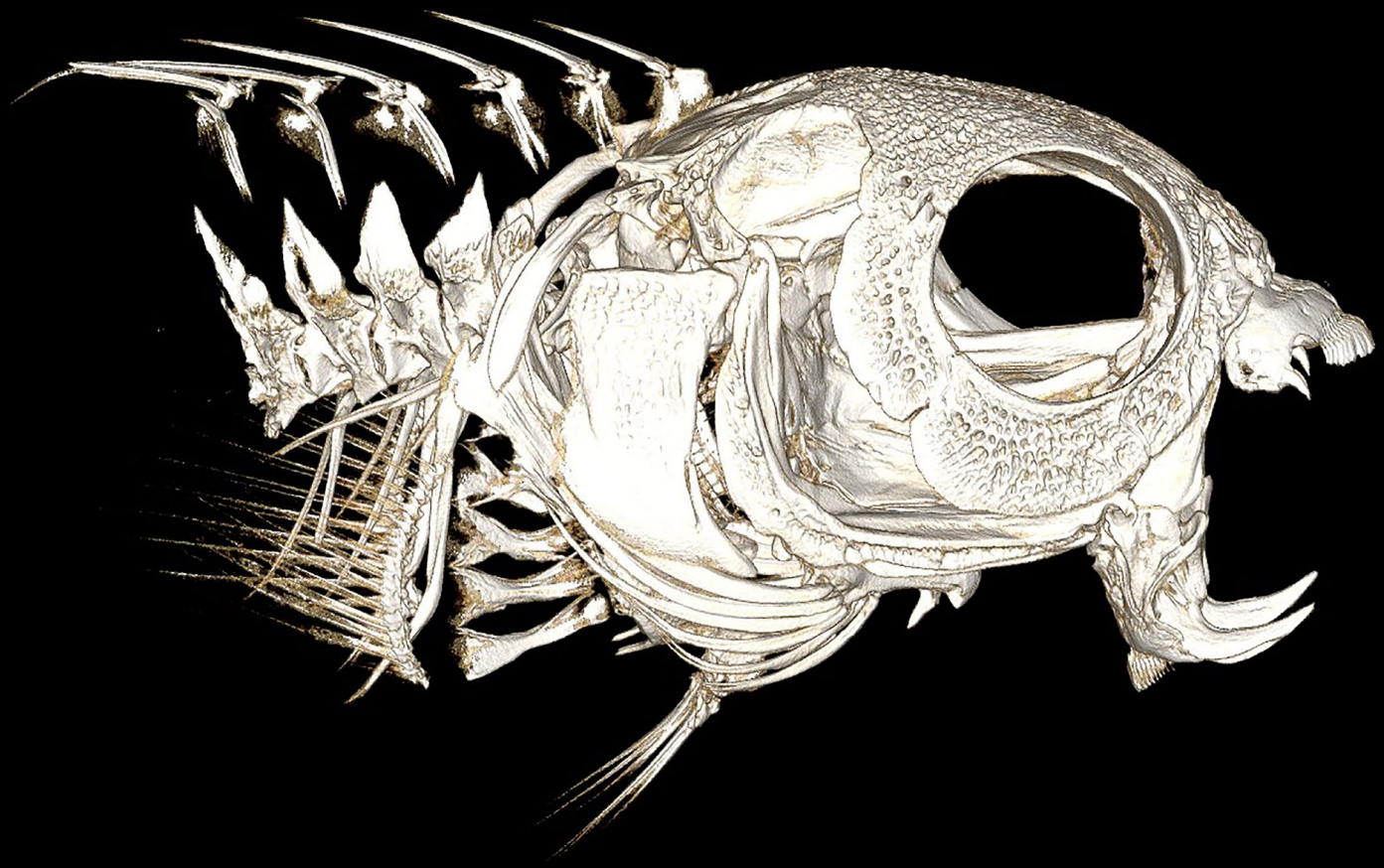
National Imaging Facility

National Imaging Facility Quarterly Newsletter Issue Two 2017



Lateral view of Fang Blenny Fish showing its enlarged, venom-delivering fangs - MicroCT Imaging

Image courtesy of Dr. Karine Mardon - Centre for Advanced Imaging, The University of Queensland

In This Issue

Director's Message

The National Research Infrastructure Roadmap has been released. And the Expert Working Group, led by the Chief Scientist, Dr Alan Finkel, has confirmed that the NCRIS program is the most effective way to deliver research infrastructure, and that in vivo imaging, of the type delivered by the National Imaging Facility is a necessary part of the Characterisation Capability. Once again, it has been found that imaging is an enabling technology that crosses disciplinary boundaries.

This quarterly newsletter demonstrates the breadth of scope for NIF, from better understanding of the effects of combat on our returned service men and women, to identification of the richness of diversity in our native fauna. The staff at the NIF nodes also continue to push the boundaries of the technology, so that they have the tools to address the wide range of problems that come across their table.

As important as finding new ways to do better research, is the opportunity to share that with colleagues. NIF is committed to making new technology widely available and ensuring best practice is the standard for all researchers. So, whilst individually experts in their research fields, the Facility Fellows and Informatics Fellows can further develop through sharing with each other. This ensures that all Australian researchers benefit from developments across the national capability. Talk to your local NIF Fellow about your research problems. If they don't know the answer, they will know who does.

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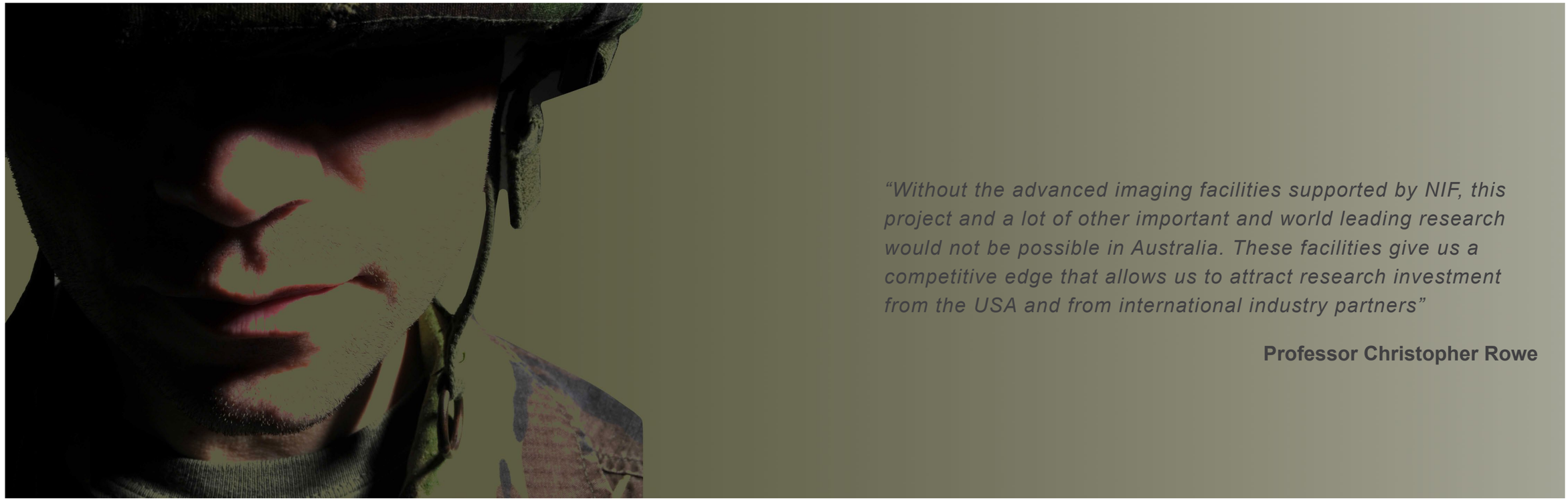
NIF is also committed to outreach, whether it be to industry, in response to the National Innovation and Science Agenda (NISA), or to school students, promoting the Science, Technology, Engineering and Maths (STEM) programs. So, whether you are a scientist of today, or one for the future, NIF is there to support your journey.

Professor Graham Galloway
Director of Operations

Are War Veterans with Traumatic Brain Injury or PTSD at Increased Risk of Alzheimer's Disease in Later Life?

Industry Project



"Without the advanced imaging facilities supported by NIF, this project and a lot of other important and world leading research would not be possible in Australia. These facilities give us a competitive edge that allows us to attract research investment from the USA and from international industry partners"

Professor Christopher Rowe

Are War veterans with Traumatic Brain Injury or PTSD at increased risk of Alzheimer's disease in later life? Australian researchers, using advanced imaging facilities supported by the National Imaging Facility (NIF), say no!

Survey studies suggest War Veterans who received a Traumatic Brain Injury (TBI) have an increased risk of later life dementia. Survey studies of persons with chronic Post Traumatic Stress Disorder (PTSD) also suggest a small increased risk of dementia in later years. The reasons for these findings are disputed and mechanisms contributing to this relationship are poorly understood.

A collaborative project, led by Professor Christopher Rowe at Austin Health and The Florey Institute of Neuroscience and Mental Health, and funded by the US Department of Defence, Piramal Imaging Pty Ltd, the NHMRC, and the Sir Edward "Weary" Dunlop Foundation, is using the NIF facilities at The University of Melbourne node to investigate the effects of TBI and PTSD on Alzheimer's disease in Australian Vietnam war veterans.

The researchers are using the advanced imaging facilities to seek evidence of increased Alzheimer's disease brain pathology such as amyloid plaques, tau tangles, and reduced glucose metabolism with Positron Emission Tomography (PET) scans, and cortical and white matter changes with MRI scans.

To date 116 Vietnam War veterans - 51 with chronic PTSD (aged 68 +/- 2 years), 37 with TBI (aged 68 +/- 2 years), and 28 with neither who are acting as controls (aged 69 +/- 5 years), have been studied. Although cognitive performance on detailed memory and other cognitive tests is mildly reduced in the TBI and PTSD participants, the researchers have found no evidence of increased Alzheimer's disease. The results have been presented at several major international meetings. Recruitment continues and the scans and data are being made available to researchers world-wide to assist further research in this area.

"Without the advanced imaging facilities supported by NIF, this project and a lot of other important and world leading research would not be possible in Australia. These facilities give us a competitive edge that allows us to attract research investment from the USA and from international industry partners" commented the study leader, Professor Rowe. "Rob Williams, NIF Fellow, has also been vital to this study as the lead scanning technologist and enthusiastic helper with veterans recruitment", said Rowe.

For more information on this project, contact the study co-ordinator Tia Cummins (tia.cummins@florey.edu.au) or Rob (williams.r@unimelb.edu.au).

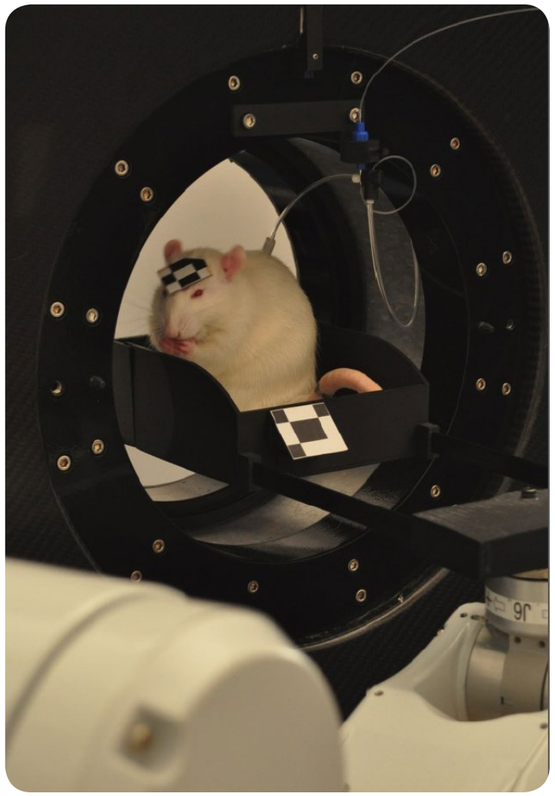
Collaborators
Austin Health
The Florey Institute of Neuroscience and Mental Health
University of Melbourne
Monash University
The Australian eHealth Research Centre, CSIRO, Brisbane.

Open-Field PET: A System For Simultaneous Brain PET and Behavioural Response Measurements in Unrestrained Laboratory Rats

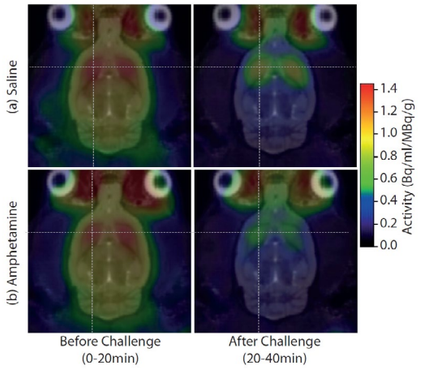
Research Project

Small animal Positron Emission Tomography (PET) imaging is a powerful research tool to gain unique insights into the complex neural circuits of mammalian brain function as an integrated whole. Conventionally, animals must be anaesthetised to avoid motion that would generate severe artefacts in the reconstructed images that can undermine regional quantification. However, anaesthesia affects many physiological processes by altering the biochemical parameter of interest, such as brain metabolism or neuroreceptor binding and precludes the opportunity to study the temporal correlation of neurotransmitter activity and changes in adaptive behaviour.

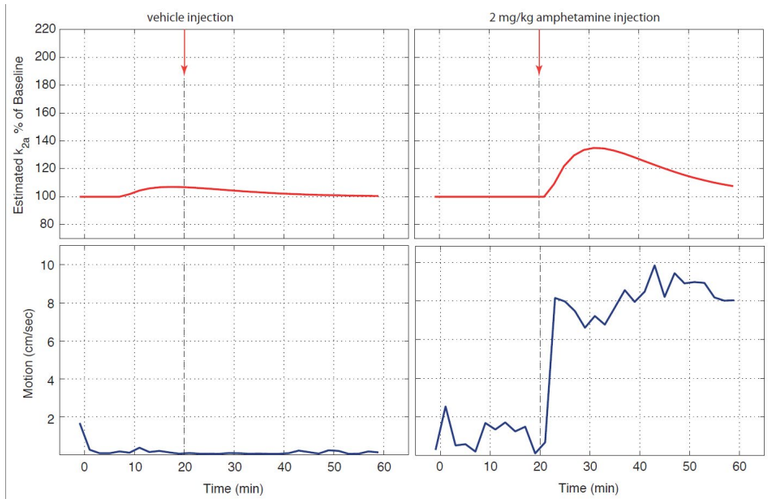
Previous work into this field has required the surgical implantation of the requisite probe. When used in combination with precise neuronal input control technologies such as optogenetics and chemogenetics, these methods provide important insights into the roles of specific populations of cells and their signalling pathways in regulating behavioural outcomes. However, the methods are invasive, prone to sampling errors and confined to small pre-determined brain regions. The desire, however, is to look at the whole brain function while maintaining cell and receptor type specificity. One method that has been used to overcome this issue is to inject the PET tracer while the animal is still conscious and applying the stimuli before anaesthetising and imaging the animal. Although, this approach avoids the confounding effects of motion, it cannot always be used with reversible receptor-binding PET tracers and can only give a delayed snapshot of brain function, rather than a full characterisation of the temporal profile of a neurotransmitter's response to a stimulus.



The experimental setup for the open-field PET. The animal is placed conscious and unrestrained within a robotically controlled enclosure which keeps the animal's head within the field of view of an unmodified small animal PET scanner. A 30 cm cannula connector is attached on the back-mount indwelling catheter and allows for the injection of the radiotracer and the drug while the animal is in the enclosure.



Motion-corrected coronal PET images of the [^{11}C]raclopride distribution in the brain of a freely moving rat, superimposed on a spatially registered MRI brain template. Images were integrated over the first 20 minutes immediately prior to the drug challenge (left column) and the next 20 minutes immediately after the drug challenge (right column). The animal underwent a vehicle injection (i.e. baseline) on the first day and an amphetamine injection (i.e. challenge) on the second day, both administered 20 minutes after the injection of the radiotracer.



Top row: the estimated D2R displacement curve obtained from kinetic modelling of the dynamic PET data for the vehicle injection (left column) and the amphetamine injection (right column). Bottom row: the recorded motion of the same animal throughout the PET study during the baseline (left) and the drug challenge study (right).

To address this problem, researchers from the University of Sydney's Brain and Mind Centre and the School of Psychology at University of New South Wales have been working closely with radiochemists from ANSTO to develop a technique called open-field PET. This system combines advances in motion tracking and compensation methods, along with a robotically-controlled animal enclosure, giving researchers the ability to acquire simultaneous measurements of transient changes in neurotransmitter concentrations in key regions of the brain and behavioural outputs following the delivery of a controlled stimuli.

During the development and evaluation of this novel imaging system, researchers focused on the quantification of receptor-ligand binding of Dopamine D2/D3 receptors, which play a vital role in many brain functions, such as learning, reward and drug addiction. The radiotracer used in this development was ^{11}C-Raclopride, which is a well understood tracer that binds to the D2 receptor in the brain. The project required productions of ^{11}C-Raclopride with high specific activity (>100MBq/nmol and <1nmol injected mass) to prevent saturation of the receptors due to cold carrier mass, as well as to allow the acquisition of images with superior signal-to-noise due to the high radioactive dose.

Sprague-Dawley rats were administered with ^{11}C-Raclopride via an indwelling jugular vein catheter and imaged in the open-field system for 60 minutes. On the first day the animals underwent a baseline scan (i.e. vehicle injection), while on the second day they received a drug challenge (i.e. amphetamine injection, which stimulates endogenous dopamine release from synaptic vesicles) 20 minutes after radiotracer injection. Dynamic PET data are analysed by least squares fitting of striatal time-activity curves using dedicated kinetic models able to quantify ligand displacement.

Using the open-field PET setup researchers could observe measurable changes in endogenous dopamine concentrations and temporally correlate it with dramatic changes in locomotor activity. Assessment of this technology continues but it already shows significant possibilities in an area that was previously unattainable.

For more information on the physics of this work contact Georgios Angelis (georgios.angelis@sydney.edu.au), and Genevra Hart (g.hart@unsw.edu.au) for animal behaviour, and NIF fellow, Gary Perkins (gary.perkins@ansto.gov.au), for radiochemistry.

Collaborators
Brain and Mind Centre, University of Sydney
School of Psychology, University of New South Wales
Australian Nuclear Science and Technology Organisation (ANSTO)

Acknowledgements: this project was supported by the Australian Research Council (project grants DP0988166 and DP120103813) and the Australian Institute of Nuclear Science and Engineering (research grant ALNGRA15022).

The Uncovered Toxins in Fang Blenny Fish Venom Could Pave the Way for New Medications

If you think that this tiny cute fish looks harmless, think again! The finger-sized and colourful fang blenny fish, which is found in Pacific coral reef, has terrifying fangs and drugs its predators with a painless bite using its two large canine teeth. These venomous bites are defensive in nature and not used for hunting. According to George Losey, a zoologist who was the first to investigate the venomousness of fang blennies through a series of experiments in 1970s, a predator that puts fang blenny into its mouth would experience a violent quivering of the head and will then open its jaws for a few seconds until the little blenny swims out unharmed.

An international team of scientists, led by Nicholas Casewell from the Liverpool School of Tropical Medicine and Bryan Fry from the Venom Evolution Lab at the University of Queensland, have recently published a study[1] that confirms although all fang blenny species share the large canines, only one group called Meiacanthus, have venom glands. The study reports that this group evolved venom glands after they developed their distinctive enlarged canines. More interestingly, the fang blenny venom does not appear to produce potent pain as it targets predators' blood pressure (instead of their pain neurons), causing a sudden drop.

The scientists went through a labor-intensive extraction of venom from these small fishes and analysed the venom to identify three toxins: The first—phospholipases—are common in the venoms of snakes, bees, and scorpions; they cause inflammation, and can damage nerves. The second—neuropeptide Y—is used by the lethal cone snail, and causes blood pressure to tank[2].

The third group—enkephalins—are opioid hormones. They're similar to the natural endorphins that give you feel-good effects during exercise or laughter, and they work by targeting the same molecules as synthetic opioid painkillers like fentanyl or oxycodone[2].

"This venom is absolutely unique," said Fry. "We have never seen anything like it." Fry is particularly excited by the newly discovered opioid toxin, as the venoms of these species may serve as a novel source of painkillers. Currently prescribed opioids have led to an epidemic of addiction, so doctors and scientists are keen to find alternatives. "We are a long way, of course, from any human medication," Fry noted, but "any new leads for opioids are always of interest."[3]

"This discovery is an excellent example as to why we must urgently protect all of nature," Fry continued. "It is impossible to predict where the next wonder drug will come from."[3]

National Imaging Facility (NIF) contributed to this breakthrough by the facilities and scientific & technical assistance provided at The University of Queensland (UQ) node - Centre for Advanced Imaging. For more information on this work, contact Nicholas Casewell (nicholas.casewell@lstmed.ac.uk) and Bryan Fry (bgfry@uq.edu.au) and for information on the Micro-CT facility and expertise at the UQ node of NIF contact Karine Mardon (k.mardon@uq.edu.au).

Collaborators
Liverpool School of Tropical Medicine, UK
Leiden University, the Netherlands
The University of Queensland, Australia
Monash University, Australia
University of Karachi, Karachi, Pakistan
Leiden University Medical Center, the Netherlands
Bangor University, UK
Anglia Ruskin University, UK

1. Casewell, Nicholas R., et al. "The Evolution of Fangs, Venom, and Mimicry Systems in Blenny Fishes." Current Biology 27.8 (2017): 1184-1191.
2. https://www.theatlantic.com/science/archive/2017/03/fangblenny-venom-opioid-oh-god-oh-god-put-it-away/521292
3. http://blogs.discovermagazine.com/science-sushi/2017/03/30/fang-blenny-venom-toxins/#.WUHsAIWGOUI

Networking within NIF

April this year marked another successful interactive workshop, which provided an invaluable opportunity for Fellows to share knowledge, exchange expertise, and further develop collaborative projects. The workshop included a number of informative presentations on opportunities for national and international engagement, talks on the future of NIF and the key role that Fellows play, as well as several group discussions that facilitated collection of constructive feedbacks from Fellows.

The workshop was held in the University of Western Australia node, Perth, in conjunction with NIF annual meetings that bring both Governing Board and Operations Committee together to discuss the future strategic direction of the NIF national network.

The NIF community also celebrated the achievement of 10 years of collaboration and partnership and renewed their commitment to providing a network that advances scientific and industrial research & development and facilitates outcomes from which the Australian economy benefits.

Marianne Keller and Brad Moffart in front of the PET/CT scanner at the Melbourne Brain Centre Imaging Unit, University of Melbourne node

Following the almost fully-attended NIF Fellows workshop in Perth, interesting discussions and visits for further collaborations between some of the NIF nodes were formed.

Marianne Keller, NIF Fellow at LARIF, went to Melbourne and met with several other Fellows including Michael de Veer and Tara Sepehrizadeh at Monash University node, and Brad Moffat and Rob Williams at the University of Melbourne node.

She visited Monash Biomedical Imaging to learn how they manage side by side human and animal imaging and the Melbourne Brain Centre Imaging Unit to discuss some of the successful projects that use the 7 Tesla Human MRI and/or the PET/CT scanners, such as the most recent advances in Alzheimer's disease research.

These visits laid foundation for future inter-node collaborations.

Special thanks to Marianne Keller for her enthusiasm and contribution of this piece.

Industry Engagement

Imaging to Innovate @UNSW

Industrial Transformation Training Centre @UQ

Imaging to Innovate @UNSW

News

The Biological Resources Imaging Lab (BRIL), which is part of UNSW's Mark Wainwright Analytical Centre and a node of the National Imaging Facility, is hosting "Imaging to Innovate" showcase on 19 July 2017. The event aims at engaging industry and commercial companies, from small to large size, to connect and support their access to the imaging research infrastructure.

BRIL is a world-class preclinical imaging facility that provides a range of imaging capabilities including high-field MRI, microPET-CT, optical imaging, ultrasound and other technologies.

This event brings the expertise of scientists, researchers and innovation managers all onto the same stage to discuss how collaborating with UNSW can support businesses' R&D and innovation.

Find out how easy it is to access cutting-edge technologies, inventions and state-of-the-art facilities and see how other companies have successfully collaborated with UNSW.

Experts will be available to provide information on collaborative funding opportunities and accessing UNSW Intellectual Property and inventions.

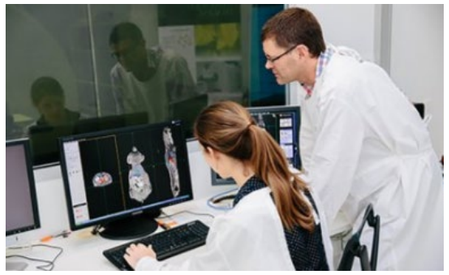
Guest speakers

Professor Bill Walsh, Director of Surgical and Orthopaedic Laboratories at UNSW
Dr Lindsay Wu, Senior Lecturer, Laboratory for Ageing Research, UNSW
Dr Josh McCarroll, Research Fellow, Children's Cancer Institute Australia, UNSW
Professor Grainne Moran, Pro-Vice Chancellor, Research Infrastructure, UNSW

For more information and registration, visit Imaging to Innovate @UNSW

Industrial Transformation Training Centre @UQ

As a result of successful collaboration with industry, a new research hub will be established at The University of Queensland node of National Imaging Facility (NIF) to train the next generation of scientists who will expand the boundaries of biomedical imaging to improve healthcare.



The Industrial Transformation Training Centre for Innovation in Biomedical Imaging Technology received $4.7 million Australian Research Council grant and $3.8 million in cash and in-kind contributions from 9 industry partners including Siemens Healthcare Pty Ltd, Clarity Pharmaceuticals Pty Ltd, Minomic International Ltd, Inter-K Peptide Therapeutics Ltd, Theranostics Australia Pty Ltd, Beijing Genomics Institute, Brisbane Veterinary Specialists Centre, Uniting Care Medical Imaging, and Red Radiology Pty Ltd.

The centre builds upon previous investments in Centre for Advanced Imaging and the National Imaging Facility from the Queensland Government and the Commonwealth Government's contributions to the NIF through the National Collaborative Research Infrastructure Strategy (NCRIS) and the Education Investment Fund (EIF).

For more information, read this story online at UQ News.

STEM Outreach

Scientists in Schools

News

Dr. Andrew Janke, one of the NIF Fellows at The University of Queensland node - Centre for Advanced Imaging (CAI), continues to contribute to STEM (Science, Technology, Engineering, and Mathematics) education voluntarily through the 'Scientists and Mathematicians in Schools' (SMiS) program, which is managed by CSIRO.

Andrew participates in schools' science classes and plans school visits to CAI frequently to create a positive, real-world experience for students and support them with the opportunities they need to develop as problem solvers, critical and creative thinkers. He also actively contributes to STEM networking events to inspire more STEM professionals and teachers to engage in such partnerships.

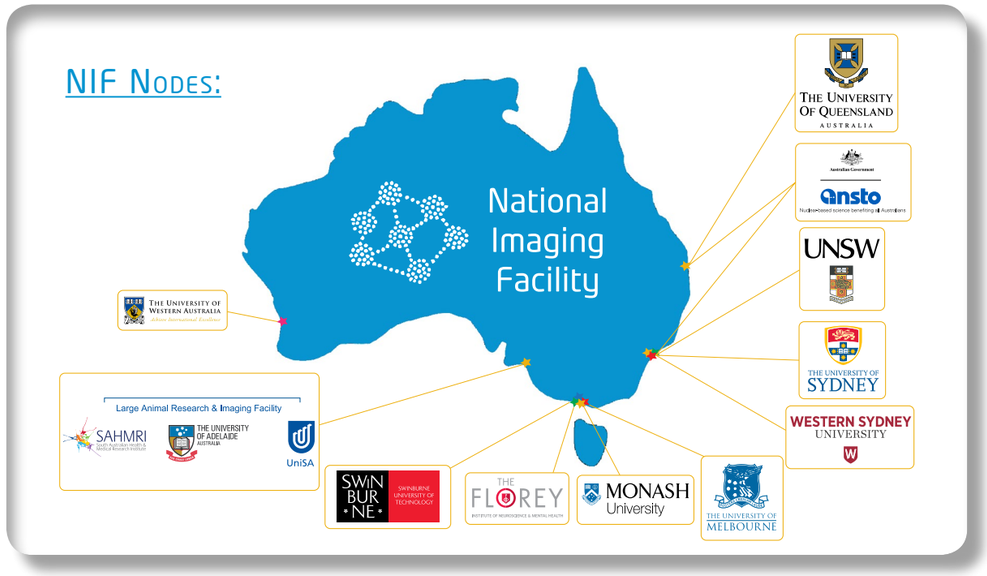
"*It is rewarding to see how the teachers integrate the work we do in NIF into some of the academy classes. We tailor the visits to be a real world example of what students are currently working on in an assignment*", said Andrew.

National Imaging Facility is committed to STEM, ensuring Australia's young adults are equipped with the necessary skills for the economy of the future.

Dr. Andrew Janke, NIF Fellow and three students participating in science academy class at Cavendish Road State High School.

Dr. Andrew Janke, NIF Fellow, and Michael Denner, head of science department at Cavendish Road State High School, guiding three students through the scientific process of a students-designed experiment.

Dr. Andrew Janke, sharing experience on his partnership with Cavendish Road State High School at the SMiS Integrated STEM Networking Event, which was held on 30 May 2017 at the CSIRO Ecosciences Precinct. The event provided a great opportunity for Scientists, STEM professionals, and teachers to meet and exchange expertise to enhance science, maths, and technology practices.



For further information regarding the newsletter, please contact Saba Salehi (communications@anif.org.au)

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