort on understanding the complex, multifaceted roles gender, age and socioeconomic status have in shaping individual identity and the associated collective impacts on our energy infrastructures.”

ENTRUST's multidisciplinary and interdisciplinary team comes from a broad range of disciplines – including engineering, sociology, political science, psychology, gender theory, and human geography – and are integral to the effective exploration of the sociodemographic factors at play. The project has made good progress to date and has already seen the completion of numerous analyses on policy and regulation, energy technologies, and market-based policy tools. Reporting on the multidisciplinary team's work on stakeholder engagement, deliberative participatory processes and the intersectional, socio-demographic analyses is now also nearing completion.



The ENTRUST team have placed particular effort on understanding the complex, multifaceted roles gender, age and socioeconomic status have in shaping individual identity and the associated collective impacts on our energy infrastructures. These influencing factors can be both positive and negative and only by understanding these drivers can we begin to fully understand our collective responses to wider energy transition initiatives. Working with the 6 communities in the project, the ENTRUST team is striving to present new and emerging knowledge within a practical framework that can improve stakeholder understanding and, ultimately, overcome the shortcomings of previous phases of the energy transition by helping to give local people a voice in the energy discourse.

Encouraging greater public participation is a perennial issue for policy

makers. A quite novel departure being taken by the ENTRUST team is the use of 'citizen juries' within the 6 communities it is working with. A citizen jury is a type of deliberative process designed to encourage people to identify and explore the issues that are of particular importance to them, within the wider framework of the energy system. Once this step has been completed participants then proceed to deliberate and posit potential solutions that they see as fair and just, both to them and to society more generally. Deliberative democracy or discursive democracy tools have been applied in numerous countries including Canada and Ireland and are increasingly seen as giving citizens a greater opportunity to contribute to the democratic process and, subsequently, lends greater legitimacy to decision makers over more traditional ballot-focused approaches. Follow us on twitter for updates of this work.

This project has received funding from the European Union's Horizon 2020 Programme for Research and Innovation under Grant Agreement no 657998.



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Understanding changes to extreme rainfall

Rainfall data can be used to help us adapt to climate change. Hayley Fowler, School of Civil Engineering and Geosciences at Newcastle University explains

Heavy rainfall events that only last a few hours or less are associated with flash flooding, which poses a significant challenge to public safety, infrastructure, and the economy. Such events are of growing concern as greenhouse gas-induced global warming will increase the level of moisture in the atmosphere, causing heavier rainfall events. New research is, therefore, trying to understand how changes to atmospheric moisture and circulation dynamics will combine to amplify or weaken regional increases in extreme precipitation events which cause flash floods. This knowledge can be used to provide a better basis for climate change adaptation planning.

The INTENSE Project

INTENSE (INTElligent use of climate models for adaptation to non-Stationary hydrological Extremes) is a large, 5 year research project (€2m) funded by the European Research Council. It is the first project to examine sub-daily precipitation extremes, enabling substantial advances to be made in observing current and past changes. It will also provide a physical understanding of processes relating to precipitation extremes necessary for improved regional prediction of change.

INTENSE is leading the global research effort in this area as a Global Energy and Water Exchanges (GEWEX) Hydroclimatology Panel Cross-Cutting project on sub-daily precipitation extremes, with a large number of international

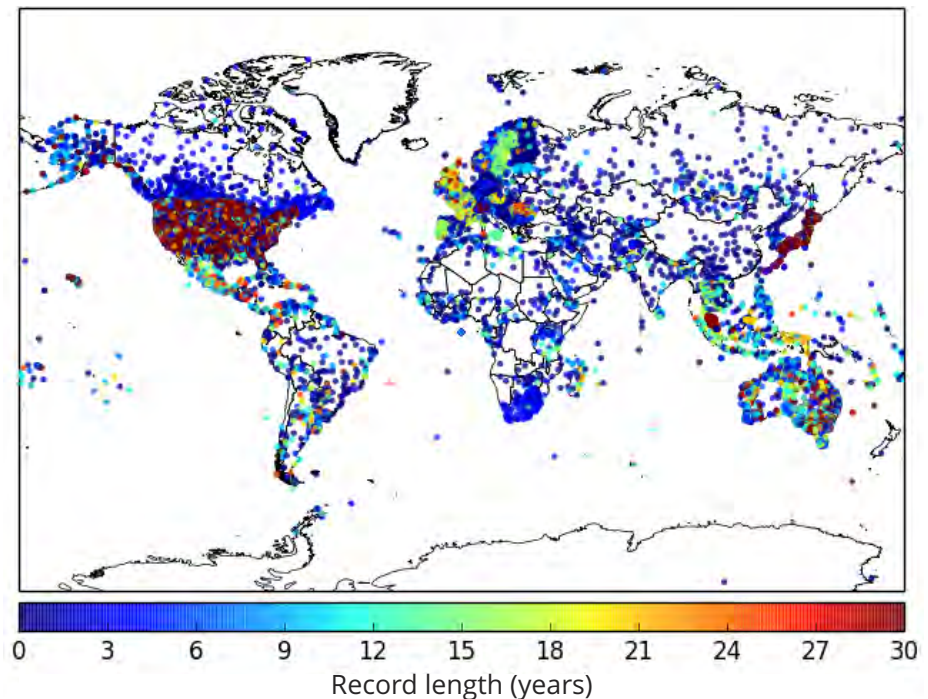


Figure 1: Location of rainfall stations collected by INTENSE and their record length in number of years

collaborators and partners. Begun in 2014, it is comprehensively analysing the response of precipitation extremes to global warming by:

- Constructing a new global sub-daily precipitation dataset;
- Using this and high-resolution climate modelling to quantify the nature and drivers of global precipitation extremes across multiple timescales;
- Examining the influence of local thermodynamics and large-scale atmospheric circulation modes on observed precipitation extremes; and

- Using these to identify climate model deficiencies in the representation of precipitation extremes.

Data collection, quality and indices

Sub-daily rainfall extremes are particularly important as causes of urban flooding, but compared with heavy rainfall on timescales of a day or longer these events have been studied relatively little in most regions. Records of sub-daily rainfall are not as extensive, either in time or space, as those for daily rainfall totals. Such data is most commonly available from the 1990s onwards, given advances in



rain gauges and electronic recording devices/telemetry. Further, sub-daily rainfall data is much harder to get access to than daily data as many organisations do not make the former freely available.

The INTENSE project is focussing on collecting gauge-based rainfall data only as it gives the most accurate representation of the amount of water reaching the ground. Many sub-daily rainfall datasets exist that cover a large proportion of the globe but are not based on gauged observations. For example, satellite datasets such as GPM record precipitation every 3 hours. Global gridded precipitation datasets also exist, such as MSWEP based on merged gauged, satellite and reanalysis data products, but these are coarse at 3hr and 0.25°. Radar and merged rainfall measurements are limited in usefulness,

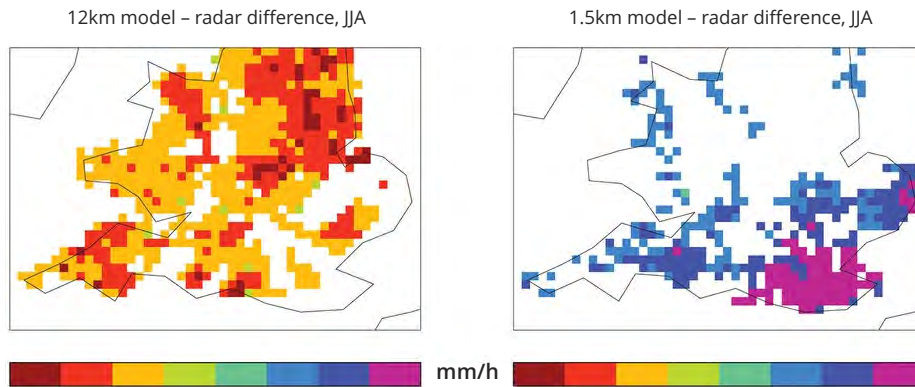
particularly for the aims of INTENSE which focus on extreme rainfall, as they are yet to be fully validated by observations as no global sub-daily gauge dataset exists.

We have collected data from 22,644 stations globally (just under half of these are from the UK Met Office's Integrated Surface Database). However, even where we have data, it may not be adequate for the analysis of extreme events – for example, undocumented gauge breakdowns may be recorded as periods without rain, daily totals may be erroneously recorded as hourly values or mechanical failure of the rain gauges may produce erroneous extreme events. Furthermore, changes such as gauge location, site characteristics, or equipment type may introduce inhomogeneities in climatic series. The detection of such errors is important for the evaluation

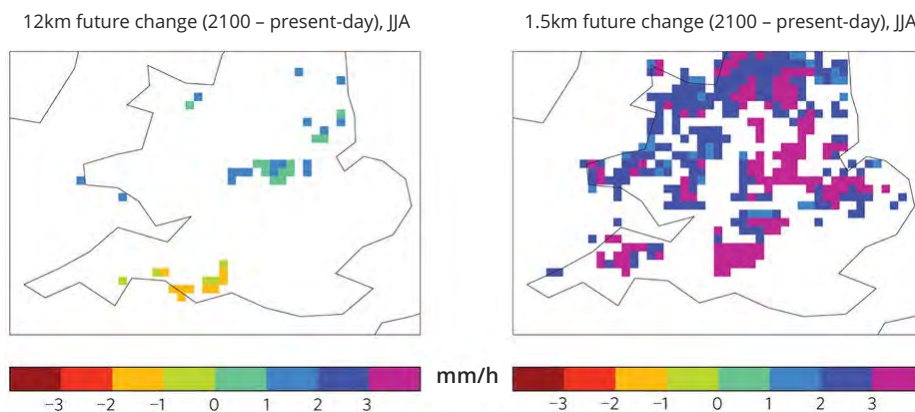
of extreme events and for the assessment of longer term variability and trends. We are therefore developing an automated quality control programme for global sub-daily data that will be applied to the station records to produce a high-quality global dataset.

We are using the data collected to produce a set of sub-daily extreme rainfall indices describing monthly maxima, frequencies over thresholds and the diurnal cycle, which will be made freely available to all users and will be very useful for understanding current patterns of extreme rainfall and for the validation of climate model outputs at sub-daily scales. Additional work will use the new dataset to validate new precipitation satellite products from NASA and explore options for combining the gauge and satellite data to produce a gridded global sub-daily dataset.

DIFFERENCE BETWEEN MODELLED AND OBSERVED HEAVY SUMMER RAINFALL (HOURLY)



CHANGE IN HEAVY SUMMER RAINFALL (HOURLY)



The dataset collected by INTENSE is a platform for future development by the larger scientific community and policy makers. In particular, we are working to find a global organisation who will maintain and update the dataset. This will require a tremendous amount of effort as licences will need to be negotiated and secured to make the data itself available to researchers to further scientific understanding.

Scaling of intense rainfall with temperature

Climate models suggest that rainfall will intensify under global warming as the physics of a warmer atmosphere are capable of holding more moisture. We expect that rainfall intensities will increase with temperature according to the Clausius–Clapeyron (CC) relation (a rate of $\sim 6\text{--}7\%$ $^{\circ}\text{C}^{-1}$), although precipitation data for some parts of the world show larger (super-Clausius–Clapeyron) rates of change for

short-duration (hourly and shorter) extremes. Historical records of UK hourly summer (June–August) rainfall show CC scaling. Our work will examine the new global dataset to see how precipitation extremes scale with temperature change and moisture availability globally.

Trends in extreme rainfall

We have produced the first analyses of trends in sub-daily rainfall records over the US. These show that hourly and daily seasonal maxima have significantly increased over the last 6 decades. The percentage of stations showing significant increasing annual maximum precipitation trends was generally higher for daily compared to hourly extremes. However, strong evidence points to more widespread increases in the magnitude and frequency of hourly extremes during winter compared to daily extremes. This work is now being extended to

examine trends globally and how these relate to global mean temperature change. Our work has indicated, though, that one of the challenges of assessing changes in historical rainfall extremes is their relatively large natural variability, in part due to their dependence on large-scale atmospheric patterns such as El Niño.

Climate modelling

Climate models are the main tools used by scientists to obtain projections of future climate from which estimates of future impacts on society are subsequently derived. Although they have a high degree of skill in simulating many features of our climate they also have a number of known weaknesses and so there are large uncertainties in regional patterns of change, making the development of efficient adaptation strategies for flooding more difficult. One major weakness is that the grids they operate on are not fine enough to incorporate surface features that influence local climate or to represent the convective storms that produce intense summer rainfall.

Working with our partners at the UK Met Office Hadley Centre we adapted a weather-forecast resolution model to study potential changes in hourly rainfall associated with climate change. This model, unlike coarser resolution climate models, is able to realistically represent hourly rainfall, allowing us to make future projections with some confidence. In *Nature Climate Change* in 2014, together with the UK Met Office Hadley Centre, we published the first evidence that summer downpours could become heavier over the UK with climate change. While we expect summers to become drier overall by 2100, our

results indicate heavier summer downpours in the future, with almost 5 times more events exceeding 28mm in 1 hour (associated with flash flooding) by 2100 than there are currently. The model also shows increases in hourly rainfall intensities in winter, consistent with projections from a coarser 12km-resolution model and previous studies at the daily timescale. The results represent the first step towards building a complete picture of how rainfall may change as our climate warms.

This work has led to the inclusion of several very-high resolution model simulations in the UK's next set of official climate change projections (UKCP18). We have now also extended this work to compare our results with the results from other international modelling centres to build up a picture of how the results from these very high-resolution models differ from those coarser resolution models generally used to create national climate scenarios used for climate adaptation. We have also extended our work within INTENSE to examine larger model domains – building towards very high-resolution global model runs.

Putting science into practice

Changes to future rainfall intensities will impact sewer flooding and so our initial work has been applied in the UK water industry. Using our high-resolution observations and model simulations and working with UK Water Industry Research, we have developed better guidance on estimates of change in rainfall intensities (uplifts) affecting water and sewerage companies, offering the potential for their application in both flooding and pollution analyses and in investment planning. INTENSE will be able to use

its high-quality observations from around the globe to provide relevant stakeholders with the most reliable return period estimates for different rainfall intensities, and so contribute to a better understanding of current flood risk. Our high-quality data could also be used to better understand how river catchments respond to intense rainfall events – for example, we have produced a high resolution gridded dataset of hourly rainfall for the UK which will be freely available to hydrologists and other practitioners. The project's advances in data provision and scientific understanding will, therefore, facilitate knowledge to help make people, business and infrastructure more resilient to flooding from intense rainfall in the future.

We have also worked hard to communicate our research with the public more generally. We recently developed a museum exhibition, FLOOD! In which we showcased our research into extreme rainfall. We aimed to help visitors navigate their way through the arguments made in the public sphere around climate change and extreme rainfall and provided a more detailed understanding of why flooding happens and what can be done to prevent it. Throughout the exhibition, visitors experienced what it's like during a flood with an immersive virtual reality headset, understood the role of landscapes and rainfall through an augmented reality sandbox and learnt about flood management, using a giant version of the childhood game Kerplunk. The exhibition also used puppets, real field kit that we use to obtain hydrological data and a peg board game to understand how the probability of extreme rainfall events will change in the future. The walls were covered in information boards

and videos explaining the causes and types of floods, how we measure and model flooding, what climate change is, how climate change will affect flooding and what we can do to reduce flood risk, and also displayed research posters from the INTENSE project. The exhibition ran from 3rd-9th July 2017 and attracted over 1000 visitors.

Outlook

Research within the INTENSE project is providing a greater understanding of the nature and drivers of change in heavy rainfall events worldwide, which will help us to better understand the mechanisms associated with flash flooding. In turn, this should lead to improved prediction of likely future changes and improvements in the use of climate models for adaptation.

Publications referred to in this report can be found on the [INTENSE website](#).



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Are m-CHP systems the answer to reducing emissions?

José Luis Viviente from TECNALIA explains how micro combined heat and power (m-CHP) systems can help to reduce CO₂ emissions in rural communities

Rural areas represent 90% of all territory in the EU 27 Member States and over 50% of the population (around 46% of population in the world). From these, there are at least 30 million homes and businesses which will probably never have access to the natural gas grid and instead largely rely on high carbon intensive energy sources. Paradoxically, rural communities have a higher carbon footprint per person than they need to and often higher than their urban compatriots.

Major concerns on anthropogenic CO₂ emissions and related greenhouse effect have pushed several governments and EU to support greenhouse gas emission reduction policies.

“By converting the biofuels into energy, it is possible to emit the same amount of CO₂ as plants do naturally in the biomass production phase.”

On-site power generation via Micro Combined Heat and Power (m-CHP) systems, has been proven to reduce Primary Energy consumption and energy cost and CO₂ emission reduction with respect to centralised generation. The main advantage is that m-CHP systems are able to recover and use the heat that in centralised systems is typically wasted, leading to particularly high efficiencies. However, wide exploitation of these systems is still hindered by high costs and reliability due to the complexity of the system.

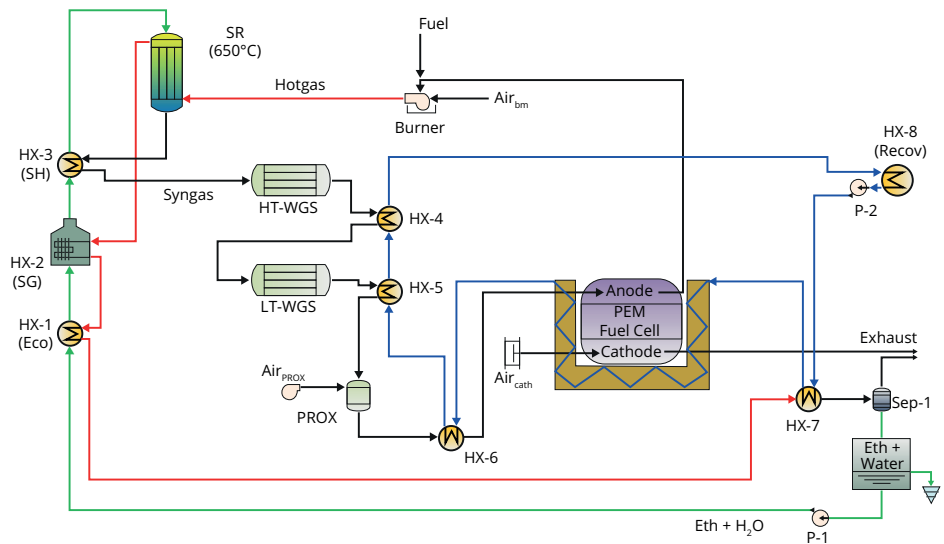


Figure 1: PEM m-CHP unit using traditional reforming

Hydrogen

Hydrogen availability is the most critical issue because it must be produced in-situ to feed the fuel cell stack. At the moment hydrogen is still being produced by fossil fuel conversion, mainly, by reforming or gasification. When looking to remote installations hydrogen can be produced from bio-renewable feedstocks. Among the various feedstocks, bioethanol is one of the preferred renewable sources for hydrogen production. Mainly when using the 2nd generation of biofuels (i.e. lignocellulosic biomass or woody crops, agricultural and forest residues, food industry and municipal biowaste and other biomass containing sugars) to produce it. By converting the biofuels into energy, it is possible to emit the same amount of CO₂ as plants do naturally in the biomass production phase. This leads to a virtually closed carbon cycle that

has not impacted on the environment and the recycling of the waste that otherwise will be lost, moving from fossil fuels to renewable energy introducing the concept of circular economy in the energy supply chain. However, the use alone of biofuels is not enough to achieve the emission reduction targets; energy-efficient conversion technologies are required to maximise the efficacy of their use.

FluidCELL FCH

The FluidCELL FCHJU/FP7 project aims at providing the Proof of Concept of an advanced high performance, cost effective bio-ethanol m-CHP cogeneration fuel cell system for decentralised off-grid applications. The main idea of FluidCELL is to develop a new bio-ethanol membrane reformer for pure hydrogen production ($3.2 \text{ Nm}^3/\text{h}$) based on membrane reactors.

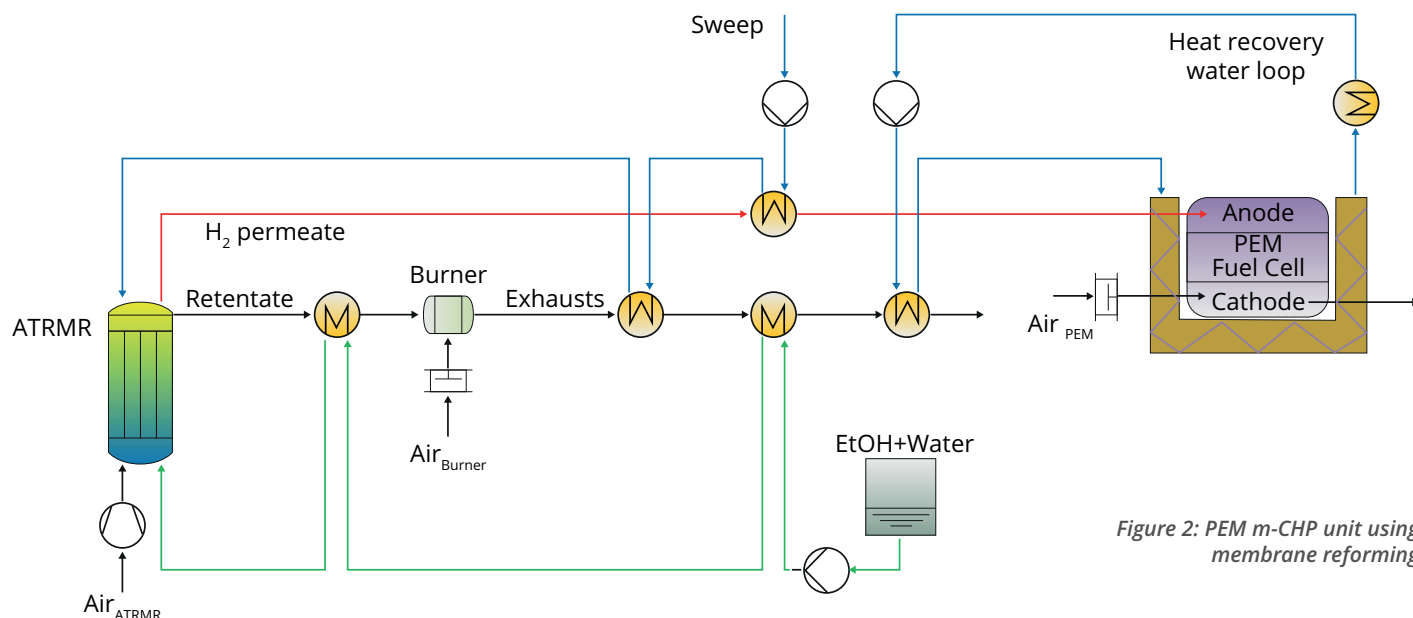


Figure 2: PEM m-CHP unit using membrane reforming

The traditional reformers include several steps for producing H_2 with adequate quality to feed the fuel cell stack (Figure 1): steam reformer for converting ethanol into H_2 and CO at high temperature (i.e. 650°C), two water gas shift reactors for converting CO into H_2 and a reactor for reducing the CO content below 10 ppm.

“Major concerns on anthropogenic CO_2 emissions and related greenhouse effect have pushed several governments and EU to support greenhouse gas emission reduction policies.”

The integration of a bioethanol membrane reactor reduces the system complexity by replacing the 4 reactors with a single reactor (Figure 2), namely the membrane reactor with expected thermodynamic advantages and reduction of the reforming temperature, ($\leq 500^\circ\text{C}$) while converting the produced bio-ethanol to hydrogen

with higher efficiencies. In addition, there is a cost reduction of the other components in the reformer and in the BoP (auxiliary elements) of the m-CHP. The hydrogen conversion and separation is carried out in this reactor and a pure hydrogen stream is produced.

The membrane reactor concept and model has been validated and lab scaled. Main components of the m-CHP system, the fuel cell stack and the reformer prototype, have been manufactured. Validation of the reformer prototype is ongoing. Once assembled in October 2017, the PEMFC m-CHP system will be validated working at least 1000 h. Finally, a life cycle assessment is also being carried out.

Visit www.fluidcell.eu for further details.

Acknowledgements

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Green energy is the solution to a number of challenges

Morten Helveg Petersen, Member and VP of the Industry, Research and Energy Committee at the European Parliament discusses the importance of green energy

We are facing 4 defining challenges of our time: climate change, Russia, economic growth and job creation. The good news is that all 4 challenges have the same solution, and it is green.

In late 2016, the European Commission presented the Winter Package. The aim of this is to fight climate change, make the EU independent of Russian oil and gas, improve competitiveness and create jobs for European citizens.

This proposal is exactly what we need to solve 4 of the defining challenges of our time. The European Commission deserves credit for the package, but I believe that we need to go further and faster.

“Along with colleagues from the European Parliament, it is my ambition that the EU follows the same path as Denmark. This will require higher ambitions and better coordination across the files constituting the Winter Package.”

Single market for energy

In the European Parliament, I am the Vice-President of the ITRE committee and the rapporteur for the revision of the ACER regulation. The revision seeks to give us more value for money, when it comes to renewable energy. Literally. A single market for energy will allow businesses and consumers to benefit from a smaller energy bill. This in turn will make businesses more competitive and able to make new and better investments. In addition, consumers will be able to spend more on other goods and services – improving economic growth and generating jobs that are highly needed across our union.

By focusing on both renewable energy and energy efficiency, we can improve economic growth and create new jobs, while fighting climate change and limiting



Morten Helveg Petersen, Member and VP of the Industry, Research and Energy Committee at the European Parliament

our reliance on Russia. However, we need to look at energy systems in their entirety. The most efficient and cost effective energy solutions are the ones that take a holistic approach, harnessing all opportunities and finding synergies between different technologies.

When the European Commission presented the Winter Package, I said that we face a unique opportunity as well as a significant challenge. We all have to coordinate, be willing to harness synergies and incorporate a systematic approach strategically across the various legislative dossiers of the Winter Package to achieve the best results. We need to overcome the false narrative and tired dichotomy between supporting European competitiveness and delivering environmental and economic sustainability. We can and must deliver on both simultaneously. Actually, the 2 only enhance each other.

Danish GDP, energy use and emissions

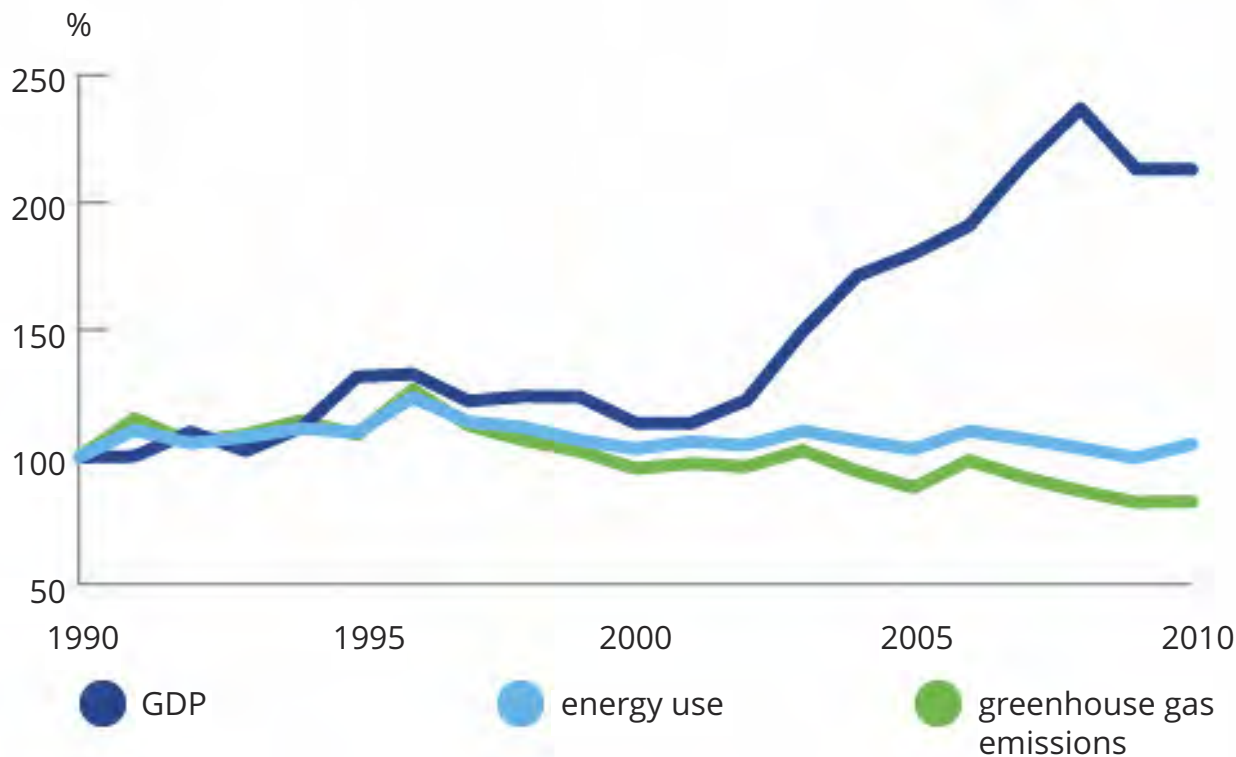


Image: © Nordic Energy Research 2012, Source: EEA/World Bank 2010

Cost effective energy

One example is Denmark, which has succeeded in decoupling economic growth from energy use and greenhouse gas emissions. Three curves that have run parallel for decades and continue to do so in most of the world.

Unlike the most famous Danish stories, this is not a fairy tale. It is a story about working diligently on delivering a cost effective transition towards an economy largely based on renewables, coupled with a highly energy efficient building stock. Our energy intensive industries ensure that their industrial production processes harness waste heat and turn it into a common good, offering cheap heating to local communities, instead of literally throwing this valuable resource out of the window.

Thus, it is possible to grow the economy and reduce the footprint. In other words, it is possible to meet all 4 challenges at once.

Along with colleagues from the European Parliament, it is my ambition that the EU follows the same path as Denmark. This will require higher ambitions and better coordination across the files constituting the Winter Package. If we are able and willing to come together, we are in a unique position to solve these fundamental challenges of our time. Even without the miracles of Hans Christian Andersen. ■

Morten Helveg Petersen (ALDE)
Member and VP of the Industry,
Research and Energy Committee

European Parliament

http://www.europarl.europa.eu/meps/en/124872/MORTEN+HELVEG_PETERSEN_home.html

www.twitter.com/mortenhelveg

Driving renewable energy research and innovation in FP9

Greg Arrowsmith, Policy Advisor at EUREC outlines how effective projects drive the EU to keep powering renewable energy research and innovation

“Why should we fund you and not them?” Decisions will be made in the European Commission in 2018 on the budget breakdown of Horizon’s 2020 successor. This programme, provisionally known as FP9, will likely fund – as in the past – research and technology demonstration in areas such as transport, energy, health, bioeconomy, ICT, and advanced materials, but with changes to the funding distribution. Now is the time when the constituencies active in a particular field make a special effort to find projects that demonstrate the positive difference that European funding has made.

The Association of European Renewable Energy Research Centres (EUREC) members will showcase their top EU-funded projects in our Projects Catalogue 2018, due out at the end of November. Among the ones put forward for inclusion are:

Cheetah, which has managed to produce thinner photovoltaic cells. Researchers at CEA-INES have made a solar panel containing individual cells of half the normal thickness. The PV industry has been slow to embrace thinner cells but by showing that industrial equipment can handle them safely, the researchers hope that these, a tenth of a millimetre across, will be adopted widely. R2RCIGS concerns an alternative to silicon, CIGS. This project, funded under Horizon 2020’s predecessor, stands out as a success. High-efficiency CIGS cells on flexible foils were transferred from the lab to the fab – they are now being manufactured commercially at the Swiss firm Flisom.

Photosynthesis is nature’s way of capturing energy from the sun, and in our space-constrained world, researchers have been looking to the sea as the place to “grow” a source of fuel. The Macrofuels project has seen 2 big harvests of seaweed in the year-and-a-half

that it has run, and a journal article has been published with details of a highest-ever yield of alcohol from seaweed, at good concentration and with few contaminants.

Fuels are easy to store – renewable energy in other forms, less so. The COMTES project developed 3 different heat storage technologies suitable for a single family home. Such stores need to be compact – these scaled-down experimental systems took up around 2 cubic metres. A EUREC member designed and built a system that achieved record storage density using water vapour adsorbed to zeolites.

Storing electricity is harder still and it’s often better to find a way to use it directly. The Orpheus project included an assessment of the advantages of using electricity for heating, focusing on Skellefteå (Sweden) and two districts in Ulm (Germany). In Skellefteå, researchers found a 35 MW electric boiler powered by electricity from a biomass-fired CHP plant was a cost-optimal alternative to meeting winter heating demand from an oil-fired boiler. It would also save 99% of CO₂ emissions. Distribution System Operators in Germany are keen to learn from the Ulm DSO how to use PV electricity to heat water when it would otherwise be wasted.

Bridge-building is often a feature of EU-funded projects. Eurosunmed brought together European and Moroccan/Egyptian research stakeholders. Staff exchanges were organised and scientists-in-training were given lectures by experts in photovoltaics, concentrating solar power (CSP) and grids. The partners also performed joint research, which saw the first CZTS/Si photovoltaic mini-modules fabricated, then tested in Morocco; protective coatings for heliostats assessed; rock-based thermal storage evaluated; innovative configurations for CSP power plants proposed,



and grid codes for renewable energy implementation in Morocco and Egypt analysed. An official progress report is [here](#).

Signals from policymakers

On June 6, the European Parliament called for a budget of €120 billion for FP9. A month later, the [High Level Group on maximising impact of EU Research and Innovation Programme's](#), chaired by Pascal Lamy, released its report calling for a budget of €120-160 billion. It did this at a large conference hosted by the European Commission. At least 2 of Brussels's 3 main policy-setting institutions seem to be signed-up to giving research a boost in the post-2020 era.

For now, sustainable development seems to be as popular a theme for FP9 as it has been in Horizon 2020. The audience at the conference spontaneously reached for the keyword "sustainable" when asked "What should be the future mission of the EU in the R&I field" and Robert-Jan Smits, Director General of DG Research, speaking a few days earlier, said, "It's only logical that sustainable development will be the leitmotif of FP9's Societal Challenges", in part because of the COP21 Paris Agreement on climate change.

Clean energy, specifically, is well positioned for the upcoming negotiations. Since early 2017 the EU is proudly at the helm of Mission Innovation, an intergovernmental pledge to double public R&D spending on energy between the years 2015-2020. This creates the expectation that the EU will push the other members towards bold pledges after 2020, using its own research budget to set an example.

Follow us on Twitter, including for news about the launch of our Projects Catalogue 2018 ([@EUREC_Info](#)). ■

Greg Arrowsmith Policy Advisor

The Association of European Renewable Energy Research Centres' (EUREC)

www.eurec.be/en/

[www.twitter.com/@EUREC_Info](https://twitter.com/EUREC_Info)

Delivering flexible and secure energy solutions

Dom Barton, of Metropolitan Infrastructure Limited explores the national challenge to deliver sustainable, affordable and secure energy solutions

With heating accounting for 40% of the UK's carbon emissions and over 2 million UK households in fuel poverty, the challenge to provide sustainable, affordable and secure energy supplies has never been greater. It directly affects the lives of individuals and their communities now and underpins the continued provision of their vital support services – including healthcare, social care, education and housing.

District energy and multi-utility solutions

Metropolitan is the leading independent district energy and multi-utility infrastructure provider in the UK. We are the only company combining all the traditional utility networks and future-proof district energy schemes as part of the complete solution for new build and regeneration sites nationwide.

We design, build, fund, own, and operate networks for decentralised and traditional energy and have delivered some of the UK's highest-profile, lowest-carbon new communities.

Our district energy networks provide sustainable, affordable and secure energy solutions for:

- High-density residential and mixed use commercial new developments;
- Urban regeneration areas;
- Combined regeneration and new development schemes;

- Retrofit of existing residential and commercial buildings.

We bring genuine choice in the delivery of district energy and multi-utility solutions, and their long-term economic operation, without the need for intervention from incumbent utility providers.

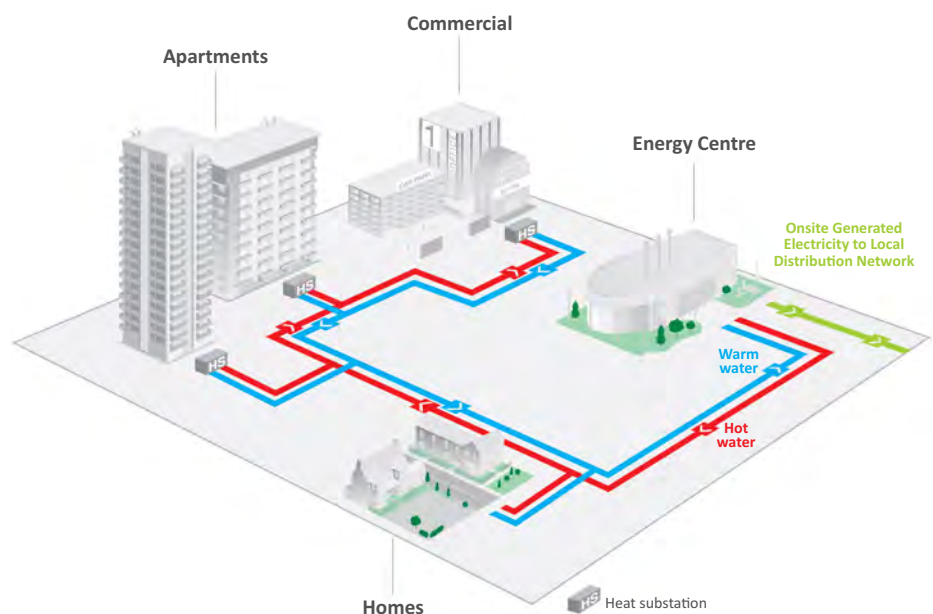
From network adoption to fully constructed and financed options, our investment models provide maximum flexibility with customers choosing the route that best suits their needs and objectives.

The only partner you need for all your energy and utility assets, Metropolitan provides solutions for:

- District energy;
- Electricity;
- Fibre-to-the-Home (FTTH);
- Water and wastewater;
- Gas.

What is district energy?

District energy reduces total carbon emissions and creates more affordable energy for all. Most importantly, it provides the opportunity to drive down fuel poverty. District energy networks allow different sources of low-carbon heating such as Combined Heat and Power (CHP), heat pumps, energy from Waste (EfW) or fuel cells



to supply heating through a network of insulated underground pipes to individual properties.

Scalable solutions

We provide solutions that are flexible, scalable and designed to evolve with the needs of the development serving the growing number of people living and working there. Once the initial part of a district energy network is operational, there are often opportunities to extend it into adjacent areas as a retrofit solution. This brings improved carbon performance to an entire area.

Transforming communities

Alongside energy networks, we deliver other enabling infrastructures, such as electric and fibre networks. These networks ensure that the provision and usage of energy are as efficient as possible while ultrafast Fibre-to-the-Home (FTTH) networks bring life-changing benefits to consumers' personal and professional lives.

Heat Trust guarantee

Metropolitan was one of the first to register a scheme with the Heat Trust, and as members, we commit to abide by the scheme which serves to protect and safeguard the interests of all heat customers.

We are committed to obtaining Heat Trust status for all our networks, to offer independent reassurance to residents that our heat tariffs are always fair. Customers connected to our electric or fibre networks have complete freedom to choose their supplier and service package.

Public sector funding

Both the UK and Scottish governments have active strategies to promote the decarbonisation of heating for buildings, and have dedicated funding available to enable district energy projects.

Funding is not limited to just local authorities and could be used to connect new loads to existing heat networks within other public sector organisations, such as NHS buildings and universities. We can incorporate such funding within our solution.

Models to reduce energy costs

Public sector organisations can choose to progress schemes themselves or look for partners in the private sector to realise their objectives. Metropolitan have proven and flexible Energy Services Company (ESCo) solutions and partnership models which allow for the separating of supply and distribution. We will also ensure scheme delivery is phased to match overall development investment timelines.

An ESCo is a commercial operation providing efficient and cost-effective energy to the development. We welcome the opportunity to share ownership of the ESCo to ensure community needs are being met both now and in the future.

With the option to sell any excess power generated back to the market, the ESCo model ultimately creates an efficient, secure and reliable community-based energy solution with reduced energy costs for residents.



Dom Barton

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CASE STUDY

Kings Cross, London

Metropolitan is already delivering one of the largest regeneration projects in the UK, at Kings Cross in London. Eventually, there will be 2,000 new homes of which 330 are affordable housing alongside commercial premises, underpinning the creation of over 5,000 jobs in high-value knowledge sectors.

Our district energy network at King's Cross uses a Combined Heat and Power (CHP) plant with natural gas driving the engines, as well as plans to install a 1.4MW fuel cell to meet the increased heat demand for future phases.

The efficiency statistics speak for themselves:

- **Carbon:** 50% saving in carbon emissions based on traditional utility solutions.
- **Electric:** 80% efficient compared to 30% in the conventional UK electricity supply.
- **Heat:** An energy centre meets almost 100% of heat demand and 80% of power demand.

A fully managed ESCo is part of the solution for the local delivery of de-centralised energy, and this includes providing professional metering and billing services to the householder. The ESCo is a joint venture with Metropolitan and Argent, who maintain a stake in its long-term success and the ongoing interests of the King's Cross residents.

Innovation is necessary to create clean, efficient energy

Open Access Government highlights how the US Department of Energy is streamlining energy use to improve economic efficiency and provide clean energy

The US Department of Energy (DOE) is looking to scientific innovation to streamline energy use, improve economic efficiency, and provide sources of clean energy. Currently, around 65% of electricity in the US is sourced from fossil fuels, around 20% is from nuclear energy, and 15% is from renewable energy (biofuels, wind power, solar).

Fusion energy

A particularly ambitious potential energy source is fusion power. Essentially recreating the energy conversion process of a star, fusion energy involves the study of plasmas, hot gases that respond to electricity and magnetic fields which form such things as stars, auroras, fire, and lightning. If successful, fusion energy would provide an eternally renewable and CO₂ neutral form of power. It also would produce no radioactive waste. A machine called a tokomak is currently being used in a DOE lab to create and experiment on fusion processes.

Currently, there are still several challenges standing in the face of achieving sustainable fusion energy. The DOE is leading an initiative to create a supercomputer 50 times faster than current technology to create simulations that will move fusion technology along. Capable of a billion calculations a second, such a computer would provide accurate predictions of fusion reactions, which would accelerate the technology and help the DOE achieve its goal of making fusion energy commercially viable.

NETL

The National Energy Technology Laboratory (NETL), an offshoot of the DOE, conducts internal and collaborative research to accelerate the DOE's goal of improving fuel efficiency in the US. The NETL's laboratories in West

Virginia are using a Fischer-tropsch reactor to develop a method to remove sulphur from fossil fuels. This aims to make them burn cleaner, as well as extracting other useful chemicals from natural gas. In their Pittsburgh, PA lab they are conducting experiments with the aim of turning fuels like biomass and coal into gas, making it easier to contain their CO₂ emissions. Innovations such as these work on a basis of improving fuel sources that are currently in use. Research into alternative renewable fuel also runs alongside this.

Biofuels

Biofuels have become a subject of debate in recent years. Long touted as a clean, renewable alternative to fossil fuels, new research suggests they may do just as much harm. The UN released a report in 2014 warning that growing plants for biofuels drives up food prices and creates just as much harm for the environment. Biofuel production relies on growing crops such as rapeseed, which means either repurposing agricultural land or clearing forests to free up more space. Some environmentalists also believe that liquid biofuels release just as much CO₂ as traditional fossil fuels, if not more.

The DOE is working on making biofuel production cleaner and more cost-effective. The Abengoa Bioenergy project in Hugoton, Kansas, is a cellulose ethanol plant financed by the DOE that converts non-edible biomass into fuel. Rather than taking up agricultural land, the plant uses corn stalks, leaves, and other non-edible plant products leftover from the farming process. Another DOE-backed project uses algae for biofuels. It does not compete for farm land in its production, and creates more usable fuel than other products such as soybeans. It can be grown in saltwater and wastewater, meaning less water wastage. It can also produce other



useful products such as fertiliser. However, the technology is still in its infancy, and requires further research to become more cost-effective and readily available.

Renewables

The DOE's [SunShot initiative](#) aims to cut the cost of solar power in half by 2030, making it an affordable go-to source of power. By increasing efficiency, improving energy storage, and speeding up the process, they intend to reduce costs from 7¢ per kilowatt hour to 3¢ by this point. Other DOE investments cover wind, water, and geothermal power. In 2008 the DOE published a report entitled '[20% Wind Energy by 2030](#)', examining the possibility of producing a fifth of the US's energy from wind. It concluded that achieving this goal would require an increase in turbine production from 2000 per year in 2006, to 7000 per year in 2017. The number of turbine installations has increased dramatically since the beginning of the year, with the [American Wind Energy Association](#) releasing a report in May stating that a new turbine was installed every 2.5 hours.

The DOE's mission involves a two-pronged approach of improving existing sources of energy in terms of cleanliness and efficiency, and investing in green and renewable sources at the same time. The US has a deeply ingrained infrastructure revolving around fuels like coal, oil, and nuclear energy, meaning a switch to alternative power would require an adaptation on many levels, and is not just a question of placing all investment in green energy. More research will be needed in fields like fusion energy and algae biofuels for them to compete with existing energy infrastructure. ■

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Exploring lower cost pathways to economical fusion power

The cost of fusion energy development is a significant reason why progress remains challenging. Scott C. Hsu of the Los Alamos National Laboratory explains

When I entered graduate school in 1993 to study plasma physics and fusion, the United States already had designs to build a “burning-plasma” fusion experiment in which the power produced by fusion would, for a short duration, exceed the heating power required to sustain those reactions¹, i.e., “scientific breakeven.” Had we proceeded then to build such an experiment, we might have achieved that milestone a decade ago. The experiment was never built, and, instead, the multi-national collaboration ITER² is now aiming to fulfill this mission. ITER’s final cost is projected to exceed US\$20bn³, and it will take nearly another 20 years from today before ITER might demonstrate scientific breakeven. Fusion science and technology have advanced significantly since 1993, but we have frustratingly regressed with respect to the timeline for realising commercial fusion power. Why?

The two biggest, interrelated reasons that progress toward fusion power has slowed to a crawl, in this author’s opinion, are (a) the significant cost (>US\$10bn) of constructing a burning-plasma experiment based on the most scientifically mature approach (the tokamak), and (b) the absence of consensus that fusion energy is urgently needed. Such consensus, if it can be established, would increase the available public funding and therefore the rate of progress. At the

present rate of progress, commercial fusion power will not be realised in time to impact midcentury carbon-emission targets. All projected energy solutions (e.g., renewables with storage, fossil fuels with carbon sequestration, and advanced nuclear fission) have daunting challenges of their own to overcome in order to achieve the scales needed to meet midcentury energy demands. More timely development of fusion energy would greatly increase our chances of achieving an adequate carbon-free energy mix. But how do we increase the rate of progress toward realising economical fusion power, given the socio-political realities?

Lowering costs

There are many proposed pathways to fusion energy that are potentially “faster and cheaper” compared to the development path based on ITER. In the remainder of this and a series of subsequent articles, we draw from the story of our own fusion research to explore and advance a lower-cost development pathway toward economical fusion power, benefitting from and complementing mainstream fusion research that is centred around ITER. We assert that lowering fusion-development costs is essential to



Figure 1. Photo of the outer (top) and inner (bottom) electrodes of a (disassembled) coaxial plasma gun used to launch supersonic plasma jets in our fusion research. Photo courtesy of HyperV Technologies Corp.

accelerate fusion development, such that fusion might penetrate power-generation markets by 2050. Our journey over the past decade benefitted from desirable aspects of a public-private partnership to develop fusion, but our path occurred against great odds, whereas such paths should be enabled systematically throughout the worldwide fusion-development enterprise to improve its chances of timely success.

Our research is focused on developing a reactor-friendly embodiment of magneto-inertial fusion (MIF), aka magnetised target fusion (MTF). MIF is a class of approaches involving the compression of a magnetised target plasma (consisting of the fusion fuel)

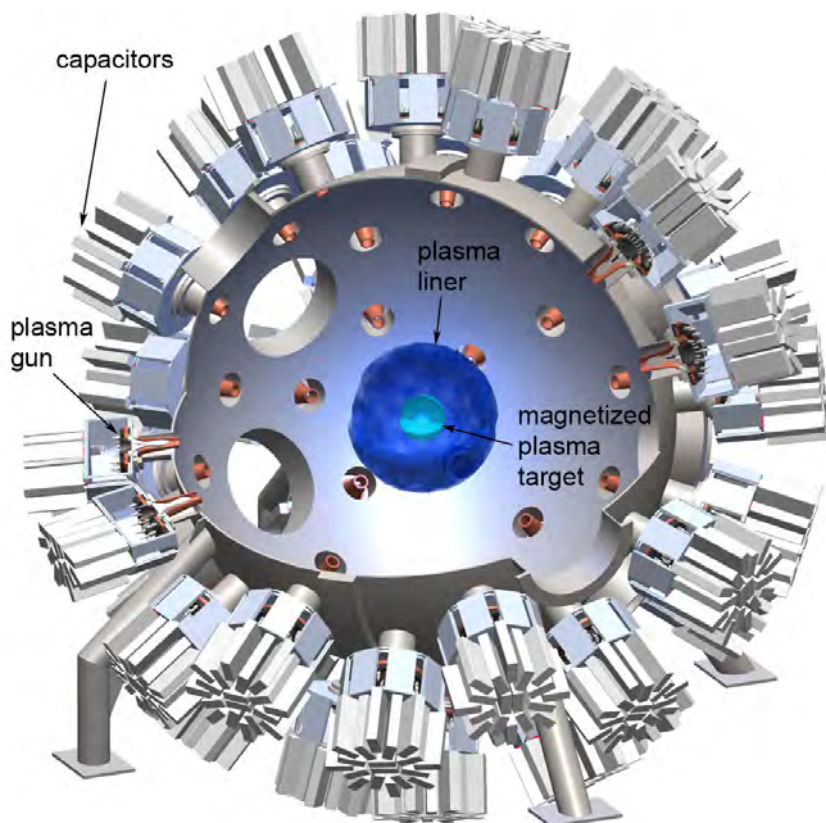


Figure 2. The objective of our research: to form a spherically imploding plasma liner (by merging 60 plasma jets) that will be used to compress a magnetized target plasma to fusion conditions. The cutaway spherical vacuum chamber is 2.7 m in diameter. Figure courtesy of HyperV Technologies Corp.

to fusion conditions by an imploding pusher, called a “liner.” For example, the Canadian company General Fusion is developing MTF via acoustically driven liquid lead-lithium as their liner. MIF is inherently lower cost than other fusion approaches because MIF aims to achieve a compressed fuel density that optimises the combination of plasma heating power and stored energy required to achieve fusion conditions⁴, thereby minimising the capital cost of the required facility. On the other hand, for historical and myriad other reasons, the mainstream, most scientifically mature approaches of magnetic-confinement fusion (MCF, such as ITER) and inertial-confinement fusion (ICF) operate at the lowest and highest extremes of fuel density, respectively. As a result, due to basic laws of plasma physics, MCF requires very large size and stored energy, and ICF requires very high power to compress the fuel, which both drive costs

into the multi-billion (\$US) range for breakeven-scale facilities. In contrast, a breakeven-class MIF facility is expected to cost as little as a few hundred million dollars (\$US).

Our project, the Plasma Liner Experiment-ALPHA (PLX- α)⁵, is one of nine projects supported by the ALPHA Program⁶ of the Advanced Research Projects Agency-Energy (ARPA-E) of the U.S. Department of Energy (DOE). We use innovative, low-cost coaxial plasma guns (Fig. 1), developed and built by partner HyperV Technologies Corp.⁷, to launch a spherically converging array of supersonic plasma jets toward the middle of a large, spherical vacuum chamber (Fig. 2). A key near-term goal of PLX- α is to merge up to 60 plasma jets to form a spherically imploding plasma liner, as a low-cost, high-shot-rate driver for compressing magnetised target plasmas to fusion conditions. This approach is

known as plasma-jet-driven MIF (or PJMIF)⁸. A new startup company HyperJet Fusion Corporation (which recently received seed funding from Strong Atomics, LLC, a new fusion venture fund) aims to develop PJMIF under continued public and private sponsorship.

In an ensuing article, we will describe the key elements that led to joint public/private sponsorship of this research, in hopes of motivating public policymakers and private-sector investors to make such sponsorships more commonplace throughout the fusion-development enterprise.

¹ For example, Burning Plasma Experiment Special, Fusion Technology 21, 1045-1308 (1992); http://fire.pppl.gov/fusion_library.htm (accessed July 9, 2017)

² www.iter.org

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⁴ I. R. Lindemuth and R. E. Siemon, Amer. J. Phys. 77, 407 (2009)

⁵ <https://arpa-e.energy.gov/?q=slick-sheet-project/plasma-liners-fusion> (accessed July 9, 2017)

⁶ <https://arpa-e.energy.gov/?q=arpa-e-programs/alpha> (accessed July 9, 2017)

⁷ www.hyperv.com

⁸ Y. C. F. Thio et al., “Magnetized Target Fusion in a Spheroidal Geometry with Standoff Drivers,” in Current Trends in International Fusion Research – Proc. 2nd International Symp. (NRC Canada, Ottawa, 1999), p. 113; S. C. Hsu et al., IEEE Trans. Plasma Sci. 40, 1287 (2012).



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Sustainability through technology: The power of N

Popularism and bumper sticker science should not stop us tackling sustainability through technology, argues Ingenuity Lab Director Carlo Montemagno

Ingenuity Lab is a unique organisation, designed and created to solve many of the grand challenges facing a modern world. Ingenuity Lab is a research organisation that focuses on the development and deployment of effective solutions to seemingly intractable challenges.

It works using a formal connect-and-develop process which involves building teams from members of government, industry, and academia. Central to this process is problem identification and the visualisation of the ideal solution. Often the identified problem is not the problem, but a symptom. Symptoms tend to be obvious, but quite often provide little insight into the most effective solution. With the recent intense discussion surrounding the newly imposed carbon tax in Canada, I think that it is time to extract ourselves from the emotion of the issue surrounding climate change, examine the impact of humanity on our environment, and identify the salient challenges needed to ensure global sustainability.

The unassailable fact is that the Earth's climate is changing. But the Earth's climate has been changing since its creation. The Earth's atmosphere, governed by complex, non-linear physical processes is easily perturbed. Changes in solar radiation, volcanic activity, deforestation, construction of cities and roads, large-scale irrigation and, yes, the release of CO₂ into the atmosphere, can all impact the Earth's climate. The

challenge is teasing out the climate variations caused by natural phenomena which we cannot manage from the impacts caused by anthropomorphic activities.

Firstly, we need to understand the impact of human activity versus natural processes on the climate. Then, isolate the impact of different human activities to further identify the effect that each activity has on the environment, especially when many of the activities occur simultaneously. For example, the change in albedo – the amount of solar energy absorbed/reflected – caused by the expansion of population centres is usually accompanied by an increase in CO₂ emissions. Which of the two impacts is more important? Are their collective impacts additive or multiplicative? There are many questions yet unanswered. If we cannot clearly define and quantify the “cause”, how can we craft an effective solution?

Disagreeing with Malthus

The bottom line is that human activity has impacted the Earth's environment since our society transitioned from hunter-gatherers. In 1798, Thomas Malthus postulated that humans were quickly going to exceed the carrying capacity of the Earth and that the positive population checks of starvation, disease, and war were necessary. He also dismissed the idea that technological advances in agriculture would provide the solution to the Earth's resource limits. I hear echoes of Malthus in much

of the dialogue surrounding climate change. While no one is proposing eugenic behaviour for addressing man's impact on the environment, there is a distinct tenor in the dialogue that humankind must accept a lower quality of life and reduced opportunity for future generations. There is also the implied truth that the human race cannot address the challenges associated with man's impact on the environment through advances in technology. I soundly reject both premises.

When I was growing up one of my favorite TV shows was *Get Smart*. I always waited for the moment in the show when Maxwell Smart would use his shoe phone. It was hilarious because most people perceived it as ridiculous. The concept of portable communication was outlandish. Nine years ago when Apple introduced the iPhone, it revolutionised global communication. In just 30 years, the technologies of science fiction fantasy transformed the way we engage in commerce, deliver healthcare, and interact as people. It effectively shrunk the world, making the Earth a single village where virtually every voice can be heard.

Popularism politics and bumper sticker science

Unfortunately, not every voice should be heard at the same volume. The cult of personality has enabled individuals without the requisite gravitas to seed popularism politics and bumper sticker

science. By feeding personal prejudices, rational discussion has been kicked to the curb and has been replaced by intensely polarised emotion. Culturally, Canadians have an intense connection to the environment. I believe that it is fair to say that the wonder of nature is strongly woven into the fabric of Canadian society. This is why Canadians feel compelled to lead the charge against global warming and why Canada has acted to impose a significant tax on the use of carbon. The question that many are asking, both inside and outside of Canada is, is this an effective path for addressing the global warming challenge?

Canada is currently responsible for releasing approximately 1.6% of all of the global CO₂ emissions. The European Union, China, India, Russia, Japan, and the United States are collectively responsible for releasing over 70% of the global CO₂ emissions. It is doubtful that even a 50% reduction of Canadian CO₂ emissions would have any material impact on global warming. To have any real effect on global warming, CO₂ emission reductions must occur in concert with all six of the major emitters. Even with over 10 years of significant effort, it has not been possible to achieve a meaningful coordinated global response to CO₂ emissions. Acting in isolation will only stress the Canadian economy and place an unnecessary burden on Canadians without achieving the desired goal of reducing man's impact on global warming. There is a better path forward.

We must recognise that humankind has impacted and will continue to impact the Earth. It is our responsibility to access the Earth's bounty in a sustainable way. Our ultimate goal should be to consume each of Earth's resources within cyclic processes to maximise the utility of all of the

resources that we harvest. The economic reusing of resources would ensure their continued availability for future generations. Achieving this vision can only be accomplished through technological innovation.

Examining the challenge of CO₂ emissions you find opportunity. Let's flip our perspective; instead of labeling CO₂ as a waste product we should recognise it as a valuable raw material. Carbon is the foundation, the building block of all living organisms. At the very core of the global ecosystem, nature uses the Sun's energy to assemble all living organisms from CO₂. Visioning the solution to CO₂ atmospheric emissions, suppose we can generically insert our industrial processes within the web of nature's carbon cycle. We take the CO₂ which would normally be emitted into the atmosphere, such as from an electrical power generating plant, and instead, using light, repurpose the CO₂ into valuable products. Effectively we insert the carbon that would have been wasted and transform it into the fabric of our society. Ingenuity Lab is currently commercialising this new technology.

Using the power of N – inspiration from nature to guide the manipulation of matter using nanotechnology to build networks – Ingenuity Lab succeeded in replicating the natural process of carbon assembly and translated it into an industrial process. The process required learning how to convert light into the various chemical fuels of life and the ability to cheaply fabricate nano-compartmented systems to assemble an artificial metabolism that fixes and transforms CO₂ into valuable products. While not the total solution to the global climate warming challenge, it does pull back the curtain to display the possible. It shows that the potential for technological achievement is boundless.

Advancing sustainability through technology

We must consider the past technological achievements of modern man as governments assess the optimum strategy for addressing global sustainability challenges. These achievements speak loudly about the human potential for creative innovation. Canada needs to occupy the position of a leading global steward of the environment, but must achieve it as a champion of sustainability through technology. It is the path forward.

Set the stage for a bright future for coming generations by embracing the potential of the possible, as well as understanding that technological achievement can drive market forces that lead to a more sustainable world. World leaders need to focus on providing an environment that supports the crafting of solutions to the global warming challenge and not at regulatory instruments as the primary weapon of choice. This strategy will accelerate economic and societal prosperity and has a much higher likelihood of long-term success. Canada, believe in the inventiveness and creativity of your citizenry. Provide the needed environment, and the people will deliver. The future belongs to the bold.

 ingenuity lab

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Creating a modern transportation network for Canada

Marc Garneau, Minister for Transport in Canada outlines the importance of the transportation network for Canadian communities as well as the economy

As an exporting country, Canada strongly depends on the effectiveness and fluidity of its transportation network.

In order to create jobs, help the middle class and stimulate our economy and competitiveness, we must be able to count on a modern, integrated and effective transportation network, and we must invest carefully in it.

It must also be recognised that the network is under national and global pressure, and our adaptation will be essential for the future of the country.

Further to the recommendations of the Canada Transportation Act Review Report, I and Transport Canada representatives conducted a cross-Canada consultation to hear the views of Canadians, industry stakeholders, the provinces and territories, and Indigenous groups.

The information gathered allowed me to identify in depth the issues on which we must act in the short, medium and long-term, and the solutions to implement to resolve these issues. In November 2016, I presented my strategic plan for the future of transportation in Canada: Transportation 2030.

Transportation 2030 is a whole-system approach that ensures that all parts of Canada's transportation network work well together and support the actualisation of the government's general priorities.

Since this strategy was presented, we have begun to review the regulations and acts to amend in order to transform Canada's transportation network so that it better supports economic growth, job creation and the Canadian middle class.

Furthermore, in March, the Minister of Finance presented the 2017 budget, which includes initiatives and funding to modernise our transportation network.

Thus, on May 16, 2017, I tabled Bill C49, the Transportation Modernization Act. It represents a first legislative step to provide Canadians with a safe, reliable, clean and effective transportation network that will facilitate trade and travel while promoting environmental sustainability.

The tabling of the Transportation Modernization Act will allow Canada to take advantage of opportunities that arise on the international stage, contribute to a highly productive economy and respond to Canadians' needs and service expectations.

To do so, Canada will have to collaborate closely with the United States so that our activities take place seamlessly on both sides of our shared border.

As Canadians, we have always been aware of the challenges and privileges associated with such a vast country. To travel, we depend on roads, waterways, railways and airways. They connect us to our friends and families, to our work and to our leisure activities.

This important milestone will make our transportation network into one that can better serve Canadians. ■



Marc Garneau
Minister of Transport

Transport Canada
www.tc.gc.ca/eng/menu.htm
[www.twitter.com/Transport_gc](https://twitter.com/Transport_gc)



Is aviation climate policy heading in the right direction?

Cait Hewitt, Deputy Director of the Aviation Environment Federation looks at aviation emissions and whether we're on course to tackle them

If the aviation sector was a country it would be seventh in a world ranking of CO₂ emitters. Unchecked, its climate impact is set to triple by 2050. Technology improvements can't keep pace with passenger growth, and while most sectors are on course to decarbonise over the coming years and decades, aircraft will remain dependent on fossil fuels for as far into the future as anyone can see.

When the Kyoto Protocol was agreed in 1997, unresolved questions about how best to allocate international aviation emissions among states led to them being left out of national targets, and the UN's specialist aviation agency ICAO (International Civil Aviation Organization) was instead given the task of tackling the sector's growing emissions. A decade of prevarication followed.

But in 2008 progress on the issue suddenly moved up the agenda. With the EU's plans to bypass ICAO and incorporate all flights to and from EU airports in its Emissions Trading System, generating acrimonious retaliatory talk of widespread non-compliance and trade wars, plans for a global solution that all states could get behind finally started to get some attention.

Will carbon offsetting be effective?

In 2016 ICAO celebrated its agreement to implement a Carbon Offsetting and Reduction Scheme for International Aviation (CORSIA) beginning in 2020 and requiring any growth in aviation emissions from that year on to be 'offset' through the purchase of emissions units generated by CO₂ cuts in other sectors. Whether or not the scheme will be effective remains to be seen, however.

At present, CORSIA is far less ambitious than the 2015 Paris Agreement – the landmark global climate deal which aims for no more than 1.5 degrees of warming and total decarbonisation of our economies. Environmental organisations successfully lobbied for the inclusion of a review mechanism in CORSIA, to allow for tougher carbon targets to be set over time, but it is not certain that these periodic opportunities will lead to improvements. Negotiations about what offset credits and activities will be eligible – whether to allow contentious forestry credits, for example – are ongoing. Also Trump's determination to withdraw from the Paris Agreement, while not directly impacting CORSIA, casts a shadow of doubt over whether the US will continue to support the scheme.

“While CORSIA was at one level ground-breaking – it signalled a global acceptance that aviation emissions are a problem and that policy action is needed to tackle it – critical questions about what role aviation should play in a zero carbon future remain, for the most part, even to be asked let alone answered.”

More fundamentally, does carbon offsetting offer an effective response to the global climate challenge, as its advocates argue, or is it merely a way of putting off difficult decisions? The UK's statutory advisory body, the Committee on Climate Change, has advised that market based measures should be seen as only a short to medium term solution for tackling aviation emissions, arguing that the sector should be preparing for deep cuts in its own emissions. Europe voted this year not to accept international offset credits for compliance with its emissions reduction targets under the Paris Agreement.

The need for domestic action

What action, then, should EU states themselves be taking to ensure that their aviation activity doesn't undermine climate change commitments? It's a question that is perhaps only just starting to bite. In February this year an Austrian court overruled a planned airport expansion on the basis that it would be incom-

patible with the country's climate change law. The UK government is currently pursuing an expansion of Heathrow Airport, but has presented no answers on how the scheme can be compatible with the country's Climate Change Act, despite a court ruling in 2010, the last time a third runway was on the table, that the government's suggestion that airport expansion was somehow divorced from climate law was “untenable in law and common sense” and that it must review its plans.

While CORSIA was at one level ground-breaking – it signalled a global acceptance that aviation emissions are a problem and that policy action is needed to tackle it – critical questions about what role aviation should play in a zero carbon future remain, for the most part, even to be asked let alone answered. Does a globalised outlook make it impossible to question the continued growth in air travel? Or will the digital age allow us to find ways to stay connected without the need to travel? Are direct air connections critical for global trade, or can our future connectivity needs be met without a continued proliferation of expansion by states seeking to out-compete each other with boasts about having the biggest and best airports?

Decisions we take now can have far-reaching consequences. Airport infrastructure is seen as long-term investment, for example, and the economic case for a new Heathrow runway is based on an assessment over 60 years. But while analysis suggests that achieving the Paris Agreement will require our economies to be zero emissions by 2070, we have yet to have a public or political conversation about what that could mean for the role of flying in our economies and our lives. ■

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EUFAR – Coordinating airborne environmental sciences

Instrumented aircraft are an important scientific tool, allowing researchers to support a range of applications in environmental sciences, says EUFAR

EUFAR is currently supported by the 7th Framework Programme (FP7) of the European Commission. It combines 24 European institutions and organisations involved in airborne research, operating 19 instrumented aircraft and 5 remote-sensing instruments, providing a broad measurement capability.

There is a long history of airborne observational research contributing towards incremental developments in the scientific understanding of Earth-system processes. These developments have proceeded in parallel with similar developments in the capabilities to observe these processes on a global scale from space and to model them in operational Numerical Weather Prediction (NWP), Climate and Earth-System Models. The fields of science that are impacted by an airborne research observing capability are very broad and span the atmosphere, ocean, land surface and biological systems. Maintaining access to a broad range of airborne observing facilities is critically important to our future ability to study processes in the environment and to develop and use the models that will, for example, be used to study mitigation strategies in a changing climate.

EUFAR aims to:

- improve the quality of the services provided by aircraft and instrument operators by strengthening expertise through knowledge exchange;
- develop and maintain a central database of airborne data and the standards for this database to be interoperable with other environmental science and Earth observation databases;
- support joint instrumental research activities centred on the development of improved data processing and calibration techniques;
- promote the use of research aircraft and instruments by providing education and training courses on airborne research topics;
- support innovation in airborne research, working with industry to transform airborne research instruments, methodologies and software into new products and services.

EUFAR activities

i) Transnational access

Transnational Access provides fully-funded flight time to Principal Investigators and User Groups without access to the required airborne observing facilities via national funding within their country of employment. To maximise the scientific impact, applications are encouraged that can be



Figure 1. The 4 aircraft operated by DLR, the German Aerospace Research Centre at Oberpfaffenhofen. From front to back: HALO Gulfstream 550, Dornier 228, Cessna Caravan and Falcon-20. The latter three aircraft have all participated in Transnational Access projects.

clustered with larger nationally- or internationally-supported flight campaigns. 32 projects have been approved for funding, evenly split between the use of in-situ atmospheric measurements and the use of imaging systems for Earth Observation. As a result of clustering, TA flight activities have been possible in West Africa as part of the multi-national DACCWA campaign, in the Cape Verde Islands and also in Namibia.

ii) Networking activities

EUFAR supports a number of Networking Activities that share its objectives of improving efficiency and spreading best practice in airborne research observations.

Education and Training are designed to attract and train both early-stage researchers and university lecturers in airborne atmospheric research observations and remote sensing of the



Figure 2. Students at a lecture during the SWAMP training course on the use of airborne imaging for studies of photosynthesis in a wetland region that was held in Poland in 2015.

Earth surface and to develop/consolidate EUFAR training course educational material. By the end of its present contract, EUFAR will have supported a further four summer schools on airborne research topics hosting approximately 80 students.

Standards and protocols aim to harmonise and document processes in the management of data within EUFAR, including both in-situ and Earth observation data. A focus has been on the update and extension of previously-developed common protocols and standards and assuring their compatibility with international standards. EUFAR is engaging with the ENVRplus community of research infrastructures via the implementation of its data Reference Model. This promotes interoperability and will put access to airborne data on the same footing as that from other infrastructures.

A database ensures that valuable data, metadata and documentation are widely available to facilitate data discovery, exchange, collaboration and re-use. The archive is maintained by the Centre for Environmental Data Analysis (CEDA) in the UK and is accessible via the EUFAR website.

iii) Joint Research Activities (JRA)

Two JRAs are currently being undertaken, both aiming to improve the quality of airborne data and developing new data products and services supplied to scientific users.

HYLIGHT is working to develop, test and validate improved software tools for the combined use of Hyperspectral Image (HSI) and Airborne Laser Scanning (ALS) data and improved ALS data processing using HSI and to make them freely available. These tools will, for example, contribute to better management of forest ecosystems for both recreational and economic purposes, where the combined measurements yield more detailed information on the nature of the forest canopy. HYLIGHT tools, installation guides and user manuals can be downloaded from the EUFAR website

TGOE is working to develop robust calibration systems for gas-phase chemical measurements made on board research aircraft.

These contribute substantially to the development of numerical models used for both air-quality forecasting and longer-term climate studies, providing information on the vertical distribution of species that are difficult to obtain by other means. They are also an important source of local and regional validation for satellite observations that are used for global-scale measurements. Studies of trace gas emissions and evolution often involve one or more aircraft together with fixed, ground-based measurements. Working with the IAGOS and ACTRIS communities to develop the best calibration techniques, TGOE seeks to reduce measurement uncertainties and so enable them to be used to provide more detailed analyses of the processes involved in the

transport and chemical evolution of atmospheric trace gases.

The future of EUFAR

EUFAR is seeking to establish itself as an AISBL (international non-profit association). Such an association, supported by members' cash and in-kind contributions will ensure that key EUFAR activities can continue beyond its present funding by the European Commission. These activities will include the maintenance of its website and broadening access both to the aircraft themselves and to data obtained from flight campaigns. EUFAR is also currently seeking Expressions of Interest in future Joint Research Activities that may be undertaken within the framework of the AISBL.

Significant progress has been made by a core group of members to form such an association. Agreements will enable as wide a range of organisations as possible to participate in its work, as members or partners, hence broadening its impact in countries not presently operating their own research aircraft. The AISBL will be formally established at the start of 2018.



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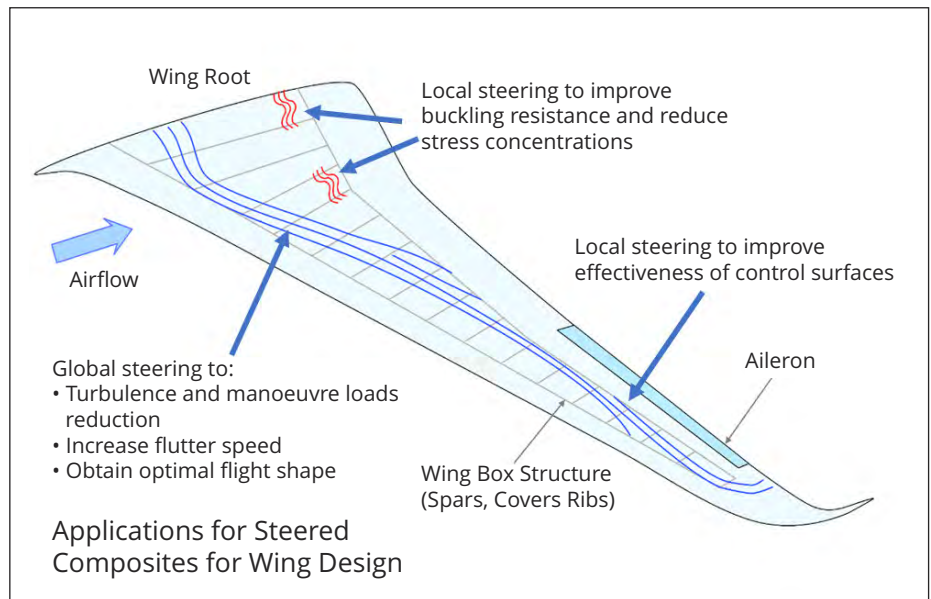
Tailoring composite materials to achieve optimised wing designs

University of Bristol's Jonathan Cooper and Olivia Stodieck explore different ways that composite materials can be used to build aircraft wings

Carbon fibre composites were developed in the 1960s and consist of thin carbon fibres which are combined within a plastic resin to form a composite material, often referred to as CFRP (Carbon Fibre Reinforced Plastic). Typically, the fibres are aligned together in the same direction to produce a 'ply', and then these thin layers (often referred to as 'lamina') are placed upon each other onto a mould to form the required shape. Finally, they are cured in an autoclave (a pressurised oven) in order to achieve the final manufactured component.

"The benefits from a design viewpoint for the use of tailored composites are clear, so it is likely that industry will overcome the constraints that have held back the implementation of uni-directional composite tailored wings in the near future, leading to improved environmentally friendly aircraft designs."

Carbon fibres have a very good strength to weight ratio (i.e. they are strong and light) compared to metals and also enable complicated shapes to be manufactured as a single component. Consequently, they have been used increasingly in aircraft designs over the past 40 years as they enable aircraft to be lighter and hence more fuel efficient and environmentally friendly¹. For example, the two most recent commercial jet aircraft designs, the Boeing 787 and the Airbus 350, have over 50% of their

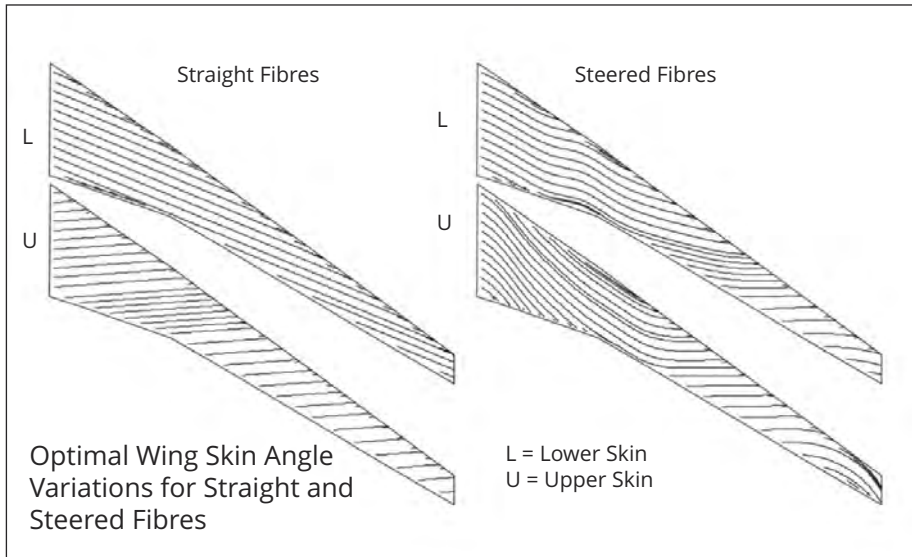


structure made from composites.

However, these designs are based upon laying up the plies in such a way, typically using symmetric combinations of $0^\circ / 90^\circ / +45^\circ / -45^\circ$ orientated layers, so that the material behaves in a uniform manner in every direction, often referred to as 'black metal'. Consequently, the full possibilities of using carbon fibre are not being exploited. As the fibres are very strong in one direction, it is possible to use them in different orientations, an approach known as 'aeroelastic tailoring', so that the coupling between the wing bending and twist deflections with the aerodynamic forces in-flight (a phenomenon that provides the underlying physics of the science of aeroelasticity) can be used to allow the wings deform to achieve the most fuel-efficient shapes,

reduce the loads from turbulence and manoeuvres², and eliminate any potentially dangerous vibrations such as flutter (a violent oscillation that can result in catastrophic structural failure).

Such a tailoring capability was demonstrated in the early 1980s by NASA on the X-29 experimental aircraft which had composite wings that were swept forwards rather than backwards in the conventional manner³. Through the use of optimised orientations of the composite layers in the wing surfaces, it was possible to control the wing deflections to enable good aircraft performance. However, in the past 30+ years, this technology has still not found its way onto modern commercial aircraft, primarily due to manufacturing constraints and certification requirements.



Steered fibres

A recent development that builds upon the tailoring approach described above is to 'steer' the fibres in each layer so that it is possible to vary the angle of the plies throughout each laminate. Studies related to wing design⁴ have shown that it is possible to use these variations in the fibre orientations to improve local behaviour such as buckling whilst also ensuring optimal turbulence loads reduction. Testing⁵ is currently being performed at the University of Bristol to demonstrate the potential of steered composite layers in order to optimise the deflection and vibration of wings whilst also reducing weight. Results have shown that the use of steered fibres does enable improved performance. The major problem with the steered design lies in the current manufacturing capability; it requires some very specialised machinery to be able to vary the orientation of the layers without obtaining either gaps or overlaps in the material. Therefore, the process

required to make a structure using these novel designs is very slow and is also not capable of producing the large components needed in aircraft structures.

"Carbon fibres have a very good strength to weight ratio (i.e. they are strong and light) compared to metals and also enable complicated shapes to be manufactured as a single component."

The benefits from a design viewpoint for the use of tailored composites are clear, so it is likely that industry will overcome the constraints that have held back the implementation of uni-directional composite tailored wings in the near future, leading to improved environmentally friendly aircraft designs. However, due to the high rates of manufacture that are required, it is likely to be a very long time before it is possible to produce aircraft wings with steered composite designs.

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The evolution of the European rail industry

UNIFE – The European Rail Industry discusses how rail has evolved to become more attractive to customers and investors through technology and innovation

In the early 20th century, Nietzsche famously listed the railway as one of 4 ground-breaking inventions ‘whose thousand-year conclusion no one has yet dared to draw.’ Since then, European rail has evolved almost beyond recognition. Modern rail vehicles are equipped with driverless and automatic systems (e.g. metros), efficient signalling systems (e.g. ERTMS – European Rail Traffic Management System), energy-savings systems and more. Yet, as other industries and the demands of the public evolve, rail must continue to modernise in order to play a key role in the increasingly multimodal environment and become more attractive to both customers and investors.

“With the right resources – both financially and politically – the future of the European rail industry can and will be as bright as its past.”

The industry has made tremendous strides towards harmonising the European rail systems and creating an integrated EU railway area – but we are still a few steps away from creating a true single European railway area as targeted by the European Commission. Hailed as the single most significant achievement in railway legislation to date, the technical pillar of the fourth railway package, adopted in 2016, aims to remove the remaining barriers to achieving this.

It is clear that the current fragmented national approaches cannot answer the challenges faced by today’s sector. To become competitive with other modes of transport, European railways must remove the regulatory burden it currently suffers by working closer together, thereby having simpler, clearer, and more efficient processes across Europe. A harmonised European process with the European Union Agency for Railways as a rail system authority should result in a convergence of process and requirements, less duplication of checks and

testing, and importantly, more consistency in decisions given to the applicants. A quicker process will also see a reduced lead time in placing a vehicle in service, and thus quicker returns on investments.

It is estimated that the technical pillar of the fourth railway package will bring about a 20% reduction in cost and duration for rolling stock authorisations by 2025 – that’s no small amount.

What does the future hold for rail?

However, the future of the European rail industry relies on much more than this key proposal. Our industry is facing fierce competition from outside of Europe, mainly from Asia, as well as increasingly difficult to penetrate external markets. Just like in any other industry, the key is to stay ahead of the curve – and to find the funding to do so. Innovation in rail technology is a major lever to create a sustainable transport system that meets the rising needs of end-users (passengers and logistics), cities, and the environment.

European research public-private partnerships like Shift2Rail are poised to deliver such innovation – and it is crucial that the European railway industry builds on the current momentum. Shift2Rail aims to double the capacity of the European rail system, increase its reliability and service quality by 50%, all while halving lifecycle costs. These are bold objectives, but they are what the industry needs to meet tomorrow’s challenges. That’s why it is equally important for the European Union to make sure that the second iteration of this programme – Shift2Rail 2.0 – is a part of the next European Research Framework Programme (FP9) that is currently under preparation by the European Commission. This type of long-term commitment is of paramount importance to enable European rail supply industry to tackle the global trends and upcoming challenges that will impact the



future of transport, including rapid urbanisation, congestion, environmental issues, and societal changes.

“It is estimated that the technical pillar of the fourth railway package will bring about a 20% reduction in cost and duration for rolling stock authorisations by 2025 – that’s no small amount.”

Finally, ensuring the long-term competitiveness of European industry as a whole, and rail, in particular, is a role that the European Institutions must take on with alacrity to safeguard its future. Member States have also positioned themselves firmly on the supporting side. Most recently, at a July 2017 meeting between France’s President Macron and Germany’s Chancellor Merkel, both reiterated their support for an ambitious EU industrial policy, announcing that they will be working together to make concrete proposals to the Commission by the end of the year for an action plan to be adopted in early 2018.

Support from the European Parliament was solidified with their 2016 resolution on the competitiveness of the

European rail industry. Over 130 associations representing a vast spectrum of manufacturing industries have recently come together in Brussels under the banner #Industry4Europe to call on the European Commission to develop an ambitious EU industrial policy. It is now up to the Commission to move forward with an action plan that is forward thinking, measurable, and bold.

With the right resources – both financially and politically – the future of the European rail industry can and will be as bright as its past. ■

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Asset management must be a consideration for the rail sector

During holiday season asset management is very important to the rail industry. Here, Marcel Van Velthoven, CEO of ZNAPZ explains why

When I am writing this, the sun is shining and the temperature in the office is actual too warm to do any work. Clouds are drifting and many people passing by are definitely dressed to enjoy the summer.

Without their knowledge, asset management played a key role

Many people take the train to go on holiday, to take them to their final destination or to the airport. Going on holiday is for many people a stressful event and having a reliable form of transport is very important.

Without our knowledge the railway industry has fully prepared for the holiday season. Since the rail industry has many stakeholders, not only the availability of the trains was planned, but also the work schedule for the activities to be done during this period has been changed to fit with busy time.

Expectations vs reality

The first question we ask with regards to this is, what do we expect from our assets? The railway company should align the assets with their strategic business plan. Which has an immediate effect on the schedule of the

trains. Also all activities, the transport of the passengers and the maintenance of the tracks and all other activities should be done in a healthy and safe environment. Defining those deliverables, e.g. 90% of the passengers should have a seat on journeys of more than 20 minutes – must be done thoroughly and well measured if the objectives are met.

During the holiday season we have different passengers who have different journeys. Also the availability of the rail staff is different than outside of that period, since the train drivers



and other personnel also take holiday breaks. Not only the train personnel, but also the maintenance personnel of the trains and the tracks take holiday during this period. How can we manage this?

Maintenance on the tracks is required and is an on-going process 24 hours a day, 7 days a week, 365 days a year. A maintenance is not taking a holiday. On the contrary, if additional trains are scheduled to be driven on the track this may have an additional load effect on the maintenance. However there is help available in the form of big data.

In today's environment we are more and more able to predict the required maintenance of our assets. Not based on the preventive maintenance schedule logged in the calendar, but based on the actual status of the assets, condition based, and this is based on realistic models that indicate when

maintenance really needs to happen. Is this of importance during normal operations? Even more so during the holiday season where we have a changed demand and capacity to deal with, as well as even more of a demand on reliable services.

So without the knowledge of the public, asset management has supported the rail industry in enabling its staff to take well-deserved holidays. At the same time the schedule was maintained. Prior to the holiday season additional work was done to have the railways and the trains prepared for this period.

This is all achieved using big data. Combining different data sources to have an accurate prediction of the use of our assets and the demand of our assets for service or maintenance. One of the key questions is how do we make this predictable?

Big data

There are two trends that enable big data to play a far bigger role in our life than ever before. First we have our social networks. People like to share many activities they plan and perform. This often unstructured data is now being analysed, not only by the likes of Google but also by IBM's Watson. Based on these analysis trends, in time are becoming predictable with a high accuracy. The second development is the Internet of Things (IoT). Many assets, pieces of equipment and other devices are equipped with a variety of sensors. The information of one sensor doesn't tell us a lot, but the information of various sensors combined is giving quite an accurate picture of what is going to

happen. Adding to this the cognitive computing technologies that Watson offers gives a realistic prediction. Now we have our steer in our hands and we can choose which direction to go.

"Many people take the train to go on holiday, to take them to their final destination or to the airport. Going on holiday is for many people a stressful event and having a reliable form of transport is very important."

A more challenging question is how will this affect our behavior? The rail industry can fine tune their capacity on the need of the passengers and they will be able to adjust their maintenance schedules to align with the required capacity. Information about the capacity and any changes in schedules will be able to be shared with the passengers quickly. Slowly but surely we can expect trains to drive on demand with Swiss accuracy. Taking away part of the stress a holiday can bring.



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PAN-LNG Project: Developing Trans-European transport in Hungary

With funding from the Connecting Europe Facility, the PAN-LNG Project is developing a Trans-European transport infrastructure, starting in Hungary

MGKKE, the Hungarian NGV Association, developed the PAN-LNG Project for the liquefied natural gas (LNG) fuelling infrastructure, which has been selected in 2015 for co-finance by the INEA under the Connecting Europe Facility (CEF). The main goal of the project is to prepare the necessary infrastructure in Hungary for LNG-based transportation, to construct the first five filling stations and also establish a supply chain.

To increase its impact, in 2016 the PAN-LNG Project developers introduced further project proposals for the call of CEF 2015 Innovation, which were

eligible for a grant by the INEA evaluation team, and gained the approval of the European Commission. On that basis, nearly 40 new LNG-based compressed natural gas (CNG) vehicle filling points will be established by 2018 along the TEN-T corridors.

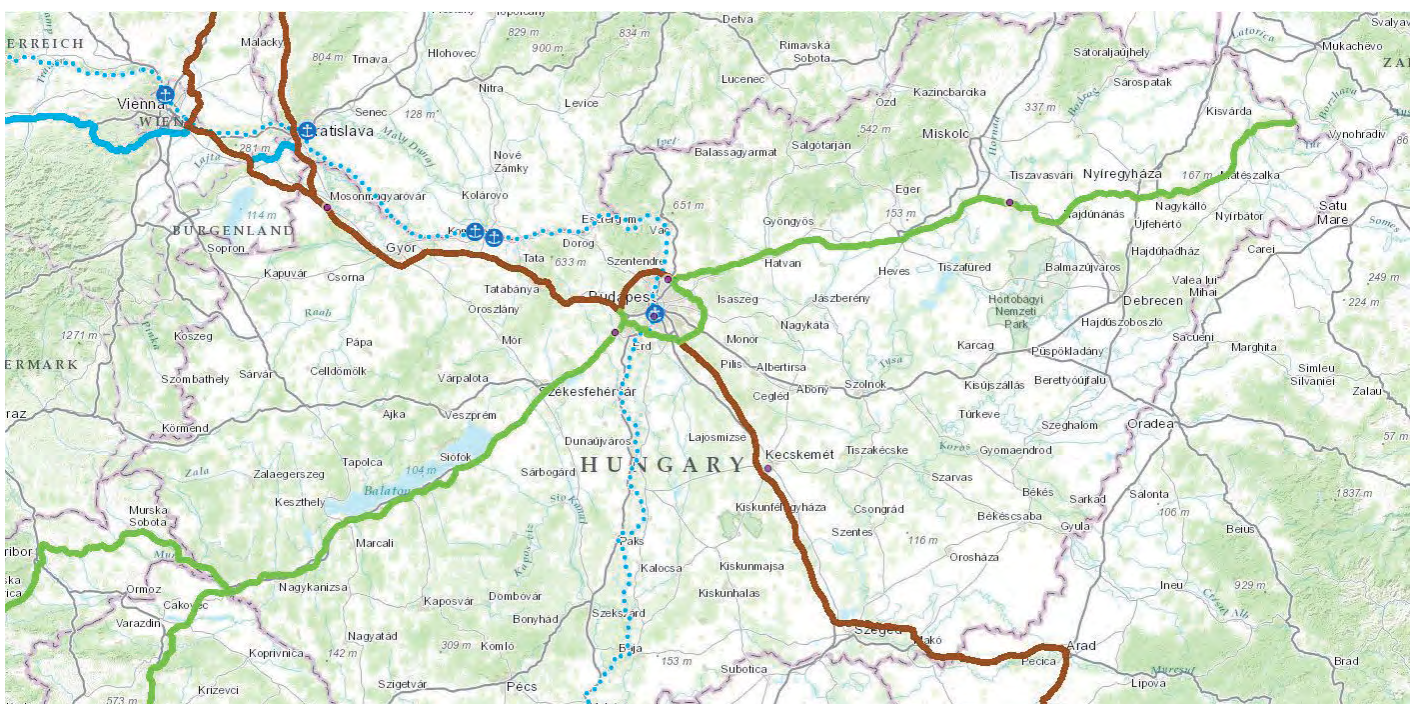
This will most likely boost interest in CNG and dynamically grow the number of motorists using vehicles powered by environmentally friendly fuels.

Expanding the network to shipping

We expect a similar breakthrough effect from the PAN-LNG-4-DANUBE

Project, which built the first LNG fuelling solution for shipping on the Danube, which will serve ships as well as trucks. In 2018, fuelling is expected to start at the middle point of the EU's longest inland waterway, the Budapest-based international port, which is also a tri-modal transportation centre. For the future, upgrading the railway will provide another opportunity; the non-electrified lanes can be revamped with soot-free LNG operation.

Of the propellants that are available today, bio-methane is proven to be the most advantageous, based on emissions of greenhouse gases. The





feedstock is an organic material, which is not adding new carbon into the air, meanwhile the energy requirement is beneficial and is able to establish truly CO₂-free transport, even for heavy duty vehicles.

On the other hand, bio-methane can secure the cleanest possible burning in internal combustion engines: by virtue of the fact that it is soot- and sulfur-free, it has very low NO_x and

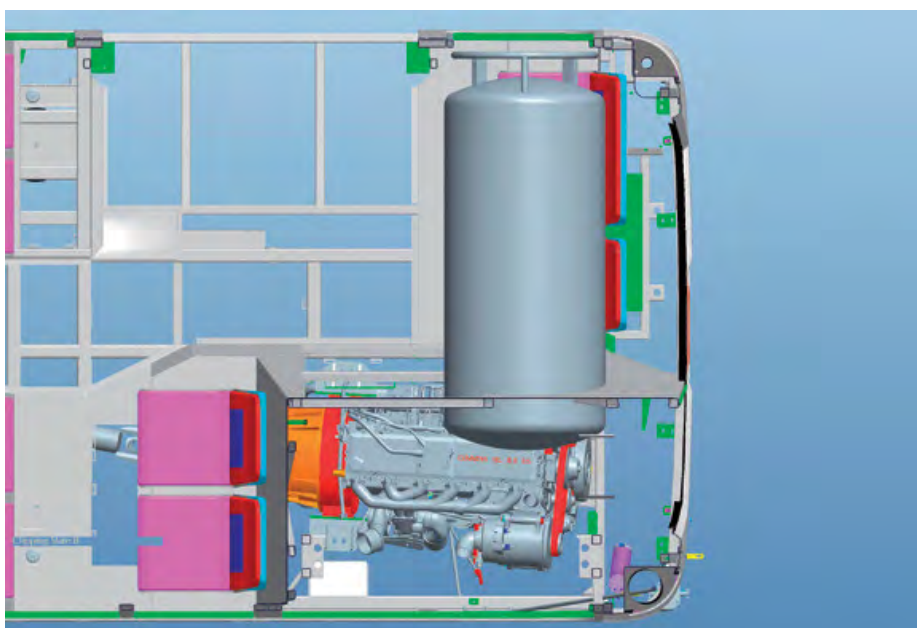
hydrocarbon emissions. The level of environmental load and its social costs are only one tenth of that of today's diesel vehicles.

PAN-LNG Project will fill in missing links

Thanks to funding from the European Commission's CEF fund for the PAN-LNG Project, the new LNG filling points for environmentally friendly transport will completely fill the miss-

ing links along the Mediterranean and Orient-East/Med, as well as the Rhine-Danube corridors in Hungary. The development will link the whole European LNG network, and at the same time create the opportunity to continue progress towards Greece and Turkey, increasing the use of LNG-based Trans-European transport.

The main beneficiary of the grant, Pannon Fuel Ltd (investors in the LNG filling stations), is working closely together with the long-standing Ikarus bus manufacturer to enter the market with a new, innovative LNG-fuelled city and intercity bus family. By obtaining type approvals for the modifications, the production of the outstanding seating ability alternative propelled bus can start in 2017. Based on the intention of Ikarus, the near-zero emission vehicle, which is far cleaner and smoother than the Euro VI diesels but has the same drive and range ability, will have better TCO (Total Cost of Ownership) than any other bus.



IKARUS

PannonFuel

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Securing large scale events in the aftermath of terrorism

James Kelly, Chief Executive of the British Security Industry Association, looks at some of the most effective methods of securing large scale events

In the wake of recent terror attacks on British soil, such as that of Westminster, Manchester and London Bridge, it is essential that the general public are aware of, and have confidence in, the vital role that security products and services play in keeping our nation safe.

Hostile vehicle mitigation

Recently, terror attacks in both England and Europe have seen vehicles as being a primary method of attack, targeting public open spaces, which are more vulnerable to these types of threats. Discussing hostile vehicle attacks, Alan Meyrick, Senior Risk Analyst at G4S Risk Consultancy, commented: “the main focus of such attacks are public open spaces and temporary events – such as markets, outdoor music events and

festivals, sites that have limited permanent perimeter security and that are considered ‘soft targets’, thus increasing the likelihood of mass casualties.” As a result of this growing threat, it is important that event organisers build hostile vehicle mitigation (HVM) tactics into their security plans. This requires careful thought out planning of the necessary security barriers as well as how they fit into the surrounding streetscape. “Hostile vehicle mitigation in various forms, is – and has been – the initial ‘go-to’ products to stop such attacks (as those in Nice, Berlin and London), as well as Vehicle Borne Improvised Explosive Devices (VBIED) attacks such as the Glasgow Airport attack in 2007,” explains Alan. “HVM in different forms, including bollards, concrete planters, concrete benches and other physical architecture, are all used.”



Event organisers will need to consider the most suitable HVM techniques to suit the event, taking into account the cost of the installation and the suitability of the solution. "Existing infrastructure and utilities, existing hardware and hard landscaping, the proximity to points of egress or access, as well as integration with the existing streetscape and how HVM methods may impact pedestrians and vehicular movement are all key considerations," Alan adds. If HVM methods are employed, it is also important to be aware of the standards that such methods should meet with. There are a number of standards that provide a benchmark for HVM equipment, as well as guidance for the installation of products. Perhaps the most relevant for HVM is the British Standard Institute's PAS 68 – Impact Test Specification for Vehicle Security Barriers, which is the UK standard and the security industry benchmark for HVM equipment. Any equipment should be tested in conjunction with PAS 69 – Guidance for the Selection, Installation and Use of Vehicle Security Barrier Systems, which provides product installation guidance.

Event security – best practice

With large-scale events finding themselves as the targets of terror attacks in recent years, the importance of choosing quality event security suppliers should not be overlooked. Discussing some of the essential elements of event security, Andrew Murphy, Managing Director of Eventsec, explained: "When reviewing security at events, purchasers should consider various factors prior to their decision. Many companies offer event security, however, many do not have the relevant experience or operational capacity to perform the role. It is very important that the organiser checks if the prospective company has appropriate insurance. It is also important that purchasers review the insurance

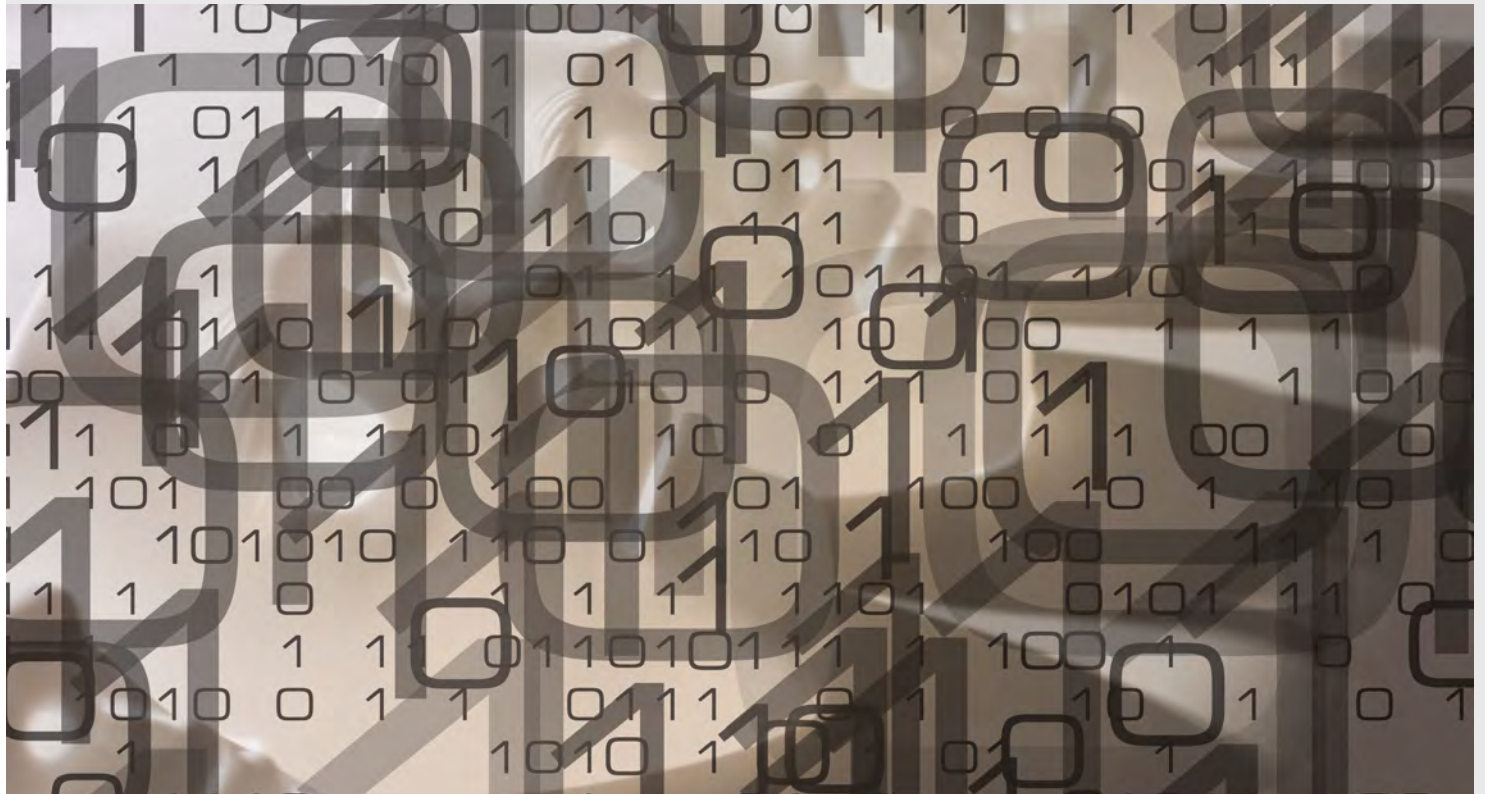
cover and clarify with the underwriter as to what insurance is in place and whether it covers events and issues such as wilful acts, front of stage and ejection."

Andrew went on to add that: "With the present severe UK warning, it is important that we constantly monitor our security provision. It is essential that whoever is engaged, has relevant experience, has the operational capacity and can provide assurances to the organiser with regards to recruitment, vetting and training. This can be ascertained and qualified by companies who hold membership of trade bodies and have external accreditations such as ISO 9001 and Investors in People as an example.

"Events are complex and often have multi layered security plans. It is important that the organiser, statutory agencies and the public, have confidence in the security provider. Often, cost is the most important factor to organisers, but in light of recent events, staff experience, training and the supporting management structure will help mitigate the impact of incidents and should help the procurement decision. The staff employed in Manchester during the recent attack should be commended, demonstrating immense bravery and resilience as the first responders in what was a truly awful situation. Events will continue and resolve is strong, I would encourage event organisers to review their procedures and decision making procedures when procuring security. They should ensure when it comes to procuring security that they engage with experienced and reputable operators. It is important that we minimise the impact of all hazards, and events pose many risks. Therefore, it is very important that event organisers understand and recognise their responsibilities. The procurement of experienced and reputable companies will help ensure the safety of all attending events and mitigate when incidents occur." ■

James Kelly Chief Executive

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www.bsia.co.uk/#
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A long term strategy for cyber security

Challenges remain in the fight for cyber security. Open Access Government's Ciara Ruane highlights the work being undertaken to keep the UK safe

Following the cyber-attack on the NHS earlier this year questions have been raised as to how both the public and private sector can protect themselves from hackers. The recently launched National Cyber Security Centre (NCSC) released a statement at the time of the attack, saying: "The NCSC is aware of an incident and is working around the clock with the UK Parliamentary digital security team to understand what has happened and advise on the necessary mitigating actions."

Launched in 2016, the NCSC collaborates with other government departments such as defence, intelligence, and law enforcement. Speaking about the launch of the centre, Chancellor Phillip Hammond, said: "The cyber-attacks that we are seeing are increasing in their frequency, their severity, and their sophistication. In the first 3 months of its existence, the NCSC has already mobilised to respond to attacks on 188 occasions.

"The NCSC will play a unique and crucial role bringing together the public and the business community on the one hand, and our intelligence and security agencies on the other."

Strategy for security

In November 2016, the government announced the new [National Cyber Security Strategy](#), which was part of the Active Cyber Defence (ACD) programme. The centre aims to work with other national and international organisations to gather information needed to detect, prevent, and solve potential threats to digital infrastructure. They aim to register government and other high-profile domains and emails through the DMARC (domain-based message authentication, reporting and conformance), a move which will soon become mandatory, as well as creating a centralised registry system for the public sector. They have partnered with Nominet, a Domain Name Service (DNS) that prevents access to

known harmful domains, and provides analytics data to provide insight into the state of IT in the public sector.

The NCSC has also set up a free WebCheck service, which aims to scan sites for common vulnerabilities. Currently running on a prototype with 150 users, the service targets points such as security certificates and out of date domains, notifying the organisations responsible for them. They have also been working with Netcraft, a private company, creating an email address where public sector organisations can provide the URLs of potential scam sites, to identify and take them down within around 24 hours of their creation. This is a service which they aim to expand, which will identify both malware and phishing sites and issue takedown notifications within a few hours.

They have also outlined plans to develop new identification techniques beyond current protocol such as password registration. Facial recognition software and other such technologies would, they claim, provide a more airtight identification process. Through the GOV.UK verify service, the government offers choices of certified companies, such as the Post Office, which can verify your identity with the information you give them. It aims to shorten and simplify the registration process while providing an extra layer of security. The NCSC has also identified the need to gather wide ranging unbiased data on the digital landscape so that future threats can be identified, which is a key aim for their overall defence strategy.

Protecting organisations from attack

The NHS attack itself was caused by a group of hackers using a 'cyber weapon' called Eternal Blue developed by the US government to access the files of suspected terrorists. 'WannaCry' exploited a weakness in Microsoft, which has now been patched. Microsoft's legal head Brad Smith criticised the US government for developing the system and urged them to become more transparent, saying the attack could have been prevented otherwise. Edward Snowden also criticised the government for not identifying the flaw in Microsoft operating systems when they found it. The ransomware tricked victims into opening links that corrupted their systems and blocked their files, requiring bitcoin

payments to regain access. Hence, the emphasis on avoiding opening links in suspect emails.

After the attack, Microsoft said that those using the most up to date version of their antivirus software would be protected. One researcher is said to have accidentally found a way to prevent further spread for the time being. The NCSC has a section of their website dedicated to advising protection against WannaCry. It names the patches and updates available through Microsoft, and offer their own 'Cyber Essentials' programme, which is now mandatory for government contract suppliers and can be installed for small businesses and other organisations.

"The NCSC will play a unique and crucial role bringing together the public and the business community on the one hand, and our intelligence and security agencies on the other."

Speaking at London Tech Week, NCSC CEO Ciaren Martin outlined how organisations can protect themselves from such threats. "There are a whole range of basic protections that can be layered to build up your defences.

"Understanding the threat environment is important of course. During WannaCry we sent out three simple messages: keep security software patches up to date, use AV and back up as you can't be held to ransom if you're backed up." ■

Ciara Ruane Commissioning Editor

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How do we build safer digital environments?

Identify, Protect, Defend, Respond are the four key components to ensure safer digital environments. Here, Fujitsu provide insight

A decade ago, primary security concerns were satisfied by deploying and maintaining an effective firewall, in addition to keeping the permissions for devices and physical locations up to date. While organisations used the internet to maintain a website and for communications, an online presence wasn't as ubiquitous as it has become today.

How things have changed! Today users expect to access information and departments on any device – and to do so from almost anywhere, at any time. Information really has become the new currency – and it's available 24x7. It is commonplace today that employees bring their own devices into the organisation's network, download and install software they have selected, and interact with corporate data on their own personal devices. What's more, these devices are taken outside the workplace – still carrying access to valuable and sensitive data.

Citizens want to be empowered to reach services as and when they desire which creates huge challenges for national and local bodies to provide platforms that are resilient and information that is protected. The issues of data management, storage, access, and rights need to be paramount within any business or organisation where there is a transaction of information.

This new level of being interconnected brings untold benefits but it also

creates new security challenges.

Against this backdrop, Fujitsu's Global Cyber Security business protects government departments around the world against cybercrime of all kinds, strengthening their resilience against cyber-attack, as part of a globally-integrated security offering.

Fujitsu provides Managed Security Services from Security Operation Centres (SOCs) in Japan, North America, UK, Germany, Finland, and Spain, and aims to bring to market a wider range of security solutions, upgrading its SOCs to Advanced Cyber Threat Centres.

Our philosophy: Identify, Protect, Defend, Respond

Fujitsu's portfolio of security solutions and services provides public sector organisations with peace of mind that their security is in good hands while they get on with running their business. Fujitsu aims to be the trusted digital security services provider, helping its customers predict and respond to cyber threats to protect their business reputation with an intelligence-led approach.

Our key services lie in 3 areas:

- Predictive intelligent threat detection;
- Trusted delivery - expert-led professional and managed security services;
- Global 24x7 monitoring & response.

Managed Security

One key service that Fujitsu offers to address this lack of time and skills is a fully managed security service. A key feature of this is continuous system monitoring that constantly keeps a watchful eye on internet traffic, looking out for potential attacks before they can do harm.

Fujitsu takes an intelligence led-approach to cyber security. Artificial intelligence systems monitor customers' internet traffic for potential risks. Once identified, the team of experts located in one of the global SOCs can help customers rapidly take action.

Advanced Biometrics

Security challenges are not limited to the cyber world and the implications of sensitive information falling into the wrong hands remain significant. The most basic level of prevention involves controlling physical access to hardware or facilities. Traditionally, access to doors, devices, computers, and border controls have been managed by PIN code entry systems or by door tags – both systems which can be easily lost, shared, or stolen.

Fujitsu's answer to the challenge lies in sophisticated biometric authentication – which can be applied to gain access to physical locations such as office buildings, server rooms or even to access personal mail boxes. Devices such as laptops can also deploy biometric authentication. The



authentication is deployed in the easy-to-use form of palm vein readers. Called PalmSecure, this technology that is uniquely offered by Fujitsu, takes advantage of the fact that everybody has a unique pattern of veins in their body which can be used for highly secure authentication. It is hygienic, as no contact is required – users just need to wave their hands in front of the sensor. And of course, vein patterns can't be lost or stolen and are only visible when blood is flowing through them.

Fujitsu Identity Access as a Service

Users of public systems today have dozens if not hundreds of usernames and passwords that allow them to log-on to countless on-premise systems and cloud services. Fujitsu's identity as a Service is designed to reduce this complexity and to help businesses prevent hacks or fraud, by ensuring that only verified users can access selected systems, applications, data, and resources.

The browser-based service makes it easy to manage, create, adjust, and remove permissions from any connected device or location. It incorporates a variety of strong authentication

methods, including user ID and password, Windows desktop login, single sign-on (SSO), CallSign authentication (based on a phone call and PIN code) and biometric authentication.

As well as the recent growth of ransomware, there are a number of trends that we expect to see in the near future which illustrates the increasing sophistication of cyberattacks:

- Many systems have 'a blind spot' – this lies in the encrypted channels that are designed to give remote workers easier access to networks. If taken over by a cyber-criminal, these channels can essentially provide access to the heart of a critical computing system and mean that nefarious activities are largely undetectable.
- Our state-of-the-art Fujitsu SOC's also expect to see cybercriminals continue to target financial applications. In particular, our experts predict that the SWIFT global payment network will be targeted, in addition to further growth in banking Trojans that are targeting older, more vulnerable back office applications. Although SWIFT is moving to establish mandatory controls, we still think it is a window of opportunity for cybercriminals.

- Smart cities will also find themselves targeted – many of the protocols designed for smart connected devices have their own potential flaws and vulnerabilities. The implications of this are wide-ranging and could include allowing hackers to disable power supplies or other infrastructure services. This would plunge entire cities not only into darkness but into disarray – because it's also likely that phone systems would stop working – and could even impact on water supplies.

"Did you know?"

Fujitsu uncovered a massive 'hit list' of 385 million email addresses including many from government agencies and banks on a server hosted in Russia as part of its activity tracking a Dridex Trojan. The server was found in 2015, by following a trail of major customers who had fallen victim to hackers. For more information, see [this video](#).

Further information:

[The Fujitsu 2017 Security Predictions report](#).

[Inside the Security Operations Centre:](#)

Secure thinking: When it comes to cyber security there will always be vulnerabilities. How can you be confident that your information is protected?

[Inside the Gates](#) – The Banking Trojan Threat (Dridex Case study).

FUJITSU

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Cyber security, GDPR and the public sector

Jayne Goble, public sector security expert at PwC looks at what the General Data Protection Regulation means for cyber security and if we're prepared

Public sector organisations need to focus on data and cyber security, not simply because of the costs and the reputational damage breaches cause, but also because of incoming legislation which steps up security and breach reporting requirements, and provides sanctions for non-compliance.

The EU Commission has reached an agreement on 2 key data protection regulations – the General Data Protection Regulation (GDPR) and the Network and Information Security Directive (NISD), also known as the Cyber Security Directive.

The GDPR will give individuals stronger rights, empowering them with better control of their data, and ensuring that their privacy remains protected in the digital age. Whereas the Cyber Security Directive will complement the GDPR, providing protection of IT systems in critical national infrastructure.

The GDPR and Cyber Security Directive will apply to all public sector organisations collecting and/or processing EU citizen's personal data.

The GDPR and Cyber Security Directive are both EU pieces of legislation. This, of course, begs the question as to how far UK businesses need take notice following the results of the EU Referendum.

The Information Commissioner's Office (ICO) has said that all organisations with operations and/or services within the EU, should work on the assumption that the GDPR will apply. This will ensure the UK maintains 'adequacy' for EU purposes and can continue to receive EU personal data.

The Cyber Security Directive will also apply to organisations that provide elements of a country's critical

national infrastructure – i.e. operators in energy, transport, health, and banking – and operate and/or provide services within the EU.

The new Cyber Security Directive, coupled with the GDPR, means another element of compliance for all public sector organisations. They must adjust how they handle data and, in turn, their cybersecurity.

GDPR & the National cyber Security Directive, and its main implications for public sector organisations

Although the GDPR and Cyber Security Directive came into force in April 2016, they will not apply until May 2018. This has provided a 2-year transition period before both pieces of legislation become enforceable across EU countries, including the UK.

A 2-year grace period may sound generous, but in reality, given the number of teams that will need to be involved to help a public sector organisations comply with the new regulations (such as IT, marketing, legal and compliance, as well as management and operations teams) it is important to consider the implications and plan for the new regulations right now.

As the GDPR and Cyber Directive will not apply until May 2018, many public sector organisations will still be in the early phases of understanding the requirements. We have been leading the way in performing GDPR maturity assessments and specific privacy transformation services. Based on this wealth of experience and knowledge, we have identified 5 key implications to public sector organisations:

Changes to the definition of 'personal data' and 'sensitive' personal data

The definition of what constitutes personal data will



expand under GDPR, with personal data now extending to location, IP address, as well as whole new swathes of medical data, including genetic information. This means that more public sector data will be subject to data protection laws and higher level protections (that apply to sensitive personal data).

Processing based on the 'legitimate interests' ground

Public sector organisations who currently rely on 'legitimate interests' (i.e. legitimate reasons for processing personal data that the other conditions for processing do not specifically deal with) will need to find alternative grounds to justify personal data processing.

Data breaches

The GDPR introduces a requirement for all data breaches to be reported to the Information Commissioner's office and to data subjects in certain circumstances. Public sector organisations will need to put appropriate internal procedures in place to detect, report, and investigate personal data breaches in accordance with the new rules and applicable timescales.

Subject Access Requests

Under the Data Protection Acts, data subjects already

have a right to be provided with a copy of the data and certain amounts of information. However, under the GDPR, more detailed information must be supplied. This may require additional administrative effort from public sector organisations to comply with detailed rules set out in the articles.

Cyber Security Directive

The Cyber Security Directive required operators of essential services in the energy, transport, banking, and healthcare sectors, as well as providers of critical digital services like search engines and cloud computing will be expected to take 'appropriate security measures relating to breach detection, response and reporting'. ■

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Public sector security expert

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Using proactive security to protect against cyber attacks

Aaron Pickett, Digital Forensic Examiner at IT Group UK Ltd highlights proactive security as a way to protect the public sector from possible cyber attacks



There are many out there who claim that online criminal activity proliferation, such as the spread of ransomware, the attack of large corporate networks and website defacing, is one of the biggest emerging threats to businesses, government bodies and public sector organisations worldwide. This is something of a myth; online criminal activity has been around in large quantities for a very long time, the so-called proliferation is more the result of increased media and public interest.

Despite this, high-profile cases, such as the WannaCry attack that took a grip on many sectors of the NHS, are increasing public awareness. Where once it was not understood, ransomware (and other malware types) are becoming common-knowledge.

The addition of legislation requiring some element of disclosure following an attack has meant that fewer and fewer 'cyber attacks' are being swept under the carpet. The net result of this is that organisations are required to do far more to protect their data and interests.

What you can do

Preventative strategies are key elements of an effective cyber security programme. Proactive security, as it is known, can ensure that an attack is less likely to succeed and there are many ways to accomplish this (see below). In addition, one of the key strategies employed against malicious software (malware) is user education. The importance of updating hardware and software, not opening unknown attachments and remaining vigilant against network

attacks is the most effective method of protecting any organisation. In spite of this, pushing these lessons in a way that individuals will learn, act upon and make part of their daily routine is one of the main challenges facing security in the 21st century. The technology is there to protect the majority of systems, but the human element remains the biggest weakness.

What we can do

IT Group provides all of the proactive security services listed below, and additional areas including Wi-Fi security testing, White-Box Phishing Campaigns and Security Consultation. Reactive services, including post-event Penetration Testing and Digital Forensic Imaging for the preservation of evidence can build a picture of what has happened, allowing reporting to



the Information Commissioner, shareholders and the public at large with accurate facts that show the extent of the damage caused.

Penetration testing is one of the most well-known strategies of proactive security. Penetration testing uses a simulated scenario of an attack, testing the defences that are currently in place on the network and exploiting any areas that a weakness can be found. Penetration testing can be conducted in a way that will test the IT technicians' responses to an attack by not informing them of the test, or a more thorough attack that will use the IT Technicians' knowledge to target the different areas of the network more accurately.

One of the key areas that many forget to test is internal. A network attack

from a person with malicious intent (a hacker, for example) will not necessarily come from an external source, such as across the internet. It is just as likely that the attack could come from an insider who is already within the network; a rogue ex-employee whose access was not revoked, an employee with a grudge, or a temporary sub-contractor. Internal penetration tests are, therefore, just as important as the testing of any external endpoints such as websites, remote access gates or network firewalls.

Vulnerability scanning is the practice of scanning open ports on machines and creating a list of potential vulnerabilities that an attacker could be used to leverage access to a machine on the network. This is a stage that will be conducted during a penetration

test, but does not perform any further attacks to see which vulnerabilities are exploitable. Despite this, vulnerability scanning is an effective way of gaining a picture of how the network is protected and what, if any, weaknesses are present.

Incident response planning is an important step for any business to take. No matter how many precautions are taken to stop a security incident from occurring, there is always the chance that an attacker could slip through the net, or a user may accidentally create a new hole in the security defences. Planning for this event removes many of the incorrect decisions made following an event (reactive) and means all relevant members of staff are aware of the actions they have to take. This particularly lends itself to forensic readiness, specifically focusing on the preservation of evidential data that could then be relied upon following a malicious event.



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The challenge of maintaining cyber security

After a number of high profile breaches cyber security has become a key focus for the public sector, says Meg Hillier MP, Chair, Public Accounts Committee

The NHS was hardest hit by the recent ransomware attack in May which affected businesses and public services across the world. During the attack operations were cancelled, ambulances diverted, medical records inaccessible and patients left adrift. Reports suggest that hackers used out of date software on NHS computers as their way in. Software that should have been updated many months ago.

In 2010 the government ranked cyber security as one of the top 4 security threats to the UK. Seven years later this threat remains. With the cyber-attack on the NHS and more recently Parliament itself, the importance of protecting not only government data but the data of people it represents is paramount.

Monitoring

When the Public Accounts Committee looked at the government's efforts to protect information last year we found a lack of joined up action across Whitehall. Each government department determined what it considered to be a data protection breach and recorded this data differently. This chaotic approach meant that central government could not monitor the problem.

This lack of monitoring concerned the Committee. Threats to cyber security are growing rapidly – with 200 incidents a month which were serious enough to alert GCHQ to in 2015, up from 100 a month in 2014. Ministers realise the challenge they face but the government has taken too long to consolidate and coordinate its response to protecting the UK.

As recently as April last year there were at least 12 separate organisations and teams in central government with a role in protecting information. The Committee's report highlighted the former Chancellor George Osborne's criticism of the "alphabet soup" of

agencies involved. The establishment of the National Cyber Security Centre (NCSC) was a welcome step in beginning to bring these bodies together to provide a unified source of guidance and support, including the management of critical cyber security incidents. But there is a lot still to do to make sure that this centre lives up to expectation.

"The NCSC has the potential to provide national leadership, but it is only just making its first baby steps in 2017 despite the government committing to take action in 2010."

It is not clear for instance how an organisation outside of Whitehall such as a local authority, charity or business would know whether a cyber breach needed to be escalated to the NCSC.

Challenges

An area of real concern, and one harder to tackle is the recruitment of staff with the right skills to tackle the problem. A particular challenge is too often the private sector can outbid government rates of pay. In 2013 the Cabinet Office established a security profession to develop the professional skills of civil servants working in this field. It is attempting to paper over the cracks by setting up large clusters where civil servants can share their skills – amalgamating 40 different departmental security teams into 4 larger clusters.

There are patches of good practice in Whitehall. The Department for Work and Pensions (DWP) is working to ensure its staff buy in to their role in maintaining security. As one of only a few command and control departments where there's a direct line between Whitehall and the front line this is easier to achieve compared with a department made up of a disparate group of organisations such as the Department of Health and



Meg Hillier MP, Chair

the NHS. The National Archives is also providing training courses for civil servants from across Whitehall. This is all welcome but the government has to make sure it has the capability to provide support in the event of an attack.

“An area of real concern, and one harder to tackle is the recruitment of staff with the right skills to tackle the problem.”

The NCSC has the potential to provide national leadership, but it is only just making its first baby steps in 2017 despite the government committing to take action in 2010. We are 7 years off the pace.

However, the NCSC can only provide guidance and has no statutory power to enforce its recommendations.

Whilst the NCSC must ensure its advice is acted upon, cyber security relies on us all – individuals, private companies, public bodies and government. The fact that Britain ranks below Brazil, South Africa and China in keeping personal phones and laptops secure is worrying.

There are also other concerns coming down the line. The possible security threat of foreign investment in major infrastructure projects such as Hinkley Point. How EU directives being brought into force to ensure a strategic approach to cyber security across Member States will work in a post-Brexit world. And the growing concerns around the Internet of Things. The hacking of smart gadgets in people’s homes can not only be used against one consumer but linked to cause wider disruption of services. With new smart technology anything is hackable – cars, security cameras, televisions, even children’s toys.

Government has a vital role to play but it needs to raise its game. Its approach to handling basic data breaches is chaotic and my Committee did not have confidence in its ability to take swift, coordinated and effective action in the event of an attack.

The UK can be ahead of the game – it was a British cybersecurity researcher who halted the recent global attack, but across government departments there is much work to do to keep up with the staggering pace of change. ■

Meg Hillier MP
Chair

Public Accounts Committee

<http://www.parliament.uk/business/committees/committees-a-z/commons-select/public-accounts-committee/>

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How can UK universities protect themselves from cybercriminals?

Robert Stoneman, Analyst at GlobalData highlights why UK universities are key targets for cybercriminals and how to safeguard from an attack

UK universities will find it sobering that over 4,000 Chinese universities and research institutions were also affected by the same piece of ransomware that crippled NHS IT systems last month. Universities are ripe targets for cybercriminals, and potentially even foreign governments, due to the wide range of information they hold, from personal and financial data to commercially sensitive and potentially highly sensitive research data. Therefore, to safeguard this and avoid a potential PR bombshell, they will be keen to learn the lessons in case the next big attack has UK higher education in its sight. Aside from ensuring the basics are up to scratch, universities face particular challenges, particularly the growing trend for staff and students to bring their own devices onto campus (BYOD) or to access systems and services remotely.

Vulnerable academia

The cat and mouse nature of cyber security means that even the most diligent of universities can fall victim to a major cyber-attack, even if events of the scale that hit the NHS recently are relatively rare. Research carried out last year by the cloud and virtualisation provider VMware found that 87% of UK universities surveyed (among 75 ICT decision makers at over 50 UK universities) had suffered some form of cyber-attack. Shockingly, one in three said they faced attack on average once or more every hour. What is even more worrying is that 25% said critical intellectual property had been infiltrated, while 43% reported student data being attacked. It is, therefore, no surprise that 85% of those surveyed argued more funding is needed for IT security. As cyber-attacks increase in frequency and sophistication,

universities will need to focus more resources on ensuring they are ready.

Getting the basics right

The most effective cyber security strategy is built on getting the basics right. Universities not only have to consider their staff, but also the many thousands of students who log into and use IT systems and services daily. It is crucial all are up to speed with the basics of cyber security since even the ablest defences can be circumvented by basic human error. Firstly, they should put in place a cyber security policy that is reviewed and updated regularly. Secondly, they must ensure everyone connecting to the network is aware of this policy and up to scratch with the basics of cyber security, for instance, not clicking on links in suspicious emails from unknown parties. Thirdly, universities should regularly drill in preparation for an attack. Regular penetration testing will help discover weaknesses which can then be plugged while testing your data recovery procedures will make dealing with any attack far easier to manage. Fourthly, universities should audit what data they possess, where it is held and how long for. This will help in terms of planning backups and in making sure that they do not hold any sensitive or personal data unnecessarily, reducing the potential risk of a security breach. Finally, and most important of all, universities must ensure they keep their security systems up-to-date by implementing the latest security patches as soon as possible after they are available.

BYOD

Arguably the greatest cyber security challenge universities face is the growing tendency for students and staff to access IT systems and services through their own devices. Whether or not this is on campus or via remote access, universities need to mitigate the risks posed by devices outside of their control accessing their networks. The initial temptation might be to put the brakes on such measures in order to re-centralise control over hardware. However, this would be a major misstep: students have come to expect to be able to use their own devices to access university systems and service at their convenience. Academic staff too will be unhappy about losing access to systems on the go, especially considering that most spend significant time away from campus for research. Instead of turning back the clock, universities need to be proactive and put in place procedures that allow them to maintain as much

oversight as possible. From the outset they need to consider the potential risks that BYOD brings: what data devices hold and how it is transferred; the potential for data leakage; the implications of those not associated with the university accessing devices; devices' security capacities; how to deal with the loss of devices; and the procedure in case someone leaves their studies or employment. All this considered, universities need to make sure devices connecting to their network meet the requirements laid out in their cyber security policy, for instance, ensuring they run up-to-date operating systems and security software. This should be supplemented with a BYOD acceptable use policy outlining what data can and cannot be accessed or stored on personal devices. Furthermore, larger institutions may want to consider enterprise-level remote access solutions which allow greater administrative control over what users can access on the network, all whilst offering a more seamless user experience.

High stakes for negligence

If the high-profile attack on NHS IT services fails to prompt universities to improve their cyber security, the potential financial penalties certainly will. Brexit will not be enough to prevent UK universities from falling under the remit of the EU's General Data Protection Regulation (GDPR), coming into force from May 2018. This brings with it the sobering prospect of substantial fines for the most serious negligence, way in excess of the current maximum fine of £500,000. GDPR will mean that, for the most severe data protection violations or negligence, universities could be liable for a maximum fine of €40m or 4% of global annual turnover, whatever is higher. Even less serious violations could see fines of up to €20m or 2% of global annual turnover. Although it is very unlikely a tidal wave of major fines will emerge from May onwards, as many institutions are still putting in place measures to become compliant, it is clear the financial equivalent of a 'slap on the wrist' will no longer cut the mustard. ■

Robert Stoneman

Analyst

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Digital Europe: digitising industry, empowering people

Andrus Ansip, European Commission VP for the Digital Single Market outlines why science and research play an integral role in creating a digital Europe

Wherever we look, digital issues are firmly on the global political agenda: a clear sign of their socio-economic importance and political relevance.

We have entered a new era of digital globalisation, defined by data flows that transmit information, ideas and innovation. As data flows go global, Europe has to look beyond its borders, which means being linked into the global digital economy and accompanied by the right infrastructure.

This is true for any country. Connections are a social and economic lifeline. Affordable and inclusive global connectivity is in everyone's interests, wherever they are located.

It is why the EU is strongly committed, politically and financially, to science and research cooperation on a

wide range of related issues. These include high-performance computing (HPC), cybersecurity, cloud computing, interoperability and the common technical standards needed to develop 5G and Internet of Things technologies.

In all these areas, open cooperation and innovation are vital, for the simple reason that they affect the entire global digital community. The increasing importance of data flows in every type of international exchange makes that all the more relevant.

Investing in computing power

A key part of the philosophy that underpins our plan to build a Digital Single Market (DSM) is to help Europe's industry go digital as much as possible.

Companies across many industry sectors are coming to rely on supercomputer power to innovate, cut costs

and the time to get their products and services to market. That is why HPC is a vital tool to increase competitiveness and should be seen as a strategic resource for the future of EU industry.

HPC has countless applications with a direct positive impact on people's lives: designing and simulating new medical treatments; designing energy-efficient buildings; providing accurate weather forecasting. To get the full benefit from this sheer supercomputing power, industry must be able to access adequate and available HPC infrastructure. Until very recently, the EU did not have any HPC machine in the world's top 10 – we expect one, from Spain, to make it just now. What is clear is that not every EU country is in a position to build and maintain such infrastructure – and that it is more efficient to join forces to do so.

Other countries around the world are moving fast. Since we cannot afford to lag behind, the EU has to work together. In March, in a spirit of true European cooperation, seven EU countries pledged to work together to build the next generation of computing and data infrastructure: France, Germany, Italy, Luxembourg, Netherlands, Portugal and Spain. We want more countries to follow their lead and indeed Belgium and Slovenia have done so recently.

Our aim is for every research centre and project, every researcher, to have access to high-quality supercomputing, storage and data facilities across Europe. This infrastructure will be available for scientific communities, industry and the public sector – wherever the users are located.

We should also remember that it is not only industry, scientists and engineers that stand to gain from HPC availability: Europe's researchers also depend on HPC and are among its major users.

Our future HPC infrastructure will support the European Open Science Cloud, allowing millions of researchers to share and analyse data in a trusted environment across technologies, disciplines and borders.

People power

We often talk about digital transformation in the context of technology and data. But above all, it is about people, about their being at ease in the cyberspace,

and of course about jobs. Digitisation directly affects employment, it will, inevitably, change some jobs, replace some by machines and new processes.

As this happens, however, digital progress will also create other new jobs and services. Europe's app economy is a good example. Until quite recently, it did not even exist. But it is hard to think of another industry that has created so many jobs in so little time.

In today's increasingly digital world, it is essential to have the right skills. Unfortunately, Europe is no stranger to the digital skills gap: nearly 40% of the workforce does not have basic digital skills.

Rectifying this situation is another major element of the Digital Single Market project. We know that in the near future, some 90% of jobs – in careers such as engineering, accountancy, nursing, medicine, art, architecture, and many more – will require some level of digital skills.

This is where the EU can help, and already does a lot of work – for example, with the Digital Skills and Jobs Coalition launched in December, which aims to develop and expand the pool of European digital talent. It will help to provide people – young and old, the employed as well as jobseekers – with the skills they need to use digital technologies and then apply them in a working environment.

The Digital Single Market is about investing more in new technologies – whether HPC, cloud, quantum computing or microelectronics – but also as much in people.

Without a digitally skilled workforce, Europe's peoples and businesses will not be able to make the most out of the data economy that the Digital Single Market promises to provide. ■

Andrus Ansip

Vice-President for the Digital Single Market

European Commission

https://ec.europa.eu/commission/commissioners/2014-2019/ansip_en

www.twitter.com/Ansip_EU

Strategic value of high-performance computing for innovation

Wim Slagter, Director HPC & Cloud Alliances, ANSYS, highlights the importance of a sustained investment in high-performance computing

High-performance computing (HPC) is an enormous part of the present and future of engineering simulation. HPC enables engineers and researchers to gain high-fidelity insight into product behaviour – insight that cannot be obtained without detailed simulation models. When applied to design exploration, HPC can lead to robust product performance and reduced warranty and maintenance costs. Wim Slagter, Director HPC & Cloud Alliances at ANSYS, gives his perspective on HPC adoption challenges and threats on a European scale, and explains how these can be addressed by strategic partnerships.

What are the main challenges of today's HPC in your field?

While hardware and software enhancements have enabled HPC to deliver significant value to engineering simulation users, important challenges remain in ensuring that every organisation is strategically deploying HPC to gain the greatest return on investment. For small and medium enterprises (SMEs), for example, specifying, provisioning and managing HPC resources involves a significant learning curve and requires highly skilled IT staff. We have addressed these challenges by developing an ecosystem of cloud-hosting partners who provide HPC infrastructure and IT services to customers for burst or steady-state extension of in-house computing capacity. For those who are not ready for cloud computing yet, we

have developed, with HPC partners, out-of-the-box, plug-and-simulate, externally managed HPC clusters that are optimised for ANSYS and pre-configured with ANSYS simulation solutions and job management software.

What is the future of HPC?

The future of HPC is great. Increasingly, customers are looking for ways to scale up to HPC for more, bigger and faster simulations. The main reason is that the computer industry continues to deliver enormous increases in computing speed and power at consistently lower costs. The average workstation that you use today is equivalent in power to the entry-level HPC cluster of just a few years ago. While compute power has increased a thousand-fold over the last decade, large scale computing is now within reach of more and more engineering teams, with new trends, like cloud computing, promising to make access even more widespread. Today, parallel simulations using 128–256 processor cores are increasingly common, and there is an increasing demand for scaling to thousands of cores per simulation. Organisations like Airbus and Rolls-Royce are demanding “extreme scalability” for running huge simulation models, either in the form of complete aircraft engines or real-time CFD-based in-flight simulations. The packaging company Tetra Pak wants to be able to tackle package sterilisation problems with advanced Large Eddy Simulation (LES) models using ten to one hundred thousand cores.

ANSYS is committed to delivering HPC performance and capability to provide our customers with higher levels of simulation fidelity, engineering insight and innovation. To achieve this goal, we will continue to focus on HPC software developments and partnerships which include:



- Ongoing optimisation of our software. Here, we work with processor vendors like Intel and NVIDIA to understand and optimise the mapping of the simulation workload to the compute resources (e.g., using new compiler options, enabling the use of hardware accelerators and dynamically adjusting how the workload is balanced across multiple processors).
- Extension of parallelism and HPC performance across all aspects of the simulation process – from meshing and setup to file handling, visualisation and automated optimisation techniques. We are driving toward a unified environment – across solver components – for defining, submitting and monitoring customers' parallel workloads.
- Supercomputing partnerships. We work closely with HPC centres to profile and benchmark our software at "extreme" scaling. These partnerships also benefit our customers, who need a platform to demonstrate how increased HPC scale can impact their real-world simulation workflows. Most recently, ANSYS, Saudi Aramco and KAUST have set a new supercomputing milestone by scaling our software to 200,000 processor cores.

What are the expectations and threats in Europe?

The expectations of HPC are very high. After all, HPC is without doubt a key enabler of scientific and industrial innovation today. HPC enables high-fidelity simulation (bigger, more detailed, more accurate, more complete, as well as system-level simulation), which is critical for organisations that rely on simulation to support product innovation. HPC also enables design exploration, leading to early identification of optimal and more robust designs, and making the

engineering process more productive. It is quite clear that the global economies that invest in HPC are those that will, over time, gain the greatest competitive advantage and reap the largest economic benefits. Hence, the current scramble to invest in large-scale leading-edge HPC systems worldwide.

It is evident that Europe is "threatened" by global competitors making huge investments. Among the new economic powers, China and India have very ambitious HPC programmes, and are investing vast sums of public money on related infrastructure. In my opinion, Europe must view these challenges as an opportunity to invest for its future by developing new HPC technology, exploiting synergies with other domains, providing advanced facilities, educating its workforce and promoting innovative use of HPC.

As the HPC landscape continues to change, the economies which adapt the fastest will be the ones that will most likely reap the greatest benefits. In this landscape, ANSYS wants to play a leading role and has the commitment, expertise and support from key partners like Cray, DELL EMC, Fujitsu, HPE, Intel, Lenovo, NVIDIA and others to ensure that customers' return on investment in HPC is maximised today and into the future.



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In 2018 PRACE will organise
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**HPC for Innovation: When
Science Meets Industry**
29–31 May 2018
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www.prace-ri.eu

Partnership for Advanced Computing in Europe



High-performance computing can create new opportunities

Alison Kennedy of the STFC Hartree Centre shares the benefits of high-performance computing and how it can be utilised to make the UK more competitive

Previously known as parallel computing, high-performance computing (HPC) involves using a computer system with many processors to undertake a specific activity, by running tasks in parallel rather than serially. Sometimes referred to as supercomputing, HPC is relatively new, but has been traditionally used mainly by scientists. However, organisations such as the Science and Technology Facilities Council's (STFC) Hartree Centre are working with companies to make the technology more accessible to a wider range of people. As technology develops, more people are using computer systems such as laptops and iPads with several different processors and are therefore more aware of the potential for speeding up everyday tasks by using more powerful computing devices. As technology evolves it's important for its users to evolve with it and develop the skills needed to use these novel technologies effectively.

Here, Open Access Government Editor Laura Evans chats with Alison Kennedy, Director of the Hartree Centre to find out why the UK should be taking full advantage of HPC, and why it's important to ensure that more people are trained to use these supercomputers.

What is HPC's role in the UK's digital revolution?

There are a few ways that HPC is used in the UK. One of the more traditional ways involves using a computer to build complex models and virtual simulations that allow you to explore some of the challenges we face today. This enables you to undertake certain areas of research in a more effective way, rather than doing experiments or observations over a longer period of time. Climate change, for example, takes place over thousands of millions of years, whereas a computer model would enable you to compare historical data to live measurements, allowing you to look forward,

identify patterns and make predictions about what's likely to happen in the future. HPC means that we can investigate some of the big challenges that the UK faces socially and economically, identifying new, industrially-relevant applications.

How beneficial is it to the UK and how should it be utilised?

Primarily, HPC is used to help make the UK more globally competitive, both in our academic research and in creating opportunities for industry. For example, in product development, there is a drive to reduce development and manufacturing costs, testing to make products more reliable and reducing the environmental impact. HPC can be applied in all of these areas to help explore options for businesses.

On the research side of things, HPC has been used for key science projects, such as in the discovery of the Higgs Boson, as well as in a number of environmental challenges, like predicting earthquakes. It enables you to build models and predict when things are likely to happen in the future. Another benefit is being able to use computers to analyse very large amounts of data that you wouldn't be able to analyse using traditional methods.

What impact can HPC have on key challenges such as climate change?

HPC opens up a different area for discovery. Scientists will develop a theory about what could happen, but HPC allows you to run through a large number of different scenarios to work out which ones are most likely to happen. It means that you don't have to wait; you can try to foresee ahead. Predicting weather forecasts, climate change, earthquakes are the big environmental applications. However, you can also look at the spread of disease and the resistance to antibiotics. HPC allows



you to use your existing data to try to bring together a number of different pieces of information and use the computer to integrate that data while producing a model for what is likely to occur, providing valuable insight.

What role does HPC play within research and innovation?

It enables 2 things. It opens up some areas of research we couldn't previously look at; for example, there is some work that is being done on molecules, atoms and neurons etc... Some items of interest are too small to be investigated experimentally, but they can be examined theoretically on the computer. There is some work in fields like astronomy, where HPC has played a part in discovering new planets and new stars. The computer simulations are even more advanced for what can actually be seen from the new telescopes, but they can identify meaningful patterns in existing data and measurements to make sure the telescopes are focussed to where they think the interesting things will be.

New materials are particularly big as well because it's very expensive to experiment with every possible combination. Scientists try to predict what is likely to work well together. HPC is used to cut down the experimental space and try to get some ideas of which materials are

going to be the most promising areas to be investigated in academic or industrial research. Then, hopefully, you can get results faster.

Where do you hope HPC to go in the future?

There are several things that we are hoping to achieve at the Hartree Centre. One of them is to continue to make HPC more accessible for a range of new industries because it is clearly an important technology. But at the moment the barriers to using it can be quite challenging because people typically will need to have specific programming skills and will need to be comfortable working with things like Linux which is the operating system used by big computers.

There are a lot of areas where new packages, programming packages or languages can be used to make it easier. One of the big fields which is currently taking advantage of HPC is the life sciences sector. These people do not tend to come from a computing background, so we're looking at where the challenges are and what can be put in place to make it easier for a wider range of people to access the technology.

At the Hartree Centre we're primarily working with groups of companies to try to identify common challenges across sectors. Where companies say they experience a barrier to the UK being competitive or if



Image: © @revorpalin2015/palimimages

Alison Kennedy, Director of the Hartree Centre

something stops them from developing a new product we'll work with them and look at what research is being done in the UK and how it can be applied to their organisation. We'll work out how the research can be used in combination with our computers and our expertise to deliver a proof of technology or a proof of concept solution. We'll then go back to the companies and work out in more detail exactly how it can be used to solve their particular problems

What are the key challenges that come with novel technologies such as HPC?

One of them clearly is education and training, because the technology develops very quickly. For example, we essentially need a new computer every 3 or 4 years. This means you need to have people in place who can understand how to use the latest technology. Most companies are keen to take advantage of HPC, but they can't afford to have large numbers of people who need to learn how to use new systems that often. It's about getting the balance between identifying who are the earlier adopters who would benefit most from it and supporting them.

It's important to highlight the challenges in the UK when it comes to developing the skill sets we need. The computers themselves are just tools and what we need is a skilled population who understands both the science and the technology. Traditionally, HPC has been portrayed as big computers which are difficult to use. That's partly true, but on the other side of things we really should be trying to get across the great potential this tool has for driving economic and social change in the UK. ■

Alison Kennedy

Director of the Hartree Centre

Science and Technology Facilities Council's (STFC)

www.hartree.stfc.ac.uk

[www.twitter.com/HartreeCentre](https://twitter.com/HartreeCentre)

[www.twitter.com/STFC_Matters](https://twitter.com/STFC_Matters)

Blockchain provides many opportunities for government

The European Union Agency for Network and Information Security (ENISA) explains what Blockchain is and how it is revolutionising the public sector

As more and more services are offered by governments in electronic format, the sector has to continually evolve into the modern era. Blockchain is considered one technology that could revolutionise many sectors, one of which could be the public government sector. This technology has many opportunities and challenges, which are not very well known. The EU¹ is setting up a new Blockchain observatory to monitor and encourage the use of the technology. The European Union Agency for Network and Information Security (ENISA) as part of its cyber protection of critical sectors, more specifically finance sector, has been advised to give an initial overview of the cyber challenges in the technology.

What is Blockchain

Distributed ledger technology, or commonly known as Blockchain, is a distributed peer-to-peer network in which all nodes could have a copy of the ledger. The transactions are added to the ledger through a consensus agreed between all participants in the network. Consensus is the way a given transaction is proved valid and accepted to the ledger and all transactions are recorded in the ledger without the possibility to be modified at a later stage. This is also due to the fact that every transaction is tied cryptographically to the previous transaction. This way there is continuation and traceability of the transactions. One unique feature of the Blockchain is that information could only be added to the ledger.

The distributed ledger allows participants to use smart contracts². Smart contracts are essentially actions that could be triggered after a certain event has occurred. They allow participants to verify that counterparties have fulfilled their obligations and provide for an accelerated, automated, settlement once the required conditions have been met (such as a payment or asset transfer).

The distributed ledger also provides enhanced transaction security and privacy. The transactions in the ledger are signed and/or encrypted by a public key. The private key associated with that public key is only available to the owner.

What is very interesting for governmental organisations is the use of permissioned ledgers. This type of ledgers operates as a “members club”. Participants in this type of ledger could be allowed only after approval of the members. Also, if encryption is enabled in the ledger, visibility inside the ledger is not available for the outside world.

Opportunities for governments

Trust

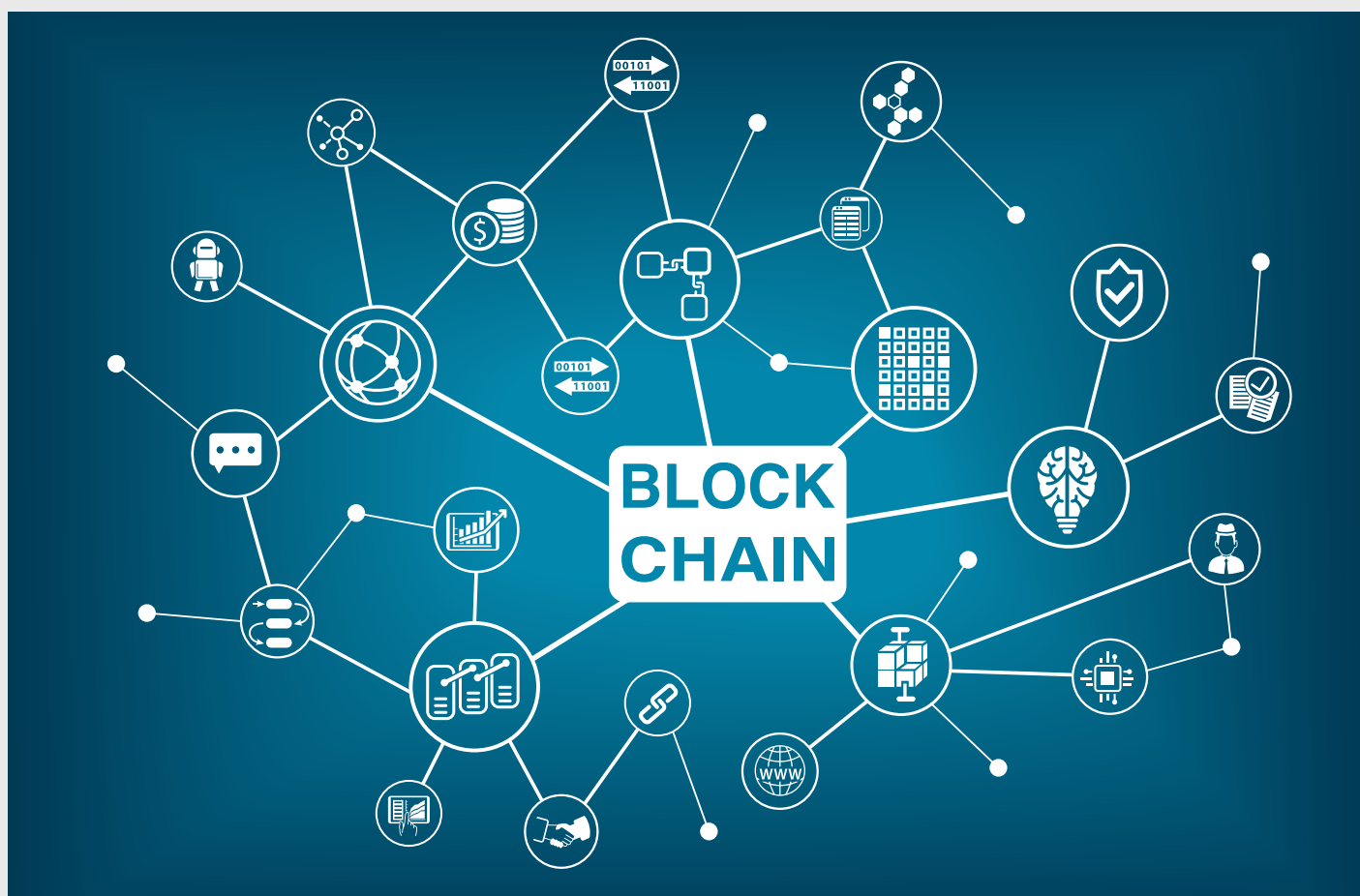
Traditionally, in order to make a transaction one needed to rely on trusted third party to provide ownership verification. With the distributed ledger, if one could provide a signature which is associated with a given asset, then this is sufficient.

Traceability

Since in the distributed ledger one transaction is tied to the previous it is possibility to trace the ownership of an asset from the beginning of the system. This way it would be very easy to verify if a painting, for instance, is original or not.

Privacy

Without a public information as to whom a given key belongs to, it is virtually impossible to determine who the owner is. If the transaction is also encrypted it would be only visible to the participants involved, and not to the general public. This does not prohibit the use of a know-your-client (KYC) systems, where one could have a match between identity and keys.



Challenges coming out of the technology

Due to its nature key management becomes paramount for the operating of the assets on the Blockchain. Since keys could be copied from a machine without leaving a trace, the owner might not even realise that key have been compromised until it is too late.

Consensus hijack is another challenge that could potentially render the Blockchain system unusable. Depending on the case and where consensus is formed through majority, taking control of a large enough portion of participants could allow an attacker to tamper the validation process. This accepting fraudulent transactions – like double spending an amount.

A key challenge is also denial of service to the system. This could be done if sufficient participants in a system try to add bogus transactions. Since time and computing power are required for the validation of a certain transaction, wasting these resources on bogus transactions, could block the processing of legitimate ones.

Smart contracts are essentially code written by people. Based on previous experience written code could have bugs and make actions which are not intended. Since

transactions once accepted to the ledger are irreversible, this could lead to potential problems. In addition, based on the fact that smart contracts are code, this could potentially mean that one could store malware on the system.

Another key challenge is also that the current anti-money laundering/ anti-fraud tools are not working in Blockchain system. Though it might be possible to identify who owns a given key, it is not possible to block transactions in advance.

You may find more information about these and other challenges on ENISA [website](https://ec.europa.eu/digital-single-market/en/news/pre-information-notice-eu-blockchain-observatory-forum).

1 <https://ec.europa.eu/digital-single-market/en/news/pre-information-notice-eu-blockchain-observatory-forum>

2 Szabo, Nick. "The idea of smart contracts, 1 997." (1997).

European Union Agency for Network and Information Security (ENISA) –
The EU Cyber Security Agency
www.enisa.europa.eu
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Outsourced IT fail: Why government must use the cloud

Alistair Smith, Government and Public Sector lead, Contino outlines why moving to the cloud could help government departments ditch toxic vendor relationships

I've spent the last few years working on projects across a number of public sector organisations and have seen many of them hamstrung by legacy vendor relationships, typically with the large outsourcers. As a recent [computing.co.uk](https://www.computing.co.uk) article has it: "[w]ith Capgemini and Accenture again signed in to long-term deals at HMRC, the tax collector can now celebrate 22 years of outsourced IT failure".

Due to long (read: costly) procurement processes, an inability to hire enabled staff, and low risk appetites, no doubt it made sense at the time to outsource technical responsibility to third parties, and stick with them over the years. But as the technological landscape has shifted, so have the requirements – for infrastructure automation, configuration management, frequent software deployments and DevOps-style team structures – and these legacy vendors are simply no longer suitable.

As a result of legacy relationships, public sector teams can be distanced from their own platforms, unable to leverage the benefits of owning their own capabilities, such as swift server provisioning and frequent application deployments. Instead, they're forced to shell out whatever price their third party demands for routine changes to their platform: "You want to change your VPN configuration? Oooh, that'll be £15k, thanks."

A public sector department that is locked into an expensive contract with an outdated vendor that is delivering in accordance with outdated delivery models represents incredibly poor value for money for the taxpayer, and can severely impact the effectiveness of the good work done in government by limiting how that value reaches the consumer.

The taxpayer is essentially subsidising large consultancies for the privilege of keeping their government

departments stuck in inefficient modes of working. I've seen forward-thinking teams within the government then have to innovate around the dominant vendor, annexing tiny portions of their territory in an attempt to get things done quicker.

The cloud as an opportunity to revisit your relationships

But migrating to the cloud – besides the obvious up-front benefits of improved visibility, agility and scalability – is an opportunity to leave behind outdated, sour, or potentially toxic vendor relations and to 'bring back home' some core technological competencies that historically may have been outsourced or managed by third parties.

Undertaking a digital transformation programme brings with it the opportunity to bring some of these capabilities back in-house and transform the way that services are delivered: pick a low-risk application or service and put together a cross-functional team that can leverage the power of ubiquitous APIs: think automated infrastructure provisioning, developer enablement, rapid software prototyping and iteration, and build/test/deploy automation. Begin to seed this knowledge throughout the organisation and change is already underway.

Using this kind of transformational approach can be a catalyst for the organisational changes that must necessarily accompany technical ones, including which third parties you engage with and why. While of course there may be contractual lock-in, sometimes revisiting a relationship from a new standpoint can bring about discussion that is mutually beneficial and results in a more focused and productive service.

While there may initially be an internal skills gap, an upfront upskilling program can mean that time-to-value



is reduced. As well as this, some early assistance with common patterns and best-practices tends to help organisations avoid common pitfalls when working with cloud platforms and modern software delivery practices for the first time.

The principal drivers of cloud adoption – increased organisational agility and simultaneous potential cost savings – are incredibly compelling. Despite this, as well as the government's Cloud First policy, security concerns still linger.

However, with appropriate governance and controls in place, and assurance that cloud adoption does not necessarily imply a "wild west" security model, public sector organisations are increasingly empowered to shed legacy technologies and practices, and move towards more modern ideals, assured by appropriate compliance controls.

Controls intrinsic to cloud platforms can, when correctly configured, provide deep and valuable visibility – building on this with in-platform software solutions allows organisations to improve rather than reduce their workload and security visibility.

Over the last two years we've seen the traditionally risk-averse financial services industry embrace public cloud, with this happening slowly at first but now gaining huge momentum. Parallel to this, the public sector has also been waking up to these potential wins, and we're now seeing significant pace in this market sector as well.

The government must take the opportunity to maximise the value of the cloud by using it as a springboard to new ways of working internally, as well as externally, as they increasingly look for transformation partners that are able to impart the skills and mind-sets to allow government departments to own their own capability, rather than relying on an old guard that can only ever provide more of the same. ■

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Government and Public Sector Lead

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Building success at the Agile Business Conference

Mary Henson from the Agile Business Consortium highlights how the Agile Business Conference on the 4 & 5 October aims to support businesses at an unpredictable time

As the UK comes to terms with the uncertainties arising from Brexit and a hung parliament, the focus of this year's Agile Business Conference will be building success during unpredictable times.

Hosted by Daniel Thornton, Programme Director at the Institute for Government, the first day of the event will feature keynote addresses from experts including Chris Roebuck, Visiting Professor of Transformational Leadership at Cass Business School London, and Dr Patrick Dixon, ranked as one of today's 20 most influential business thinkers (Thinkers 50-Awards).

"Agile has been shown to be a powerful tool for business transformation whether in the public or private sector. These presentations by some of the world's leading international business thinkers will give delegates the opportunity to learn more about the latest developments in Agile, how it has been successfully implemented and the lessons that can be drawn."

The Conference, which takes place in London on the 4 & 5 October, is being organised by the Agile Business Consortium, the not-for-profit body that pioneered Agile business thinking some 20 years ago. The Consortium continues to be at the forefront of Agile as it expands from its IT and project management origins to enable enterprise-wide Business Agility.

Image: © Tom Hampson, Visual Eye Creative



Professor Roebuck, who has been a regular on the HR Most Influential Thinkers list since 2010, will reveal how to get the best from your people – including the role of emotion and creating a 'we not me' culture – and how to focus that energy on delivering organisational success so that it could deliver 10%+ on the bottom line for virtually no cost. Dr Dixon will examine how global trends are set to transform retail markets, whether in terms of demographics, Agile packaging, niche marketing, faster delivery or sustainability. Companies that correctly identify and respond to these trends will, he says, be able to delight customers with small changes that have a huge impact at little cost.

Other talks will cover some of the many ways using Agile techniques can help organisations with issues as

diverse as better budgeting, managing risk and developing digital services.

Daniel Thornton said: "Agile has been shown to be a powerful tool for business transformation whether in the public or private sector. These presentations by some of the world's leading international business thinkers will give delegates the opportunity to learn more about the latest developments in Agile, how it has been successfully implemented and the lessons that can be drawn."

Agile Business Conference: day two

The second day of the Conference will feature a diverse programme of collaborative workshops and roundtables to support further learning around three main themes: Transformation and Leadership, People and Culture,

Image: © Tom Hampson, Visual Eye Creative



Image: © Tom Hampson, Visual Eye Creative

and Digital Services. The keynote speakers from day one will attend and facilitate this work.

“The Consortium continues to be at the forefront of Agile as it expands from its IT and project management origins to enable enterprise-wide Business Agility.”

Mary Henson, Chief Executive of the Agile Business Consortium, said: “The Agile Business Conference provides a single forum for everyone interested in the application of Agile, or moving towards an Agile way of working. It is a unique gathering of influential Agile practitioners and leaders, interested in learning more about how they can help their organisations thrive in an increasingly uncertain world. The programme of hands-on workshops will guarantee attendees a full day of

interaction with Agile experts and thought leaders, and help prepare them for success in an unpredictable world.”

For full details about the Agile Business Conference 2017 or to book a place, visit www.agileconference.org.



Mary Henson
CEO

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Success with Agile in Unpredictable Times

London, 4 & 5 October 2017

The Agile Business Conference 2017 is a major, two-day annual event which provides a single forum for everyone interested in the application of Agile, or moving towards an Agile way of working.

“There are a number of different approaches that deal with elements of what organisations need to do if they are to respond successfully to unpredictable events. However, Agile is the only model I have seen that actually takes an holistic approach, encompassing the whole organisational environment.”

Prof Chris Roebuck



Conference Host

Daniel Thornton - Programme Director, Institute for Government

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Author “The Little Book of Beyond Budgeting”

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The rise of data and its impact on government IT departments

Joe Kim, EVP, Engineering & Global CTO at SolarWinds, explores how government IT departments can utilise the large amounts of data they collect effectively

The past few decades have seen a digital revolution across the globe. Breakthroughs in technology have transformed society and day-to-day life for millions. The Internet of Things (IoT) and the rise of connected devices have been at the centre of this change, and their numbers and applications continue to grow.

However, one of the most astonishing developments of this revolution is the volume of data that has been, and continues to be, created. It's unclear just how much data there is in the world right now, but in 2013, there was about [4.4 zettabytes of data](#) in total. With one zettabyte being equivalent to a trillion gigabytes, this was already a huge amount. What's scary is that from [today until 2020](#), the digital universe is predicted to double every 2 years.

As always, it's up to IT professionals to manage and analyse this ever-growing magnitude of data. This places a huge strain on IT departments, particularly in organisations that deal with exceptionally large amounts of data, such as the government. After years of seeing the amount of data rise, it's only now that government IT professionals are realising they need to change their data-mining methodology to better handle the big data challenge more effectively.

New [SolarWinds research](#) has found that 95% of government organisations have adopted hybrid IT. So when applying these new data mining strategies, the first thing government IT professionals need to think about is adopting an approach that is ideal for a hybrid cloud environment. At [SolarWinds](#), our advice is to implement automated and intelligent decision-making that's driven by predictive analytics, this not only helps with data mining in a hybrid environment, but also improves the efficiency of the network.

Changing the approach

Before the amount of stored data skyrocketed to its current, unimaginable levels, data analysis was largely a matter of manual labour – a task that could be accomplished by data scientists diving into the data to retrieve vital information. However, the speed at which data is now being created, combined with IoT, connected devices, and hybrid cloud environments, means this traditional approach would be a near-impossible task for even a small business today, let alone a government organisation.

In a government organisation, data will not only live in numerous departmental silos, but will also be scattered across multiple IT environments, making it even harder for IT departments to keep track of. With the data hidden across the organisation, traditional data mining approaches also make it difficult to identify insights within the data, and even harder to use these insights to create a consistent and flawless network performance.

Tools need to be implemented to make it easier for government IT professionals to monitor and analyse data that lives both on-premises and across multiple clouds. Having this cross-stack view of IT data can help the IT team compare disparate metrics and events across hybrid infrastructure, identify patterns and the root of problems, and analyse historical data to help pinpoint the causes of system behaviour.

What's coming next?

The best way for government IT organisations to effectively identify data patterns and use that insight to predict and prevent potential network issues is through pairing predictive analysis with automated data mining. Predictive analytics allow IT professionals to foretell the future states of systems by automatically



analysing and acting on past trends. Historical performance issues can be assessed alongside current environments, which teaches the network to “learn” from prior incidents and avert future issues.

The idea behind predictive analysis is to give network admins more time to jump on a problem by alerting them to a potential issue, such as disk space running out or a patch failing upon installation, before it actually occurs. The system will be able to use the knowledge of past experiences and performance issues and apply it to the present situation to avoid a network slowdown or downtime. By comparing both historical and recent data, predictive analytics can help IT professionals make informed predictions about the future.

Take it to the next level

Government IT professionals could even take things a step further and incorporate prescriptive analytics and machine learning into their data analysis mix as well. While predictive analytics is needed to highlight opportunities and possible risks, prescriptive analytics and machine learning can go to the next level and provide recommendations to prevent problems, such

as intrusions, before they occur. Prescriptive analytics will allow IT organisations to overcome threats and react appropriately to suspicious behaviour by establishing what “normal” network activity looks like.

Government IT professionals need to tackle the big data challenge head on before they get too hard to manage. Implementing sophisticated and modern approaches to data mining such as predictive and prescriptive analysis, along with machine learning, can help prevent potential issues before they occur and keep the network running smoothly. All of this will be invaluable for government IT professionals who, without a doubt, will see the level of data they deal with continue to rise. ■

Joe Kim
EVP, Engineering & Global CTO

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Bridging the digital skills gap: What can the government do?

Civica Digital Managing Director, Chris Doutney explores how the digital skills gap can be tackled and addresses some of the challenges

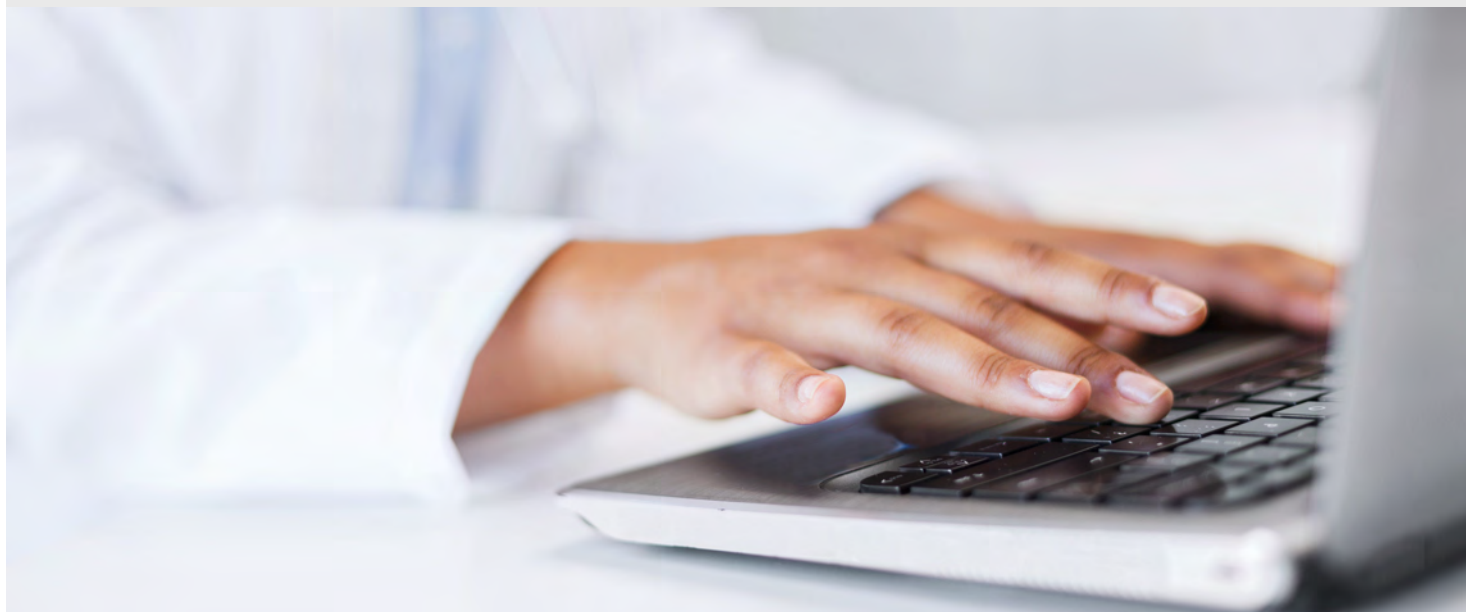
In a recent report, the National Audit Office (NAO) warned that government department's face being unable to take advantage of the opportunities of digital transformation. The report identified 3 main gaps in our civil service capabilities – commercial, project delivery and digital skills. But what can be done now to address these shortfalls?

Under pressure

The combination of increased expectations from citizens and pressure to make greater savings has created significant pressure on the civil service. There's no doubt that the shift to digital has been a real success story,

leading to a wave of transformation programmes across departments, but it's also led to an increased demand for scarce skills to deliver this service transformation.

The 'Capability in the civil service' report highlights a key challenge for continuing the pace of digital transformation. Over the last decade, there has been a 26% reduction in the number of civil servants, despite pressure to deliver increasingly complex and evolving solutions. The report also estimates that the civil service will need an additional 2,000 people in digital roles by 2022 – with the Government Digital Service estimating the figure to be even greater.



Barriers to success

There's an almost 'perfect storm' brewing around the evolution of digital in government service delivery. There will be a continued reduction in budgets, putting further pressure on overall civil service numbers over the next 5 years. Then there are the combined factors of quickly resourcing the Department for Exiting the European Union, increasing numbers at the DTI and handling reform to tax legislation (IR35) – which may make the civil service a less attractive option for private contractors. There is also a drive to bring government IT jobs back in-house, but this takes time and risks limiting the talent pool available.

A lack of understanding?

The NAO report highlighted the calls for 'greater urgency' from government and suggests that it doesn't have sufficient understanding of how the private sector can supply the skills it lacks. Transformation projects need people with specialist skills and real-world experience, who are often rare and in-demand. And we don't just need technical skills and experience. Effective service transformation programmes require an understanding of people, business processes and the process of change itself.

We're all digital

The real answer to the challenge is that the civil service needs to maintain a collaborative approach with the private sector to access the skills and resources it needs for continued digital change.

In parallel, we need a change in mindset where we see people as either 'digital' or 'non-digital.' We are all digital. A digital divide within teams will create duplication and inefficiency; so employees should be encouraged to further embrace digital. Government departments need to continue to look to private sector suppliers to assist the process of cross-skilling to help civil servants embrace approaches such as Agile, DevOps and Cloud.

Continuous evolution

In the longer-term, we all need to embrace continuous change to deliver effective service transformation. What we see as cutting-edge digital skills today will rapidly evolve into something even bigger and better. But by working in partnership, we can continually expand and adapt our skillsets to suit the requirements of our evolving landscape. This will not only enable our teams and organisations to fully harness future digital opportunities, but also deliver better outcomes and more efficient government services. ■

Chris Doutney
Managing Director

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[www.twitter.com/CivicaUK](https://twitter.com/CivicaUK)

Why local government should embrace technology

Andrew Cowling at Fujitsu Scanners outlines how local government could benefit from document management for efficiency gains and a reduction in costs

Local government bodies are under growing pressure as they are increasingly being faced with challenges that question the current status quo; demands for instant access to information online such as public records, freedom of information legislation, heightened security, compliance, and regulations are all areas that raise the need and desire for more efficient ways of working. Indeed, the upcoming GDPR that becomes law on the 25th of May next year poses several challenges, not least the ability to be compliant with stricter data protection rules but also to be able to prove it in a court of law.

Outdated, paper-based processes are draining departments of valuable time and money, thereby reducing the quality of public services and making having a controlled retention policy tough, threatening the privacy, security, and ultimately the ability to provide complete transparency or in the case of GDPR erasure and proof thereof.

Document management

Document management enables the demands for higher productivity and improved service delivery to be met at a significantly reduced cost, both in terms of money and time. Capturing, routing, sharing and storing information effectively are simultaneously driving sustainable performance improvements and providing significant cost reductions.



Technology is seen as a catalyst for change, not only will the service to the public be increased but embracing digital transformation will also help create and retain a more efficient and motivated workforce who are enabled for mobile working, for enhanced collaboration and ultimately seeing a shift in man hours from admin related tasks to those of higher perceived value to the overall cause.

With the benefits and rapid return on the investment, ECM deployments can provide core systems that will allow public sector organisations to tackle the challenges facing the industry in the coming years.

Find out more about how Fujitsu document scanners can help support local government bodies in adopting or developing their document management capabilities by contacting us at scannersales@uk.fujitsu.com.

David Taylor, a Senior Information Governance Officer commented – “It’s

not just the removal of the manual file management processes or the ability to access the files wherever we are. It’s the all-round capability to manage the whole response process from request to disclosure and beyond from one system. Fujitsu’s scanner hardware is integral to the whole solution enabling all documents to be digitised, reviewed, redacted, compiled and released electronically. We now respond to almost 95% of all requests electronically compared to approximately 55% just two years prior. Response times have fallen from an average of 12 days per request to under 8 and still falling.”

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Measuring the success of digital services in local government

John McMahon, Product Director at IEG4 talks about the transformation of public sector digital services and explains the Digital Offset Effect

"For every action, there is an equal and opposite reaction." Isaac Newton penned his Third Law in the year 1687, and it's fair to say he was not considering its relevance to digital transformation which would happen some 330 years later. But such is the use-case agnostic nature of this law that it very much holds true in the case of digital transformation in the public sector today.

Why the destination is as important as the journey

At a rudimentary level, the tangible relationship is that for every digital service introduced to reduce telephone calls and improve automation in local government, there should be an equal reduction in calls and operational costs. Thinking about this makes me question the nature of commonly used terms in digital transformation. While well-known and understood, both of the most common terms are about the journey of digital transformation without measuring the effectiveness or the outcome.

So what should be considered, the destination or end game measure for digital transformation? Is a utopian 100% digital model so fantastical it shouldn't be considered a reality?

One could argue that digital transformation is a persistent activity without end. This is true in terms of continually improving the user experience, take up levels or saturation and conversion to actions, but not in terms of what technically can be done to make the entirety of a process digitally enabled.

Digital ubiquity versus digital transformation

Digital ubiquity in the public sector is where all contacts and transactions are handled entirely through the digital

medium. Now, knowing what the goal is – how does one measure how close one is to achieving it; and whether the action from the introduction of digital services has had the appropriate reaction? There needs to be a new term to measure the level of reaction to digital transformation. Digital transformation is largely down to reducing operational costs; so it could make sense to use the financial term 'offset', as the crux of this novel effect.

The Digital Offset Effect (DOE)

The Digital Offset Effect's basis is that for every digital service introduced there should be an equal ratio of reduced activities through alternative channels. Therefore, if a council were to make every service it offered such as paying council tax and benefit applications a digitally complete one, it would remove all alternative channels of access.

Whilst certain areas in the public sector, such as social care, mean that it may not be possible to make every service digital, the principle holds true for those that can be digitised. Therefore, the de facto DOE measurement would be 100%. This harks back to Newton's 1:1 action and reaction ratio.

When reviewing and creating digital transformation business cases, DOE should be measured to establish the efficacy of the new digital service in achieving its intended goal. Clearly, unless alternative channels are removed, not all digital services will achieve the gold standard of 100% DOE. Not achieving this rate of success may also be a consequence of the fact that not all services which are digital are designed very well. Not just in terms of how they look (e.g. they may not be mobile device friendly) but also in terms of the user experience (e.g. they may suffer from slow registration processes).

Human nature is like water

The American poet, Wallace Stevens, said: “Human nature is like water. It takes the shape of its container.” I like to think of service delivery like this. Humans will choose the quickest and simplest way to flow through a process such as applying for benefits or paying for their council tax. If that route is not the digital channel because of a poor user interface or experience, then invariably DOE will be sub-optimal. So, achieving a DOE of close to 100% is directly proportionate to the effectiveness of the digital service. Thus, it is a barometer for project sponsors and senior managers to understand whether the service is achieving or whether it will achieve the expected return on investment in the business case.

Is digital ubiquity possible?

It is true that a DOE of 100% is difficult to achieve for public sector organisations with a legacy investment in alternative methods of delivery, but it is certainly not impossible. The private sector shows time and time again that in a bid to minimise operational costs, it is possible to innovate on service development to keep a high DOE level over time.

When easyJet launched 21 years ago emblazoned on the side of its first plane was a big, Boeing 737-sized telephone number. With the eCommerce element of the internet at an embryonic stage this was then the primary medium of finding and booking flights. Fast forward to today and there is, almost no ability to contact a human at easyJet, certainly not by telephone. Unlike most websites there is no “contact us” option available either. This has been part of its digital by design strategy. Answering telephones is now simply too costly for a well-oiled digital machine.

Rather than focus on call waiting times and costly phone numbers, the philosophy has been to stop this channel and instead prioritise the provision of web services and mobile applications. This enables customers to access the activities and services they most want to use in the most convenient and user friendly fashion. So, this example shows that if one understands all the transactions and engagements people

wish to carry out with a specific organisation, it is possible to achieve near or total digital ubiquity even from a company that started off with costlier and less user-friendly channels.

What this illustrates is that, where relevant, councils are able to copy best practice in the private sector.

Digital transformation is happening in every sector and the private sector has a huge vested interest to deliver innovative solutions in the interest of minimising operational costs while simultaneously improving customer service.

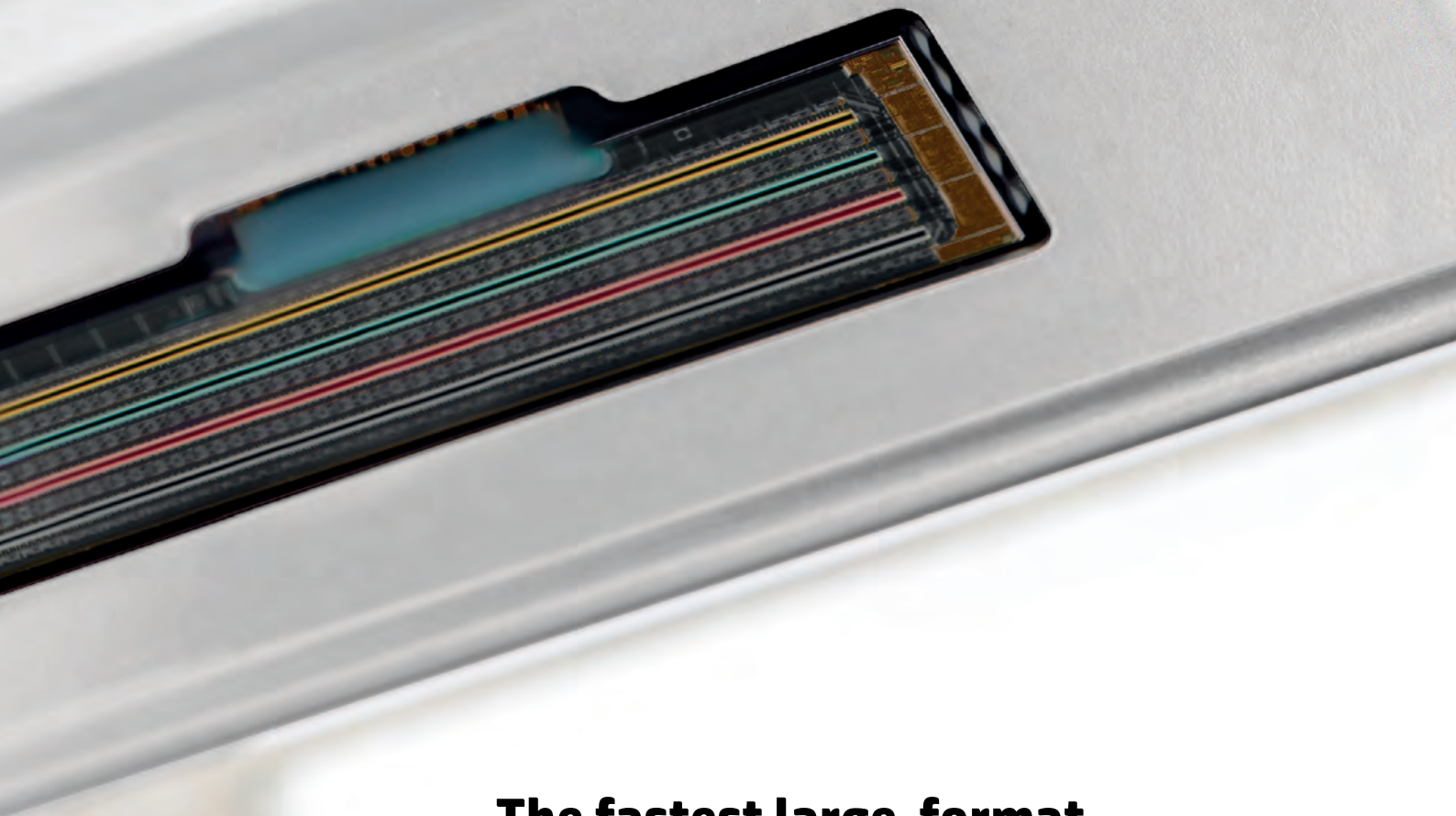
Progress tracking, proactive updates and real-time communication within a single council-wide digital platform are critical to the next generation of public sector services – achieving high DOE and close to digital ubiquity.

Of course, in reality, all of this should be balanced up with the fact that the public sector has significantly more processes than the private sector, as well as a political balancing act to do in terms of a carrot and stick approach to digital. While there remains a service delivery paradox which public sector leaders and politicians are versed in (or should be), digital is about providing better services for citizens, not just alternative ones. The digital channel just happens to be significantly cheaper, and, because it provides a better service, is the one that citizens increasingly want to use.

I’m sure that if an explanation of the Digital Offset Effect were to be provided to Isaac Newton, he would tell you it is a no-brainer – that every action has an equal and opposite reaction. ■

John McMahon
Product Director

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Encouraging the digital workforce of the future

Holly Ellis from the Government Digital Service outlines how they are helping young people develop the key skills needed for a future digital workforce

Our [Civil Service Talent Action Plan](#), sets out our ambition to be “the UK’s most inclusive employer, representative of modern Britain and the public that we serve.”

One of the 5 main themes of the [Government Transformation Strategy](#) is to develop the right skills and culture among our people and leaders.

We want to show that there’s an opportunity for everyone in the Civil Service. It’s only by reaching out beyond our usual audience that we can transform government. We want to attract and retain a diverse and inspired workforce and equip them with the skills they need for the future.

In the digital world, knowledge is a commodity so we need to shift our thinking on how we skill and upskill our future digital workforce. Complex problem-solving, critical thinking, creativity, people management and emotional intelligence will be critical skills to possess in 2020.

We’re reaching out across schools, colleges and universities. We manage cross government emerging talent schemes aimed at developing the digital specialists of the future.

Graduate programme

The graduate programme – the [Digital, Data and Technology Fast Stream](#) currently has 150 graduates working right across government on large scale and ambitious transformation projects. It’s encouraging to know that the programme attracted its highest number of applicants in 2016 and was ranked 12 in the Top 50 Social Mobility Employer Index in June 2017. Applications for the 2018 scheme open in September 2017.



Apprenticeship programme

The apprenticeship programme [Fast Track](#) – aimed at non-graduates offers opportunities across a wide range of roles within digital, data and technology, with a direct, practical route into a digital career. The 2017 Fast Track attracted a record number of 8570 applicants, this is an encouraging step in an increasingly competitive apprenticeship market and digital sector.

Our flagship skills programme the [GDS Academy](#) is partnering with universities and currently has students from Leeds and Manchester universities attending its course and experiencing what a digital career in government might be like. Last year, following a successful 8 week internship partnership with University of Leeds the Academy received a nomination for a [National Undergraduate Employability Awards 2017](#) in the category ‘Best Collaboration between a University and Employer’.

We’re working across government departments, with tech industry and charities to ensure we have a joined up understanding of the people, behaviours and skills that we want to develop.



It doesn't stop once we've successfully attracted, recruited and on boarded. We then need to figure out how to keep our teams engaged and inspired, working towards a clear career pathway with transparent and fair pay, reward and expectations across government.

We have been working together with departments and communities to create a single common structure of digital job roles in government.

Immediate benefits include a more visible route for career progression and a better grasp of the huge scale of job opportunities in digital, data and technology across government. We hope this will encourage technical specialists to have a long-term career in government.

What next?

There are few quick fixes for building the skills for the future and so we're working on multiple medium to long-term strategies to attract people into the Civil Service and to better develop the skills of the people we have.

An important part of that is encouraging young people, and those at the start of their careers into our profession so we're working with charities, including [Dragon Hall Trust](#), [the Tinder Foundation](#), [Stemettes](#) and [Codebar](#). We're also working with schools to explore the best ways of [showing young people what it's really like](#) to work in the civil service. We want to support young people on their journey of learning, creating and flourishing in the digital world.

Find out more about the [Digital, Data and Technology profession](#) and [digital career opportunities](#) in government. ■

Holly Ellis

Director of Capability – Digital, Data and Technology Profession

Government Digital Service

<https://digitalpeople.blog.gov.uk/>

[www.twitter.com/gdsteam](https://twitter.com/gdsteam)

OUR MISSION IS “TO PROVIDE GLOBAL LEADERSHIP IN PROMOTING, SUPPORTING AND PROVIDING GUIDANCE AND ACCREDITED PRODUCTS AND SERVICES TO ORGANISATIONS”

User research from ICT2.0, etc

What we learned from ICT 2.0

The UK Government's Digital Service Standard puts user needs first, literally; the first two criteria in the Standard are “understand user needs” and “do ongoing user research”. So it makes sense that our work to design a new course and qualification for people developing digital services using Agile methods, should do the same.

Our journey started at the Government ICT 2.0 Conference last year, where the Agile Business Consortium facilitated a seminar on “creating effective Agile governance for digital service delivery”.

Many of the challenges raised by delegates at the seminar echoed those identified by Daniel Thornton in the editorial to this ebook:

- Governance needs to become less bureaucratic, more flexible and more focused on setting clear goals, delegating decision-making and facilitating cross-programme conversations
- A shared understanding of Agile delivery and digital services needs to be cultivated at all levels, from senior civil servants to ICT developers
- The focus of attention must be on meeting user and business needs, not on the process, and staff need to understand how to select and adapt Agile tools and frameworks flexibly

- People need more support and guidance in how to put the GOV.UK Service Manual into practice

When we reviewed these findings, it seemed clear that there was an educational need that the Agile Business Consortium could help with, and we decided to adapt our widely recognised Agile Project Management (AgilePM®) framework and qualification. This is specifically targeted at digital service development and teaching key elements of the GOV.UK Digital Service Standard and Service Manual.

What we are learning from our alpha programme

Like government digital services, we believe in testing our products with real users, so we've put delegates in both central and local government through a prototype of our new course to find out what works and what doesn't.

We've heard some things we hoped to hear; that the course is engaging and of practical value, that it increases confidence, and that delegates are pleased that the exam will test their knowledge of how their own organisation really works, using language and terms familiar to them.

We've also learned that some of the language we use on the course and in the exams is confusing, and we're working on simplifying things before we launch our beta programme in the summer.

SUPPORTING AND ENABLING BUSINESS AGILITY” BY OFFERING ADVICE,
THROUGH AN INTERNATIONAL NETWORK OF PARTNERS.

Framework for Public Sector Business Agility



Framework for Business Agility: Enabling public sector bodies to develop and embed business agility at any scale – from a single team focused on a single service, to Agile programmes with many teams delivering complex services. All positioned within a continuously dynamic, strategically aligned portfolio.

Agile Culture and Leadership: Delivering genuine empowerment and flexibility within a robust framework of accountability. Inspiring the public to engage with each other and their service users, collaborating to meet the needs of citizens while preserving value for money.

Agile Strategy and Portfolio: Agile business change scaled to the highest level. Ensuring that change strategy remains under continuous review and reflects shifts in the operating environment. Providing a spectrum of coordination and control, from “full-on” Agile enablement at one extreme to a “halfway house” of Agile tolerance at the other. Features include Agile portfolio planning, Agile monitoring and control, active and effective business ownership of initiatives and, where appropriate, Agile budgeting.

Agile Programmes: AgilePgM® is Agile at scale for significant whole-business capability change; embracing Agile and non-Agile projects in a universally applicable Agile framework of governance, coordination and control.

Agile Projects: AgilePM® is a tried, tested and trusted Agile project management approach with more than 60,000 certified practitioners worldwide. For public sector bodies delivering digital services, it is now complemented by a new qualification in AgilePM® and digital services.

Agile Service Evolution: With or without IT enablement or support, business services are at the heart of the way organisations connect with and serve their customers. Agile Service Evolution is an exciting new concept inspired by the pioneering work from UK government digital services and a key element of the Framework for Business Agility.

Agile Product Evolution: For over 20 years, the primary focus of Agile has been software development. Agile Product Evolution will embrace this most popular and critical focus whilst broadening the scope of product evolution to include business products too.

Agile Enablement and Governance: Public sector organisations face a challenging balancing act in adopting business agility, while strengthening public accountability and transparency. We believe the starting point should be governance that engages people with the right knowledge and skills to do the right thing in the right way whilst promoting an environment where truth, trust and transparency is the norm.



AgilePM® and Digital Services



What will the new course allow us to do?

The new AgilePM® and Digital Services course will help organisations to develop a consistent Agile approach, a common language and a skilled workforce (with appropriate accreditation opportunities) for the successful design and delivery of digital services, whether through evolving improvements or step-change transformation.

The Agile Business Consortium has adapted the AgilePM® qualification to explain how its concepts can be easily aligned to the GDS life-cycle and roles, to provide a flexible governance structure to use alongside Scrum, Kanban or any other Agile IT development methodology. The new course will also cover some of the distinctive elements that GDS has injected into Agile discourse, such as “Citizen over Government” and “Assisted Digital”. It will also include the tried and tested concepts of alpha, private beta and public beta within the project lifecycle.

Do we really need a new course?

Yes, absolutely. Although there is some good Agile training available, including our own AgilePM® qualification, none of it focuses on how to apply the Digital Service Standard, and the language used is often different to that in use within government departments.

In response to the special complexity of government, GDS has created the GOV.UK Service Standard and supporting Service Manual, which defines a development lifecycle for digital services (Discovery-Alpha-Beta-Live) and provides a set of design standards and a host of supporting guidance. This has produced

some excellent results in the design of citizen-facing services (e.g. Tax your Vehicle). However, there is often the need to deliver more complex and far-reaching changes through projects and programmes, and this is where challenges emerge. There is currently no Agile method which effectively addresses the Agile development of Digital Services within a project or programme structure.

More broadly, it's clear from the research we've done that government is struggling to adapt the way it leads and manages change to get the most out of the speed and flexibility that Agile promises. As Daniel Thornton from the Institute of Government observes in the editorial, “Agile development involves decision-making which is swift, and as close to the user as possible. This is not how decisions are made in government, with its overlapping layers of control from the centre and within departments and agencies. Public servants need to learn the specialist skills to do this...”

Who is the new course aimed at?

The course is aimed at all those involved in the delivery of digital services to the public, including central government, local government, the NHS, and the private sector organisations that support them with training and consultancy services.

We want the new course to be useful to both delivery teams and the civil servants who support them as change managers, service managers and product owners. For those with a good grasp of Agile methods, we will introduce guidance on elements that might be new, such as user research, user experience design and digital performance analysis.



INNOVATION AND LEARNING OVER THE STATUS QUO.

At the same time, we will cover the fundamentals of Agile culture and delivery as well as demystify Agile jargon for civil servants and others who are new to Agile.

What is Agile anyway?

Agile is built on simple principles which were radical when they first emerged 20 years ago, and still remain relevant today. Yet they are challenging to put into practice in large, complex and hierarchical organisations like government departments. These ideas are articulated in many different lists – here's a short one:

Agile is collaborative – we have users, technologists, front-line staff and managers working together, often in the same room, throughout the design and delivery of a new service.

Agile is flexible – we know that requirements will change throughout a project, and welcome the improved understanding of user needs that this change represents... we don't hate "scope creep" but embrace change and aim to make decisions quickly and as close to the problem as possible.

Agile is about people, not technology or other "stuff" – we focus on what users and businesses need, and how the people who deliver services can meet those needs – often, but not always, with the help of technology.

Agile is transparent – we prefer showing models, prototypes and the actual product, rather than producing reports, spreadsheets and presentations. We prefer sharing our challenges to hiding them.

How and when can I get involved?

The course is in alpha at the moment (meaning we're trialling a prototype with real people to see how it works), and we'll be sharing those experiences and launching our public beta programme in May 2017.

If you'd like to participate in the public beta programme and get early access to the new course, please email the Agile Business Consortium info@agilebusiness.org



At the Agile Business Conference 2017 –

Success with Agile in Unpredictable Times, the topics of Digital Services, Transformation and Leadership, and People and Culture will be explored in more detail. The Conference is a major, two-day annual event which provides a single forum for everyone interested in the application of Agile, or moving towards an Agile way of working. This unique gathering of influential Agile practitioners and leaders takes place on Wednesday 4 and Thursday 5 October at etc. venues., 155 Bishopsgate in Central London. To find out more information, or to book tickets please go to our website:

www.agileconference.org

Keep your personal and business data secured with iStorage's encrypted data storage devices

iStorage Limited reveals their new diskAshur range, which consists of ultra-secure hard drives, solid state and desktop drives

iStorage, the award winning and trusted global leader of PIN authenticated, hardware encrypted portable data storage devices, has announced the launch of their new range of USB 3.1 Hard Disk Drives (HDD) and Solid State Drives (SSD). This consists of the diskAshur², diskAshur² SSD, diskAshur PRO², diskAshur PRO² SSD and the diskAshur DT² all of which are designed, developed and assembled in the UK.

"The GDPR, which comes into force on 25th May 2018, compels organisations who process or hold personally identifiable information of EU residents, to implement adequate security measures to protect personal data loss or face tough fines."

The new drives feature Enhanced Dual Generating Encryption (EDGE) technology making them the most secure HDD/SSD and desktop drives currently on the market.

EDGE™ Security Features:

One of the unique and underlying security features of the GDPR compliant diskAshur range is the dedicated hardware based secure microproces-

sor (Common Criteria EAL4+ ready), which employs built-in physical protection mechanisms designed to defend against external tamper, bypass laser attacks and fault injections.

Unlike other solutions, all the drives within this range react to automated hacking attempts by entering the deadlock frozen state, which renders all such attacks as useless.

In plain and simple terms, without the PIN, there's no way in!

With software free set up and operation, the diskAshur range is platform/device independent and works across all operating systems including all versions of MS Windows, macOS, Linux, Android, Chrome, Thin Clients, Zero Clients and embedded systems. In fact, the drives will work on any device with a USB port!

The diskAshur PRO² USB 3.1 portable hard drive is available in a stylish graphite housing and is the ultimate secure data storage device. The diskAshur PRO², diskAshur PRO² SSD portable drives and diskAshur DT² desktop hard drive are designed to be FIPS 140-2 Level 2 and 3, NCSC CPA Foundation Level, Common Criteria and NLNCSA government certified. The diskAshur range consists of the diskAshur² and diskAshur PRO² portable HDDs (both available up to 2TB), diskAshur² SSD and diskAshur PRO² SSD (both available up to 1TB)

and diskAshur DT² desktop hard drive (available up to 8TB).

About iStorage Limited

iStorage is the trusted global leader of award winning PIN authenticated, hardware encrypted data storage devices. Delivering the most innovative products to securely store and protect data to military specified encryption levels; safeguarding valuable business information whilst ensuring compliance to regulations and directives.

About the General Data

Protection Regulation (GDPR)

The European Union will have the power to fine companies €20 million or 4% of their global turnover if they are found to be in breach of the new government legislation. The GDPR, which comes into force on 25th May 2018, compels organisations who process or hold personally identifiable information of EU residents, to implement adequate security measures to protect personal data loss or face tough fines.

iStorage®

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- OS & Platform independent Works on any device with a USB port
- No software or drivers required



CITRIX

Data availability: the building block for digital transformation

Massimo Merlo, VP of EMEA Enterprise and Regional VP of UK&I at Veeam details why data should be at the heart of digital transformation in the public sector

Earlier this year the UK government unveiled its transformation strategy aimed at harnessing digital technology to change the way it does business. Formally known as the [Government Transformation Strategy \(GTS\)](#), it recognises that ‘data acts as the foundation upon which everything else rests’ and that digital transformation has an important role to play in raising productivity and meeting increasing demands on public services. In short, the public sector needs to be in tune with technological change, and the knock-on effect on citizen expectations, security, and public service delivery.

Digital transformation is a key priority for the overwhelming majority of UK businesses according to [recent research](#), with 94% seeing it as a central pillar of their technology roadmap. Clearly, businesses of all shapes, sizes, and sectors are keen to use digital innovation for competitive advantage.

What we constantly remind ourselves of, however, is that to achieve this, we must be able to deliver access to services, data, and applications at any time and from anywhere.

Around 70% of UK businesses acknowledge that data availability and continuous access to services are a vital requirement for digital transformation. Yet, two thirds of senior IT leaders surveyed (66%) felt their efforts to go digital are being hampered by unplanned downtime of services as a result of cyber-attacks, infrastructure failures, network outages, and natural disasters. While many businesses are still ‘planning’ or ‘just beginning’ their transformational journeys, more than two thirds (67%) agree that these initiatives are critical.

Ushering in the fourth industrial revolution

In addition to the GTS, the Chancellor outlined plans

to make £270m available to ‘keep the UK at the forefront of disruptive technologies’, including artificial intelligence and robotics, as part of the Spring Budget. Against a backdrop of political and economic uncertainty, the Chancellor’s proposed investment in innovation and technology was warmly welcomed. With money being pumped into areas such as robotics and artificial intelligence it presents a golden opportunity to forcibly move the UK into the 4th industrial revolution.

However, we have a chicken and egg situation on our hands. True innovation will only be realised if it has the right infrastructure to support it. If the UK is to become the de-facto standard of future-facing technologies, it must go deeper than simply paying lip-service to innovation and consider how technology can truly support it behind-the-scenes. As technology becomes ubiquitous from connected devices to connected services, the pressure increases on the public sector to ensure those services go uninterrupted. Data availability must be at the heart of the digital economy and if the UK is to become data-driven it will require continual access to that data.

Downtime is hampering digital transformation

To be reliable, service levels cannot waiver from continual availability. Immediacy is key in this digital age and the public has zero tolerance for downtime – whether that’s on an application or in their personal lives. The majority (90%) admit that their IT teams cannot deliver the level of service expected by their employees, a shortfall known as the ‘[Availability Gap](#)’. The financial implications of the Availability Gap are huge, costing UK businesses an average of £17.9m every year – potentially costing the economy hundreds of millions of pounds a year when proportioned on a public-sector scale.



The UK economy simply can't afford to haemorrhage hundreds of millions of pounds a year through suffering unplanned downtime. When you consider that the UK's economic position is under global scrutiny post Brexit- with a weakened economy, devalued British pound, and poor national productivity- UK businesses must do better to retain a seat at the top table and ensure they are globally competitive.

Meeting the expectations of an always-on world

It's imperative that business and government leaders ask questions of their digital transformation plans and begin to have different conversations about their existing IT infrastructure. Maintaining availability of data is a relatively easy win with the right technologies in place.

The data outages and system failures that are becoming mainstream news come as UK businesses and bodies remain incapable of meeting employee and end-user expectations for services, applications, and other data to be constantly online. While some businesses are

succeeding in improving their efforts, these increased expectations, combined with an evolving IT landscape, continue to create significant challenges.

“Around 70% of UK businesses acknowledge that data availability and continuous access to services are a vital requirement for digital transformation.”

If the public sector doesn't rise to the challenge, the gulf in class with the commercial sector will become ever greater. The new digital economy dictates that old rules don't apply and businesses of all sizes must ensure they deliver services at any time, from anywhere. Ensuring data availability is an area that is within most businesses capabilities to suitably manage and in 2017 it must move from the 'wish list' to the 'check list'. ■

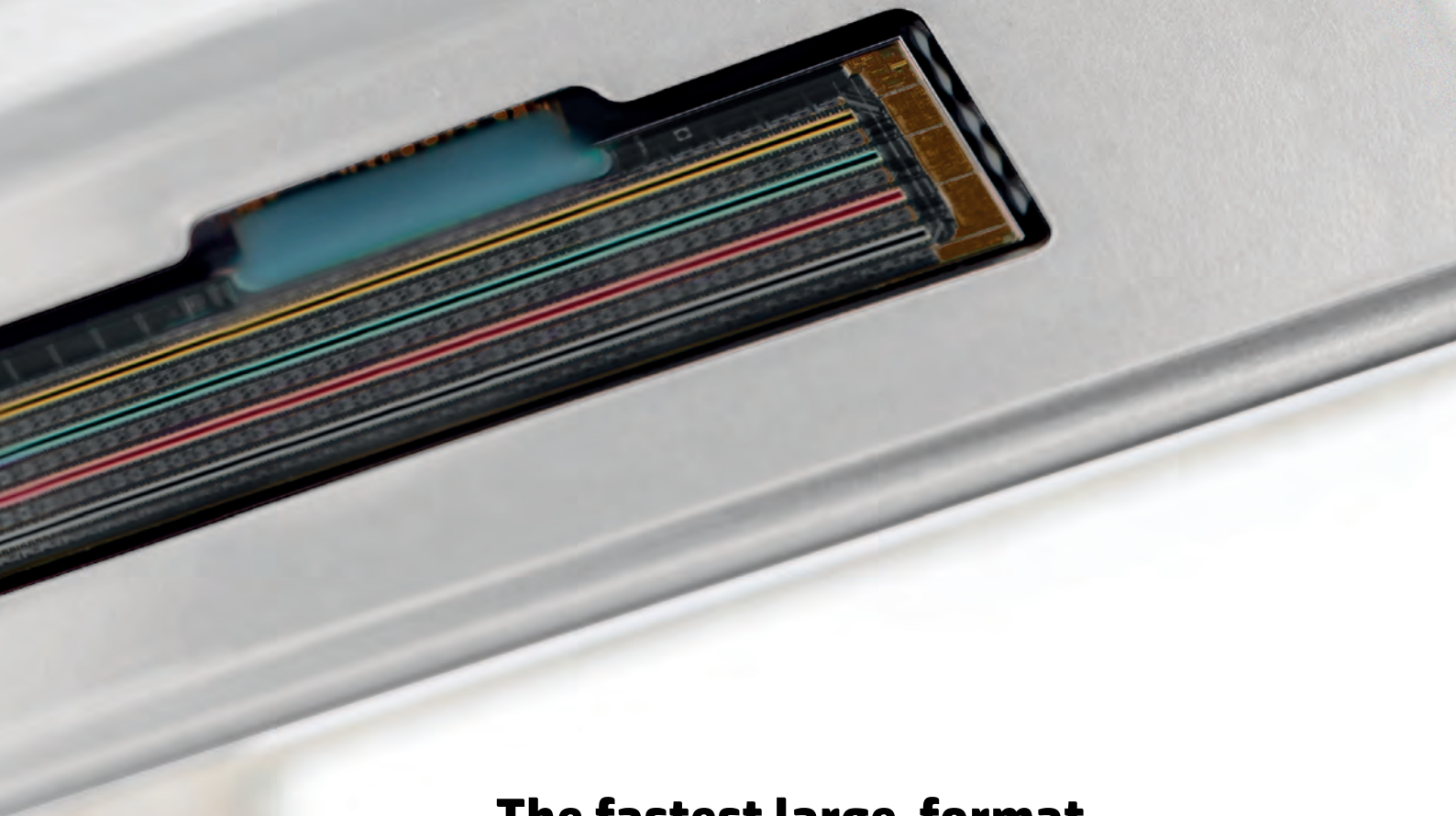
Massimo Merlo

VP of EMEA Enterprise and Regional VP of UK&I

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1. Fastest based on internal HP testing and methodology compared to alternatives for large-format printing of technical documents, GIS maps, and point-of-sale (POS) posters under \$200,000 USD as of March, 2015. Production costs savings based on comparison to a setup consisting of one monochrome LED printer and one colour production printer, both under \$150,000 USD, as of April, 2015. Production costs consist of supplies and service costs, printer energy costs, and operator costs. For testing criteria, see www.hp.com/go/pagewidexlclaims.
2. With a maximum linear speed of 23 meters/minute (75 feet/minute), the HP PageWide XL 8000 Printer is 60% faster than the KIP 9900 printer which, at 14 meters/minute (47 feet/minute), is the fastest rated LED printer as of March, 2015.
3. Using HP SmartStream software compared with using equivalent software programs. For testing criteria, see www.hp.com/go/pagewidexlclaims.

Meeting the Printing needs of the AEC Industry

How new technology enables the production of high-quality prints more efficiently and cost-effectively



Thomas Valjak, EMEA Head of Large Format Printing HP Inc in the Graphics Experience Center in Barcelona, Spain

Repro houses play a critical role in reproducing high-quality technical drawings and other documents for AEC customers. This includes architectural and engineering blueprints and renderings, and folded and finished bid sets containing all the drawings and construction sets needed to complete a project.

Although traditionally a high number of AEC technical documents are produced in black and white, coloured prints are increasingly becoming a pre-requisite. The move into colour can be attributed to the belief that it improves communication, readiness and indirectly saves time and costs throughout the bid, design and construction process.

Eliminating complex workflows

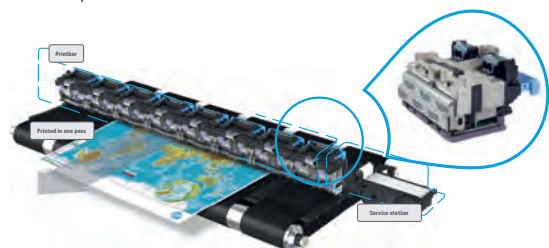
Many repro houses use an LED printer for monochrome print runs and an inkjet printer for colour. Managing both monochrome and colour printing, along with bid sets that consist of a mixture of small format and large format pages, means having to rely on a wide range of printing hardware and software. This has often led to inefficient processes, where costs are greater and workflows can contain an increase in the number of stages needed. As AEC clients face tighter project completion times, repro houses are also under increasing pressure to deliver high-quality short-run print runs with quick turn-around capabilities.

Automation is one of the key factors of a smoother and faster print process. Technology including end-to-end workflow software, combined with peripherals such as on-line folders, makes print management more efficient. Additionally, automatic detection and correction of corrupted PDFs, automatic selection of small and large format pages and on-screen soft-proofing can all help reduce job preparation time by up to 50 per cent. This frees up time to take on more jobs. Easy-to-use workflow software like HP SmartStream can also make a repro house better able to weather workforce turn-over, as it minimises the need to train new workers in complex operations.

When speed matters

Streamlining workflows is one way to speed up turn-around times but increasing the speed of printers is also critical. In 2015 HP was bringing the record-breaking speed of HP's PageWide Technology to large-format printing. HP PageWide Technology uses tens of thousands of tiny nozzles on a stationary print bar rather than a scanning print-head. This results in print speeds of up to 30 A1 pages/minute. Instead of using two separate devices, one printer can be installed for both monochrome and colour, and colour prints can be produced at the same cost as black-and-white. In addition, new graphic applications such as retail temporary posters and maps can be added to the offering.

Based on proven HP Thermal Inkjet technology, HP PageWide print heads are designed to have a long life. The reliable drop ejection process reduces print quality defects from 'nozzle outs'. Automated print head servicing and calibration, including nozzle compensation, ensure consistent operation and minimal service intervention.



HP 841 PageWide XL Printhead module

Costs under control

For print service providers looking to meet the demands of AEC clients, gone are the days of the LED and inkjet printer sitting side-by-side. Both colour and black & white printing will be able to be produced at much lower costs than ever before. This will make it easier to meet clients' increasingly high expectations whilst having a much needed positive effect on the bottom line.

Additional information under [hp.com/go/pagewidexl](https://www.hp.com/go/pagewidexl)

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