OPEN ACCESS GOVERNMENT NORTH AMERICA ANALYSIS

EYE HEALTH PROGRESS AND IMPACT

TO MARK ITS 50-YEAR ANNIVERSARY, THE NATIONAL EYE INSTITUTE (NEI) TAKES STOCK OF ITS PROGRESS IN ADVANCING VISION RESEARCH AND DEVELOPING NEW THERAPIES TO TREAT BLINDING DISEASES

IN THIS ISSUE

Dr Arthur Lupia, at the National Science Foundation in the U.S. provides a compelling glimpse into how supporting social and behavioural science improves the quality of life **Dr David Weinberg** from the Human Placenta Project, a program of the NICHD, details why the human placenta is a short-lived organ, yet has a long-lasting impact **William Leith**, Senior Science Advisor for Earthquake and Geologic Hazards at USGS explains the important aspects of their Earthquake Hazards Program

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Gene expression and Huntington's disease

Naoko Tanese from New York University explores how monitoring gene expression can be used to treat neurodegenerative diseases such as Huntington's.



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





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INTRODUCTION

elcome to the January 2019 edition of North America Analysis. Heading up this publication, the National Eye Institute (NEI) takes stock of its progress in advancing vision research and developing new therapies to treat blinding diseases, to mark its 50-year anniversary.

On the subject of research & innovation, Dr Arthur Lupia, Assistant Director, Directorate for Social, Behavioral, and Economic Sciences (SBE) at the National Science Foundation (NSF) in the U.S. provides a compelling glimpse into how supporting social and behavioural science improves the quality of life.

Another fascinating insight comes from Dr David Weinberg from the Human Placenta Project, a program of the Eunice Kennedy Shriver, National Institute of Child Health and Human Development (NICHD), part of the U.S. National Institutes of Health. In his article, he details why the human placenta is a short-lived organ, yet has a long-lasting impact.

Turning to Canada, the work of The Canadian Space Agency (CSA) in advancing the knowledge of space, through science and using its discoveries to benefit Canadians and all of humanity, is detailed here. Finally, Shawn Yarnes from The Integrated Breeding Platform in Mexico highlights harnessing the genetic diversity of a dynamic crop, cowpea and why it is important today.

I hope that you find this publication insightful. Please do get in touch with me if you have any ideas for compelling content for the future, or perhaps you'd just like to provide your remarks on this edition.

Jonathan Miles Editor





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Eye health progress and impact: Protecting and prolonging vision by research

To mark its 50-year anniversary, the National Eye Institute (NEI) takes stock of its progress in advancing vision research and developing new therapies to treat blinding diseases

The National Eye Institute (NEI) was established by Congress in 1968 with an urgent mission: to protect and prolong vision. At the time, millions of Americans were going blind from common eye diseases and facing isolation and a diminished quality of life.

Over the past 50 years, public investment in vision research has paid remarkable dividends. Research supported by NEI and conducted at medical centres, universities, and other institutions across the country and around the world – as well as in laboratory and clinical settings at NIH – has led to breakthrough discoveries and treatments.

Today, many eye diseases can be treated with sightsaving therapies that stabilise or even reverse vision loss. NEI-supported advances have led to major improvements in the treatment of glaucoma, uveitis, retinopathy of prematurity, and childhood amblyopia. We have more effective treatments and preventive strategies for age-related macular degeneration and diabetic retinopathy. Recent successes in gene therapy and regenerative medicine suggest the future looks even brighter for both rare and common eye diseases.

Basic research has revealed new insights about the structure and function of the eye, which also offers a unique window into the brain. In fact, much of what we know about how the brain works come from studies of the retina. Decades of NEI research on retinal cells has led to fundamental discoveries about how one nerve cell communicates with another, how sets of cells

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Paul A. Sieving, MD, PhD, NEI Director

organise into circuits that process different kinds of sensory information, and how neural tissue develops and organises itself.

People with vision impairment can take advantage of assistive technologies that can help them work, read, navigate their home or city and otherwise remain productive. Many of these technologies have been developed with NEI funding. Ongoing research continues to improve the available options – from prosthetic devices to prism glasses to electronic navigation aids.

This is a remarkable time of discovery. We can view the functioning eye in greater and greater detail and gain a better understanding of the biology, at the level of cells, genes and proteins, that make vision possible – and how things can go wrong with disease or trauma.

In 2012, I challenged our advisory body, the National Advisory Eye Council, and the vision community to identify a novel and ambitious goal that pushed the boundaries of vision science and tackled the most devastating and difficult-to-treat eye diseases. The resulting NEI Audacious Goals Initiative (AGI) gathered a set of targeted proposals with the overall goal to "restore vision through the regeneration of neurons and neural connections in the eye and visual system."

Regenerative medicine is a new frontier in biomedicine that uses stem cells, engineered biomaterials, and gene editing to repair, replace, or regrow damaged cells, tissues, or organs. AGI builds on the understanding that many leading causes of blindness, such as age-related macular degeneration, diabetic retinopathy, and glaucoma, result from the death of photoreceptor cells and ganglion cells (neurons) in the eye.

In the eye and brain, lost and damaged nerve cells must be replaced and coaxed to grow long connections to other nerve cells. This complicated process requires scientists to understand not only biochemical guidance cues but also how to train the visual system to form the right connections. AGI will greatly influence regenerative approaches to eye diseases, as well as to other neurodegenerative diseases, such as Parkinson's disease and Alzheimer's disease.

AGI is designed to be nimble and responsive to rapidly evolving scientific opportunities to reach its goals. It will take a lot of planning, with input from a variety of experts, to be successful. As a first step, NEI assembled several research consortia to tackle the most pressing needs and gaps in science. The first goal is inventing new, noninvasive imaging technology to watch cells grow and form connections over time in animals and, ultimately, in patients responding to therapy.

Other AGI consortia are trying to identify new regeneration factors that may be turned into therapy and to create new models to evaluate the survival of regenerated neurons and cells. Through this initiative, with continuous input from the research community, NEI is supporting the cutting edge of vision science and beyond.

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Diabetic retinopathy research and thioredoxin-interacting protein (TXNIP)

When it comes to the field of diabetic retinopathy research, Dr Lalit Pukhrambam at Wayne State University is exploring ways to prevent blinding eye diseases due to diabetes by targeting a protein called thioredoxin-interacting protein (TXNIP). Gene therapy is, therefore, a promising option

way of an introduction, diabetic retinopathy (DR) is a devastating eve disease causing blindness; yet, there is no cure. Thioredoxin-interacting protein (TXNIP) is strongly induced by high glucose and inhibited by insulin. Therefore, chronic hyperglycaemiainduced TXNIP expression in tissues remains elevated in diabetes. TXNIP inhibits the anti-oxidant and thiol reducing the capacity of thioredoxin, thereby, causing cellular oxidative stress, inflammation and cell death. Gene therapy targeting TXNIP is one way to prevent DR.

TXNIPlogy: The study of the role of TXNIP in health and disease

Diabetes global epidemic

Diabetes mellitus (DM) is a metabolic disease in which high blood sugar level persists over a prolonged period. Two main types of DM are Type 1 (insulin-dependent or Juvenile diabetes, an autoimmune disease, ~10%) and Type 2 diabetes (insulin-resistant or adult-onset diabetes, associated mainly with obesity and lifestyle change, ~90%). DR is a severe complication of diabetes causing damage to retinal microvasculature and neurons. It can eventually lead to blindness. DR affects up to 80% of all diabetic patients who have had diabetes for 10 vears or more. DR accounts for ~12% of all new cases of blindness each

year in the United States and is the leading cause of blindness among the working adult population.

With a global increase in diabetes, obesity and hypertension (*Diabesithy*, a term I coined for risk factors for DR), the number of people affected by DR will increase in the coming years. Therefore, there is an urgent need for cure or methods to prevent diabetes and its complications.

"Diabetic retinopathy DR is a severe complication of diabetes causing damage to retinal microvasculature and neurons. It can eventually lead to blindness. DR affects up to 80% of all diabetic patients who have had diabetes for 10 years or more."

TXNIP and diabetic retinopathy

Diabetic retinopathy has been defined by complications of retinal microvascular capillaries due to blood vessel leakage/blockade and the development of new and fragile blood vessels (neovascularization). Early DR involves non-proliferative DR (NPDR), which progress to a more serious disease of proliferative DR (PDR). Laser coagulation, anti-inflammatory steroid and anti-VEGF antibody injection into the vitreous are current treatment methods.

However, these treatments do not produce satisfactory results for most

patients. Therefore, there is an unmet need for developing effective therapies via the identification of new gene targets and metabolic pathways. Currently, it is recognised that microvascular damages are late pathologies in DR and there is an early neuronal injury. This is where new therapeutic methods need to be targeted in the early stages of DR, as diabetic eye diseases develop after a prolonged exposure to hyperglycaemia and diabetes duration. Most common retinal cell dysfunctions (including neurons, glia, pigmented epithelium, pericytes and endothelial cells) in hyperglycaemia and/or hyperlipidaemia involve oxidative stress, mitochondrial dysfunction, low-grade inflammation and premature cell death.

Recently, we identified TXNIP as a gene strongly induced by diabetes and high glucose in retinal cells causing oxidative stress, mitophagy dysregulation and inflammation. Knocking down TXNIP by small inhibitory RNAs (RNAi) in the retina prevents early abnormalities of DR, which include capillary basement membrane thickening, glial activation, and neuronal injury. Therefore, we proposed that TXNIP itself and/or its downstream partners, including the NLRP3 inflammasome, are potential targets for gene and drug therapies.

Furthermore, we showed that the

TXNIP promoter exists as an opened and poised configuration that it is activated strongly by high glucose and histone deacetylase inhibitors (HDACi). Therefore, this TXNIP promoter may be operably linked with a therapeutic gene or RNAi to increase/decrease gene expression in diabetes, DR and agerelated neurodegenerative diseases.

Nucleic acid constructs containing a TXNIP promoter for gene therapy

As mentioned above, TXNIP is induced by high glucose and diabetes in most tissues tested so far, including pancreatic beta and retinal cells. Therefore, the TXNIP promoter may be linked with a therapeutic gene or an RNAi and induce their expression under hyperglycaemia, such as encountered in diabetes or after a meal. In particular, the TXNIP promoter may be operably linked to a gene encoding as follows:

- (i) Insulin or an insulin promoting protein (PDX1);
- (ii) A protein that reduces oxidative stress, inflammation and cell death (Trx1 or Gpx4);
- (iii) An RNAi that reduces expression of a protein, which promotes oxidative stress, inflammation and cell death (including TXNIP itself and NLRP3); or
- (iv) A neurotrophic factor (BDNF or GDNF).

Advantages are that the TXNIP promoter will remain active when hyperglycaemia prevails; while mostly unresponsive under physiological glucose.

Gene delivery

Gene delivery into the retina may be achieved by packaging the TXNIP promoter-gene construct into an appropriate vector, such as recombinant adeno-associated viral vector, rAAV2. The eye provides an exceptional opportunity for gene therapy because it is a closed organ and relatively an immune privileged site. Therefore, cross-contamination from an intravitreal injection to another organ or systemic immune response will be minimal. Additionally, genetic material needed for the retinal gene therapy is small (cost effective) compared to a systemic gene delivery for other organs.

In fact, most current trials in human gene therapy are conducted for retinal diseases, e.g., retinitis pigmentosa. Gene therapy using the TXNIP promoter is simple, yet innovative, potentially mitigating DR progression. Furthermore, gene and tissue bioengineering methods may be applied in ex vivo systems using autologous adiposederived stromal stem cells (ASCs) or inducible pluripotent stem cells (iPSC) to produce insulin via a TXNIP-promoter-linked insulin gene expression and subsequent subcutaneous transplant of the manufactured cells. These autologous cells, if producing insulin under hyperglycaemia, will avoid immune responses and survive longer in their own subcutaneous environment, as opposed to a pancreatic beta cell transplant.

Conclusion

Diabetes and its complications affect, not only individuals but also families directly and the society at large. One in ten people in the world is considered to have diabetes, yet many are to be diagnosed. The loss in work productivity and economy due to chronic diabetes diseases are enormous. Tinkering with simple, yet innovative, ideas may lead to diabetes cure and/or prevention of organ damages. There are promises in the horizon for gene and cell therapy for curing diabetes or preventing DR. TXNIP may be an answer.

Supports

American Diabetes Association Juvenile Diabetes Research Foundation Mid-West Eye Banks National Kidney Foundation National Institutes of Health Research to Prevent Blindness (RPB)



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HEALTH & SOCIAL CARE

Critical care nursing: Reshaping professional talent roadmap over the coming years

Cecilia Van Cauwenberghe from Frost & Sullivan's TechVision Group turns the spotlight on to the key issues around critical care nursing, with a focus on reshaping the professional talent roadmap over the coming years plus clinical competence

During the past five years, nursing programmes focussed on critical care began to encourage the admittance of a greater number of students in order to provide a more innovative education system-based on higher care quality and safer clinical practice. In fact, clinical and professional competence in intensive nursing play a significant role as a specific knowledge base, skill base, attitude and value base that build its foundations over the professional experience in intensive and critical care nursing (Ääri et al., 2018). Broadly speaking, the nursing competence involves adherence to clinical guidelines and nursing interventions standards, absolute ethical behaviour, smart decision making, development work, and multidisciplinary collaboration.

Encompassing this vision of critical care nursing, a number of clinical teaching models based on standardised and customised simulation labs were performed to improve intra-professional collaboration among complex clinical centres and healthcare professionals and junior/senior-level nursing students (Boothby et al., 2018).

Future skills and talent nursery roadmap

Leading healthcare companies are presently redesigning its talent attraction policies in order to improve the effectiveness of their graduate and undergraduate programmes (Das, 2015). Therefore, a certain level of diversity around their recruitment process, based on student profiles and universities prestige is crucial to attracting high potential candidates. To achieve this goal, twin track approaches to career development, that is, professional and management approaches, focus on an in-depth understanding of success profiles resulting from competency models that should be in place in the future for both potential career pathways and the development of future managers.

The road ahead in Europe

Regional commitment and collaboration work These strategies are also stimulated by the European Federation of Critical Care Nursing Associations (EfCCNa), a formal network of nursing associations in Europe focussed on promoting collaboration and equity among the national critical care member associations. According to EfCCNa, collaboration is crucial to advance critical care practice, education, management and research in Europe. Indeed, the Belfast Declaration, established in recognition of the First Global Critical Care Nursing Organizations Joint Meeting reflect the commitment of most relevant European nursing associations to promote and support optimal nursing practices worldwide.

Among the most important goals defined by the organisations, the identification of novel opportunities to collaborate in further advancing nursing education, practice, and research, advocating for the highest standards of critical care nursing practice worldwide, are of note. The commitment is extended to the advancement of the state of critical care nursing based on the constitution of multi-professional team-based practices to promote in-depth knowledge, as well as, the engagement of patient and family-centred care to support ongoing care and recovery beyond clinical institutions (Butcher et al., 2018).

Big themes for discussion

Among the most relevant issues to be covered in order



to significantly improve critical care nursing, EfCCNa has selected the following items to be discussed by 2019:

- · Pain management;
- Family-centred care;
- Critical care education;
- Critical care simulation;
- Rescue therapy;
- Clinical research;
- Patient safety;
- Post-operative care;
- · Airway care, ventilation loops and waves;
- Infection control;
- Palliation and end of life;
- Early mobilisation;
- Sleep and comfort management;
- Intensive care unit (ICU) multicultural organisation.

It is important to highlight that according to the latest Eurostat data, migration has become one of the key drivers of population change, hence revealing the importance of cultural diversity as one of the most important factors in the healthcare area. ICU multicultural organisation will be essential to address critical care nursing in Europe by the coming years.

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References

Ääri, R.L., Tarja, S. and Helena, L.K., 2018. Competence in intensive and critical care nursing: a literature review. Intensive and critical care nursing, 24(2), pp.78-89.

Boothby, J., Gropelli, T. and Succheralli, L., 2018. An Innovative Teaching Model Using Intraprofessional Simulations. Nursing education perspectives.

Butcher, H.K., Bulechek, G.M., Dochterman, J.M.M. and Wagner, C., 2018. Nursing Interventions classification (NIC)-E-Book. Elsevier Health Sciences.

Das, R. 2015. Acuity-Based Staffing as the Key to Hospital Competitiveness - Why the Smartest Hospitals are Tying their Nurse Labor Investment to Patient Care. Frost & Sullivan Research Service. Frost Perspectives. Healthcare.

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A trans-disciplinary approach to cancer research

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Tumors are extremely complex systems, involving biological interactions of pathological and normal cells with the extracellular biochemical microenvironment, where all important transport processes, such as nutrients delivery and waste removal, play a key role as well. Recapitulating all these factors into a comprehensive modelling framework is a formidable task in cancer medicine.

Different research approaches are typically proposed, including *in-vivo*, *in-vitro*, *in-silico*, and mathematical

models to study cancer growth and treatment. Each of these methodologies alone can only provide and examine a partial description of the interplay between complex microenvironment and drug transport efficiency, and hardly allows to provide patient-specific information, to be used to design personalized precision treatments.

We believe a trans-disciplinary experimental-theoretical approach needs to be implemented to identify quantitative mechanistic correlations between tumor stromal/microenvironmental parameters and cell behavior. The results will provide insight on resistance factors that limit drug delivery for cancer therapies, and suggest the design of novel nano-carriers to enhance drug transport and release by integrating *in vitro*, theoretical, and *in vivo* models, superior to any actually existing experimental approach.

We are developing a novel Elementary Tissue Unit (ETU) based on spatial and temporal microfluidic technology integrated with *ex vivo* 3D co-cultures and



advanced mathematical modelling, enabling us to deliver the full potential of each technology and their combination toward predictive precision medicine. We have set up 3D cultures of patient-derived breast cancer organoids. The latter are miniature forms of tissues that exhibit threedimensional architecture and are able to maintain phenotypical properties when cultured in a dish.

The proposed integrated experimental-theoretical approach overcomes the limitations of typical *in-vivo*, *invitro*, *in-silico* models, when taken alone, since it is based on a highly interdisciplinary collaborative effort of engineers, mathematicians, biologists, chemists and oncologists exceeding research activities that can be offered by each expertise individually.

Advanced mathematical models can be used to abstract key parameters responsible of the description of cancer growth, evolution and treatment. The same parameters can be reproduced in an *ex-vivo* model, where advanced microfabrication techniques can be used to reproduce the microenvironment surrounding elementary tissues in the patient body mimicking the human *in-vivo* environment. The engineered ETU will reproduce the complexity of cell microenvironment present in-vivo and will be specifically designed to investigate the biophysical barriers affecting drug transport, including convective and diffusive gradients limiting cancer drug perfusion, as identified and predicted by the advanced mathematical models. The ETU will include extracellular matrix and blood vessels models, and host *ex-vivo* co-cultures of tumor and healthy cells, directly from the patient, allowing to study tumorstroma interactions. ETU can be also used to evaluate the patient specific response to novel drug carriers.

As targeting moieties for active drug transport through nanocarriers, we developed aptamer ligands for transmembrane receptors overexpressed on the cancer cell surface. Indeed, aptamers have easy synthetic synthesis and modifications to improve their pharmacokinetics (stability and biodistribution) and pharmacodynamics (toxicity and immunogenicity), and show an improved tissue penetration. The functional effects of treatments is experimentally determined by measuring morphological and chemical parameters and will be fed to the mathematical models developed. The output of this analysis will be used to identify the controlling barriers to drug transport and to optimize nanovector design.

In other terms cancer and heathy cell samples taken from the patient can be growth in the ETU. Since ETU mimics the environment originally surrounding the tissue sample, the cancer will develop in vitro following the same trends, as in the human patient. Quantitative analysis of tumor growth, invasion, and response to external stimuli, such as specific controlled therapies, can provide a measurement of key physico-chemical parameters, able to instruct advanced mathematical models. The models can be finally used to predict the response of patient to therapies.

Similar approach is typically applied in the engineering design of complex processes, such as the design of complex industrial plants or complex mechanical equipments, such as a modern, advanced vehicles. In the engineering approach, mathematical models are used to suggest lab-scale experimental models and tests, that can be also a simplified version of the final product, but still contain all the key parameters needed to provide information relevant to the final design of the product. The final result is a non trivial scale-up from lab to full scale.

In the approach we are here proposing the final result will be to design a complex, patient specific, precision therapy.

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HEALTH & SOCIAL CARE

Reducing the burden of neurological disease: A focus on stroke research

The wider work of The National Institute of Neurological Disorders and Stroke in the U.S. when it comes to reducing the burden of neurological disease is detailed here by North America Analysis

The National Institute of Neurological Disorders and Stroke (NINDS) is an Institute within the National Institutes of Health (NIH) in the U.S which seeks to gain fundamental knowledge about the brain and nervous system to reduce the burden of neurological disease.⁽¹⁾

The current Director of the new Division of Neuroscience is Lyn Jakeman, PhD, appointed in October 2018. When appointed, she painted a very positive picture of neuroscience research. "We are in the midst of amazing technological and analytical advances that are rapidly accelerating the pace of discovery in fundamental and applied neuroscience research", she said ⁽²⁾

A balance of basic, translational and clinical research

Going into further detail, we know that NINDS fosters a balance of basic, translational and clinical research. Indeed, it is said that scientists and physicians in academia and industry agree that basic research is crucial for long-term progress against neurological diseases. In essence, basic research aims to help us understand how the nervous system develops and works and what goes wrong in disease.

While the private sector in the U.S. supports little basic neuroscience research because the return on investment in this type of research is unpredictable, the NIH, therefore, supports most basic medical research in the U.S in this field.

Following on from this, it's worth noting that NINDS basic research is divided between research on the normal development and working of the nervous system, plus research related to disease mechanisms.

The cluster organisation of the NINDS extramural program focuses on the following areas, amongst others: neurodegeneration, such as shared mechanisms of nerve cell death that contribute to many diseases; the control of the environment of nerve cells by supporting cells; systems and cognitive neuroscience, including attention, thinking, sensation, perception, movement, learning, memory and emotion; as well as the role of genes in the normal and diseased nervous system; nervous system repair and plasticity, such as neural prostheses, stem cells, and regeneration. Maintaining this remarkable breadth of basic research is essential to the Institute's mission. ⁽³⁾

When it comes to NINDS Division of Translational Research (DTR), we know that they provide funding and resources (approximately \$100 million annually) for neurological disorders and stroke through grants, cooperative agreements, and contracts to academic and industry researchers to advance early-stage neurological technologies, as well as therapeutic programmes to industry adoption and devices.⁽⁴⁾

Stroke research

There are many examples of NIH-funded stroke research that we read about online, such as this <u>NIH-funded trial</u> which finds a lower rate of secondary stroke but a small risk of bleeding, and how preliminary research results suggest that <u>strokes also affect the eye</u>.

Let's, however, take a look now at a more recent example, an NINDS funded study that suggests a change in diet could mitigate increased risk for stroke. These recent research findings suggest that diet is a major contributor to the increased risk of hypertension in black compared to white Americans.

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We find out that the results, published in the Journal of the American Medical Association, examine the incidence of stroke in around 30,000 individuals. "This study addresses a lead cause of racial disparity in mortality and identifies potential lifestyle changes that could reduce racial disparities in both stroke and heart disease," says Claudia Moy, Ph.D., NINDS program director and one of the authors of the study.

"We are in the midst of amazing technological and analytical advances that are rapidly accelerating the pace of discovery in fundamental and applied neuroscience research."

In the study, researchers looked at individuals over the age of 45 over a period of 10 years and sought to identify risk factors associated with the higher likelihood of developing high blood pressure in the study participants. George Howard, a biostatistics professor at the University of Alabama, Birmingham gives his own thoughts on the study: "The majority of disparities we see in the health of black versus white Americans are cardiovascular in nature and of these, all are tied to an increase in high blood pressure."

We find out that a diet consisting of high amounts of fried and processed foods, as well as sweetened beverages, was the greatest factor as to why blacks are at a greater risk of developing high blood pressure compared to whites, for both sexes. Important factors for men and women include salt intake and education level. For women, extra factors contributing to the racial difference in high blood pressure included waist size and obesity.

"One of the main factors affecting the difference between the black and white population is cardiovascular disease, and the increased risk of high blood pressure among black Americans could help explain why their life expectancy is four years shorter than that of whites," says Dr Howard. "Understanding how we can prevent this increased risk of hypertension in blacks is critical for reducing health disparities among the black population", he adds. As this article comes to a close, we know that these researchers hope that these findings might be applied to reduce the prevalence of hypertension and, therefore, the risk of stroke and heart attack in the black American population. This study recommends that lifestyle changes, such as changes in diet, could help to lower the disparities evidenced in black versus white Americans.

The last word goes to Dr Howard, who provides a very sensible piece of advice on how to treat high blood pressure. "The best way to treat high blood pressure is to prevent it from occurring in the first place," states Dr Howard. ⁽⁵⁾

References

- 1 https://www.ninds.nih.gov/About-NINDS
- 2 https://www.ninds.nih.gov/News-Events/News-and-Press-Releases/Press-Releases/NINDS-Names-Dr-Lyn-Jakeman-Neuroscience-Director
- 3 https://www.ninds.nih.gov/Current-Research/Research-Funded-NINDS/Basic-Neuroscience
- 4 https://www.ninds.nih.gov/Current-Research/Research-Funded-NINDS/Translational-Research
- 5 https://www.ninds.nih.gov/News-Events/News-and-Press-Releases/Press-Releases/Diet-rich-fried-and-processed-foods-linked

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Stroke recovery research: The exciting trends of the future

Steven A. Kautz, Professor at the Ralph H. Johnson VA Medical Center and the Medical University of South Carolina College of Health Professions gives a glimpse into the future trends for stroke recovery research

here is a crucial need for research into recovery from a stroke that leads to improvements in the long-term quality of life of those who have suffered a stroke. The term "Recovery from Stroke" almost always describes an incomplete process that includes compensatory behaviour and modified neural circuits rather than recovery of the function of pre-morbid neural tissue. This term broadly describes events, such as recovery of damaged neural tissue by neuroprotection, recovery of damaged neural circuitry by reorganisation, recovery of behaviour through rehabilitation, and recovery of quality of life through increased participation in daily living activities.

Most stroke research focuses on acute treatment or prevention within hours or days after stroke, with research to help those with chronic disabilities after stroke having long been underemphasised. Current understanding of how the nervous system repairs and reorganises neural circuitry (i.e., neural plasticity) to promote behaviour, and how neural plasticity can be harnessed to maximise recovery of behaviour through rehabilitation, is inadequate. There is a pressing need to conduct animal and human studies to improve understanding of the mechanisms involved in functional behavioural change and neural plasticity induced by interventional studies, and build a framework

to help researchers develop more efficacious, evidence-based interventions.

Such studies will help identify the neural substrates and processes underlying specific behaviours and recovery of these behaviours after stroke, including translational studies in which we model human studies in animals with complementary intervention and measurement paradigms. Multidisciplinary translational research into stroke recovery is of special importance to the people of my state of South Carolina in the U.S. due to their disproportionate rate of stroke and the economic and societal burdens of resulting post-stroke disabilities.

I believe that better understanding of the experience-dependent nature of neural plasticity will allow researchers to investigate and exploit inherent neural recovery processes, develop and translate novel mechanism-based interventional strategies and ultimately, improve the function and quality of life of individuals recovering from a stroke. Currently, outcomes following stroke are suboptimal because of major gaps in foundational understanding of the neural circuitry (substrates and processes) underlying behaviour, as well as their repair and reorganisation (i.e., neural plasticity).

While the translation of methods to augment plasticity inspired by basic

science knowledge holds exceptional promise for advancing the field, rehabilitation interventions will necessarily play a central role in advancing recovery from stroke. Even if the highest hopes for cell-based therapies (i.e., neural repair by stem cells), pharmaceuticals or other adjuvant methods of enhancing neural plasticity, such as invasive or non-invasive brain stimulation techniques are realised, rehabilitation will be crucial as the behavioural engine to 'teach' the new neural circuitry to perform the necessary functions. Thus, a major focus of current research is to develop and test novel methodologies for performing and augmenting rehabilitation interventions, based on principles consistent with the mechanisms of experiencebased plasticity in the nervous system.

I am fortunate to direct a talented team of multidisciplinary researchers at the NIH-funded Center of Biomedical Research Excellence (COBRE) in Stroke Recovery, a collaboration between the Colleges of Health Professions and Medicine at the Medical University of South Carolina in Charleston, South Carolina. The initiative is supported by the NIH's Institutional Development Award (IDeA) program put in place to promote, augment and strengthen the biomedical research capabilities of institutes in IDeA states. I believe that there are four aspects of our centre that offer insights into the future of stroke recovery research.

Four insights into the future of stroke recovery research

First, multidisciplinary team science is the clear future of stroke recovery research, and these teams should include both clinical and basic scientists. Our centre includes teams with experts in rehabilitation, neuromodulation. statistics, bioinformatics. neuroimaging and neuroscience. In addition, those teams include scientists from the clinical professions that are on the front lines of stroke recovery and rehabilitation – stroke neurologists, physical therapists, occupational therapists, speech-language pathologists, neuropsychologists and psychiatrists, among others.

Second, neuromodulation offers incredible opportunities for application to stroke recovery. Stroke is a disease that affects the nervous system. After the stroke, there are neurons that have died. However, the deficits do not just result from the loss of those neurons, but also from the changes induced in all of the neural circuits and pathways in which those neurons participated. Neuromodulation offers a potential methodology to modify aberrant circuits and improve, or even restore, some of the poststroke deficits negatively impacting the quality of life. The BRAIN initiative at NIH has led to the development of a number of new tools that allow researchers to better understand how to modify neural circuits. That many of these neuromodulation methods use electricity directly at the aberrant circuit, instead of pharmaceuticals delivered systemically, offers the promise of an approach with greatly reduced potential for side effects.

Third, a better understanding of the experience-dependent nature of neural

plasticity and its translation into clinically effective interventions will be crucially facilitated by the development of a theory-based measurement framework that includes quantitative behavioural, neurophysiological and imaging based measures of:

- 1) Normal neurological function;
- 2) Underlying structural and functional damage after stroke;
- 3) Experience-dependent neural plasticity during rehabilitation;
- 4) Structural and functional changes post-rehabilitation and;
- 5) The functional recovery of each individual patient.

Fourth, comprehensive multidisciplinary databases enabled by data sharing between studies and between centres offer incredible promise for tackling the difficult problem of determining which treatment or treatments are needed for each stroke survivor. Stroke is heterogeneous and recovery is likely to need to be personalised to the specific deficits and available neural substrates of each individual. Thus, there is a need for a theory-based measurement framework and the data from multidisciplinary domains neurophysiology, like imaging, behaviour, cognition, language, etc. in order to better define the various phenotypes of stroke recovery - what has been called dense phenotyping. The ultimate goal is to connect this dense phenotype data with the electronic health-care records and genomic data.

This is an exciting time in the field of stroke recovery as these emerging

trends leave researchers well positioned for breakthroughs that can truly improve the quality of life for stroke survivors. Research centres, such as our COBRE and others throughout the world are assembling innovative multidisciplinary research teams, testing promising technology like neuromodulatory devices, and sharing data to assemble rich multidisciplinary data sets to allow dense phenotyping. I foresee great progress in personalised stroke recovery in the next decade.



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Providing a path to advanced degrees in biomedical fields

The NYU Sackler Institute of Graduate Biomedical Sciences aims to train the next generation of scientists to make breakthroughs and advances in society at large, explains Naoko Tanese

Becoming an accomplished researcher requires an inquisitive mind and perseverance. It calls for hands-on research experience and active mentorship. Sackler students receive rigorous training to become independent scientists. We also instil in them a strong sense of social and ethical responsibility through interactions with our diverse research community.

PhD programme

Students matriculating at NYU Sackler Institute of Graduate Biomedical Sciences begin their training in an Open Program. While some students enter graduate school with a speciality in mind, in the Open Program students are encouraged to explore multiple fields. First-years wait to select a training discipline until they have taken several courses, completed two or three laboratory rotations, and selected a faculty mentor for their PhD thesis work. They have a full year to make final decisions.

We recently expanded the scope of our program to include new training tracks in Biomaterials Science, Biostatistics, and Epidemiology, in addition to all of the existing traditional disciplines in biomedical sciences. As we recruit students interested in the new tracks, we are faced with balancing the unique background of each student with the spirit of the Open Program. How can the curriculum of an Open Program satisfy students with varying interests and backgrounds?

To address this challenge all incoming students are required to take the course Introduction to Research, which starts immediately after Orientation with an immersive lab experience called Research Adventure. The Introduction to Research course is intended to not only help incoming students begin graduate school with the same basic knowledge, but also to provide them with a sense of community.

The Research Adventure is an intensive, week-long, hands-on research experience, where students working in a team carry out a structured project in a faculty's lab on a topic different from their previous research. This exposes them to new possibilities that perhaps they may not have considered. We continue to evaluate best practices to keep the spirit of the Open Program alive while accommodating the different interests and backgrounds of our matriculating students.

Career

In higher education, there is an increasing trend for PhD students to pursue alternative careers (non-academic positions). For this reason, we strive to prepare them for any career. We emphasise how PhD training teaches students to be critical thinkers, problem solvers, productive team members, collaborators, independent workers, and effective leaders. These are qualities useful to any career path.

NYU's centre for career development offers services such as resume and cover letter preparation as well as networking and interviewing practice sessions. Students participate in many job and internship fairs. We also invite alumni back to give career talks and meet with students to discuss their experiences.

Our students also take advantage of a variety of workshops and courses offered by the postdoctoral affairs office. To improve their career training, they actively engage in career planning while assessing their personal values and translating them to individual goals. They are introduced to all the diverse career opportunities outside of academic research. For those interested in teaching, students learn how to design and implement courses both at the college and post-graduate level. Communication is another skill critical to any career. We host workshops and seminars to help our students with their communication skills, both written and oral, to a variety of audiences.

Inspiring the next generation

The future of our society depends on training the next generation of highly capable scientific workforce. For this



Participants of the Sackler Institute's Summer Undergraduate Research Program

reason, we place a great deal of effort in mentoring young people interested in pursuing careers in science. We are increasingly wary of losing students' interests in STEM – Science, Technology, Engineering, and Mathematics. We are also concerned that not enough young people from diverse backgrounds are entering the STEM field. The current makeup of scientists in biomedical fields does not reflect the composition of the US population.

Numerous studies have reported the benefits of a diverse research community in advancing scientific endeavours. We are committed to making this happen by reaching out to students from diverse racial, ethnic, and socioeconomic backgrounds. One mechanism that has been in place at the Sackler Institute is our Summer Undergraduate Research Program (SURP).

Established in 1990, the SURP has been one of the cornerstones of minority recruitment for MD, PhD, and MD/PhD programs. The purpose of SURP is to give students who have the interest in biomedical sciences an opportunity to conduct research at a major medical centre. Over 700 students have participated in this program and >95% of the participants subsequently entered graduate or professional degree programs. We make an effort to provide a supportive community where students from all backgrounds feel at home. This is critical to our mission to promote diversity and inclusion at the Sackler Institute.

In many ways, STEM training needs to start earlier than college. We have been reaching out to students in nearby high schools to introduce them to scientific research. It's never too early to show them what it's like to be a grown-up scientist. We have visited local schools to give presentations and met one-on-one with young students. We have invited them to research laboratories to observe scientists at work, and in some cases perform experiments as student interns.

Ambitious and determined students commit to commuting long distances for these hard-to-find opportunities to satisfy their curiosity and challenge themselves to unfamiliar but exciting tasks. Some students never give up looking for a chance to enter research labs. This makes it worthwhile to mentor and see them thrive in a new environment. Scientific discoveries are made by following one's passion. We are here to inspire young people to find their passion in the biomedical sciences.



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Duchenne muscular dystrophy (DMD): Correcting the dystrophin gene

Dr Ahlke Heydemann, Associate Professor and Director of Medical School Curriculum at University of Illinois, Chicago explains Duchenne muscular dystrophy (DMD), focussing on the issue of correcting the dystrophin gene

uchenne muscular dystrophy (DMD) is an inherited progressive disease that affects skeletal, diaphragm and cardiac muscles. The pathology initiates with muscle weakness, particularly noticeable on the leg muscles of the young - two to three-year-old – boys. The dystrophin gene is located on the X-chromosome; therefore, it is sex-linked and only boys get the full disease. Women are carriers and can develop cardiomyopathy much later in life. As time goes on, the skeletal muscles continue to weaken, and corticosteroid treatments are initiated, usually at around six years of age.

A few years later, night-time assisted ventilation and then prophylactic ACE inhibitors for the maintenance of respiratory and cardiac function, respectively, are added to the treatment regimen. These combined treatments have extended the quality and quantity of the patients' lives, but more effective treatments or even cures are still urgently required. Within MD, there is some relationship between the specific mutation in the dystrophin gene and the protein levels of dystrophin and the severity of the disease.

The mildest cases are classified as Becker MD (BMD). These mild cases reveal that a relatively low expression level of dystrophin – only 20 to 40 % of normal levels – is required to establish a mild disease course. This very important trait can be utilised to set a reasonably achievable goal for a highly beneficial and successful therapy.

Treatments in the preclinical and clinical trial pipeline

There are many promising treatments in the preclinical and clinical trial pipeline. These can be subdivided into overlapping categories.

- Inflammation/immune inhibitors.
- Modulators of metabolism.
- The reestablishment of the dystrophin glycoprotein complex without dystrophin and
- Gene correction.

The gene correction strategy can be further subdivided as shown below.

Gene correction

- 1. Cell transplantation.
 - a. Stem cells
 - i. Embryonic.
 - ii. Induced.
 - 1. From normal donors.
 - 2. From the patient, corrected in vitro
 - b. Muscle satellite cells.
 - i. From normal donors.
 - ii. From the patient, corrected in vitro.
- 2. Premature stop codon read-through.
- 3. Exon skipping.
- 4. CRISPR/Cas.

Utilising cells to reintroduce a wild-type dystrophin gene into diseased muscle has been investigated for many years. Recent progress has given new hope to this particular therapy for MD. Stem cells (SC) can be harvested from a number of sources: embryonic (ESC) tissues or induced (induced pluripotent stem cells) (iPSC) from adult tissues. These SCs have the potential to become permanently engrafted into the host muscles, proliferate, express dystrophin and respond to injury. ESCs have the benefit of being immune privileged, meaning the host tissue will not reject the cells as foreign. However, obtaining the number of ESCs required to treat a patient has been difficult. Proliferating the ESCs in culture causes functional changes that impede their effectiveness in establishing themselves in the host tissue.

One of the benefits of iPSCs is that scientists can produce large numbers without changing their effectiveness for transplant. ESCs are usually derived from normal donors and therefore, contain and deliver the intact dystrophin gene to all muscles that the cells populate. iPSCs can be derived from a normal donor or the patient themselves. If derived from the patient, the genetic defect will have to be corrected while the cells are in culture. An additional step, but a highly effective one, and using the patient's cells ensures that a large immune response will not be



mounted upon transplantation. One of the most positive aspects of this stem cell transplantation approach is that it can be a true cure. If the cells engraft and repopulate the muscles appropriately, they could survive and provide sufficient dystrophin for the life of the patient.

Muscle satellite cells (muscle resident stem cells) are another source of cells that could potentially engraft all muscle groups and be a true cure. These cells are derived from adults and are, therefore, more plentiful and tolerate proliferation in cell culture very well and their use has fewer ethical ramifications. The donor is a normal volunteer or the patient themselves, with the same considerations as mentioned above for the iPSCc. Recent work identifies a procedure that fuses normal donor satellite cells with the patient's satellite cells. This results in cells which express dystrophin and are immune privileged. And, as mentioned above, the cells tolerate proliferation, so the clinicians can have a large number of cells available for transplantation.

Clinical trials are also being conducted upon premature stop codon read-

through strategies. This approach is based upon a fortuitous discovery that some antibiotics impede bacterial proliferation by causing the protein-making machinery to ignore the bacterial stop codons, thereby, making longer and less functional proteins. A subset of dystrophin mutations in patients causes a premature stop codon, by the selective use of antibiotic-like pharmaceuticals, the mammalian ribosomes will ignore the stop codon and continue making the remainder of the dystrophin protein, with just one amino acid change, instead of no protein at all. In addition, advanced generation read-through pharmaceuticals have a much higher efficiency of ignoring the stop codon then the original antibiotics, providing higher levels of dystrophin expression.

Recent news has highlighted the success of exon-skipping strategies. This strategy is based upon aligning two synthetic nucleotide strands, with specific sites of the native DNA which causes the normal mRNA processing machinery to skip exons which contain the mutation. So far, this strategy has caused almost normal dystrophin protein to be expressed at close to

therapeutically beneficial levels. Researchers are still perfecting this technique to produce more protein.

The CRISPR system is also being investigated for gene correction in isolated cells from DMD patients and for gene correction within the patient. The final stages of preclinical testing will soon be completed. The exon-skipping and CRISPR systems are largely patient specific. Therefore, each patient will require specific chemistries to guide the editing machinery.

The further good news is that these genetic correction strategies can be utilised with other strategies that treat the symptoms to provide the most patient benefit with the lowest sideeffects. Very importantly, transplantation, read-through and exon skipping studies are currently being tested in patients for efficacy. In the near future, multiple options will be available for clinicians and their patients to combat this disease.

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HEALTH & SOCIAL CARE

Supporting biomedical research: A focus on hearing loss

The work of the National Institute on Deafness and Other Communication Disorders (NIDCD) in the United States is profiled here, with a focus on their work around helping those with hearing loss, as well as tips to prevent it and their hopes for the future

The National Institute on Deafness and Other Communication Disorders (NIDCD) is one of the many parts of the National Institutes of Health (NIH) in the United States today. By way of an introduction, it's important to know that NIH is the federal government's focus where the support of biomedical research is concerned. In essence, the NIH's mission is to unveil new knowledge that will result in better health for everybody. In very simple terms, the aim of NIH research is to gain new knowledge to help prevent, detect, diagnose and treat both disease and disability.

It's very fitting that we're looking at the work of NIDCD here as they have recently celebrated their 30-year anniversary, established in 1988 and since then they have been supporting research that has led to remarkable discoveries in hearing, balance, smell, taste, speech, voice plus language. Their work has brought into focus disorders of human communication plus an impressive contribution to biomedical and behavioural research that improves and advances the lives of millions of people with communication disorders.¹

Advancing research to improve lives

Judith A. Cooper, PhD, acting director of the NIDCD and director of the NIDCD Division of Scientific Programs highlights in a message for this 30th anniversary that at least 20% of adults in the U.S. have a significant impairment where hearing, balance, taste, smell, voice, speech, or language are concerned. In her view, the basic components of communication (sensing, interpreting and responding to their environment) can be challenging for these people.

Let's now focus on the hearing aspect of NIDCD, indeed, according to Judith, a number of factors contribute to hearing loss, as well as balance dysfunction, which can happen at any age and impact upon communication, safety and the quality of life. In her own words, Judith explains NIDCD's research aims in this vein, as well as her thoughts on hearing aids and cochlear implant technology.

"The NIDCD's robust program of basic and clinical research on hearing and balance includes genetics, genomics, and proteomics. This research focuses, in part, on the identification of genes involved in hearing loss to lead to earlier diagnosis and treatment, and to new therapies.

"Nearly 30 million adults in the United States could benefit from using hearing aids, but only one in four has used them. The NIDCD supports innovative clinical and translational research to lay the foundation for making hearing health care more accessible and affordable. Current research includes identifying barriers to care and assessing novel service delivery and screening models.

"Researchers are also applying cochlear implant technology to develop other neural prostheses. These devices will, for example, provide a sense of hearing for people whose auditory nerve is removed or damaged; normalize balance by electrically stimulating the vestibular nerve; and help patients with severe speech and physical impairments express themselves using speech synthesized from brain-computer interfaces."

Takings steps to protect your hearing

One initiative to highlight here is the one that took place during October 2018, which was National Protect Your Hearing Month, and at the time, the NIDCD promoted noise-induced hearing loss (NIHL) and the steps you can take to prevent it, which we'll highlight

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here. One important point in this vein is that sounds that are too loud for too long can damage your hearing permanently, indeed the louder the noise, the quicker it can damage hearing.

Incredibly loud noises can damage your hearing for life, and in just 15 minutes your hearing can be damaged by listening to loud music on headphones or attending a concert, for example. It's also worth bearing in mind that lower levels of noise over prolonged periods can also damage human hearing, an instance of which is those working in a noisy yard using farm equipment. The NIDCD also stresses that when sounds are too loud for too long, "tiny bundles of hair-like structures that sit on top of hair cells in the inner ear are damaged."

"The NIDCD's robust program of basic and clinical research on hearing and balance includes genetics, genomics, and proteomics. This research focuses, in part, on the identification of genes involved in hearing loss to lead to earlier diagnosis and treatment, and to new therapies."

The NIDCD provides the following helpful hints to protect your hearing:

- Reduce the volume. Know which noises can cause damage is important for those at or above 85 decibels. If you use headphones or earbuds, it is vital to ensure that the volume is always low.
- Move away from the noise. The advice here is that if you are unable to lower the volume, create some distance between you and the source.
- Wear hearing protectors, such as earplugs or earmuffs, when you're involved in a noisy activity is very important. This could be done whether you are using power tools, mowing the lawn, playing loud music or attending a loud sporting event or a concert. Activity-specific earplugs and earmuffs can be purchased online and at sporting goods, hardware, as well as other stores.
- Protect the ears of children who are not old enough to protect their own.
- Spread the news to your family, friends and colleagues about noise hazards.²

NIDCD-supported research in the future

Looking at the wider picture, we know that NIDCD-supported research also concerns voice, speech, and language impairments linked to stroke, injury and neurodegenerative disorders, such as Parkinson's disease. Such communication problems, like aphasia, apraxia and dysarthria frequently lead to a poor quality of life and increased isolation for an individual.

Looking ahead, Judith A. Cooper, PhD, acting director of the NIDCD and director of the NIDCD Division of Scientific Programs paints a picture of a journey towards brand new frontiers in precision medicine and scientific discovery and she believes that the NIDCD is in a very good position to support innovative studies to produce more effective, sensitive, and individually tailored interventions. We leave the closing words of this article with Judith herself who underlines that the NIDCD's research will expand in the future to help people of all ages who are experiencing the challenges of communication disorders, including, of course, hearing.

"NIDCD-supported researchers are dedicated to expanding our understanding of hearing, balance, taste, smell, voice, speech, and language and improving rehabilitation strategies for children and adults who face the challenges of communication disorders."³

For more information on hearing, ear infections and deafness, go to: www.nidcd.nih.gov/health/hearing-ear-infections-deafness

References

- 1 https://www.nidcd.nih.gov/
- 2 https://www.nidcd.nih.gov/news/2018/october-is-npyhm
- 3 https://www.nidcd.nih.gov/about/advancing-research-improve-livespeople-communication-disorders-message-nidcd-director

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The genetically modified chicken: A sound approach to the study of hearing

Jason Tait Sanchez, Assistant Professor at Northwestern University provides insight into why the genetically modified chicken is a sound approach to the study of hearing. We discover how tonotopic properties are established in the chicken auditory brainstem by using novel and innovated genetic research methods

t is well established that the chicken is a valuable research tool to study basic biological questions in numerous health-related areas, including immunology and infectious diseases^{1,2}.

Recent applications of gene editing in chickens also suggests an innovative era is on the horizon for developmental and sensory neurobiology as well^{3,4}. With respect to hearing development, mammals and birds share comparable auditory functions at the cellular, synaptic, and neural circuit level^{5,6} and both species encode sound similarly across the frequency axis, a process known as tonotopic tuning^{7,8}.

Tonotopy is the spatial arrangement of where sounds of different frequencies are processed. Tonotopy originates along the peripheral sensory epithelium and is preserved throughout the entire auditory system. Tonotopy in the central auditory pathway is arranged not only by the specific locations of neurons and their inputs, but by differences in their structural and functional properties along the tonotopic axis^{9,10}. Exemplars of this are found in the mammalian anteroventral cochlear nucleus and the chicken cochlear nucleus magnocellularis (NM), which are analogous, first-order auditory brainstem structures. In this article, I will provide recent insight into how tonotopic properties are established in

the chicken auditory brainstem by using novel and innovated genetic research methods.

Development of tonotopic properties

Despite more than a half-century of work on the development of tonotopic properties in the peripheral auditory system (i.e., the cochlea), little is known about its establishment in the central auditory system¹¹. This fundamental lack of knowledge is noteworthy, and several questions warrant discussion.

First, do tonotopic properties emerge from indiscriminate connections, or are there precise projections early in development? If precision exists early on, does refinement improve with maturation? Anatomical evidence argues that the topography of connections between the periphery and central pathway develops with considerable precision, well before hearing onset, and with substantial refinement thereafter¹²⁻¹⁸.

Second, what role, if any, does spontaneous neuronal activity – as opposed to sound-driven activity – have on the development or maintenance of tonotopic properties? Physiological studies show that early in development, functional mapping along the tonotopic axis supports precise tuning independent of sound-driven activity ¹⁹⁻²³. Finally, what are the molecular and cellular signals responsible for establishing and maintaining distinct neuronal phenotypes along the tonotopic axis in the central pathway? The answer to this final question remains elusive, making it a significant and timely problem in developmental and sensory neurobiology in general³.

Potential genes-of-interest

One thing is clear, however; both presynaptic axons and postsynaptic target neurons express genes - like neurotrophins - that may be responsible for establishing tonotopic properties in the central pathway. Neurotrophins, along with their cognate receptors, are growth factor proteins that support numerous aspects of normal nervous system development²⁴⁻²⁷, and irregular neurotrophin signalling is implicated in pathophysiological conditions in both the peripheral and central nervous systems²⁸⁻³⁰. This makes them a critical factor that promotes normal and abnormal biologically relevant properties³¹.

The idea that neurotrophin signalling is important for the tonotopic establishment in the auditory system is supported by the following observations from the chicken NM.

First, the retraction of neuronal dendrites takes places along a spatial gradient that matches the tonotopic



axis ³². Mid- to high-frequency NM neurons lose their dendrites while low-frequency neurons maintain them.

Second, the expression pattern of a very specific neurotrophin receptor (known as TrkB) is spatially and temporally dynamic; TrkB is present at embryonic (E) day 7, significantly reduced by E15 and absent at hatch (E21), but only in mid- to high-frequency regions³³.

Third, this expression pattern parallels a developmental period when functional properties are also differentially established along the tonotopic axis^{34.37} and coincides with hearing maturation³⁸.

Finally, genetically modified maintenance of TrkB receptors in mid- to high-frequency NM prevents dendrite retraction and promotes aberrant neuronal excitability³⁹, properties that more closely resemble their low-frequency neuronal counterparts^{10,40}. The dynamic expression pattern of TrkB receptors regulates the development of distinct tonotopic properties found in NM and strongly supports the hypothesis that neurotrophin signalling establishes different neuronal phenotypes along the tonotopic axis in the central auditory pathway.

Why the chicken?

The chicken is an ideal model system over other mammalian research tools because they have tonotopic properties more commonly shared with humans. Chickens, like humans, utilise both low- and high-frequency sounds to perform behaviourally relevant auditory tasks, such as sound localisation and signal discrimination^{41,42}. This is unlike most mammalian research models, such as mice and rats, which rely primarily on ultrasonic hearing.



Figure 1. In ovo electroporation in the chicken auditory brainstem

(A) Schematic of electroporation in the hindbrain of a Hamburger Hamilton (HH) stage 12 chicken embryo. The injection pipette is filled with plasmid DNA and fast green dye for visualisation of the injected hindbrain (rhombomeres 5/6 [R5/R6]). In this study, a plasmid that coexpressed the gene-of-interest and the yellow fluorescent protein (YFP) reporter was used. Electroporated embryos are further incubated until the desired developmental stage is reached. (B) Embryonic (E) day 4 chicken showing the site of YFP expression relative to the left eye (arrow, E) and left otocyst (arrow, O). The dashed white line represents the dorsal brain and brainstem border. Scale bar = 480 μm. (C & C1). Brainstem slice (300 μm thick) from an E12 chicken under differential interference contrast (DIC, C) and fluorescent (YFP, C1) illumination. Dashed white lines represent the borders of nucleus magnocellularis (NM) and nucleus laminaris (NL). Note, the brainstem slice shows only one side of the tissue. White arrowheads represent midline cleft of the brainstem slice. White arrows show YFP expressing regions of NM and NL. V = ventral, M = medial. Scale bar = 240 μm. (D & D1). High magnification (80X water immersion objective) of an E18 chicken brainstem slice containing NM. The classic adendritic cell bodies37 are clearly visible under DIC illumination (upward arrow, D). With fluorescent illumination for the same slice, a transfected NM neuron identified by YFP fluorescence is clearly visible (upward arrow, D1). Asterisks = YFP expressing NM neurons just below the focal plane. Scale bar = 30 μ m. Figure from Lu et al., 2017⁴⁸.

With respect to the development of hearing acuity, chickens (like humans) are also precocious animals. The chicken's auditory system is near functional maturity at hatch, and the onset and refinement of hearing occur during embryonic stages³⁸. This is unlike other low-frequency hearing mammalian research models (e.g., gerbil, guinea pig), whose hearing emerges ~10-16 days postnatal⁴³ and are susceptible to extrinsic factors that influence development.

Finally, the spatial and temporal expression of limited neurotrophin

factors in the chicken NM^{33,44} provides a novel opportunity to evaluate highlyspecific neurotrophin signalling and its role in establishing neuronal topology. This is unlike the mammalian auditory system, which expresses many more neurotrophin factors across numerous developmental periods⁴⁵, ultimately confounding the study of neurotrophin signalling in regulating tonotopic development in these species.

"Our research aims at addressing these issues by providing a comprehensive understanding of neurotrophin signalling and its role in establishing neuronal phenotypes along the tonotopic axis in the developing auditory brainstem, a biologically relevant structure which is essential for sound processing."

A sound approach

Electroporation is a method that introduces genes into biologically relevant organisms like the chicken embryo. In ovo electroporation is a formidable tool to study neuron-specific development in the auditory brainstem^{3,46}. It permits the over-expression or knockdown of specific genes-of-interest (like neurotrophin factors) in order to analyse in vivo gene function^{39,47}. We and others have recently introduced genetic methods to obtain focal, stable and temporally regulated transgene expression of neurotrophins at multiple stages of chicken embryo development^{3,39,48} (Fig. 1). It is advantageous over mammalian model systems for several reasons. First and foremost, because electroporation is performed in ovo, it permits gene expression in a normally developing biological system.

Second, genes are focally injected, allowing spatial control of expression in highly specific brain regions⁴⁹. Third, genes are temporally regulated by drug applications, enabling expression at precise developmental time periods^{39,48}.

Finally, genes are only expressed by a subset of neurons, allowing nontransfected neurons to serve as internal controls. This provides a rigorous and quantitative comparison of the neuron-autonomous effects of gene expression. The in ovo electroporation technique – together with either biochemical, pharmacological, and or in vivo functional assays – provides a genetic approach to study auditory neuron development associated with tonotopic differences in neuronal structure and function, as well as associated pathophysiological phenomena.

Indeed, a better understanding of normal auditory circuit assembly along with unique structural and functional properties associated with tonotopic gradients - will provide a significant foundation for developing stem cell-based therapies for auditoryrelated disorders. However, stem cellderived auditory neurons will only prove useful - therapeutically - if they are able to re-create neuronal properties that are characteristic of normal circuit maturation⁵⁰. A careful characterisation of neurotrophin signalling, the underlying molecular mechanism by which it operates, the role it plays in establishing normal neuronal properties, and the functional consequence of altering this biological process is necessary and appropriate.

Our research aims at addressing these issues by providing a comprehensive understanding of neurotrophin signalling and its role in establishing neuronal phenotypes along the tonotopic axis in the developing auditory brainstem, a biologically relevant structure which is essential for sound processing. References

- 1 Lyall, J. et al. Suppression of avian influenza transmission in genetically modified chickens. Science 331, 223-226, doi:10.1126/science.1198020 (2011).
- 2 Farzaneh, M., Hassani, S. N., Mozdziak, P. & Baharvand, H. Avian embryos and related cell lines: A convenient platform for recombinant proteins and vaccine production. Biotechnol J 12, doi:10.1002/biot.201600598 (2017).
- 3 Sid, H. & Schusser, B. Applications of Gene Editing in Chickens: A New Era Is on the Horizon. Frontiers in Genetics 9, doi:10.3389/fgene.2018.00456 (2018).
- 4 Dimitrov, L. et al. Germline Gene Editing in Chickens by Efficient CRISPR-Mediated Homologous Recombination in Primordial Germ Cells. PloS one 11, e0154303, doi:10.1371/journal.pone.0154303 (2016).
- 5 Koppl, C. Evolution of sound localisation in land vertebrates. Current biology: CB 19, R635-639, doi:10.1016/j.cub.2009.05.035 (2009).
- 6 Carr, C. E., Soares, D., Parameshwaran, S. & Perney, T. Evolution and development of time coding systems. Current opinion in neurobiology 11, 727-733 (2001).
- 7 Grothe, B., Pecka, M. & McAlpine, D. Mechanisms of sound localization in mammals. Physiological reviews 90, 983-1012, doi:10.1152/physrev.00026.2009 (2010).
- 8 Carr, C. E. & Soares, D. Evolutionary convergence and shared computational principles in the auditory system. Brain, behavior and evolution 59, 294-311 (2002).
- 9 Brew, H. M. & Forsythe, I. D. Systematic variation of potassium current amplitudes across the tonotopic axis of the rat medial nucleus of the trapezoid body. Hearing research 206, 116-132, doi:10.1016/j.heares.2004.12.012 (2005).
- 10 Wang, X., Hong, H., Brown, D. H., Sanchez, J. T. & Wang, Y. Distinct Neural Properties in the Low-Frequency Region of the Chicken Cochlear Nucleus Magnocellularis. eNeuro 4, doi:10.1523/eneuro.0016-17.2017 (2017).
- 11 Rubel, E. W. & Fritzsch, B. Auditory system development: primary auditory neurons and their targets. Annual review of neuroscience 25, 51-101, doi:10.1146/annurev.neuro.25.112701.142849 (2002).
- 12 Angulo, A., Merchan, J. A. & Merchan, M. A. Morphology of the rat cochlear primary afferents during prenatal development: a Cajal's reduced silver and rapid Golgi study. Journal of anatomy 168, 241-255 (1990).
- 13 Friauf, E. Tonotopic Order in the Adult and Developing Auditory System of the Rat as Shown by c-fos Immunocytochemistry. The European journal of neuroscience 4, 798-812 (1992).
- 14 Fritzsch, B., Farinas, I. & Reichardt, L. F. Lack of neurotrophin 3 causes losses of both classes of spiral ganglion neurons in the cochlea in a region-specific fashion. The Journal of neuroscience: the official journal of the Society for Neuroscience 17, 6213-6225 (1997).

- 15 Willard, F. H. & Martin, G. F. The development and migration of large multipolar neurons into the cochlear nucleus of the North American opossum. The Journal of comparative neurology 248, 119-132, doi:10.1002/cne.902480109 (1986).
- 16 Schweitzer, L. & Cant, N. B. Development of the cochlear innervation of the dorsal cochlear nucleus of the hamster. The Journal of comparative neurology 225, 228-243, doi:10.1002/cne.902250208 (1984).
- 17 Schweitzer, L. & Cecil, T. Morphology of HRP-labelled cochlear nerve axons in the dorsal cochlear nucleus of the developing hamster. Hearing research 60, 34-44 (1992).
- 18 Snyder, R. L. & Leake, P. A. Topography of spiral ganglion projections to cochlear nucleus during postnatal development in cats. The Journal of comparative neurology 384, 293-311 (1997).
- 19 Lippe, W. & Rubel, E. W. Ontogeny of tonotopic organization of brain stem auditory nuclei in the chicken: implications for development of the place principle. The Journal of comparative neurology 237, 273-289 (1985).
- 20 Sanes, D. H., Merickel, M. & Rubel, E. W. Evidence for an alteration of the tonotopic map in the gerbil cochlea during development. The Journal of comparative neurology 279, 436-444, doi:10.1002/cne.902790308 (1989).
- 21 Lippe, W. R. Relationship between frequency of spontaneous bursting and tonotopic position in the developing avian auditory system. Brain research 703, 205-213 (1995).
- 22 Sterbing, S. J., Schmidt, U. & Rubsamen, R. The postnatal development of frequency-place code and tuning characteristics in the auditory midbrain of the phyllostomid bat, Carollia perspicillata. Hearing research 76, 133-146 (1994).
- 23 Ryan, A. F. & Woolf, N. K. Development of tonotopic representation in the Mongolian gerbil: a 2-deoxyglucose study. Brain research 469, 61-70 (1988).
- 24 Ibanez, C. F. Emerging themes in structural biology of neurotrophic factors. Trends in neurosciences 21, 438-444 (1998).
- 25 Schecterson, L. C. & Bothwell, M. Neurotrophin receptors: Old friends with new partners. Dev Neurobiol 70, 332-338, doi:10.1002/dneu.20767 (2010).
- 26 Schuman, E. M. Neurotrophin regulation of synaptic transmission. Current opinion in neurobiology 9, 105-109 (1999).
- 27 Arevalo, J. C. & Wu, S. H. Neurotrophin signaling: many exciting surprises! Cell Mol Life Sci 63, 1523-1537, doi:10.1007/s00018-006-6010-1 (2006).
- 28 Hu, Y. & Russek, S. J. BDNF and the diseased nervous system: a delicate balance between adaptive and pathological processes of gene regulation. Journal of neurochemistry 105, 1-17, doi:10.1111/j.1471-4159.2008.05237.x (2008).
- 29 Gupta, V. K., You, Y., Gupta, V. B., Klistorner, A. & Graham, S. L. TrkB receptor signalling: implications in neurodegenerative, psychiatric and proliferative disorders. Int J Mol Sci 14, 10122-

10142, doi:10.3390/ijms140510122 (2013).

- 30 Singer, W., Panford-Walsh, R. & Knipper, M. The function of BDNF in the adult auditory system. Neuropharmacology 76 Pt C, 719-728, doi:10.1016/j.neuropharm.2013.05.008 (2014).
- 31 Bramham, C. R. & Messaoudi, E. BDNF function in adult synaptic plasticity: the synaptic consolidation hypothesis. Progress in neurobiology 76, 99-125, doi:10.1016/j.pneurobio.2005.06.003 (2005).
- 32 Rubel, E. W. & Parks, T. N. Organization and development of brain stem auditory nuclei of the chicken: tonotopic organization of n. magnocellularis and n. laminaris. The Journal of comparative neurology 164, 411-433 (1975).
- 33 Cochran, S. L. et al. Ontogenetic expression of trk neurotrophin receptors in the chick auditory system. The Journal of comparative neurology 413, 271-288 (1999).
- 34 Hong, H., Rollman, L., Feinstein, B. & Sanchez, J. T. Developmental Profile of Ion Channel Specializations in the Avian Nucleus Magnocellularis. Front Cell Neurosci 10, 80, doi:10.3389/fncel.2016.00080 (2016).
- 35 Lu, T. & Trussell, L. O. Development and elimination of endbulb synapses in the chick cochlear nucleus. The Journal of neuroscience: the official journal of the Society for Neuroscience 27, 808-817, doi:10.1523/JNEUROSCI.4871-06.2007 (2007).
- 36 Feng, J. J. & Morest, D. K. Development of synapses and expression of a voltage-gated potassium channel in chick embryonic auditory nuclei. Hearing research 216-217, 116-126 (2006).
- 37 Jhaveri, S. & Morest, D. K. Neuronal architecture in nucleus magnocellularis of the chicken auditory system with observations on nucleus laminaris: a light and electron microscope study. Neuroscience 7, 809-836 (1982).
- 38 Jones, T. A., Jones, S. M. & Paggett, K. C. Emergence of hearing in the chicken embryo. Journal of neurophysiology 96, 128-141, doi:10.1152/jn.00599.2005 (2006).
- 39 Schecterson, L. C., Sanchez, J. T., Rubel, E. W. & Bothwell, M. TrkB downregulation is required for dendrite retraction in developing neurons of chicken nucleus magnocellularis. The Journal of neuroscience: the official journal of the Society for Neuroscience 32, 14000-14009, doi:10.1523/INEUROSCI.2274-12.2012 (2012).
- 40 Hong, H. et al. Diverse Intrinsic Properties Shape Functional Phenotype of Low-Frequency Neurons in the Auditory Brainstem. Front Cell Neurosci 12, 175, doi:10.3389/fncel.2018.00175 (2018).
- 41 Hyson, R. L. The analysis of interaural time differences in the chick brain stem. Physiology & behavior 86, 297-305 (2005).
- 42 Shannon, R. V., Zeng, F. G., Kamath, V., Wygonski, J. & Ekelid, M. Speech recognition with primarily temporal cues. Science 270, 303-304 (1995).
- 43 McFadden, S. L., Walsh, E. J. & McGee, J. Onset and development of auditory brainstem responses in the Mongolian gerbil (Meriones unguiculatus). Hearing research 100, 68-79 (1996).

- 44 Hallbook, F., Wilson, K., Thorndyke, M. & Olinski, R. P. Formation and evolution of the chordate neurotrophin and Trk receptor genes. Brain, behavior and evolution 68, 133-144, doi:10.1159/000094083 (2006).
- 45 Green, S. H., Bailey, E., Wang, Q. & Davis, R. L. The Trk A, B, C's of neurotrophins in the cochlea. Anatomical record (Hoboken, N.J. : 2007) 295, 1877-1895, doi:10.1002/ar.22587 (2012).
- 46 Matsui, R., Tanabe, Y. & Watanabe, D. Avian adeno-associated virus vector efficiently transduces neurons in the embryonic and post-embryonic chicken brain. PloS one 7, e48730, doi:10.1371/journal.pone.0048730 (2012).
- 47 Chesnutt, C. & Niswander, L. Plasmid-based short-hairpin RNA interference in the chicken embryo. Genesis 39, 73-78, doi:10.1002/gene.20028 (2004).
- 48 Lu, T., Cohen, A. L. & Sanchez, J. T. In Ovo Electroporation in the Chicken Auditory Brainstem. Journal of visualized experiments: JoVE, doi:10.3791/55628 (2017).
- 49 Cramer, K. S., Fraser, S. E. & Rubel, E. W. Embryonic origins of auditory brain-stem nuclei in the chick hindbrain. Dev Biol 224, 138-151 (2000).
- 50 Appler, J. M. & Goodrich, L. V. Connecting the ear to the brain: Molecular mechanisms of auditory circuit assembly. Progress in neurobiology 93, 488-508, doi:10.1016/j.pneurobio.2011.01.004 (2011).



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RESEARCH & INNOVATION

Supporting social and behavioural science improves the quality of life

Dr Arthur Lupia, Assistant Director, Directorate for Social, Behavioral, and Economic Sciences (SBE) at the National Science Foundation (NSF) in the U.S. provides a compelling glimpse into how supporting social and behavioural science improves the quality of life

Today, the social and behavioural sciences focus on the United States' most critical issues. Through dynamic collaborations with one another, and with other scientists, social and behavioural scientists are pursuing many new approaches to our nation's largest challenges and opportunities. Through vast networks of relationships with public and private sector actors, social and behavioural science insights are increasing the effectiveness of the public sector, the efficiency of the private sector, and quality of life for millions of people throughout the world.

To see how these effects are happening, consider the context of safety, security, and preparedness. Think about soldiers on a field of battle. Think about first responders in a city whose infrastructure is unexpectedly compromised. Think about a new mother whose automated vehicle is going a bit too fast towards a crowd of unsuspecting people. Each is in a time of crisis.

Critical infrastructure and technology will be built for these moments. Will humans react as planners expect? Will prior instructions be comprehensible? What do we know about the neural and behavioural underpinnings of these split-second reactions?

We know that neuroscience has made great strides in understanding the brain. We know that other scholars have supported important discoveries about human decision making. Yet the gap between what we know about brains and what we know about behaviour is often too wide to apply to split-second decisions. While electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) allow us to infer certain types of neural activity, helping the soldier, the first responder, and the mother requires neural observations that are more closely linked to behaviour – observations that are beyond our current ability.

Closing the brain-behaviour gap

Today, the National Science Foundation's Social, Behavioral, and Economic Sciences Directorate (SBE) is helping to close the brain-behaviour gap. On the brain side, we know that the neuromodulators that influence attentional control are different from the neuromodulators that affect other functions. Today, we lack non-invasive means of recording and understanding these differences. Change is coming.

SBE-supported scholars are using an evolving process called resting-state fMRI to link increasingly complex forms of brain activity to performance on split-second tasks. Understanding these linkages gives us great potential to improve performance in many cognitive domains.

This is exciting. Now think about what these discoveries can teach us when combined with new work using single-neuron recording in behavioural contexts.

SBE-supported researchers are recording how single neurons change during memory encoding and memory retrieval. A recent finding from this work clarifies why people can be confident even when their memories are wrong. This work identifies two different neuron populations in the parietal cortex. One neuron population signals whether an item is familiar or unfamiliar. Another population reflects people's confidence in their judgments. At moments of overconfidence, the two neural networks send very different signals about the likely consequences of a decision. The

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Dr Arthur Lupia, Assistant Director

"confidence green light" overwhelms the "reality red light." We are on the verge of learning a lot more about when this type of cognitive conflict occurs.

When we combine new abilities to observe neuromodulators with gains in single neuron recording, brain-behaviour gaps become smaller. When the gaps become smaller, planners, engineers, and programmers can more effectively anticipate split-second reactions. They can use this information to better tailor technology to the needs of soldiers, first responders, parents and other important decision makers. With these changes, transformative advances in safety, security and preparedness are more likely.

Tackling many formidable problems

SBE-funded researchers are tackling so many formidable problems, from the origins of violent extremism to effective ways to mitigate the opioid epidemic; from examining how babies acquire language to clarifying how reading teachers can detect learning impediments. Social and behavioural sciences are also examining how the perception of risk affects decision making in contexts ranging from personal finance to extreme weather. SBE-funded research into human movement has assisted in the development of prosthetics that enable people with disabilities to live independent and full lives. In the same spirit, our agency also supported the basic research on page-rank algorithms that produced search engines like Google.

The world is undergoing rapid change, and SBE-funded research is examining how our citizens and nation can adapt to a fast-changing world. Current research emphases include:

• How women and men returning from military service are transitioning back to civilian life.

 What opportunities and challenges face workers, and others who want to work, when employment landscapes and requirements for new kinds of work are changing at unprecedented speed.

SBE-funded research is examining the effects of these changes on jobs and ways of life for communities, the United States, and the world.

SBE-funded researchers also work with the public sector to improve the delivery and effectiveness of critical public services. For example, although advances in weather forecasting increased the window of time for people to seek safety from life-threatening storms, many people were not listening to governmentgenerated warnings. The National Weather Service and other parts of the National Oceanic and Atmospheric Administration worked with SBE-funded researchers to improve how this critical information is conveyed to the people who need it.

SBE-funded scientists are tackling many of today's most important questions. Their answers are helping us improve our security, bolster our economy, and advance the progress of science. While there are so many ways to measure the impact of this work, one easy measure is the fact that NSF-supported researchers have won 57 Nobel prizes in economics – more than two-thirds of all such prizes. In fact, NSF has supported every economics Nobelist since 1997.

It is an exciting time for the social, behavioural, and economic sciences, and SBE is grateful for the opportunity to work with so many talented researchers, institutions, and citizens whose work improves quality of life for so many.

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Gender science: Multifractal geometry in predicting the development of a gender stereotype

Damian G. Kelty-Stephen, Assistant Professor at Grinnell College lifts the lid on gender science research, including the work of Anne Fausto-Sterling and the role of multifractal geometry in predicting the development of a gender stereotype

Gender science epitomises the complexity of goal-directed experience: it exemplifies nonlinear interaction across many scales of space and time. Nonlinear dynamics provides a particularly good geometry – called "multifractal" – for quantifying, modelling, and predicting such interactions across scales of space and time. That sounds complex which I regret, but I think multifractal geometry is complexity that gender science needs.

Introducing gender science

For what it's worth, simplicity in scientific advertising has rarely been good news for gender science. First, developmental science tried to boil gender down into "nature" versus "nurture" probably because the science did not know better. Next, it continued boiling gender down into nature to protect gender diversity against bigoted appeals to unlearn or opt out of nonheterosexual and non-cis identity.

Now, taking oversimplified "born that way" defences of gender to dangerously literal extremes, the Trump administration wants to enact a legal definition tying gender to biological sex. My piece here is about gender, so I will just recommend Sarah Richardson's book Sex Itself for readers interested in how sex is not a simple function a so-called "sex chromosome." Generally calling for more nuance in our discourse about gender, I write this piece specifically to recommend multifractal geometry as one of many tools that nonlinear dynamics has to offer an account of gender respectful of gender's complexity.

The current wisdom in development psychobiology is that nature and nurture are completely entangled. They interact at many scales, to such a degree that they are not even separate. Genetic "nature" exerts no effects separate from experiential "nurture." Epigeneticists in the tradition of Gilbert Gottlieb have shown any simple accounting of "what genes do" separate from "what you learn" absurd, rendering weary statements that "nature and nurture interact" meaningless. Whereas developmental psychology once only envisioned maturational unfoldings of a genetic programme, it now respects the "active child" driving its own trajectory, a bustling organism reaching out to design its own experiences.

And intuitive as it is to imagine an "active child" exploring the playground and leaving a charming path of exploratory destruction in its wake,

developmental psychobiology has struggled to make as clear the epigenetics wrapping everything we thought was "natural" in experientially produced constraints. But epigenetics has been very clear about its complex truths: genes only do what cellular contexts prompt, and behaviour has cascading effects rippling across time and down from the full-body organismic scale, traversing physiological terrain, to the finest systematic changes in gene expression.

The research of Anne Fausto-Sterling

Gender science is at the forefront of researching this developmental tangle wrought by the active child. Anne Fausto-Sterling explores the rich pattern of touch-based experiences and interactions that children have with their caretakers long before children learn the social codes of gender. With such rich haptic experiences crafting all other aspects of organism development, it becomes less tenable that genetic codes should proceed so smoothly - through the creative chaos of a developing child's activity - to cleanly transmute into gender outcomes.

Fausto Sterling aligns her work with the expectation that gender emerges

from the necessarily intersectional experience of a developing organism. Intersectionality refers to a pattern of several overlapping constraints at very many scales, from the cultural to the biological, and gender is no simple sum of these constraints – gender is rather the result of the interaction these multi-scale constraints. Gender is neither coded by genes nor a fluke of nurture, and it is instead emergent from the self-same interactions governing the rest of organism-wide development.

Multifractal geometry – predicting a gender stereotype

To unlock the creative chaos of this active child, Fausto Sterling and Adrienne Harris have both pointed gender science towards nonlinear dynamics. Nonlinear dynamics offers mathematical lenses for modelling interactions across scales. One such intriguing lens is multifractal geometry. Nonlinear interactions across scale generate "multifractal structure." When development follows from nonlinear interactions across scale, developing systems exhibit very many large slow changes and progressively fewer and smaller fast changes. Using what mathematicians call an "inverse power law," we can quantify progressive decay in the relationship between size-of-change with speed-of-change. Intriguingly, power-laws are "scale invariant," meaning that the decay of size-of-change with speed-of-change is the same throughout, suggesting widespread permeability of entire organism to epigenetic-like interactions from grand-scale behaviours to finest gene expressions. Power laws are "fractal" because power-law exponents are often not integers but fractions. Now, nonlinear cross-scale interactions do not just produce one power law but multiple power laws. So, if we study development with an eye to how many and how strong these power-laws we find in time-series of measured fluctuations, then we might get to test the hypothesis that the variety of power-laws (i.e., the multiple fractal patterns: multifractality) could predict the gender outcomes.

Surely, mathematizing gender sounds like a fool's errand. However, the mathematics that speaks to the convolution and complexity of subtle constructs like gender can speak to interactions across scales even in a brief span of time. You may only need a 2000-word narrative with just enough information to suggest a gender stereotype about an ambiguously-named protagonist and then measure how long people take to read each word. I did just that with collaborators Hannah Brown, Chase Booth, Lizzie Eason, and Sebastian Wallot. We asked whether multifractality geometry in word-reading times could predict the development of a gender stereotype. When readers reached the 1000th word with a plot twist thwarting the cued gender stereotype and showing the ambiguously named protagonist having an unexpected gender, readers slowed down to gather their startled thoughts before pressing forward again. Multifractal geometry of word-readings

series up to that point predicted individual readers' differences in how much and how long readers slowed down. After almost as brief a text as appears here, multifractal geometry allowed us to predict the development of a gender stereotype. Interestingly, the startled readers went on to read the remaining text with markedly increased multifractal structure.

Certainly, learning new math sounds dreary and intimidating, and maths seems too harsh and unfeeling a thing to reveal the heart of our experience of gender. But simplicity is cheap. Nonlinear-dynamical complexity respecting the known intersectionality of gender may reap quicker insights.

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The social context of innovation

Professor John F. Padgett uses social network analysis to illuminate how borrowing tactics from seemingly unrelated social phenomena converged to facilitate revolutionary change across Florence

The Renaissance in Florence, Italy was one of the most innovative times and places in Western Europe, generating world-altering advances in art, political thought, science, banking, public finance and republicanism. Scholars have long sought to understand the social context in this city that produced not only particular innovations, with their own local histories, but also spill overs in innovation from one domain to another.

Using primary archival sources, Professor John F. Padgett of the University of Chicago has devoted 30 years to assembling a database that traces the historical evolution of multiple social networks in the city, among about 80,000 persons over 150 years (1350– 1500). These range from kinship and marriage networks, to economic partnerships and commercial credit, to political elections, factions, and public debates. This research has been funded by the US National Science Foundation, the Hewlett Foundation, and the Neubauer Collegium.

Inspired by the biological sciences, where relationships between

molecules within an organism, and organisms within an ecosystem, are often context dependent and best understood through network representations, Professor Padgett's work seeks to understand how complex social networks facilitated innovation in Renaissance Florence. As with a biochemical reaction, innovations in one social network were often catalysed by activity in adjacent social networks.

In a series of studies into each of the evolving social networks listed above, Professor Padgett and his team have identified an organisational innovation



or change of focal interest, and have situated that innovation in the multiple-network context of its production. For example, if focal attention is on banking innovation, Professor Padgett and his collaborators reconstruct in person-by-person detail not only the economic networks of those bankers but also their kinship and political networks. Florentines, after all, were the historical source for our current stereotype of 'Renaissance Men' (and perhaps not as many women as we would like, but some).

Though revolutionary innovations often appear to have sprung from thin air, the team's work demonstrates that they are often the product of a combination of forces that may seem unrelated on the surface. These networks illuminate factors adjacent to an innovation that shaped its emergence and ultimate form.

Social network structure enables revolutionary political change

In a study of the rise to power of Cosimo de' Medici, the founder of the Medici political dynasty during the Florence Renaissance, Professor Padgett traced the unusual degree of centralisation of this revolutionary faction in the marriage- and business-network social foundations of its emergence. This unique example represents Florence's transition from the late medieval tradition of numerous urban political factions to the birth of a united Renaissance state.

Prior to Medici, Florentine politics consisted largely of competition between guilds and wars between urban feudal houses. Professor Padgett and his colleagues focused on Medici's 'social embeddedness' – the ways in which his social relationships shaped and enabled his rise to power to form the Florence state.

Cosimo de' Mendici had many vocations and connections and was a member of both elite marriage networks and numerous business partnerships, which allowed him to behave opportunistically in each of his circles to shape interactions between them. Since he was the singular point of overlap between some of these circles, he was at low risk of being found out when supplying contradictory information to different groups.

This allowed him to take robust action when opportunities to advance his own interests or hinder his opponents' power presented themselves, ultimately moving the Medici family into a position of power over a much broader region than ever before. Through his social connectedness,



Cosimo de' Mendici was able to leverage the existing system of inter-guild and inter-family feuding to create an entirely new system.

Economics shaped by family and friendship

In the 1380s, a new form of business organisation emerged in Florence – the partnership system. For the first time, rather than companies being exclusively run by a single person or family, businesses emerged with multiple legal owners or partners from different families.

These partnerships formed the basis for financial capitalism by protecting business owners from financial ruin in the case of a business failure. It also allowed companies to simultaneously become more generalist and more specialised: the overarching company could cover many markets, while the various partners could specialise in their market within the company.

"Though revolutionary innovations often appear to have sprung from thin air, the team's work demonstrates that they are often the product of a combination of forces that may seem unrelated on the surface. These networks illuminate factors adjacent to an innovation that shaped its emergence and ultimate form."

Through a network analysis inspired by biochemical pathways, Professor Padgett found that the business innovations, in this case, were not strategized, rather an unintended consequence of repression of class revolt. Prior to the partnership system, businesses were based primarily on paternal inheritance or membership in a guild. As these systems became destabilised in a changing urban political environment, marital ties and client pressure began to determine the direction of businesses. This reorganisation of elite social networks to favour victorious pairings encouraged the partnership system to emerge.

Another critical innovation in capitalism was the development of economic credit markets. Businesses relying on commercial credit was unheard of prior to the Renaissance, but in Florence, a system emerged by which trading partners began offering and tracking credits and debts of goods.

By analysing records of credits and debts between Florentine businesses along with marital and political ties, Professor Padgett and his team were able to construct a more complex understanding of how the credit system emerged. As with many of Florence's innovations, social ties played a

major role. The public reputation and social status of a business owner influenced their ability to secure a loan. Friendship and kinship were the initial determiners of who got credit or not, but increasing tax scrutiny from an evolving political landscape eventually forced the formalisation of a mathematically advanced credit system.

These Florentine multiple-networkrewiring processes have been generalised to the other historical cases of the emergence of organisational novelty: the stock market in early-modern Amsterdam, the consolidation of Germany in the 19th century, the divergent outcomes of similar economic reforms in the Soviet Union and China, and the emergence of the biotechnology industry in late 20th-century America. Underlying this generalisation of Florentine insights to new applications is Professor Padgett's adaptation of the concept and models of 'autocatalysis' from the biological literature on the origins of life.

Blurring class lines through new status symbols

Kinship and marriage have long played a major role in determining social status in class-based societies. Medieval class structures based on feudal systems were rigid and categorical, with limited class mobility and marriage prospects relegated to within one's designated group; elite families only married to other elite families. During the Renaissance, Florence saw the breakdown of this medieval social status and hierarchy among categorical groups into a continuous hierarchical status with potential for mobility.

Once again, Professor Padgett and his colleagues were able to use records to determine the social networks that made this transition possible. They found that during this time, social stratification could be determined by either wealth, political office, or age of family. However, rankings of a family within each of these three systems often did not align. Thus, a member of a family with great wealth but poor political standing could marry a member of a less wealthy family with an old name.

"Another critical innovation in capitalism was the development of economic credit markets. Businesses relying on commercial credit was unheard of prior to the Renaissance, but in Florence, a system emerged by which trading partners began offering and tracking credits and debts of goods."

As families sought to make suitable matches across these three components, it opened the door for new men who were successful in politics or business to marry into old families, gaining upward social mobility. As a result, distinctions between elite families began to blur and become more fluid. Just as marital ties shaped Florentine economics and politics, developments in economics and politics made novel marriage pairings possible.

Expanding social understanding

Currently, Professor Padgett is in the process of extending his multiple-network and autocatalysis ideas about social innovation to language. He is studying William Faulkner and political debate in the Florentine Consulte e Pratiche to uncover how social networks shaped the linguistic landscape of the Renaissance.

Nothing occurs in a vacuum

In all of these cases and others, socialorganisational innovation came from cross-network advances and the recombination of multiple networks. Every Renaissance innovation can be tied to activity in adjacent social networks. For example, radical economic change does not occur through the evolution of one network in isolation, but rather the evolution of that network in the surrounding 'catalytic' context of kinship and political networks. Advances in any one network fuelled new processes in others, creating an innovation feedback loop that ultimately shaped the course of European history.

One of Professor Padgett's most intriguing findings is that innovative Florentines were usually conservative in their motivation; seldom were they setting out to create something novel, instead simply working to improve upon the familiar. Innovation occurred not so much by the intentional invention of new tools for old purposes, as by the opportunistic adaptation of old tools for new purposes.



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Building a university climate of inclusive excellence for women and minorities in the fields of STEM

Dr Suzanna M. Rose from the Office to Advance Women, Equity & Diversity, Academic Affairs shares her views on working towards a university climate of inclusive excellence when it comes to the representation of women and minorities in the fields of science, technology, engineering, and mathematics (STEM)

he representation of women and minorities in the fields of science, technology, engineering, and mathematics (STEM) has not kept up with the dramatic growth in the STEM fields over the past few decades. This is true both in the workforce and in academia.

The Office to Advance Women, Equity & Diversity (AWED) at Florida International University (FIU) was established to address this issue by achieving and sustaining faculty equity and diversity in STEM, as well as other fields. With the award of a National Science Foundation Institutional Transformation grant, AWED set out to combat the issue by launching FIU ADVANCE, a five-year, \$3.2 million dollar programme to develop innovative organisational strategies that would produce comprehensive change across STEM and other disciplines.

FIU is both a Hispanic-Serving Institution (HSI) and a Minority-Serving Institution (MSI) that is designated as a Very High Research University within the Carnegie classification. FIU is among the ten largest universities in the U.S. with 57,000 students. Its students are 61% Hispanic and 20% from other underrepresented groups (URGs). FIU is one of the top schools in the country in the number of bachelor's and master's degrees awarded to Hispanic students, as well as in awarding STEM degrees. However, like many academic institutions across the country, the same levels of diversity are not seen at the faculty level. In 2016, the percentage of women in tenure-line, research faculty positions in STEM was just 18%, and only four of the 255 combined STEM faculty members were women of colour.

The goals of FIU ADVANCE were influenced partly by previous research completed by Rose and colleagues showing that foreign-born STEM men faculty demonstrated strong preferences for hiring from within their own cultural group (Rose & Farhangi, 2016). This led the team to explore the intersectional identities of foreign-born men STEM faculty to see if their cultural beliefs also might pose an unaddressed barrier to attracting and hiring Hispanic-American and African-American women in STEM. For instance, findings based on interviews and focus groups indicated that some international faculty members tended to have beliefs about women and gender from their home cultures that were at odds with the more egalitarian ideas

common in the U.S. Others considered racial issues as being a "U.S. thing" and believed themselves to immune from it, even while expressing U.S.-based racial stereotypes and prejudices.

"A diverse faculty has positive effects on our diverse student body. More perspectives are taken into account and increased diversity gives us access to talent currently not represented among faculty and students."

The team, thus, determined that, in order to create a truly diverse community, an atmosphere of inclusion and openness must be fashioned and underlying biases of both U.S. and international faculty must be addressed in order to succeed at hiring more women and members of underrepresented groups.

Building an inclusive culture at FIU

In response, several programmes have created that focus on building an inclusive culture at FIU. Even before search committees begin their work to recruit candidates for a particular faculty position, committee members are required to attend a STRIDE Workshop (Strategies and Tactics for Recruiting to Improve Diversity and


Prof. Svetlana Roudenko, Mathematician and Diversity Mentor Professor, and Suzanna Rose, Associate Provost, AWED

Excellence). The faculty-led workshops provide participants with background information and concrete advice about practices that make searches more effective at producing diverse candidate pools and more successful at hiring the candidates that departments want to attract.

Faculty also may participate in the Bystander Leadership Program, a workshop that is intended to raise awareness of implicit bias and provides experience with using a variety of diplomatic responses to both subtle and obvious situations involving gender or race bias. A crucial component of the programme is AWED theater, that presents skits tailored to the academic setting using professional actors to encourage attendees to interact with each other and the curriculum. Attendees discuss a toolkit of response options available to them and then take part in simulations in which they practice the techniques. Participants attest that the practice sessions are especially important for increasing their confidence in using intervention skills and strategies.

FIU's Diversity Mentor Professorships programme

Another initiative aimed at increasing diversity is FIU's new Diversity Mentor Professorships, a programme launched in 2017-2018 to recruit excellent research scientists and engineers with a history and commitment to the mentorship of women students and students from traditionally underrepresented groups. Research has shown that having a female role model has a powerful positive effect on women's performance in maths and science classes.

Suzanna Rose, associate provost, AWED, says that: "A diverse faculty has positive effects on our diverse student body. More perspectives are taken into account and increased diversity gives us access to talent currently not represented among faculty and students."

Helping create female role models and leaders

A further programme run by AWED and designed to help create female role models and leaders on campus is the Women Faculty Leadership Institute (WFLI). This annual symposium is designed to promote women's leadership and strategic career planning. WFLI focuses on enhancing skills and thinking broadly about women's issues.

As of fall 2018, the STRIDE workshops were institutionalised (with a threeyear phase-in) to be required of faculty search committee members in all colleges and departments, and more than a hundred faculty members have taken part in a Bystander Leadership workshop. Additionally, the development of university-wide faculty diversity and inclusion plans was launched during the same semester.

The number of women in STEM is now at 20%. FIU ADVANCE, therefore, can already claim positive results in its goal to create a faculty-based social system that proactively enhances a culture of inclusion for all faculty at FIU.

Rose, S. M. & Farhangi, S. (2016). The intersectionalities of men STEM faculty: An unexplored barrier for recruiting women of color? Association for Women in Science, 48, 16-19.



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RESEARCH & INNOVATION



The Human Placenta: A short-lived organ, with a long-lasting impact

Dr David Weinberg from the Human Placenta Project, a program of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), part of the U.S. National Institutes of Health, details why the human placenta is a short-lived organ, yet has a long-lasting impact

The placenta is the least understood human organ and arguably one of the most important, not only for the health of a woman and her foetus during pregnancy but also for the lifelong health of mother and child. Though we've all been connected to a placenta, many of us rarely think about the role of this sophisticated, multi-tasking organ in launching our lives.

The placenta serves as the lungs, kidneys, and liver for a developing foetus. It brings oxygen and nutrients and

discards waste. Yet, the organ is immediately discarded after birth, under-appreciated and under-studied.

We hope to change that.

Our ambitious Human Placenta Project (HPP) aims to monitor the placenta in real time as it changes shape and form during the course of pregnancy. Our goal is to harness advanced technology and developing tools that can detect when the placenta fails to function properly. If we can learn early on that typical develop-

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Placenta oximeter



Dr David Weinberg Project Lead

ment has gone awry, we can identify possible pregnancy complications, such as preterm birth, preeclampsia, or fetal growth restrictions – and make it possible to intervene.

New advanced monitoring tools allow us to glean information about the placenta as it develops, without compromising the health of mother and foetus.

Global expertise to make a difference

Recognising the need to tap scientists from diverse fields, HPP has invested more than \$60 million to support the development of novel technologies, from MRI and ultrasound to measurement tools that read signals in the mother's blood. Achieving our goals will require a concerted commitment from across the globe. HPP was launched with input from the Trophoblast Centre for Research in Cambridge, as well as researchers at Oxford University and King's College of London.

Progress and novel approaches

Imaging the placenta presents unique challenges. Even the slightest movement by the foetus or simply the mother's breathing can temporarily distort the shape of the placenta shape and make it difficult to get clear images. Advances in imaging technology have allowed researchers to capture clear images of the placenta doing its job transporting blood and oxygen between mother and foetus. The placenta releases small particles, called vesicles, into the maternal blood that may yield clues to the health and function of the placenta. Since the Human Placenta Project started five years ago, researchers already have developed new methods for isolating and analysing these vesicles. Scientists are studying their content looking for clues that would possibly identify biomarkers to show when pregnancies face problems.

One of the newest research developments at NICHD is a small, hand-held device, the size of a mobile phone, that can be strapped around a pregnant woman's belly to monitor oxygen levels to the foetus – a key to detecting early pregnancy complications. While still at the early stage of development, such a device might be a cost-effective tool for use in low-resource settings.

Hope for the future

At the very first HPP workshop, I remember a physician telling me that in the past there had always been only two choices for doctors facing a pregnancy complication: deliver the baby early or wait and hope for the best. Such limited choices should be unacceptable. The goal of the HPP is to make them archaic.

For more information about the Human Placenta Project, visit: https://www.nichd.nih.gov/research/supported/HPP/default

To read about the most recent research projects funded in 2018: visit: http://bit.ly/2qTFxAN

Dr David Weinberg Project Lead

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Love as medicine

Dr Sue Carter, Director of the Kinsey Institute provides an expert insight into the role of oxytocin, a hormone that helps to explain the healing power of love

ove is intrinsically beautiful, but also complex and mysterious. Although love can be difficult to define, the list of love's functions is long. Love influences all aspects of human existence. Love is powerful medicine. Healthy relationships can protect against disease and restore the body in the face of illness.

Without loving relationships, humans fail to flourish, even if all of their basic needs are met. "Love lost" is one of the most powerful forms of stress and trauma. We now understand that the causes and consequences of love or its absence are grounded in a biology that operates largely below the level of human consciousness.

"The mechanisms through which love protects and heals are only now being discovered."

Remarkably, the origins of this knowledge began in research conducted in a small field mouse known as the prairie vole. In the 1980s, working at the University of Illinois, my colleague Lowell Getz and I uncovered evidence that both in nature and in the laboratory, prairie voles were capable of forming life-long pair bonds. In this species, both parents nurtured the young, with fathers sharing all aspects of infant care except nursing. Older siblings also cared for younger babies. Juvenile prairie voles left the family to find mates and scrupulously avoided incest. Prairie voles exhibited the

traits of the mating system that humans associated with monogamy.

As in humans, the core of the prairie vole monogamy was based on social bonds, not simply defined by sexual exclusivity. The capacity for pair bond formation was regulated physiological and emotional states, based on neural systems also found in humans. We also found that prairie voles have high levels of oxytocin, a human-like autonomic nervous system, and they are exquisitely sensitive to the neural and epigenetic effects of early nurture. Thus, by studying pair bonding in voles, we had created a laboratory model allowing us to examine the neurobiology of what humans call "love."

The evolutionary and biochemical prototype for love and social bonds is the mother-child interaction. The physiological pathways that permit social bonds are shared with parental behaviour, as well as birth and lactation. Our research in prairie voles revealed that two ancient neuropeptides and their receptors are foundational to the capacity to form pair bonds and also show defensive aggression. Those molecules are oxytocin and vasopressin. Both oxytocin and vasopressin are important to the social bond formation, but their functions are strikingly different.

Vasopressin is the more primitive of the two and is associated with adap-

tive functions that protect humans against dehydration and regulate blood pressure. Vasopressin has been associated with the neurobiology of anxiety, fear and avoidance learning. Both males and females synthesise vasopressin. However, in areas of the brain implicated in defensiveness and territorial aggression, vasopressin production is increased by androgens, and may play a central role in sex differences in the expression of aggression.

Oxytocin, in contrast, is associated with prosocial behaviours, including social engagement and the formation of social bonds. Oxytocin also may induce a sense of safety, reduce reactivity to stressors, block fear and increase trust. Processes that help to define mammals, including lactation and maternal behaviour are facilitated by oxytocin. Although both sexes synthesise oxytocin, in some cases estrogen increases sensitivity to the actions of oxytocin, favouring this peptide in females. Oxytocin was essential to human evolution, facilitating the birth, growth and nurture of our immature babies.

Oxytocin helps, directly and indirectly, to promote healing and restoration. For example, oxytocin has anti-oxidant and anti-inflammatory properties. Oxytocin also regulates the immune system and the highly protective parasympathetic, vagal branch of the autonomic nervous system. Vagal pathways, regulated by oxytocin, are



necessary for social communication and engagement through actions on the muscles of the face and head.

Furthermore, the autonomic nervous system regulates all of our internal organs, as well as the distribution of blood and nutrients throughout the body. Through effects on the autonomic nervous system, oxytocin regulates blood flow and oxygen to the brain, thus further supporting human cognition, culture and eventually civilisation.

Thus oxytocin-vasopressin effects on the autonomic nervous system are likely a critical component of the healing power of love. The autonomic nervous system is one portal through which the peptide systems and love may be accessed and influenced.

Oxytocin and vasopressin evolved from a common ancestral peptide. Oxytocin and vasopressin are similar in structure and interact dynamically with each other's receptors. However, for several reasons, these molecules are difficult to study. Their actions are adaptive, quickly changing and also strongly affected by emotional context. Under conditions of safety, oxytocin promotes social engagement. But in a context of anxiety or fear, oxytocin may function like vasopressin, possibly by binding to vasopressin receptors.

Generally, oxytocin tempers fear and increases both trust and social behaviour. But in individuals who have a history of trauma or extreme stress, oxytocin may trigger the vasopressin system, enhancing fear and protective responses. The unique properties of the oxytocin and vasopressin systems allow these two molecules to be highly adaptive and support emotions such as love, but also jealousy and defensive aggression. The same novel properties that give oxytocin and vasopressin great power, also create serious challenges for understanding their functions.

The oxytocin-vasopressin system is constantly changing across the life cycle. Oxytocin affects the development of the brain, cardiovascular and immune systems. Recently, my colleagues and I have demonstrated that the expression of the gene for the oxytocin receptor in voles is epigenetically tuned by early experience. Loving relationships, especially in early life can influence behaviour and physiology across the lifespan, in part through changes in the sensitivity of the oxytocin system. The absence of nurture may create a pattern of self-defensive and a sense of threat that could inhibit the capacity for love in later life.

The mechanisms through which love protects and heals are only now being discovered. Oxytocin influences sociality and social experiences influence oxytocin. Knowledge of the neurobiology of love helps to explain the exceptional reproductive success of humans and also our resilience in the face of fear and aggression. The emotional and physical health and longevity of our species, and perhaps our planet, depends on our capacity to understand and apply our knowledge of the biology of the love, especially in this time of trauma.

Early nurture epigenetically tunes the oxytocin receptor. https://www.ncbi.nlm.nih.gov/pubmed/30227351

The Oxytocin-Vasopressin Pathway in the Context of Love and Fear. https://www.ncbi.nlm.nih.gov/pubmed/?term=Carter+love+and+fear



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Are environmental chemicals contributing to the obesity epidemic?

A group of experts from the University of California, Davis and the University of Southern California explain the extent to which environmental chemicals are contributing to the obesity epidemic

besity is a metabolic disease characterised by excessive body fat that is defined clinically as having a body mass index (BMI) over 30. For the first time in human history, the number of obese and overweight people is greater than the number of those who are underweight. An estimated 1/3 of the world's population currently meet the clinical definition of obese, and it is predicted that approximately half the world's population will be obese by 2030.

Obesity is a major risk factor for numerous life-threatening diseases, including cardiovascular disease, cancer, and Type 2 diabetes, and in 2014, the global economic burden of obesity was estimated to be \$2 trillion. Given the significant health and economic impacts of obesity, there is an urgent need to identify the risk factors involved in the development of obesity. While caloric excess and sedentary lifestyle are classically identified as the main drivers of obesity, these two factors do not explain the recent dramatic rise in the global incidence of obesity.

Factors that are receiving increased scrutiny as potential risk factors for obesity are chemicals that interfere with the action of hormones that regulate metabolism and weight gain. These chemicals, which are referred to as "environmental obesogens", are thought to promote obesity by interfering with metabolic homeostasis.

In support of the obesogen hypothesis, several human studies have demonstrated a positive association between exposure to environmental chemicals and obesity. For example, increased levels of dichlorodiphenyltrichloroethane (DDT), a pesticide once widely used to control mosquitoes, have been linked to higher BMI in both children and adults in multiple populations around the world. More recently, maternal smoking or exposure to near roadway air pollution have been reported to increase the risk of childhood obesity.

While human studies are essential for assessing the feasibility of the environmental obesogen hypothesis, they do not establish that exposure to DDT, air pollutants, or other environmental chemicals, actually cause obesity. This is because it is difficult to tease out whether other factors that coincide with environmental exposure, such as socioeconomic stressors, may be the actual cause. However, studies of laboratory animals maintained in a controlled environment on a fixed diet have confirmed that at least some environmental chemicals can increase the risk of obesity.

Studies of animal and cell culture models are also providing insight as to

how environmental chemicals promote an obese phenotype. For example, environmental chemicals can increase fat storage capacity by increasing the number and/or size of fat cells, known as adipocytes. Cell culture experiments suggest that the industrial chemical tributyltin (TBT) increases the number of adipocytes by activating a receptor that promotes the differentiation of stem cells into adipocytes.

"Obesity is a global epidemic that affects adults, children and infants, and the rising incidence of obesity and its related diseases shows no signs of levelling off."

Consistent with these observations, experimental animal models exposed to environmentally relevant concentrations of TBT during development have increased fat accumulation in adipose tissues and the liver compared to control animals. Of concern, these studies suggest that the obesogenic effect of TBT is transgenerational, meaning that TBT may influence obesity risk in not only the individual exposed during development but also in the children and even grandchildren of the exposed individual.

Obesogens have also been shown to affect adipocyte function. Healthy adipocytes not only store energy but also produce hormones that signal throughout the body to control



appetite and energy balance. Air pollutants can interfere with both of these processes, increasing the body's ability to store energy while also decreasing the production of hormones important for metabolic health. The body also contains a special type of adipose tissue called brown adipose, which burns energy to create heat to maintain body temperature. This process is thermogenesis, known as and decreased thermogenesis has been linked to obesity in humans. Developmental exposure to DDT hinders thermogenesis in mice and decreases the expression of genes involved in burning energy.

The hypothalamus is a region of the brain that monitors and responds to changes in the body's hormonal and nutritional status to maintain metabolic homeostasis, and disruption of hypothalamic function can lead to obese phenotypes in animal models. Recent studies in mice have shown that exposure to air pollutants increases inflammation in the hypothalamus, which can interfere with hypothalamic function, and this effect coincides with increased body weight. Another animal study of the obesogenic effects of air pollution linked increased obesity with decreased expression of hormone receptors involved in appetite regulation. Whether environmental chemicals alter the hypothalamus in other ways remains a critical data gap.

Obesity is a global epidemic that affects adults, children and infants, and the rising incidence of obesity and its related diseases shows no signs of levelling off. These alarming trends warrant research focused on understanding the relative contribution of environmental chemicals to the development of obesity, especially since exposures to environmental chemicals are modifiable risks. However, an effective public health strategy requires determining which of the tens of thousands of chemicals in the human environment have obesogenic activity. It may be possible to address this problem by leveraging cell culture models that express receptors that drive adipocyte differentiation or are implicated in controlling feeding behaviours. Chemicals found to activate these receptors in cell culture at environmentally relevant concentrations could then be studied in preclinical models to confirm obesogenic potential at the organism level. In addition, it will be important to educate the public – especially pregnant women – as to the effects of environmental exposures on the disease risk in their child. Given the increasing evidence linking chemical exposure in utero to increased risk of obesity, it will be important to educate parents on the approaches for mitigating or reducing their exposure to suspected environmental obesogens before, during and after pregnancy, with the goal of reducing the risk of obesity in their children.

References

- 1 Heindel, J. J. et al. Metabolism disrupting chemicals and metabolic disorders. Reprod. Toxicol. 68, 3-33, doi:10.1016/j.reprotox.2016.10.001 (2017).
- 2 Janesick, A. S. & Blumberg, B. Obesogens: an emerging threat to public health. Am. J. Obstet. Gynecol. 214, 559-565, doi:10.1016/j.ajog.2016.01.182 (2016).

VETERINARY MEDICINE

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Challenges in creating open data policies for universities

Anne Mims Adrian, PhD, PUSH Open Data Project Manager charts the challenges in creating open data policies for universities

s government agencies and private foundations are increasingly requiring public access to scientific publications and to the supporting research data as terms of their grants, universities struggle to meet these new requirements.

Though open data practices at <u>universities seem to be</u> <u>driven</u> by funders' requirements, university leaders and researchers also recognise the benefits of open access and open data. They see the values of data as accelerating the pace of discovery, facilitating transparency, confirming of scientific results, increasing collaborations, building faculty and universities reputations and credibility, and supporting education.

Although universities recognise these benefits of open access and open data, they also have some concerns and hesitations. At the centre of this conflict is the protection of intellectual property – who owns the work and research conducted at universities. Since the passage of the Bayh–Dole Act of 1980 which gave rights to universities to own inventions and research obtained through federal dollars, U.S. universities have been increasingly motivated to protect research and intellectual property for potential income opportunities, especially with those prospects that may yield big profits through patents and royalties. Prior to the passage of the Bayh-Dole Act, federal research funded contracts assigned inventions to the federal government.

The current intellectual property paradox for universities arises from the protection of potential profits that can be absorbed back into universities and the growing beliefs in the benefits to the public from open access to research findings and research data. Universities are asking how can they provide for open access and open



data and still protect universities' work – particularly those works that may create profits for universities.

Furthermore, universities current systems reward faculty for publishing research reviewed by their peers. Many researchers fear that with this kind of data others may scoop their work and publish similar analyses before they have had ample time to publish all findings. On the other hand, faculty are discovering that when they share their data, their work is cited more, and the possibility of collaboration is increased. Balancing sharing research data and protecting universities' and intellectual property for faculty is a challenge, but a challenge worth working through.

While some universities are evaluating their current open access and open data policies, hiring additional librarian support, and creating data repositories,

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the current university research culture, incentives, and practices are generally poorly suited to support open data.

The struggle between open data and intellectual property protection lies within the confusion of who owns the data. The confusion begins with data ownership policies. Sometimes data ownership is specified within intellectual property policies, but most often data ownership is ambiguous. And for some universities, data ownership is not mentioned in their policies at all. Confounding the issue for some is the de facto mode of practice of faculty deciding how they use the data, despite policies stating that the data and work by faculty are owned by their parent universities.

Because of funders' requirements and public expectations toward access to research findings and research data, universities are reacting with additions to infrastructure and support that will provide for open access and open data. However, to get to the bottom of this, we must affect culture and practice. And we know that culture and practice reflect policies. To change policies that will 1) help universities comply with funders' requirements of open access and open data and 2) create a notion of public access to publicly funded research, we must evaluate our current policies.

Before developing open data policies, universities need to examine and clarify current data ownership policies. From their examinations, policies can be developed that can balance the protection of potential profits and providing for the greater good.

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Detecting Specific Language Impairment (SLI) in children

Mabel L Rice analyses the cause of Specific Language Impairment (SLI) and the need to identify it early on in children to provide a solution

hildren around the world acquire their native language, or languages, without the need for explicit formal teaching. Yet children vary in how well they manage this task in comparison to their age mates. Children's language continues to grow during childhood as they acquire sentence structures, grammatical elements to mark case, person, tense, agreement of subject and verb, vocabulary, and a host of other details. Some children are behind at the beginning but catch up to their peers by four or five years of age; other children continue to trail behind their peers into adulthood, leaving them with less robust language abilities for negotiating life's educational demands, interactions with unfamiliar people, and employment positions. Most of this group of children have a language disorder that delays the mastery of language in children who have no hearing loss or other developmental delays, known as Specific Language Impairment (SLI)^(1,2).

SLI is likely to be undetected by parents and teachers, given the lack of an obvious cause of the condition. This means that a primary need is for how to identify children with SLI. Once identified, children should receive help to overcome their limitations in learning a language. Robust language skills for every child are robust assets for the individuals to contribute to their families and their societies to the benefit of others and themselves.

Around the world, solutions to these needs and increased likelihood of a good life for all children depend on a careful scientific study across languages of the children's pathways into their native languages. Detection of how one child is different from others of his or her own age requires an understanding of how children master different language skills at different ages. In turn, this knowledge requires a good understanding of the details of each language and similarities across languages. Much of the available research is based on English-speaking children, although there are rapid advances underway in documenting how children acquire many of the world's major languages.

The ultimate objective is to provide guidance for the development of effective teaching practices to assist children who do not acquire language as easily as their age peers, in order to prepare them for a productive life as an adult. Although this may seem to be obvious, perhaps just a matter of insisting a child talk better or for adults to talk more to a child. Neither of these approaches are likely to be effective. It would be like insisting that a child be taller or have different hair colour. Instead, effective teaching approaches require a consideration of four factors that vary considerably from country to country around the world.

"Some children are more at risk than others. During the toddler age range, boys are later to acquire language than are girls, a gap that can persist to five or six years of age."

Governmental/societal policies

There is considerable variation across developed countries in the organisation of governmental resources and oversight for services for children with SLI. In the United States (U.S.), the public schools are required to provide speech/language pathology services for children with language impairments, in the context of an individualised education plan (IEP) developed in teams of classroom teachers and other educational specialists. Speech/language pathologists are required to be certified at the level of a master's degree. States vary widely in the exact definitions of eligibility for services. Some states would exclude children with SLI whereas others would include them and encourage them to be enrolled in services. Schools are not the exclusive setting for services in the U.S. Private practitioners, usually but not exclusively speech/language pathologists, also enrol children with SLI in treatment, which is usually but not always paid by private health insurance plans. Less

likely are services provided through military benefits or in association with a medical practice, such as a paediatrician who specialises in SLI.

In contrast, in many countries services are implemented under a public health system, sometimes in arrangements with schools and sometimes in private practices with a governmentsponsored insurance program. Around the world, there are various configurations of these country-wide policies. The availability of speech/language pathologists with specialised training, and the level of training required, also varies greatly.

Teaching settings

The settings in which language teaching can occur also vary widely. Across the world, the most prevalent setting is a home, although home-based professional services are expensive and unlikely. Instead, the school classroom is the likely setting, as part of the teacher's approach to teaching each child in the age-defined classroom. Obviously, this has limitations related to the size of the classroom and the teacher's training. In the developed nations there is widespread recognition of the impact of preschool settings designed to enhance children's language abilities, as a strong platform for later education including the transition to reading. Private practice services are more likely to be with an individual teacher than in a group setting.

Specialised training

Teacher training, as well as paediatric training, involves a wide range of content areas and usually does not include specialised information about linguistic structures and sociolinguistic skills that are essential to the identification of children with SLI or teaching methods. Speech/language pathologists in the U.S. are likely to receive this training although training approaches vary widely. There is a great need for the specialised training that will benefit all children.

Child characteristics

Some children are more at risk than others. During the toddler age range, boys are later to acquire language than are girls, a gap that can persist to five or six years of age. Little is known about how gender differences play out over childhood. A recent well documented but surprising finding is that adolescent girls score lower than boys on vocabulary understanding, with the lowest performance by adolescent girls with SLI⁽³⁾. Some risk factors have been widely assumed, such as low levels of maternal education or low levels of a child's nonverbal intelligence, although the evidence for these generalisations is not straightforward, suggesting that the generalisations do not always hold. (1,2)

How to teach

Teaching should be culturally sensitive and effective for enhancing each child's language development across multiple dimensions of language, including grammar, vocabulary, and social uses of language. Note that the big challenge is how to teach language to a child with SLI in a way that causes them to learn language faster than their age peers in order to catch up. The catch-up period may extend over the years, requiring sustained treatments, and the age of first intervention will matter. These are formidable challenges and no one method has been shown to reliably meet them. It is most likely that a well-formulated combination of approaches will be needed, across different forms of service delivery. The new world of electronic teaching methods shows promise for how to teach in new settings, using innovative methods, at times when children are available and interested. It is essential to continue research across many languages in order to arrive at the knowledge needed to teach children with SLI what most children acquire without explicit teaching.

References

- Rice, M. Specific Language Impairment in Children. https://www.openaccessgovernment.org/specific-language-impairment-in-children/40152/ 2017.
- 2 Rice, M. Specific Language Impairment in Children. Part II. https://www.openaccessgovernment.org/specific-language-impairment-in-children/2018.
- 3 Rice ML, Hoffman L. Predicting vocabulary growth in children with and without Specific Language Impairment (SLI): A longitudinal study from 2 1/2 to 21 years of age Journal of Speech, Language & Hearing Research. 2015;58:345-359.



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Decentralising security for mobile devices: Is blockchain the viable solution?

Steven Sprague, Cofounder and CEO of Rivetz reveals a viable solution when it comes to decentralising security. He argues that there is great promise for creating mobile device security with blockchain technology

he world was introduced to the first commercial mobile phone in 1983 with the launch of the Motorola DynaTAC 800x, which stood at a height of 13 inches, weighed 1.75 pounds and took 10 hours to recharge. In the early days of the mobile phone industry, it was incredibly simple for attackers to clone a phone's identity and run up all sorts of charges on your account.

Over the last few decades, mobile has experienced quite a metamorphosis from the "brick" of the 1980s to the compact, feature-packed smartphone of today. Now, mobile is king – people across the globe use their mobile devices not only to communicate but also to read the news, get directions, stream music, check bank accounts, store assets and so much more.

As we increasingly rely on our mobile devices, new avenues of attack continue to emerge. So much of our sensitive personal information and digital assets – such as corporate data and bank account and credit card numbers – are accessible via our mobile devices. They have become treasure troves for attackers.

Blockchain and mobile device security

There is great promise for creating mobile device security by combining secure enclaves – also known as 'roots of trust' – with blockchain technology. Blockchain is a distributed ledger technology that protects a digital transaction through complex mathematical algorithms. Because of the strength of this math, the transaction can only be created by those who hold a valid private key.

Private keys were developed as a means of protecting our digital transactions. A private key is a piece of cryptographic code that allows a user to prove who he or she is – in other words, it's a digital signature that says the user is, in fact, the one who is executing a digital transaction.

Private keys are used to secure a variety of transactions on mobile, including messaging, cryptocurrency and more. Here's the downside: if an attacker steals your private key, they can impersonate you, and then access and abuse your data and digital assets. The prevalence of mobile devices has made them some of the largest repositories for private keys.

The biggest challenge in decentralised cybersecurity is that we cannot prove the transaction was intended. If an attacker steals your private key and transfers \$5,000 to a third person, there is no way to prove that the attacker – and not you – performed the transaction. Rivetz ensures an intended transaction by establishing

that it occurs from a known device, in a known condition, with an authorised user, under the required conditions. Rivetz performs "device attestation" to ensure a user's devices are in a "known" condition by executing regular health checks to ensure the device integrity. Each device's integrity is recorded on the blockchain so future health checks can be compared with the baseline, establishing that those devices are in a condition the user intended.

As the rise of the internet brought digital fraud and attacks on identity, innovative industry leaders banded together to fight that fraud and formed organisations such as the Trusted Computing Group (TCG). TCG developed specifications that have become standard for securing devices, as well as the data and identity on those devices, such as personal computers and laptops.

Trusted computing uses hardware to protect users. It ensures a device will consistently behave in the expected ways, protected by a secure enclave or a 'root of trust' embedded within the device's hardware. A root of trust is isolated from the device's software operating system (OS), allowing it to execute code that cannot be seen by the OS. One such root of trust developed by Global Platform is the Trusted Execution Environment (TEE), which



enables trusted computing technology for mobile devices. The TEE already is built into the hardware of more than 1 billion mobile devices. Today, most private keys are generated within software, which is much more susceptible to attack than hardware. The TEE is capable of protecting a user's private key within the device hardware, a method that is far more secure than performing these operations in standard software.

A single system of security may not be enough to protect against the variety of cyber-attacks possible today. It is more pressing than ever to provide multi-layered protection of digital assets across two or more security domains. That way, even if an attacker were to breach one point of security, the other(s) still would need to be compromised, offering an extra layer of protection for important digital assets – whether that's your personal information or your hard-earned money.

One of the most ubiquitous roots of trust is the subscriber identity module, or SIM card. The SIM is a protected hardware environment and was created to combat mobile fraud and to protect the device identity. With the pervasiveness of both the TEE and the SIM, Rivetz saw an innovative opportunity to use these isolated roots of trust to work together to protect mobile users. In conjunction with ElevenPaths, the cybersecurity unit of Telefónica, the world's thirdlargest mobile carrier with more than 300 million subscribers, Rivetz uses both the TEE and SIM to protect our private keys – introducing the Dual Roots of Trust.

The solution leverages the TEE along with the SIMs deployed by Telefónica. With Dual Roots of Trust, Rivetzenabled apps generate private keys in hardware, then cryptographically distribute those private keys between the TEE and the SIM. This delivers built-in security from both the mobile carrier and the device manufacturers, to create decentralised key protection.

By distributing a private key across these two roots of trust, attackers would have to breach both secure systems in order to steal a single private key. As an added security feature, two different entities - or independent control planes - aid the user in controlling their private keys. Through a special application authorised to perform activities inside the TEE, the user remains in control of the secrets stored in the TEE. If your mobile device is lost or stolen, a simple interaction with your mobile carrier can disable the SIM, permanently or temporarily until the device is found. So even if a thief has your device, you remain in control and your private keys are still safe.

The Rivetz solution has an unlimited number of use cases, such as sensitive work apps, mobile wallets, social media accounts and mobile banking. One of the most unique applications of Dual Roots of Trust is the ability to provably control specific applications on a device. This feature is especially useful for enterprises. Let's say a company has its own proprietary Rivetz-enabled app that employees use for work on their personal devices. If an employee is terminated or leaves, the company has the ability to revoke access to that app on the former employee's personal device with Dual Roots of Trust.

As our mobile devices have become more important to our everyday lives and contain so much of our personal and private data, we need better ways to protect ourselves. The solution lies in the roots of trust that already exist on millions of mobile platforms: the SIM and the TEE are two of the most common secure enclaves. Dual Roots of Trust is the next step in ensuring our assets stay safe.



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ENERGY

Why wait? Fuel cells leading the global energy transformation today

Morry Markowitz, President of the Fuel Cell and Hydrogen Energy Association argues why should we wait when fuel cells are leading the global energy transformation today

The world is undergoing an energy transformation and with that, the demand for cleaner, more reliable power is growing. Fuel cells are answering the call – emerging as the 'go-to' technology solution for a wide range of market sectors, from transportation to stationary to portable/off-grid – and are enabling the transition to renewable energy around the world.

Fuel cells generate energy through an electrochemical reaction of hydrogen and oxygen, not combustion, and when pure hydrogen is used for fuel, the only by-products are water and useful heat.

From an energy security standpoint, reducing dependence on imported fuels is key. Hydrogen can be generated from domestic sources – from conventional fuels such as natural gas to biogas generated from landfills, wastewater treatment plants, industrial farms, or food processing facilities. Hydrogen can also be produced using electricity, from the grid or renewable sources such as solar or wind power, to split water.

A fuel cell will continue to operate as long as fuel is provided, ensuring continuous, reliable power, which is critical to so many industries, governments, and the citizens they serve. Stationary fuel cells can operate in tandem with – or independent of – the grid and have proved their resilience through several major storms and power outages, servicing communications networks, grocery stores and emergency shelters.

In addition to power, the by-product heat from a fuel cell can be captured and used at the end-user facility for heating or cooling, boosting overall efficiency to more than 90%. Fuel cells are also durable, quiet, and lightweight, allowing for flexible siting – inside, outside, underground or on the roof.



Morry Markowitz, President

Fuel cells can be scaled to virtually any size to fit any power need, which is why the technology is being deployed in a range of markets. Customers today range from some of the largest global corporations to mom-and-pop small businesses, as well as utilities, municipalities, military branches, and more. Fuel cells are currently providing power to retail sites, data centres, telecommunications and railroad networks, wastewater treatment plants, hospitals, universities, and other sites.

In the transportation and mobility sector, more than 23,000 fuel cell-powered forklifts are operating in warehouses and distribution centres across the U.S. and



fuel cell buses are transporting passengers in multiple states in the U.S., as well as numerous countries abroad.

Recent momentum and announcements in fuel cells for heavy-duty trucking and medium-duty delivery vehicles has spurred significant interest and activity from major companies as current demonstrations show the potential for the technology to make a big environmental and economic impact in this sector.

For individual consumers in Japan and parts of Europe, fuel cell systems can be purchased to power homes and apartments. In California and several countries around the world, zero-emission fuel cell vehicles from top automakers are available for sale or lease.

Collectively in all these markets, there are hundreds of thousands of fuel cells in operation around the world today, and the United States is out front as an international leader for this innovative technology. This success in the U.S. is due in large part to the support of committed state and local governments, as well as public-private partnerships, a committed industry manufacturing and exporting products, and a strong foundation of R&D through academia, the U.S. Department of Energy, and the National Laboratories.

As more customers experience the benefits of fuel cells, applications for these technologies are expanding

to include ground support equipment at airports and ports, mobile lighting, unmanned land, air and sea vehicles, remote and portable power for the military, and community micro-grids. New opportunities are also emerging, including in energy storage and powerto-gas, to help transition to the large-scale and worldwide adoption of renewable energy.

With a technology that can meet the size and power requirements of virtually any application, powered by a fuel that can be produced from both conventional and renewable feedstocks and a proven record of environmental and economic benefits, the potential of fuel cells is limitless.

Fuel cells are here today and already making a huge impact helping transition the world to a better tomorrow. ■

Morry Markowitz President

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ENVIRONMENT

The USGS Earthquake Hazards Program

William Leith, Senior Science Advisor for Earthquake and Geologic Hazards at U.S. Geological Survey (USGS) explains the important aspects of the USGS Earthquake Hazards Program

September 2018's earthquake and tsunami disaster in Sulawesi, Indonesia, is our most recent reminder of the devastating power of large earthquakes. With a death toll exceeding 2,000 by recent estimates, this complex disaster, which included widespread ground failure that buried large parts of the city of Palu (pop. 335,000), now ranks among the worst earthquake disasters of the past 100 years.

It could happen here. Although Americans have not experienced a major earthquake disaster in nearly 25 years, since the 1994 earthquake that struck Northridge, California, the Federal Emergency Management Agency (FEMA) recently estimated that, when averaged over decades, annual earthquake losses in the U.S. are \$6.1 billion, with nearly half of Americans living in areas vulnerable to strong shaking in future earthquakes.

Yet earthquake losses can be reduced by improving the resilience of buildings, bridges and other structures, and by taking quick action when the ground starts shaking. Preparedness, mitigation, and informed response can reduce deaths, injuries, and economic losses from earthquakes, tsunamis, and earthquakeinduced landslides and soil liquefaction. In other words, informed and proactive communities can save both lives and money.

To help reduce losses from earthquake hazards, the USGS Earthquake Hazards Program (EHP) supports a highly coordinated set of monitoring, hazard assessment, applied research, and risk communication activities nationwide. We provide the nation with a growing suite of rapid earthquake information products, deliver regional and national seismic hazard assessments, conduct targeted research to improve these functions, and coordinate post-earthquake investigations to understand better the effect of earthquakes. The USGS program is the applied earth-science component of the four-agency National Earthquake Hazards Reduction Program (NEHRP). Through NEHRP, the USGS partners with FEMA, the National Science Foundation, and the National Institute of Standards and Technology to reduce earthquake losses (both life and property losses) in the U.S.

Response organisations require actionable earthquake information. The EHP monitors the nation's earthquakes via the Advanced National Seismic System (ANSS) which includes regional seismic networks operated by university partners. ANSS data, combined with data from the Global Seismographic Network, which the USGS co-supports with the National Science Foundation, is delivered in real-time to the NOAA Tsunami Warning Centers, enabling tsunami alerts throughout the Pacific Rim, including Alaska, Hawaii, Washington, California, and U.S. Territories, and in the Caribbean.

Through the National Earthquake Information Center (NEIC), we provide 24x7 reporting on domestic and global earthquakes and deliver rapid earthquake impact and situational-awareness products to support emergency response (the EHP website can often hosts more than 10 million visitors per month!). The NEIC catalogues more than 20,000 earthquakes a year, from imperceptible ones to great earthquakes that shake the whole globe. We also develop improved methods to improve the quality and timeliness of real-time earthquake information. We communicate earthquake information to the public and to key stakeholders that include federal and state emergency response agencies, disaster relief organisations, operators of utilities and lifelines, and local communities at risk.

ANSS earthquake products help governments and



humanitarian groups to decide how to respond in times of crisis. Rapid situational awareness of an earthquake's severity is used across the response spectrum: from how quickly search-and-rescue teams have to pack their bags, to whether or not a metropolitan area should shut down its mass-transit-rail system. Hundreds of key responders, from the Red Cross to the White House to the United Nations, rely on the USGS to tell them exactly how severe an earthquake is and look to our models for the scale of potential impacts.

The EHP also maintains the USGS National Seismic Hazard Model, which describes the likelihood and potential impacts of earthquakes nationwide, and which serves as the basis of seismic provisions in building codes. We deliver each model update to the Building Seismic Safety Council, which develops building code updates, and we maintain associated databases and tools that are widely used for site-specific engineering design and seismic risk analysis.

The EHP also conducts and supports applied field, laboratory, and theoretical research on the causes, characteristics, and effects of earthquakes. Furthermore, we support relevant research by expert partners in academia, state agencies, and the private sector via competitive grants and cooperative agreements. The latest development in earthquake safety is earthquake early warning (EEW). By recording an earthquake near its origin, one can quickly estimate its size and broadcast a warning ahead of the quake's strong ground shaking. The USGS and our university partners have built and are now testing an EEW system for the U.S. West Coast, called "ShakeAlertTM", which will begin initial alerting in the next few months. Similar systems in Japan, Taiwan, Mexico, and elsewhere have proven the utility of early warnings and demonstrated that there is demand for these alerts.

So, if you live in California, Oregon and Washington or have family and friends there, or even plan to visit, in the near future you will be seeing EEW apps that receive USGS ShakeAlerts. Then, when an alert arrives, duck, cover and hold on!

William Leith Senior Science Advisor

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Earth science: The Search for the Origin of Life

Friedemann Freund, Professor at the SETI Institute/NASA Ames Research Center provides a fascinating look at an aspect of earth science that concerns the search for the origin of life itself

, Friedemann Freund, started out studying mineralogy and crystallography, had my first academic position as Assistant Professor in Chemistry at the University of Göttingen in Germany, moved on to a professorship in the Geosciences at the University of Cologne, also in Germany, and came in the mid-1980s to the NASA Ames Research Center in California, U.S., and joined the Physics Department at San Jose State University as an Adjunct Professor.

My interests have always gravitated around defects and impurities in crystals, in particular, those that arise from the interactions of minerals with the common gas-fluid components water, carbon monoxide and dioxide, nitrogen, and sulphur. I discovered that the low-z elements H, C and N (which happen to also be the biogenic elements par excellence, on which life is built) can undergo a redox conversion that leads to an unexpected and new form of organic chemistry. At the same time, oxygen becomes oxidized - a process that introduces a good deal of semiconductor physics and opens a window of opportunity to study earthquakes from a perspective that had never before been explored.

No quest for knowledge is more profound than the search for the origin of life

On a clear moonless night, we may look up to the sky and see countless stars. We know that some of the



Figure 1: Milky Way with stars and dust clouds bearing the signs of delicate organics

speckles of light are far-away galaxies with their own countless stars. We see the Milky Way – a faintly glowing river of light marking the galactic plane, partly obscured by dark bands. These dark bands are dust clouds spreading through the interstellar space, composed of quadrillions of tiny mineral grains. These mineral grains are chockful of organics. Using a star embedded in a dust cloud as a lamp reveals the presence of aliphatic hydrocarbons, delicate organics that should not be able to survive in the harsh radiation environment of space, surely not for hundreds of millions of years. Yet, these organics are there, undeniably so, as Figure 1 shows delicate but seemingly indestructible.

...and here on Earth we have life. When Earth formed some 4.5 billion years ago, it was a lifeless orb of rocks and water, shrouded in a thick atmosphere. How could life have ever arisen here? How did it happen?

Over the past hundred years some of the world's best minds in chemistry, biochemistry, physical chemistry, chemical physics, and astrobiology have pored over this seemingly intractable question. Their goal? To find out how those complex multifunctional organic macromolecules might have formed that were needed for even the simplest life to start.

Tens of thousands of studies have been conducted, focusing on chemical reactions in the gas phase, in the liquid phase, at gas/liquid and gas/solid interfaces, even within the layers of soft clay minerals. None of them

produced the insight needed to understand how atoms of carbon, hydrogen, oxygen, nitrogen and sulphur could have combined on the barren early Earth to form the CHONS macromolecules necessary for life to start. The brutal truth is slowly sinking in that understanding the origin of life may still be quite a way off.

Something fundamentally new was needed, something different. This is where my work comes in.

At the beginning, I did not set out to study the origin of life. Far from this esoteric aspiration, I just wanted to find out how the common magmatic gases deep in the Earth – water, carbon dioxide, nitrogen and sulphur compounds – interact with the minerals that crystallize deep down.

I was in for a big surprise. To explain it, I have to become a bit technical.

When I started this work, it was well known and accepted in the science community that minerals, which gobble up magmatic gases such as water and carbon dioxide during crystallization but have no good place to put them in their solid matrix, rip these molecules apart and incorporate them as hydroxyl and carboxy anion impurities. No one suspected, however, that this was not the whole story. My work led me to recognise that, at one point upon cooling, the protons in those hydroxyls and the carbon in the carboxy anions would steal electrons from their oxygens. As a result, the protons turn into hydrogen and carbon atoms turn into chemically reduced carbon – "organic" carbon – just like that, by a purely physical process.

The follow-on steps were even more baffling: the oxygens that had given away an electron changed their bonding character. They become highly deformable, allowing the chemically reduced carbon atoms to diffuse with relative ease through dense mineral structures, even when classical diffusion theory said that they should stay put. Indeed, I found the carbon atoms to be unexpectedly mobile, able to segregate to places, where they can ease the local stresses which they produce. Other carbon atoms do the same. Thus, carbon atoms come in close contact with each other and start tying carbon-carbon bonds.



Friedemann Freund, Professor

Hydrogen molecules join in, tying carbon-hydrogen bonds. As a result, organic protomolecules form in the most unlikely place in the world: inside the seemingly forbidding densest mineral structures.

Organic synthesis in the solid state

As so often in science, when something is discovered which seems to be fundamentally new, a torrent of disapproval arises among specialists, many of whom said that this can't be true and trying to disprove the findings.



Fig. 2a: Magnesium Oxide



Fig. 2b: Olivine and MgO IR spectra



Fig. 2c: Upper Mantle Olivine





Figure 3a: Families of complex multifunctional organics released from crushed olivine single crystal grown deep in the Earth

Figure 3b: One of the few beaches of the world today, where olivine crystals still make up most of the sand

This happened to me with such vehemence that – for some time – I retreated from this field altogether to let the controversy die down.

But, of course, I could not let go. Often my thoughts returned to this nagging idea, whether this organic synthesis in the solid state may help us find an answer to humanity's most profound question: Where are we coming from and are we alone?

The tiny dust grains in the interstellar dust clouds consist mostly of olivine, a mineral that we also know on Earth. The dust grains are chockful of organics. If we take a gem-quality olivine crystal from Earth and shine an infrared beam through it, we see essentially the same organic signature as Figure 2 documents. This olivine crystal has grown in a searingly hot magma deep below. Yet, in its matrix, there are delicate organics. When we go into the laboratory and grow magnesium oxide crystals from their more than 2600°C hot melt, we see the same spectroscopic signature.

When we take such crystals and crush them to expose those internal organics, we can extract whole families of CHONS with molecular weights up to 600 atomic masses as reported in Figure 3a. In addition, these CHONS are multifunctional macromolecules – just as needed.

When the Earth was young, olivine was abundantly available at the surface, exposed to rain and all other forms of erosion. On many beaches, the sand consisted of olivine as in this rare green beach in Hawaii depicted in Figure 3b. As the olivine crystals weathered away, they must have released their load of multifunctional macromolecular CHONS into the surface waters. Charles Darwin suggested in 1871 that life might have started in some "warm little ponds". Yes, Darwin was probably right, but if my work on organic synthesis in the solid state is on target, the organics in "warm little ponds" that crossed the barrier from lifeless to life were not delivered by meteorite impacts from outer space nor generated by electric discharges in Earth's atmosphere. They were most likely released by gentle weathering from the matrix of minerals such as olivine that had gobbled up water, carbon dioxide, nitrogen and sulphur at high temperatures deep in the rock column and created - upon cooling - precursors of amazing, probably life-giving CHONS.

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AGRICULTURE

Protecting and promoting U.S. agricultural health

The Animal and Plant Health Inspection Service (APHIS) is a multi-faceted agency within the U.S. Department of Agriculture. APHIS has a wide-ranging mission that includes protecting and promoting U.S. agricultural health, as this article by North America Analysis Editor, Jonathan Miles uncovers

he Animal and Plant Health Inspection Service (APHIS) is a multi-faceted agency within the U.S. Department of Agriculture. APHIS was established in 1972, and today, it has a wide-ranging mission that includes protecting and promoting U.S. agricultural health, regulating genetically engineered organisms, carrying out wildlife damage management activities and administering the Animal Welfare Act.

The work of APHIS in protecting agricultural health

Looking more closely at the work of APHIS in protecting agricultural health, they operate 24 hours a day, seven days a week to defend the U.S.'s animal and plant resources from agricultural pests and diseases. Did you know that if the Mediterranean fruit fly and the Asian longhorn beetle (ALB), two major agricultural pests were left unchecked, several billions of dollars in production and marketing losses would result each year? Another fact to underline in this vein is that if foot-and-mouth disease or highly pathogenic avian influenza were to take hold in the U.S., foreign trading partners could invoke trade restrictions and of course, producers would suffer devastating losses.

We know that when a pest or disease of concern is detected, APHIS implements emergency protocols and partners with the affected states to speedily manage or eradicate the outbreak. Such an aggressive approach is the one APHIS likes to take and it has enabled them to successfully respond to and prevent potential pest and disease threats to U.S. agriculture.

In responding to needs expressed by Congress and the U.S. inhabitants, the mission of APHIS has grown over time to incorporate additional issues, such as regulation

of genetically engineered crops and animal welfare; wildlife damage and disease management; regulation of genetically engineered crops and animal welfare; and protection of public health and safety; plus natural resources that are vulnerable to invasive pests and pathogens.

National Fruit Fly Cooperative Control Program

A recent example of APHIS's work was highlighted on 16th November 2018 when it was announced that they had finished the final environmental impact analysis that was needed under the National Environmental Policy Act for its National Fruit Fly Cooperative Control Program, which intends to protect U.S. agriculture from exotic fruit fly incursions. With this important action complete, APHIS issues an environmental impact statement so it can carry on applying the most recent technology and science towards its efforts to control and eradicate exotic fruit flies and, therefore, support U.S. farmers.

In essence, the National Fruit Fly Cooperative Control Program protects the health and value of U.S. agricultural resources by preventing exotic fruit fly populations from becoming established in the country. The press release provides us with further details as follows: "We know that fruit flies pose a serious economic threat to agriculture because they feed on flowers and fruits, are highly mobile, and have a high reproductive potential. APHIS works in cooperation with State agriculture officials to detect and eradicate non-native fruit flies." ⁽¹⁾

The Asian longhorn beetle (ALB)

Picking up on an area of work mentioned earlier in this



article, let's take a closer look at the Asian longhorn beetle (ALB). Prior to winter 2018, APHIS reminded the public not to move wood out of areas quarantined for the ALB. The announcement makes the important point that people should follow state and federal laws, which restrict the movement of woody material, to keep the tree-killing pest from spreading outside of quarantined areas in Ohio, Massachusetts and New York.

Josie Ryan, APHIS' National Operations Manager for the Asian Longhorn Beetle Eradication Program spoke about the progress being made in the U.S. when it comes to the fight against ALB. "We're making progress in the fight against ALB. We removed quarantines in two areas of Ohio this year alone, but we still must prevent the beetle's spread to other places. As people begin using wood stoves and fireplaces, we are reminding the public to follow the quarantine laws, especially when stocking up on firewood. We cannot eliminate this beetle without the help of residents and business owners." ⁽²⁾

In 2018, APHIS reminded citizens that August is the best time of year to check trees for signs of the ALB. With August being Tree Check Month, APHIS explained in their own words the importance of checking trees. "Asian longhorn beetle-infested trees are safety hazards. You don't want them on your property because they can drop branches and treetops, and storm damage becomes much worse," said Josie Ryan. "So to make sure your trees are healthy, now is the time to go outside and look at them for signs of the beetle", she added. $^{\scriptscriptstyle (3)}$

Protecting, promoting and preserving U.S. agricultural health

In closing, these examples of agricultural pests bring us back to the wider aims of the APHIS that includes protecting, promoting and preserving U.S. agricultural health. Certainly, the APHIS' Plant Protection and Quarantine (PPQ) program specifically, "safeguards U.S. agriculture and natural resources against the entry, establishment, and spread of economically and environmentally significant pests, and facilitates the safe trade of agricultural products." ⁽⁴⁾

References

- 1 https://www.aphis.usda.gov/aphis/newsroom/stakeholderinfo/sa_by_date/sa-2018/sa-11/eis-fruit-fly
- 2 https://www.aphis.usda.gov/aphis/newsroom/news/sa_by_date/sa-2018/dont-move-wood
- 3 https://www.aphis.usda.gov/aphis/newsroom/news/sa_by_date/sa-2018/alb-tree-check-month
- 4 https://www.aphis.usda.gov/aphis/ourfocus/planthealth

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Trees in the urban environment: 'Seeing' roots underground

Dr Nina Bassuk, Professor at the Urban Horticulture Institute, School of Integrative Plant Science explores seeing roots underground when it comes to research into trees in the urban environment

cientists who study trees in the urban environment have a great challenge when it comes to measuring and 'seeing' root growth underground. In the past, if roots were studied at all, cores were pushed into the ground and then extracted provided a somewhat random sub-sample of root growth. In another instance, clear tubes called mini rhizotrons were used to visualise tree roots by placing the tubes in the soil and lowering a camera into the tube to take a picture of roots that grew near the tube. This was also a hit or miss sample of roots that may or may not have intersected with the clear tube. Still another tool, an air excavation probe, has more recently been used to uncover the roots system of a tree without damaging the root system. While effective, this process is very time consuming depending on the soil type and tree size. None of these techniques can locate and measure roots under the pavement.

The use of Ground Penetrating Radar (GPR) is a relatively new technique to study roots. GPR is an established non-invasive (i.e., non-destructive) inspection method that has been used worldwide for more than thirty years to locate subsurface objects such as pipes, utilities, and other engineering and environmental targets.

One of the main worldwide uses of GPR is in concrete inspection, where



the integrity of the structurally supporting reinforcement is examined along with the integrity of the concrete matrix itself. Although this technology has a long history of use in archaeology and engineering to locate antiquities and utilities, the practice of using it to map roots in urban soils, which can be compacted, layered and discontinuous, is comparatively new.

GPR measurement as a method of mapping tree roots has several advantages over other methods:

1) It is capable of scanning root systems of large trees under field conditions in a relatively short time;

2) It is completely non-invasive and does not disturb the soils or damage the trees examined;

3) Being non-invasive, it allows repeated measurements that reveal long-term root system development;

4) It allows observation of root distribution beneath hard surfaces (e.g., concrete, asphalt, bricks, pavers, roads, buildings) and;

5) Its accuracy is sufficient to detect structural roots with diameters as small as 1 cm.

GPR inspection employs electromagnetic waves, which will deflect, or refract from a boundary between objects with different electro-magnetic properties. The electromagnetic material property that creates the contrast and causes reflections is the dielectric, which is a dimensionless quantity relating to the materials behaviour



when subjected to an electric field. The larger the difference between the dielectrics of two different materials, the larger the radar wave.

For example, the dielectric of water is 81 and that of an average soil is approximately 13, producing a "dielectric contrast" of 6.2:1 (81/13), which is large and will cause most of the radar wave energy to be reflected back to the surface antenna. Root detection is possible in principle because of the water content within the woody root provides an excellent contrast with the soil media.

Before this technology can be used to its fullest, 'ground truth' studies needed to explore the limits and resolution of GPR as a tool or locating tree roots on development sites and under the pavement. This 'ground truth' comparison between predicted GPR and actual visualisation of the root zone was undertaken in 2011, resulting in a high degree of agreement between methods. With increasing confidence, we decided to measure tree root growth under porous and non-porous asphalt.

In 2005, a 12-car parking lot was designed and constructed in partnership with the City of Ithaca, NY, USA. This new 45-metre x 6-metre parking lot was divided in half, with the southern half of the lot paved with 8 cm of porous asphalt while the northern half used an 8 cm layer of the mediumduty traditional impervious asphalt surface. Prior to paving, the entire lot was excavated to a depth of 0.6 metres and CU-Structural Soil[®] (structural soil) was added and compacted to the required density to support the pavement and cars. Structural Soil is a highly porous medium that can support the pavement while still allowing roots to grow within it.

In 2012, 2015 and 2016, root growth of the trees under porous and nonporous asphalt was measured using Ground Penetrating Radar. Twelve GPR scans were performed on the trees growing under porous and non-porous asphalt. Each scan covered 30 cm wide by 6 metres long by 75 cm deep. Root density was measured at three depth layers and expressed as roots per linear foot. Root growth was found to be much denser and deeper in the soil under the porous asphalt presumably because of greater access to water. Additionally, tree growth above the porous asphalt was also improved.

This gave us confidence to conclude that the growth we were measuring above ground corresponded to greater root growth and water uptake below ground. Moreover, the use of Ground Penetrating Radar has added a very useful tool to the scientists' toolbox when trying to understand urban tree growth in the inner city.



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Transformative research on cowpea: "STOPCALLOSOBRUCHUS!" – Post-harvest protection for smallholder cowpea production using vegetable oil

Louis E. N. Jackai, PhD, Professor and IPM Specialist and Dr. Beatrice N. Dingha, Associate Research Professor at the Department of Natural Resources and Environmental Design share with us their thoughts on post-harvest protection for smallholder cowpea production using vegetable oil, "STOPCALLOSOBRUCHUS!"

owpea is one of the most diverse, versatile and economically important indigenous legume crops in the world. Cowpea is of vital importance to the livelihood of millions of people in the developing world, as well as in the southern U.S. where it is grown mainly by small urban and rural growers for food, income and as a summer cover crop. It enriches (feeds) the soil with nitrogen for use by the next crop, and in the Southeastern U.S. cowpea is commonly consumed as a green, frozen or canned bean, but more widely as a "Crowder" or "Blackeye" pea sold in many grocery stores across the nation.

In our recent publications (Jackai et al., 2017, 2018), we present cowpea in its historical perspective, nutritional and health value to humans and livestock, as well as its vulnerability to pests and diseases. Trap cropping was featured as a potential non-chemical approach for controlling the invasive Brown marmorated stink bug, Halyomorpha halys (Stal). Cowpea has great potential as an all-round crop for a wide range of environments. Its attributes as a versatile crop are greatly limited and diminished by a number of biotic stresses among which insect pests, weeds and diseases are clearly among

the most challenging (see review by Kumar and Kalita, 2017).

This paper in the series focuses on post-harvest protection, which we consider the most critical mitigating factor in the alleviation of food security, especially in developing countries in Africa, Asia and South/Central America which depend heavily on legumes (especially cowpea) as a source of high protein for humans and livestock and as a source of family income. Post harvest losses of cowpea typically exceed 45% worldwide.

Post-harvest losses in cowpea

The title of this paper sounds a clarion call to a lingering pest problem that has placed the realisation of the full benefits of cowpea in a state of limbo for longer than anyone could have imagined. This is most surprising especially given all the years of research and hundreds of publications on the subject at both ends of the sophistication continuum, by highly respected scholars and those not so distinguished.

So we ask ourselves what has gone wrong after all the years of intense investigation? The truth is that if we discount the use of synthetic insecticides, nothing spectacular has been accomplished in the sense that the problem persists. Many estimates of the losses from storage are underestimates, especially in traditional spaces (Kumar and Kalita, 2017). Have we focused too much on the sophisticated and played down the seemingly mundane that is usually regarded as "indigenous" knowledge (IK) and, therefore, without enough scientific merit to be useful?

That notwithstanding, a recent grain and seed storage protection technology has been deployed in West Africa with promising results. It uses hermetic storage that employs triple layer bags, a technique referred to as the "Purdue Improved Crop Storage" or PICS (Baributsa et al., 2010; Baoua et al, 2015; Murdoch et al, 2012) has the effect of reducing oxygen levels in sealed bags from 21% to 18% after almost seven months of storage. The technology followed closely behind earlier research on solarisation from the same Purdue University laboratory (Ntoukam et al., 1997) that was a scientific spin-off from a common practice by cowpea farmers in Northern Cameroon, in West Africa. This is a good indication that IK can lead to important scientific developments. The

PICS technique uses two high-density polyethylene liners (80 µm thick) woven into a polypropylene bag; however, these bags are not so secure as to be guaranteed from being pierced by sharp objects or rodents during transportation, or storage, in the supply chain. Should this happen, the entire PICS operation will be compromised. It is therefore important to build, or stack, other control measures around this concept; the work we report here using vegetable oils is an important step in this direction.

Plant oils provide lasting protection

The use of both edible vegetable and essential plant oils for the control of storage pests of legumes and grains is not a new concept, but despite many years of dedicated research on this topic, a consistent protocol for the use of oils has not been put forward. Many oils are known to be effective but the rates used and the results reported are as different as the number of reporting workers. Our understanding of how and why these oils (vegetable and essential oils) work is still somewhat vague, and only a few workers have attempted to delve into the intricacies of the underlying mechanisms.

In this report, we do not try to resolve all outstanding questions; rather we hope to advance the scientific thought on which oils work best and for what target, the concentrations required for efficacy, as well as the need to understand the science on how they work on *C. maculatus*. Knowing the structure of an effective oil is also important because it represents a biochemical signature or marker whose footprints can be searched for in the libraries of hundreds of plant oils worldwide to find the best oils for the purpose of protecting commodities in storage. It is our belief that our discussion of this subject will establish a trajectory for scaling the use of oils in the control of other insects on legumes and other grain crops.

The most important pest, of stored cowpea, from a global distribution perspective, is the so-called "cowpea weevil" which is not a weevil (does not have a snout) but a beetle in the family Bruchidae, Order Coleoptera (the beetles). In this paper, we sometimes refer to this insect, Callosobruchus maculatus (Fab.), by the abbreviated form, "Cmac". The clarion call in the title to "STOPCALLOSO-BRUCHUS" is patterned after a similar name coined by the group seeking to control the invasive brown marmorated stink bug, *H. halys* in the U.S. using the mantra "StopBMSB.org".

Most cowpea farmers are low-tomedium smallholders who are generally also limited resource growers with low income. It is therefore important for scientists target these growers with technology that is well within their grasp, both from a financial, as well as a technological standpoint. The PICS technology is an excellent example of this approach, judging from reports on its adoption (Kumar and Kalita, 2017). Vegetable oils and other cultural (IK-driven) approaches, such as the use of wood ash, various condiments (e.g. hot peppers - Capsicum spp.) and natural products, such as neem (Azadirachta indica) leaf powders and various biorational insecticides) should be deployed as toolbox components built around the nexus of plant resistance. These in conjunction with hermetic storage will, in our opinion, comprise the most reliable platform for a framework in the sustainable management of this pest. The discussion that follows on use of vegetable oils should be seen as a

component of this collective (tactics in the toolbox) that constitute a veritable attempt to provide growers and the entire cowpea value chain with a reliable and durable IPM strategy for storage beetle control.

Enhancing storage protection technology using plant oils

Both essential oils (Nenaah et al, 2015; Akami et al., 2017) and the common edible vegetable oils (Kumar and Kalita, 2007) have been reported to be effective in the control of Cmac. In studies conducted in our laboratory, we evaluated eight commonly available edible vegetable oils (including garlic, soybean, peanut, sunflower, coconut, truffle, corn and olive oil) in Greensboro, North Carolina, against Cmac on cowpea seeds for up to six month storage period in some experiments. The results were simply outstanding. We were interested in oils that would: a) cause high adult mortality to reduce egg-laying, and b) possess ovicidal activity or prevent/ greatly reduce adult emergence (by increasing within-seed mortality).

While other parameters may also be important, we believe that these two are the most critical for reducing and eventually eliminating any recurrent infestation, even in the absence of hermetic storage conditions. This is relevant given the understanding that the infestation may actually begin from the field and become exacerbated in storage. Increasing oil concentration generally increased adult mortality (Figure 1). At the lowest rate (15µl/20 grams of seed), the less susceptible Mississippi Silver cowpea variety showed a distinct difference between treated seed and the untreated control, unlike in the highly susceptible Pinkeye Purple Hull cowpea variety.

So, varieties behave differently according



Figure 1: Cumulative mortality of adult C. maculatus on cowpea seed (var. Pinkeye Purple Hull) treated with different concentrations of seven edible vegetable oils over a 2-week period.

Figure 2: Cumulative percent adult C. maculatus emergence on cowpea seed (var. Mississippi Silver) treated with different concentrations of seven edible vegetable oils and an untreated control over 44 days.

to their resistance status. With a higher number of adults dying, fewer eggs were laid and subsequently, even fewer adults were recruited into the next generation as indicated by the adult emergence levels (Figure 2). All the oils tested had a pronounced effect on adult emergence which increased with oil concentration.

In long-term studies, it is clear that oils alone could protect cowpea from Cmac damage. Obvious differences in the level of protection among the oils are observable among different oils.

One of the main bottlenecks to the adoption of vegetable oils in cowpea storage protection is the lack of consistency in their use. This is thought to be a result of poor coverage (coating of seeds or grain) when larger quantities have to be protected. There are two parts to a possible solution: a) having an appropriate carrier for the oils, and b) development of a simple but effective application process that would coat each grain/seed evenly. In studies carried out by Jackai and Dingha at NCA&T to improve coating, two essential oils (peppermint and lavender) and two edible vegetable oils (garlic and sunflower) were dissolved in ethanol to enhance coating. The results indicate that both the seed coating and biological effects of the oils were greatly improved by dilution in ethanol within 3 days (<u>Figure 3</u>). This process has obvious practical implications for seed/grain protection.

Regarding the coating process, the entomologists and biological engineers at N. Carolina A&T State University have developed a blueprint of a system that will uniformly coat each seed with a pre-determined amount of oil. Further testing is planned to determine various metrics on several biological variables in storage pest control, including persistence and shelf-life of various oils. Figures 1-4 show clearly that a range of oils can be very effective in long-term adult beetle suppression. We also know that some oils are persistent and remain effective for up to six months thus preventing, or greatly reducing, recruitment of new adults; eggs that were laid obviously did not survive (see Figure 4).

The Toolbox model for future grain storage protection for small growers

The PICS technique is by no means the first case of hermetic approach in storage protection; there have been many reports on this approach (Kumar and Kalila, 2017). The PICS technology has greatly improved the process and taken it to a different level of triple protection. But while this may be seen by some as a nexus for building a long-term, sustainable storage protection for small growers, others (including the current authors) would prefer to use cowpea resis-





Figure 3: Cumulative adult C. maculatus mortality after seven days on cowpea seed (var. Mississippi Silver) treated with edible vegetable (top) and essential oils (bottom) diluted in ethanol. Control was treated with ethanol only.

Figure 4: Seed damage and emerged C. maculatus adults on cowpea (var. Pinkeye Purple Hull) without oil treatment (left) after 6 months storage. No damage or emerged adults on cowpea treated with canola oil (right).

tance as the flagship around which to build the future scaffolding to protect legumes and other grains in storage.

Other controls (tools in the toolbox) can be built around, or anchored to, this core. Resistant varieties generally require less oil protection than do susceptible ones. This same phenomenon occurs with synthetic and biorational insecticides in the protection of field crops. Stacking resistance and oil with PICS will be a winner anywhere, any day. Relying on any single tool in the IPM toolbox is risky for the reasons outlined earlier, no matter how safe and secure the tactic looks.

The tools in this IPM toolbox should include the use of biorational insecticides such as diflubenzuron which is reported to be very effective on Cmac (Kemabonta et al., 2010), use of various plant oils (especially the more accessible and less expensive, safer and equally effective vegetable oils), in conjunction with hermitic storage on a plant resistance platform. This would be equivalent to stacking

of genes except with a different activity span and a more diverse application scope as advocated by the tenets of IPM.

References Cited

Akami, M., H. Chakira, A.A. Andongma, K. Khaeso, O.A. Gbaye, N.Y. Nicolas, E.N. Nukenine and C.Y. Niu. 2017. Essential oil optimizes susceptibility of Callosobruchus maculatus and enhances the nutritional qualities of stored cowpea, Vigna unguiculata. R. Society Open Science 4: 170692.

Baribatsu, D., I.B. Baoua, O.N. Bakoye, L. Amadou and L.L. Murdock. 2017. PICS bags safely store shelled groundnuts in Niger. J. Stored Products Research. 72: 54-58.

Jackai, L.E.N., B.N. Dingha and M. Worku 2018). Cowpea – An ancient crop for modern challenges. Scientia (http://www.scientia.global/cowpea-an-ancient-crop-for-modern-challenges/), E-Book

Jackai, L.E.N. and B.N. Dingha. 2018. Transformative Research on Cowpea: Innovative trap crop development and deployment. Open Access Government 18: 340-341. https://edition.pagesuite professional.co.uk/html5/reader/production/default.aspx?pubname=&e did=558600cb-8de9-4616-9242-f8f3b41da315 (E-Book)

Kemabonta, K., J.A. Odebiyi and A.R. Olagbaju. 2010. An Assessment of Diflubenzuron as Protectant of Cowpea Grains against Callosobruchus maculatus Fab. (Coleoptera: Bruchidae). Nigeria J. Science 44: 49-55.

Kumar, D, and P. Kalita. 2017. Reducing postharvest losses during storage of grain crops to strengthen food security in developing countries Foods 6(1), 8; https://doi.org/10.3390/foods6010008

Murdock, L.L., V.M. Margam, B.I. Baoua, S. Balfe and R.E. Shade. 2012. Death by desiccation: effects of hermetic storage on cowpea bruchids. J. Stored Product Research49: 166-170.

Nenaah, G.E., S.I.A. Ibrahim, B.A. Al-Assuity. 2015. Chemical com-

position, insecticidal activity and persistence of three Asteraceae essential oils and their nanoemultions against Callosobruchus maculatus. J. Stored Products Research 61: 9-16.

Ntoukam, G, L. Kitch , R.E. Shade and L.M. Murdock. 1997. A novel method for conserving cowpea germplasm and breeding stocks using solar disinfestation. Journal of Stored Products Research 33(2):175-179.



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Water for plant growth: The foundation of the global food supply and ecosystem services

Professor Robert Aiken, Research Crop Scientist at the Northwest Research – Extension Center and Dr. Ramesh Dhungel, Research Associate at Kansas State University both explain why water is required for plant growth, the foundation of the global food supply and ecosystem services

ater is required for plant growth – the foundation of global food supply as well as ecosystem services. Hence, the linkage of food security and water security.

Most climate change impacts are expected to affect the water sector (IPCC, 2014). These impacts include altered precipitation patterns, reduced availability of freshwater, and reduced water quality. Climate change impacts will likely exacerbate competition for water among agriculture, industry, ecosystems and settlements (MacAlister and Subramanyam, 2018).

Reliable crop water metrics provide computational tools that are particularly suited to the agricultural landscape. Robust survey tools utilise satellite imagery to detect trouble spots, such as drought monitoring services. However, satellite imagery is frequently obscured by factors such as cloud cover, limiting application to water management.

Recent advances in computational tools support use of physically-based energy balance modules to reliably calculate crop evapotranspiration (ET) at landscape and regional scales (Dhungel, et al., 2016). The Backward-



Figure 1: Scatterplot of a) daily and b) hourly evapotranspiration (ET) calculated by the revised BAITSSS energy balance model (Dhungel et al., 2016) in relation to field measure of ET (lysimeter) for corn between May 23, 2016, and September 26, 2016, near Bushland TX, USA. Linear regression (red lines) and one-to-one correspondence (black line) are also indicated.

Averaged Iterative Two-Source Surface temperature and energy balance Solution (BAITSSS) is a physically-based ET model capable of point scale and landscape simulation of soil water using a vegetative canopy, soils and weather data. Field comparisons with precise field measurements demonstrate the validity of this modeling approach (Figure 1, Dhungel et al., in review).

Application to water management is illustrated for a groundwater management district in northwest Kansas, USA. With an improved algorithm, ET was calculated for a township in western Kansas (Figure 2), a region of substantial groundwater depletion. Figure 3 shows water balance components for a particular sampled pixel. Comprehensive ET analysis provide water metrics for crop systems ranging from dryland to full irrigation. These information services support initiatives such as Local Enhanced Management Areas in Kansas, which operate multiyear water management plans that have resulted in 20% or more reductions in irrigation withdrawals.

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Figure 2: Cumulative water use (evapotranspiration, ET, May 10, 2013, through September 15, 2013) of corn for Township 9S, Range 41W, in northwest Kansas, USA. A township comprises 36 square miles (9,324 hectares). The colour scale indicates a range in ET of 8 to 30 inches (203 to 762 mm). Only pixels classified as 'corn' (U.S. National Agricultural Statistical Service) are indicated. Details of the water balance are provided (Figure 3) for a sample pixel (indicated as a red dot, 101° 50' 42" W, 39° 16 '9" N).



Figure 3: Daily evapotranspiration (ET), evaporation (E), transpiration (T), irrigation and precipitation, calculated by the BAITSSS energy balance model, is shown for a sampled pixel in northwest Kansas, as indicated in Figure 2.

Dhungel, R., Allen, R. G., Trezza, R., and Robison, C. W. 2016. Evapotranspiration between satellite overpasses: methodology and case study in agricultural dominant semi-arid areas. Meteorological Applications, 23(4), 714–730.

Dhungel, R., R. Aiken, P. Colaizzi, X. Lin, D. O'Brien, L. Baumhardt, D. Brauer, G. Marek. Evaluation of the Uncalibrated Energy Balance Model (BAITSSS) for Estimating Evapotranspiration in a Semiarid, Advective Climate. Hydrological Processes. In review.

IPCC. 2014. Climate change 2014: Impacts, adaptation, and vulnerability. Part A: Global and Sectoral Aspects. Contribution of working group II to the fifth assessment report of the Intergovernmental Panel on Climate Change. [V. R. Barros, C. B. Field, D. J. Dokken, M. D. Mastrandrea, K. J. Mach, T. E. Bilir, ... L. White, (Eds.)]. Cambridge, United Kingdom: Cambridge University Press.

MacAlister, C. and N. Subramanyam. 2018. Climate change and adaptive water management: innovative solutions from the global South. Water International. 43 (2) 133-144.



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CANADA

Advancing the knowledge of space through science

The work of The Canadian Space Agency (CSA) in advancing the knowledge of space, through science and using its discoveries to benefit Canadians and all of humanity, is detailed here

The Canadian Space Agency (CSA) is responsible for advancing the knowledge of space through science and using its discoveries to benefit Canadians and all of humanity. Set up in March 1989, the CSA is an independent federal agency that takes charge of managing all of Canada's civil space-related activities.

The CSA focuses on three main areas, which this article will examine, as well as the importance of this key sector for the Canadian economy:

1. Space exploration: Taking part in astronomy and planetary studies, astronaut missions, as well as scientific research in space (execution and support).

2. Space utilisation: Earth observation by the collection of spatial data and satellites.

3. Space science and technology: The development of innovative space technologies and applications used on Earth. ⁽¹⁾

Space exploration: Canadian Space Agency astronaut David Saint-Jacques

On space exploration, we know that astronauts today are modern-day explorers, indeed, they courageously travel to seek new scientific knowledge. At the time of writing, only a few hundred exceptional people have been beyond Earth, into space. In December 2018, Canadian Space Agency astronaut David Saint-Jacques flies to the International Space Station on his first mission. During his assignment, he conducts a number of scientific experiments, as well as robotics tasks and the testing of new technologies. ⁽²⁾

David Saint-Jacques was born on 6th January 1970 in Quebec City, Canada. Today, he is married and has

three children. He also holds a commercial pilot licence with multi-engine and instrument ratings, as well as an advanced scuba-diving licence. He is also a lifelong cyclist, mountaineer, skier and avid sailor. In addition, he is fluent in English and French and can also converse in Russian, Japanese and Spanish. In a question and answer session with David Saint-Jacques, we find out what motivated him to become an astronaut, which he details in his own words.

"As a child, I was impressed by photos of Earth taken from the moon. They showed me the immensity of the universe around us, the splendour and obvious fragility of our planet. Growing up, I was drawn to a life of adventure, exploration and discovery. I didn't think that becoming an astronaut was a real possibility, but my fascination with space remained, and that childhood dream has motivated me to reach my full potential as a human being.

"I wanted to learn everything, both about the sciences and world cultures. To be an explorer, I also had to become a responsible and trustworthy adult. Opportunities for discovery have presented themselves in many forms: science, medicine, living abroad. When I learned one day that astronauts were being recruited, the dream returned, and the little boy I once was convinced me to apply."

An interesting point raised in this interview with David Saint-Jacques is that each profession he has worked in has prepared him well to go into space. For example, his experience as an astrophysicist taught him the discipline of research and the joy of scientific discovery as he worked in observatories globally, as a part of international teams who were determined to push forward the boundaries of knowledge. "As an engineer, I especially enjoy the creativity and the satisfaction of



finding a solution to a practical problem that is so elegant, so reliable and so ergonomic that in the end, you take it for granted. When an engineer has done their job well, it works, and that's all there is to it!",

David Saint-Jacques explains. (3)

Space utilisation: Earth observation

The second aspect of the CSA's work concerns observing the Earth from space and as such, satellites give vital information on the ocean, ice, the atmosphere and land environments. Earth-observation satellites assist with the monitoring and protection of the environment, ensuring the safety and security of Canadians and managing resources. Certainly, satellite imagery and expertise are also used to support sustainable development and global humanitarian efforts.

An example of this part of the CSA's work is <u>The Inter-</u> national Charter "Space and Major Disasters", which is an international effort to put space technology at the service of rescue and emergency responders in the event of a major disaster. Certainly, we know that when the Charter is activated, its members make satellite images of devastated regions available to support relief efforts. <u>RADARSAT-2</u> imagery regularly provides support to rescue teams on the ground. Armed quickly with reliable and accurate information, response teams are better equipped to save lives and limit damage to property, infrastructure and the environment. One good example of this kind of work given on the CSA's website is October 2018's Hurricane Michael, a Category 4 storm, one of the strongest to hit the United States. ⁽⁴⁾

Space science and technology

When it comes to supporting Canada's space sector in the advancement of innovative space technologies and applications, we know that the power of science is as infinite as space. The Government of Canada believes it is vital to engage Canada's youth in science and provide them with the tools to make science a part of their lives.

On 24th October, the Honourable Navdeep Bains, Minister of Innovation, Science and Economic Development, Canadian Space Agency (CSA) astronaut David Saint-Jacque and Bonnie Schmidt, Founder and President of Let's Talk Science, launched a new youth science research project that will give students in

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Canada a unique opportunity to collect and compare environmental data from Earth and space.

The Honourable Navdeep Bains, Minister of Innovation, Science and Economic Development said at the time that when he was at school, he could only dream of contributing to experiments in space. "Now, our government is making this a reality for future Canadian scientists, engineers and leaders in innovation through the Living Space project. By investigating scientific concepts and learning digital skills, like coding and analysing data, our children will have limitless opportunities to succeed in the jobs of tomorrow", the Minister said.

David Saint-Jacques, Canadian Space Agency astronaut stated that he wants to engage young Canadians on his mission, a point he elaborated on in his own words. "I was inspired by the Apollo moon missions, and that gave way to an insatiable curiosity about technology, our planet and the universe that fueled my education and career path. I hope that through this mission and activities like Living Space, the Canadian Space Agency and I can inspire young Canadians in the same way. I can't wait to see the results of their research projects." ⁽⁵⁾

Supporting a key sector of the Canadian economy

In closing, The Honourable Navdeep Bains, Minister of Innovation, Science and Economic Development leaves

us with positive thoughts following his announcement on 15th October 2018 that the CSA is investing \$1.6 million in two concepts for lunar rovers that would use artificial intelligence (AI). His comments encompass the aspects of Canada's space sector explored in this article, including inspiration for space exploration and the development of science, technology and innovation in the field.

"Canada's space sector not only inspires Canadians to reach for the stars, it has for a long time been at the forefront of Canadian science, technology and innovation. With these investments, our government is supporting a key sector of our economy that creates good jobs and will continue to propel Canada's innovation economy to new heights." ⁽⁶⁾

References

- 1 http://www.asc-csa.gc.ca/eng/about/csa-organization.asp
- 2 http://www.asc-csa.gc.ca/eng/missions/expedition58-59/default.asp
- 3 http://www.asc-csa.gc.ca/eng/astronauts/canadian/active/bio-davidsaint-jacques.asp
- 4 http://www.asc-csa.gc.ca/eng/satellites/default-eo.asp
- 5 https://www.canada.ca/en/space-agency/news/2018/10/canadianstudents-invited-to-contribute-to-experiments-in-space.html
- 6 https://www.canada.ca/en/space-agency/news/2018/10/strengthening-canadas-leadership-in-ai-driven-robotics-to-support-jobs.html

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Dark matter: Advanced exploration at SNOLAB

Dr Gilles Gerbier, Dr Art McDonald and Dr Antony Noble delve into the unknown world of dark matter, the unidentified mass that physicists are still yet to solve

D id you know that more than 80% of the Universe's mass is unknown? The fraction that we do know about is composed of planets, stars, and well, us, but the majority of the Universe is composed of unknown mass. What exactly this unknown mass is, as it has never been directly detected, is one of the great questions left facing physicists today.

Even though this unknown mass has never been detected, it does have a name: dark matter. But wait, if it has never been detected, how do we know it exists? Based on observations, astrophysicists discovered that galaxies were spinning much faster than expected based on calculations from existing known "bright" matter, that is, there shouldn't be enough gravitational force in the glowing stars to hold the galaxies together. Yet galaxies so rarely disintegrate, there is clearly some other source of gravity that is holding everything together. This mysterious substance was dubbed dark matter.

But what is it? There have been many particle candidates over the years: axions, gravitinos, among others, but the current theoretical particle still showing the most promise is the WIMP, or Weakly Interacting Massive Particle. The "weakly interacting" part is what makes a WIMP so hard to detect. Here is the picture: the solar system and its planets, like the Earth, is bathing in a halo of WIMPs flying around and once in a while interacting with nuclei of ordinary matter.

Efforts have been made, of course, to detect it in underground labs around the world, and to 'make' it in the Large Hadron Collider, similar to its creation in the Big Bang. All of these attempts have been unsuccessful so far, and dark matter has remained as elusive as ever.

"Did you know that more than 80% of the Universe's mass is unknown? The fraction that we do know about is composed of planets, stars, and well, us, but the majority of the Universe is composed of unknown mass."

What if it is even more elusive than anticipated and/or if its properties escaped the attention of traditional searches? New ideas to enlarge the parameter space of exploration and especially include lower mass Dark Matter particles are then called for to extend the sensitivities tremendously.

The three projects described below, in which the three authors are involved, use complementary cutting-edge technologies to address these new challenges. To detect such minuscule signals, the experiments will be installed underground in SNOLAB and LNGS, Italy, to protect them from sources of "backgrounds" simulating signals. SNOLAB, near Sudbury, Ontario is one of the deepest and the cleanest underground laboratory in the world. All existing projects are international and nationally supported by NSERC and CFI. The McDonald Institute provides additional human and technical resources coordinated between 11 institutions in Canada.

The Arthur B. McDonald Canadian Astroparticle Physics Institute (McDonald Institute) is a CFREFfunded scientific network supporting Canada's Astroparticle Physics research community. Its chief concern is growing and connecting the community to solve major scientific questions like the detection of dark matter. It administers funds to expand the talent pool of faculty, graduate students and fellows working in dark matter, neutrinos and related research. The Institute works with major experimental and theoretical facilities in Canada and is maximizing economic and social benefit of large-scale research to better engage the public with the work of astroparticle physicists. See www.mcdonaldinstitute.ca for more details.

Three projects to go beyond the present status

NEWS-G: a new window on light dark matter

NEWS-G uses a new type of spherical gaseous detector developed within a Europe-North America collaboration, to be sensitive at the unexplored
PROFILE







The 3 projects : NEWS-G, PICO and DarkSide-20k

lower end of the particle mass range, comparable in mass to a proton or below. Here the ability of such detectors to detect extremely low current pulses, equivalent to a single electron, combined with the use of "light" targets, like helium, or hydrogen are keys for this exploration. The new 140 cm diameter detector with its shields will start operation in 2019 at SNOLAB.

PICO: a unique ultra-sensitive detector listening for dark matter with spin!

PICO has a very unique approach to search for dark matter. The core of the detector is a superheated fluid (C3F8). The fluid is still a liquid, despite being well above the boiling point. A small energy deposition from a WIMP interaction can initiate boiling and the creation of a gas bubble. These are easily identified using high-speed cameras, and the popping sound is heard with sensitive microphones. WIMPs can be distinguished from fake radioactivity signals through their characteristic optical and acoustic signals. PICO is world-leading in the search for dark matter particles with

spin and the collaboration are currently upgrading their detectors to increase the sensitivity by a factor of 100.

GADMC: a worldwide multi-ton scale project to reach an ultimate sensitivity using liquid argon.

Liquid argon gives out a very short burst of light from a dark matter particle, but a much longer burst from background radioactivity, so it is easy to tell them apart. Right now, there are 3 tonnes of argon operating in the DEAP detector at SNOLAB and an international collaboration of 350 scientists from 12 countries have come together to build a 20-tonne detector to be built in Italy (DarkSide-20k), followed by a 300-tonne detector, likely to be installed in SNOLAB. Increasing the sensitivity a factor of 100 may be close to the ultimate sensitivity, as the main background is neutrinos that cannot be shielded by an underground location.

Synthesis

At Queen's University, under McDonald Institute banner, G. Gerbier, holder of a CERC in astroparticle physics and PI of NEWS-G, T. Noble, PI of the PICO program, former director of SNOLAB, scientific director of MI and A. McDonald, former director of SNO project, Nobel Prize winner and active promoter of GADMC, join together their skills, enthusiasm and teams towards identifying the nature of dark matter, one of the most arduous modern physics questions, holding physicists attention for close to a century now.



Dr Gilles Gerbier Dr Art McDonald Dr Antony Noble

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Reconciliation in a higher education context: Tensions and challenges

Dawn Zinga, Associate Professor and Chair at the Department of Child and Youth Studies at Brock University explores reconciliation in a higher education context, by detailing the tensions and challenges in this area

n August 2017, I wrote about how Canadian institutes of higher education were taking up the Truth and Reconciliation Commission's calls to action. Almost a year later, higher education contexts continue to face tensions and challenges in addressing those calls to action. There has been much talk of how to address the calls and some policy changes, but it is clear that there are a lot of tensions and challenges around the implementation of any changes. Lakehead University offers an example of how those tensions and challenges can be

expressed. The university's response to Recommendation 28 was to ensure that all law students were provided with opportunities to better understand Indigenous peoples and the law by weaving Indigenous content throughout the law curriculum. However, in practice, there appear to be challenges with the implementation of significant changes. Angelique Eagle-Woman was hired by Lakehead University as the first female Indigenous law school dean in 2016 but resigned citing systemic discrimination and racism in 2018. This unfortunate situation underscores the difference between a surface response to the calls to action and meaningful action.

"The conundrum facing higher education is how to proceed to address the calls when institutions are having difficulty being able to recognise how the very structures of the institutions are getting in the way."

Universities and colleges are struggling to address the calls to action and to understand what reconciliation means. Indigenous scholars Marie

PROFILE

Battiste, Jan Hare, Jackie Ottman and Dwayne Donald spoke eloquently at the 2018 Congress of the Humanities and Social Sciences about reconciliation within a higher education context. Each of them remained committed to the conviction expressed by the Commission that education will be pivotal in putting Canada on the road to reconciliation. Battiste spoke about the importance of decolonising and how everyone has been "marinated in Eurocentrism" and that the tenets of Eurocentrism that are characterised by superiority, hegemony and a monopoly over all other knowledge systems, stand in the way of reconciliation. Battiste speaks about cognitive imperialism and how every Canadian student has been a victim and beneficiary of the same education system that has exposed them in Eurocentrism and cognitive imperialism. These act as some of the greatest barriers to reconciliation and the serve to blind people to the colonialism embedded throughout education at all levels.

Dwayne Donald agrees that it is difficult to accomplish much when the very institution that claims to want to take steps towards reconciliation gets in the way when tensions arise. He argues that part of the problem is the tendency within higher education contexts to take shortcuts by attempting to make changes without examining the embedded colonialism. When change is implemented in those contexts, tensions quickly rise and the response to those tensions is to reassert "colonial terrain". Jackie Ottman also spoke to the hidden curriculum and unconscious codes that are triggered by attempts to meaningfully address the TRC. She stated that while the Royal Commission on Aboriginal Peoples issued its report in October 1996 and offered over 400 recommendations, the TRC's 94 calls to action has engendered a more lasting response. However, she warns that the weight of addressing those calls to action within higher education contexts could not be left to Indigenous students and scholars to do all the heavy lifting, but that non-indigenous students and scholars needed to walk alongside and share the weight and the work. Jan Hare agreed with her colleagues and calls for a continued commitment to reconciliation that is grounded in an understanding of everyone's roles and responsibilities.

"Universities and colleges are struggling to address the calls to action and to understand what reconciliation means."

The conundrum facing higher education is how to proceed to address the calls when institutions are having difficulty being able to recognise how the very structures of the institutions are getting in the way. Most institutions are implementing policies and directives, but not doing the hard work of exploring what it will mean to actually implement those policies and directives. The end result is window dressing without any meaningful change or a resurgence of colonialism and a return to the status quo that hides behind claims of cultural inclusion or returns to pathologising Indigenous students and scholars.

Reconciliation requires an examination and understanding of what has happened and how current structures, systems and attitudes/biases that are conscious or unconscious continue to uphold colonialism and Eurocentrism. University mission statements can include commitments to Indigenisation but without a meaningful examination of what that term means and an appreciation that decolonisation is the first step and that such commitments will fail to produce any significant change, other than putting a new face on a continued inability to engage in reconciliation.



Dawn Zinga Profe<u>ssor</u>

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MEXICO

Harnessing the genetic diversity of a dynamic crop: Cowpea

Shawn Yarnes from The Integrated Breeding Platform highlights harnessing the genetic diversity of a dynamic crop, cowpea and why it is important today

Public plant breeders are working in international collaboration to harness the genetic diversity of cowpea (*Vigna unguiculata*). Cowpea is a leguminous crop critical to food and economic security in hot semi-arid regions of the world. Most of the 5.6 million tonnes of dried cowpea grain produced annually are grown in West and Central Africa^{1,2,3}. Nigeria is the world's largest producer of cowpea, followed by Niger and Burkina Faso⁴. Production is increasing, but yield is hampered by lack of cultivars with appropriate tolerance and resistance to biotic and abiotic stress⁵.

Cowpea is a dynamic crop and economic resource for farmers cultivating marginal agricultural land and is a food source during the "hungry season" when last year's grain stores are depleted. Cowpea is eaten as both a vegetable and as grain and can serve a dual-purpose as animal fodder. Variety development differs based on purpose, with grain-types tending to be erect and early maturing. Most grain-types mature less than 100 days after planting^{3,6}. Green leaves and young pods are edible, and mature grain is high in protein (20-25%)^{1,4}. Peas can be harvested fresh or dry but are generally collected fresh in dual-purpose cultivation to avoid leaf senescence before hay-harvest^{2,4}.

Cowpeas are well adapted to sandy soils and low input farming practices. Little nitrogenous fertiliser is needed due to N-fixation by *Bradyrhizobium* spp. in root nodules⁷. Cowpeas enrich the soil with nitrogen and are often rotated and intercropped with: maize, sorghum, millet, and cassava. In Sub-Saharan Africa rotating cereals after legumes yield significantly more than continuous cereal production, mostly due to enhanced soil nitrogen². In regions with low soil phosphorus, cowpeas do benefit from P fertilisation. Variation in P-efficiency and N-fixation rates have been characterised, but not fully optimised in cowpea cultivars^{1,8}. Cowpeas are heat and drought tolerant, with some cultivars tolerating as little as 300mm of rain³. Cowpeas recover well from early season drought, but drought during flowering and pod-filling has lasting negative impacts on yield and quality even after re-watering. Drought tolerance is a complex trait, but many components are understood. Early maturation and other traits, like photoperiod-insensitivity, confer drought tolerance because they give farmers the flexibility to plant when rain is most likely to coincide with flowering^{4,6}. Extra-early maturation (45-50 days after planting) identified in a landrace has recently been introgressed into a medium maturing Ghanaian variety⁶.

Many pests and diseases affect cowpea, resulting in partial to total crop loss. Management practices such as crop rotation, maintenance of soil fertility, and chemical applications can alleviate pests and diseases, but improved genetic resistance is imperative to sustainable intensification of production. Fortunately, resistance to many pests (aphids, root-knot nematodes, foliar thrips, and *Striga*) and diseases (*Fusarium* wilt, bacterial blight, *Macrophomina* disease, and viruses) have been identified in diverse cowpea accessions^{45,9}.

Cowpea's tremendous genetic diversity is captured in germplasm collections worldwide, and new sources of alleles are continually being identified and genetically characterised. Important traits, such as black seed coat colour, pod shattering, and seed size have been recently mapped and candidate genes proposed^{10,11}. The immediate breeding challenge is to combine multiple sources of genetic diversity into cultivars suitable to local environments and markets. Grain value is driven by the culinary preference for seed colour and texture.

One effort currently underway is the evaluation of a multiparent advanced generation inter-cross (MAGIC)

MEXICO

population created from eight genetically diverse elite lines. The MAGIC population's 305 lines contain previously uncharacterised genetic combinations⁵. The International Institute for Tropical Agriculture (IITA) along with several national agricultural research organisations are evaluating these lines across Sub-Saharan Africa and determining their suitability as breeding material and possible new varieties.

"Cowpea is a dynamic crop and economic resource for farmers cultivating marginal agricultural land and is a food source during the "hungry season" when last year's grain stores are depleted. Cowpea is eaten as both a vegetable and as grain and can serve a dual-purpose as animal fodder."

Publicly funded resources, like; gene banks, genomics initiatives, and data sharing platforms are revolutionising cowpea improvement. Playing a part in many improvement efforts is the IITA Genetic Resource Center whose aim to conserve and distribute diverse cowpea accessions for research purposes. Genomic resources, such as the cowpea <u>reference genome</u> <u>sequence</u>, the Cowpea iSelect Consortium Array, and mapping populations, like the MAGIC, are unlocking our understanding of the genetic basis of traits¹². An awareness of the genetic basis for desired traits and affordable SNP genotyping is making marker-assisted breeding possible, even for small remote breeding programmes.

The era of big data has arrived for cowpea breeding, along with the need to archive, query, and share data. Institutes, like IITA, and other international collaborations are using the Breeding Management System to record and share cowpea breeding data in a unified format. Continued characterisation of cowpea diversity and knowledge sharing are critical to fully harnessing available genetic diversity and maximising cowpea genetic gain for food security.

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References

1 Carlos, G. (2000) Cowpea: Post Harvest Operation. Food and Agricultural Organization of United Nations: Rome, Italy.

- 2 Franke, A.C., et al. (2018) Sustainable intensification through rotations with grain legumes in Sub-Saharan Africa: A review. Agriculture, Ecosystems & Environment, 261: 172-185.
- 3 Freire Filho, F.R., et al. (2012) Production, breeding and potential of cowpea crop in Brazil. Embrapa Meio-Norte-Documentos (INFOTECA-E).
- 4 Boukar, O., et al. (2018) Cowpea (Vigna unguiculata): Genetics, genomics and breeding. Plant Breeding.
- 5 Kamara, A.Y et al. (2018) "Improving cultivation of cowpea in West Africa". In Sivasankar, S., Bergvinson, D., Gaur, P., Kumar, S., Beebe, S. and Tamò, M. Eds. Achieving sustainable cultivation of grain legumes. Volume 2: Improving cultivation of particular grain legumes. Cambridge: Burleigh Dodds Science Publishing. 1-18.
- 6 Owusu, E.Y. et al. (2018) Inheritance of Early Maturity in Some Cowpea (Vigna unguiculata (L.) Walp.) Genotypes under Rain Fed Conditions in Northern Ghana. Advances in Agriculture, 2018.
- 7 Karikari, B. et al. (2015) Growth, Nodulation and Yield Response of Cowpea to Phosphorus Fertilizer Application in Ghana. Journal of Agronomy, 14: 234-240.
- 8 Saidou, A.K., et al. (2007) Variability of cowpea breeding lines to low phosphorus tolerance and response to external application of Phosphorus. In Advances in Integrated Soil Fertility Management in sub-Saharan Africa: Challenges and Opportunities. Springer, Dordrecht:413-422.
- 9 Huynh, B.L., et al. (2018). A multi-parent advanced generation inter-cross (MAGIC) population for genetic analysis and improvement of cowpea (Vigna unguiculata L. Walp.). The Plant Journal, 93(6), pp.1129-1142.
- Herniter, et al. (2018) Identification of Candidate Genes Controlling Black Seed Coat and Pod Tip Color in Cowpea (Vigna unguiculata [L.] Walp). G3: Genes, Genomes, Genetics, 8(10), pp.3347-3355.
- 11 Suanum, W., et al. (2016) Co-localization of QTLs for pod fiber content and pod shattering in F2 and backcross populations between yardlong bean and wild cowpea. Molecular Breeding, 36(6) 80.
- 12 Muñoz-Amatriaín, M. et al. (2017) Genome resources for climate-resilient cowpea, an essential crop for food security. The Plant Journal, 89(5), pp.1042-1054.

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