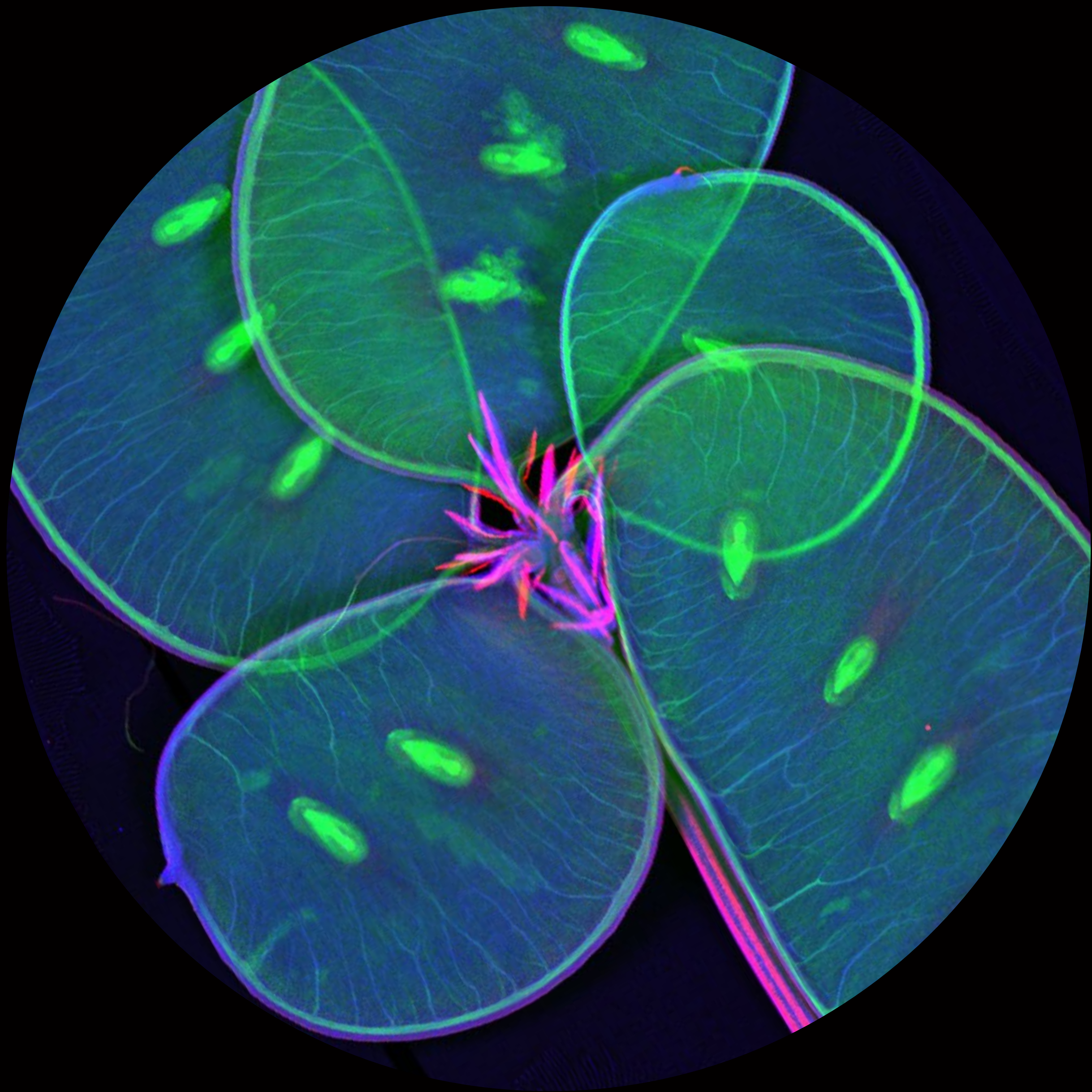
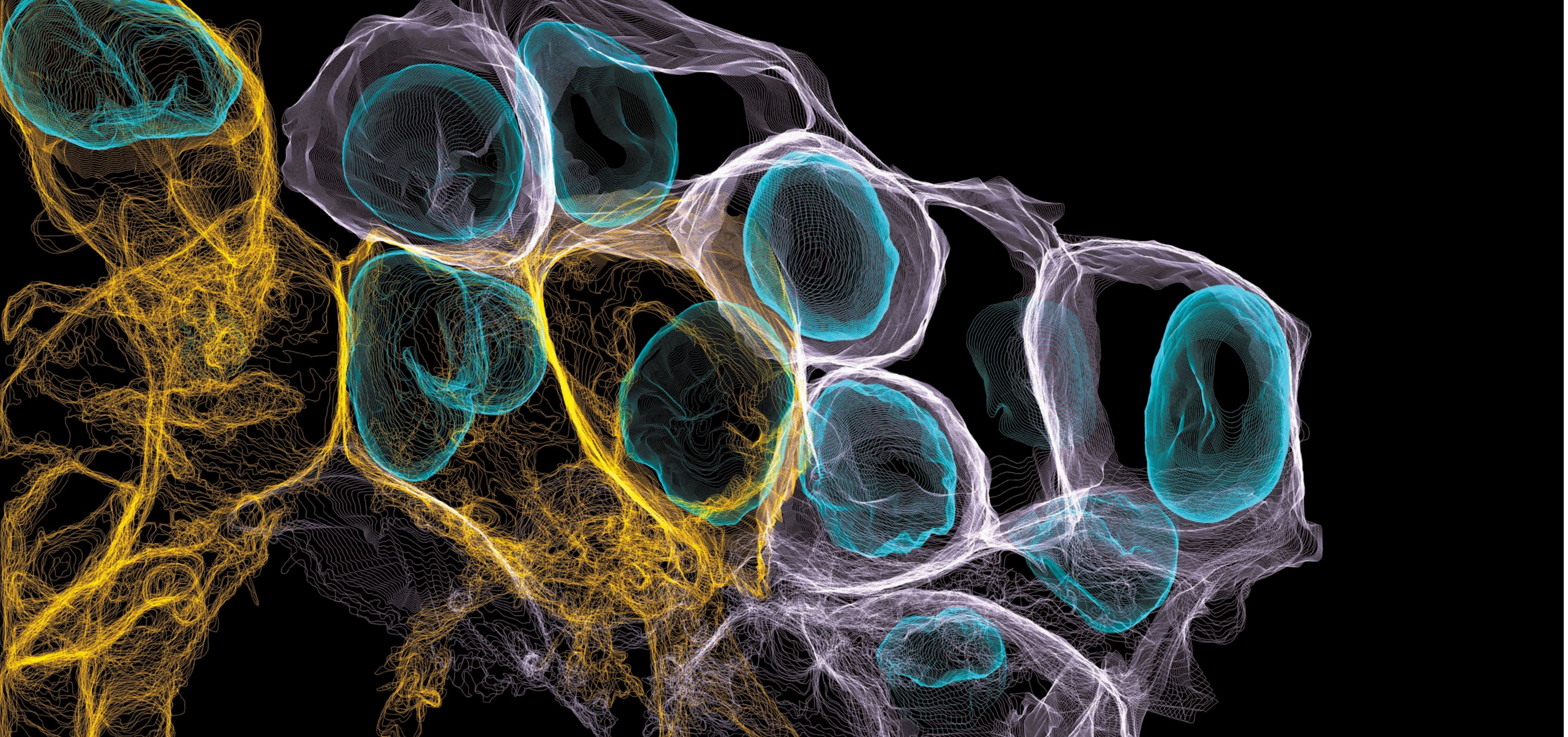
MICROSCOPY AUSTRALIA
RESEARCH HIGHLIGHTS 2022





Microscopy Australia provides researchers and businesses with access to high-end microscopes and experts, driving research excellence and innovation in Australia.

CONTENTS

Cover: Seed pods from Neptunia amplexicaulis, each approximately 10mm wide. This plant accumulates selenium and is being investigated as a tool for the remediation of mine sites (red: calcium, green: selenium, blue: potassium) by Dr Antony Van der Ent. Read more on page 41.

Left: A 3D model of a cluster of melanoma cells showing their nuclei in turquoise. The model was rendered using data from serial block-face scanning electron microscopy. Imaged by Darren Brown.

Both taken at the Centre for Microscopy and Microanalysis, University of Queensland.

LEADERSHIP REFLECTIONS

CHAIR

Dr Gregory R. Smith
Chair of Board

Microscopy Australia reached 15 years of operations in 2022, a major milestone achievement as part of Australia's National Collaborative Research Infrastructure Strategy (NCRIS). Microscopy Australia operated very effectively as pandemic restrictions eased and participated in the national research infrastructure road-mapping process.

For the 2021 Roadmap, NCRIS established an Expert Working Group (EWG) to review Australia's national research infrastructure, including NCRIS itself. The NCRIS chairs provided integrated feedback to the EWG regarding their views about opportunities and challenges related to the road-mapping process and identified numerous synergies and cross-organisational capabilities between NCRIS projects.

During the EWG assessment, the role of Microscopy Australia in the Australian research infrastructure landscape was evident. Its capability is of critical importance to the various strategic technologies identified during the review.

The review also focused on how research infrastructure supports technology step-changes that are important to the future of Australia. It was noted that Microscopy Australia provides key support to numerous step-change research activities across Australian academia and industry, including emerging government priorities, such as the National Reconstruction Fund and the List of Critical Technologies.

Microscopy Australia's Board re-examined its governance framework during 2022, focusing on the balance of Board membership, representation and skills. It also chartered a Risk and Audit sub-committee.

CEO

Prof. Julie Cairney
Chief Executive Officer

As 2022 draws to a close, we are approaching completion of our most recent five-year capital plan, with the final instruments arriving this year. The new National Research Infrastructure Roadmap has been released, framed around eight research challenges, all of which require access to the latest generation of advanced microscopy. We welcome the government's response to this Roadmap, providing continuity across the national research infrastructure landscape.

A big focus for 2022 was the development of a new approach to industry engagement, championed by our Industry Engagement Committee. We have appointed seven dedicated industry-facing platform scientists across the Microscopy Australia facilities and have convened and participated in major promotional activities such as Australian Manufacturing Week, a dedicated workshop on Microscopy in Manufacturing, the Quantum Research Infrastructure Showcase, and Australia Battery Day.

In May we enjoyed our first face-to-face strategic leadership retreat in three years. In February 2023, we are hoping to see many of our staff finally convene together at the Australian Conference for Microscopy and Microanalysis in Perth.

Left page: Confocal image of water plants and microalgae from Brisbane Botanic Gardens by John Griffin taken at the Central Analytical Research Facility, Queensland University of Technology.

THINK SMALL TO THINK BIG

We are Australia's national collaborative microscopy and microanalysis infrastructure: sharing our resources to enable research excellence for over 15 years.

Our open access model means that all Australian researchers and businesses can access a wide range of high-end instruments and expertise through our facilities around the country.

VALUES

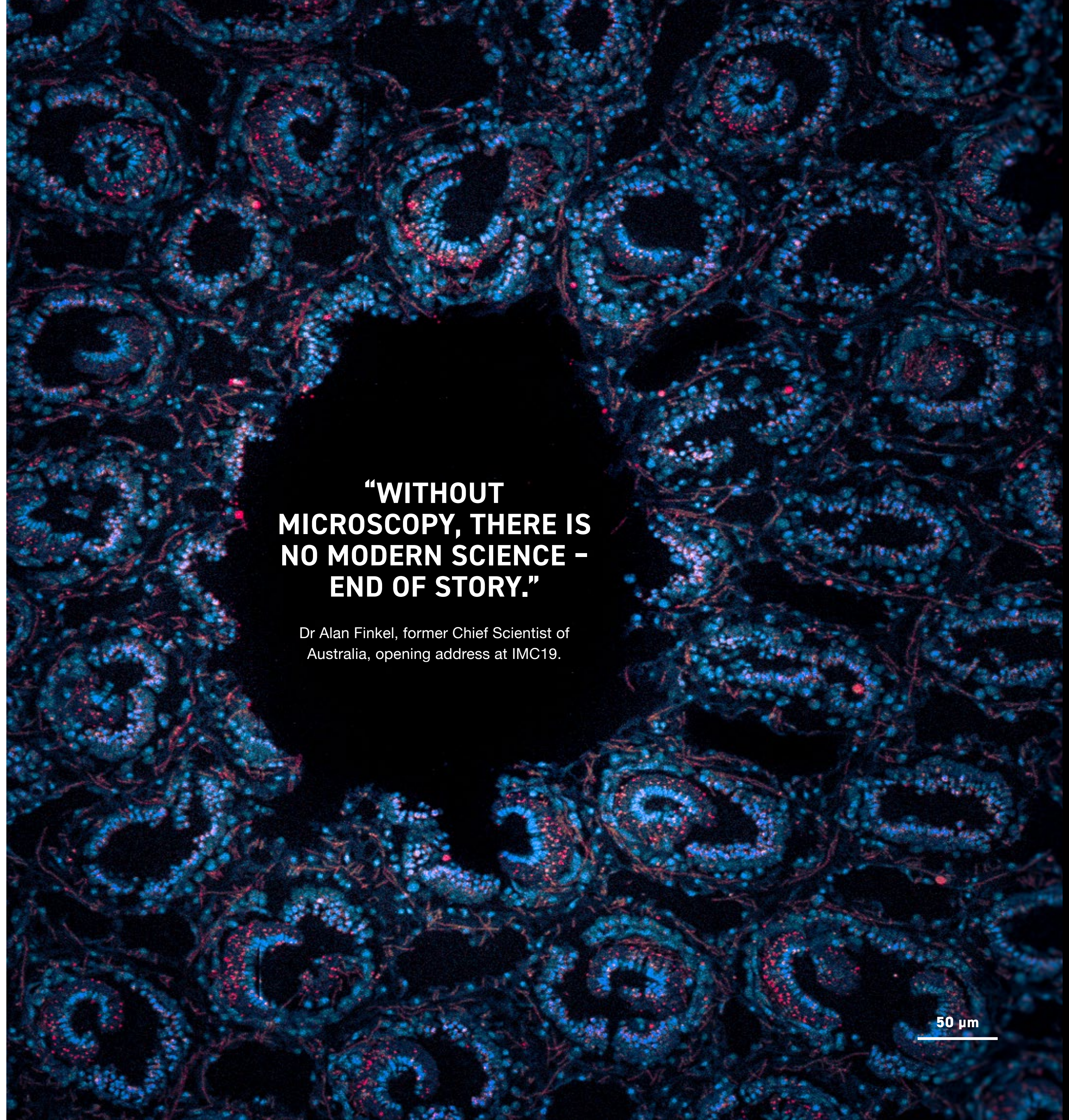
EXCELLENCE | COLLABORATION | ACCESSIBILITY | INNOVATION

VISION

To provide world-leading microscopes and expertise that keep Australia at the forefront of global research.

MISSION

To empower Australian science and innovation by making advanced microscopes accessible to all researchers.



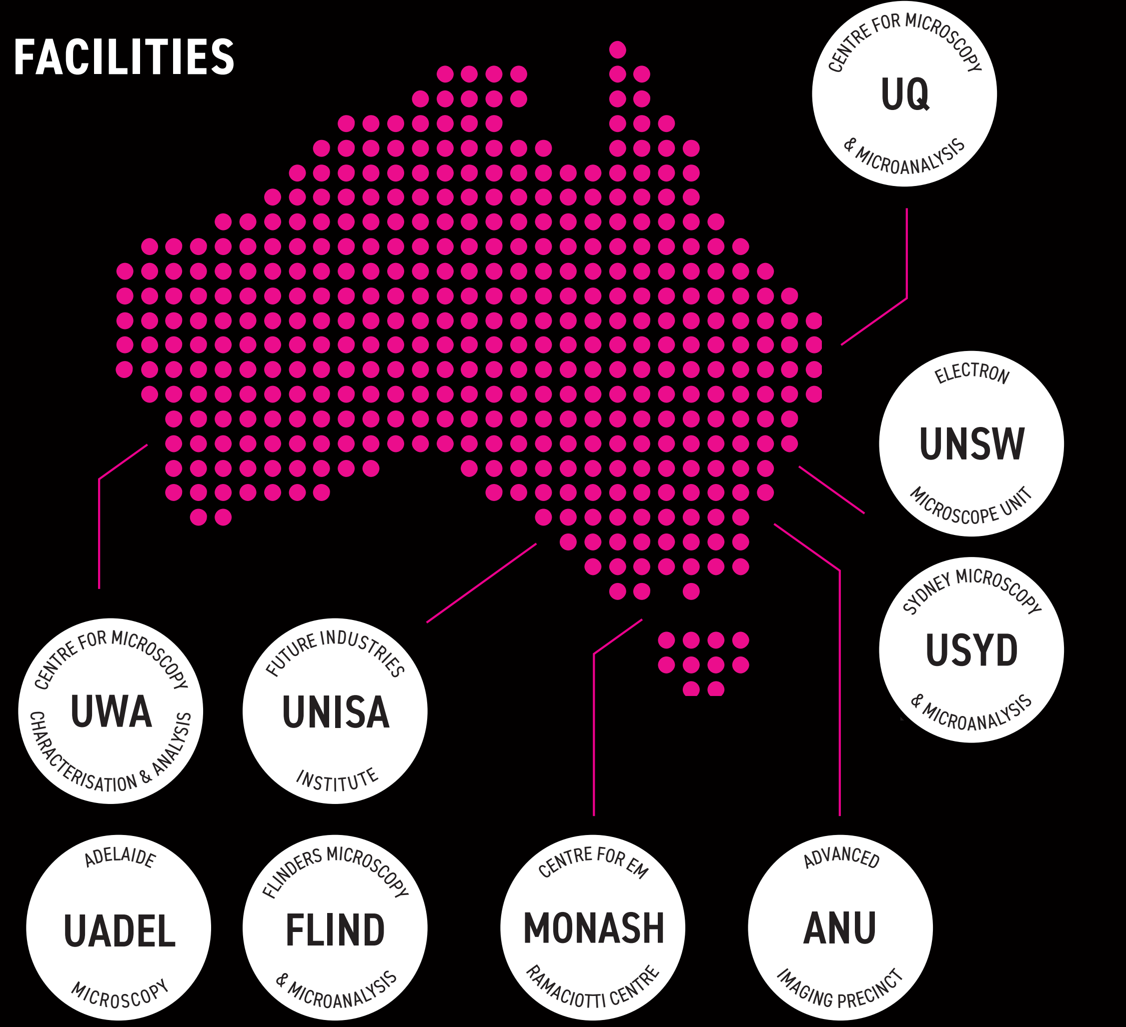
"WITHOUT MICROSCOPY, THERE IS NO MODERN SCIENCE – END OF STORY."

Dr Alan Finkel, former Chief Scientist of Australia, opening address at IMC19.

Left: Confocal image of an embryo-bearing sea sponge by Ruija Yan, Centre for Advanced Microscopy, Australian National University.

OUR LOCATIONS

FACILITIES



LINKED LABS

- QUEENSLAND UNIVERSITY OF TECHNOLOGY
- DEAKIN UNIVERSITY
- UNIVERSITY OF TECHNOLOGY SYDNEY
- CENTRE FOR DISEASE PREPAREDNESS CSIRO
- UNIVERSITY OF WOLLONGONG
- RMIT UNIVERSITY
- UNIVERSITY OF TASMANIA
- CURTIN UNIVERSITY
- JAMES COOK UNIVERSITY

Data from 2021 (2022 collection). Left: cryo-TEM image of liposomes by Dr Rhiannon Kuchel, Electron Microscope Unit, UNSW.

277
INSTRUMENTS

152
EXPERTS

3,321
USERS

315
INDUSTRY CLIENTS

280,082
HRS BEAMTIME

1,689
PUBLICATIONS

47,000
VIEWS ON YOUTUBE

44% PHYSICAL & MATERIALS
39% BIOLOGICAL & MEDICAL
17% GEOSCIENCE & ENVIRONMENT

49% MANUFACTURING
15% BIOMEDICAL
36% RESOURCES & ENVIRONMENT

99%
OF USERS REPORT MICROSCOPY WAS VALUABLE TO THEIR RESEARCH

98%
OF USERS WOULD RECOMMEND OUR FACILITIES TO A COLLEAGUE

31%
OF USERS' PUBLICATIONS ARE IN THE TOP 10% OF MOST CITED JOURNALS

MYSCOPE
MICROSCOPY TRAINING

MyScope is our free online training platform for new microscopists to learn a wide range of microscopy techniques through theory and simulated microscopes. 12 modules cover major microscopy and microanalytical techniques.

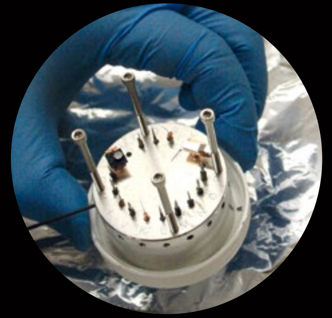
myscope.training

Complementing this is MyScope Explore, which gives individuals of all ages a chance to discover over 70 different samples on a scanning electron microscope simulator.

myscope-explore.org

EQUIPMENT & EXPERTISE

TAKE A CLOSER LOOK



SPECIMEN PREPARATION

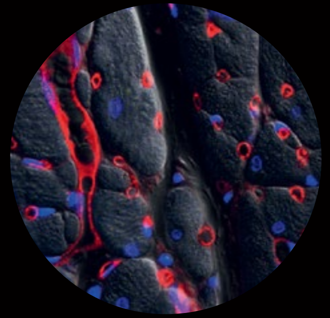
Biological & Materials

Cell Culturing & Molecular Preparation

Thermomechanical Processing

Ion Milling & Machining

Ion Implantation



LIGHT & LASER OPTICS

Confocal, Fluorescence & Optical Microscopy

Flow Cytometry & Cell Sorting

Live-cell Imaging

Vibrational & Laser Spectroscopy

Laser Microdissection

SCANNING ELECTRON MICROSCOPY

Imaging & Analytical Spectroscopy

In-situ Imaging & Testing

Cathodoluminescence

Electron Backscatter Diffraction

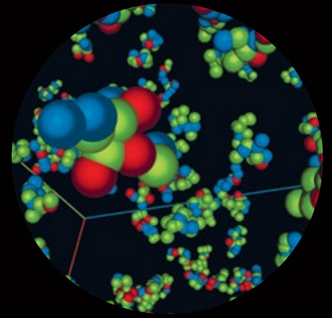
TRANSMISSION ELECTRON MICROSCOPY

Imaging & Analytical Spectroscopy

Cryo-techniques & Tomography

Phase & Z-contrast Imaging

Electron Diffraction



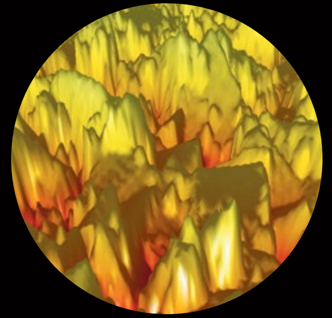
ION & SPECTROSCOPY PLATFORMS

Secondary Ion Mass Spectroscopy

Imaging Mass Spectroscopy

Atom Probe

LA-ICP-MS

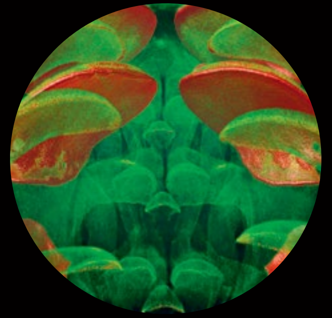


SCANNED PROBE TECHNIQUES

Atomic Force Microscopy

Scanning Tunneling Microscopy

Near-field Scanning Optical Microscopy



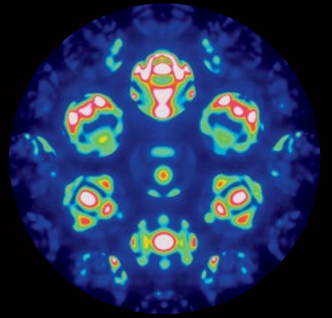
X-RAY TECHNOLOGIES

X-ray Diffraction

X-ray Fluorescence

X-ray Micro-CT

Photoemission Electron Microscopy



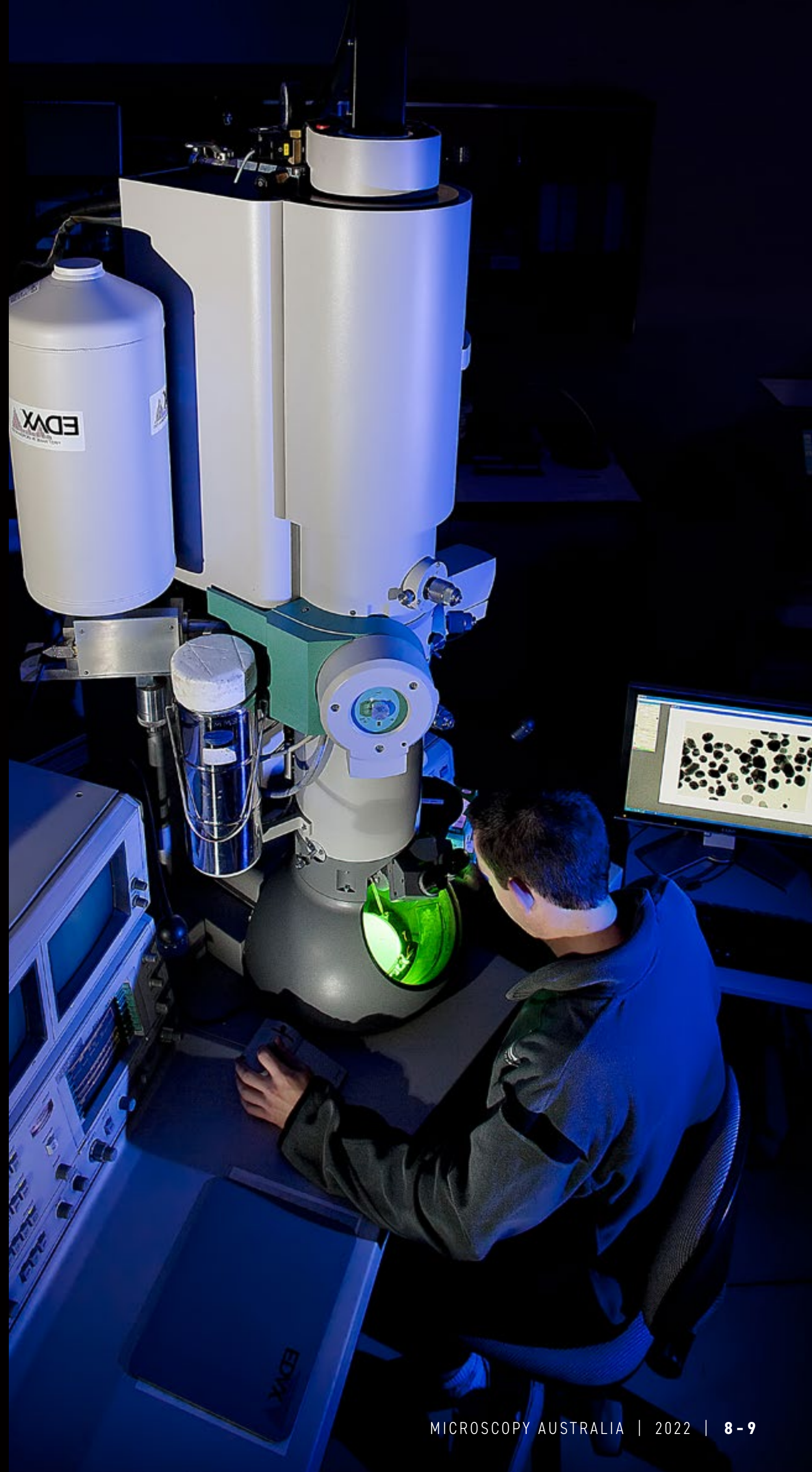
VISUALISATION & SIMULATION

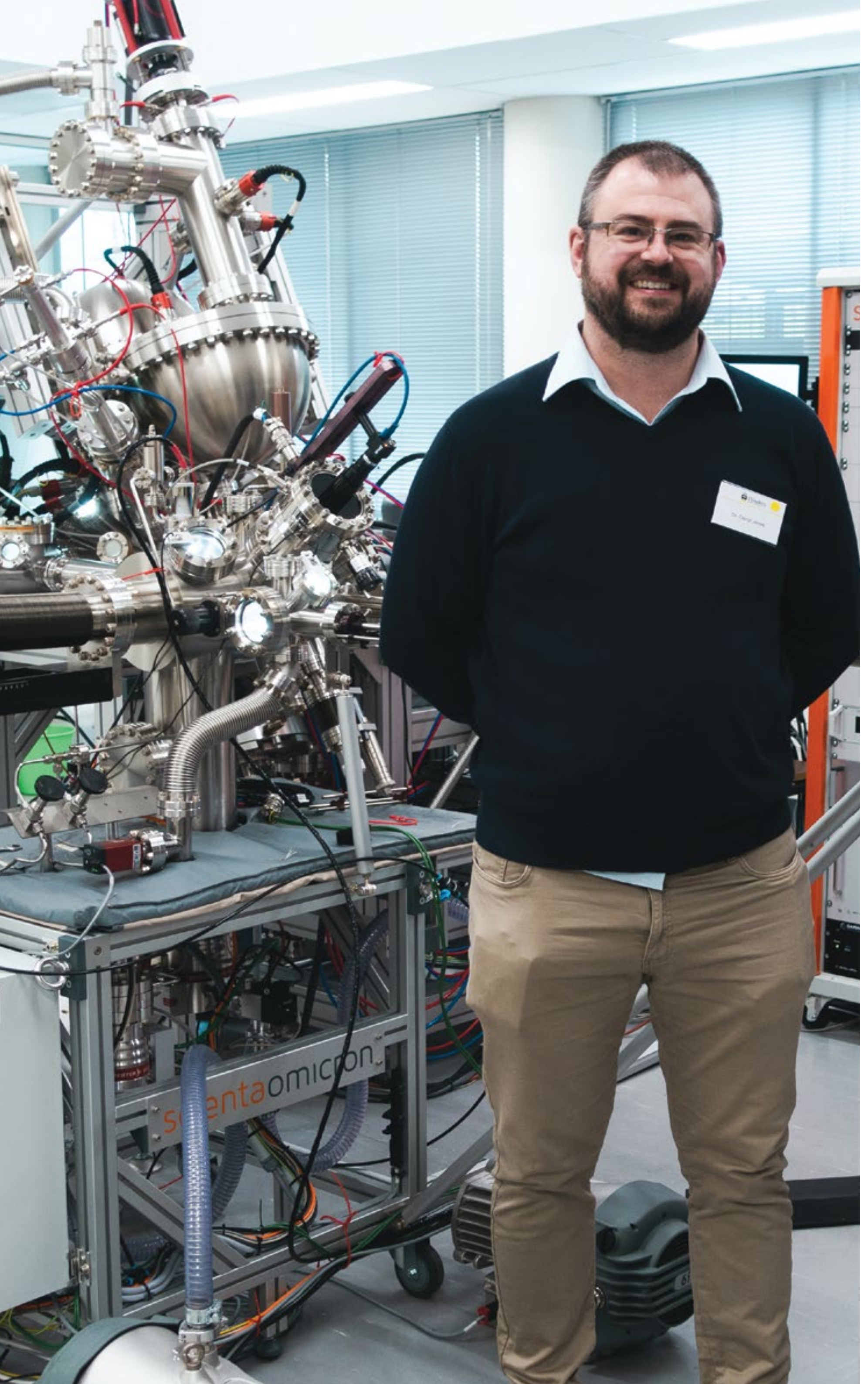
Computed Spectroscopy

Computed Diffraction

Image Simulation & Analysis

Data Mining





MICROSCOPY TO MEET AUSTRALIA'S FUTURE RESEARCH PRIORITIES

Every five years the federal government produces a National Research Infrastructure Roadmap that seeks to predict the future needs of Australian researchers in order to guide research infrastructure investment. Eight critical challenge areas were identified in the Roadmap. Microscopy Australia currently supports all of these (right) as well as four areas of step-change (below).

SUPPORTING ROADMAP STEP-CHANGES

Synthetic Biology

Microscopy is an essential tool in revealing the structures and functions of biological molecules. This is fundamental to synthetic biology. See page 22 for a case study.

National Collections

From 3D scans that reveal the internal structures of objects without destroying them, to compositional analysis, microscopy is a fundamental tool for understanding physical collections and creating digital collections. See page 34 for a case study.

Research Translation

Microscopy is essential to the development of new products, along with developing manufacturing processes and providing evidence of consistent quality in the scale-up phase. See pages 35 and 42 for case studies.

Environment & Climate

Microscopy is a key tool both in monitoring climatic and environmental change and development of new materials and technologies for adapting to it. See pages 24, 31, 32 and 42 for case studies.

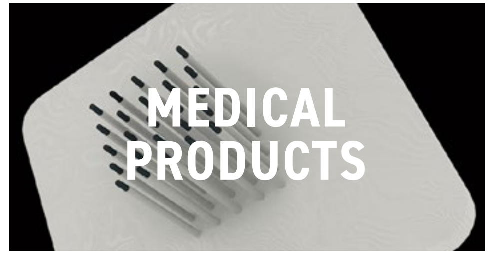
Image: Dr Darryl Jones with Australia's only Photoemission Electron Microscope at our Flinders facility.

Our facilities are regularly used to improve exploration and refine mineral processing (see pages 26 & 47). Kathy Ehrig, Superintendent Geometallurgy at BHP's Olympic Dam site, says, "I would like to stress the importance of Microscopy Australia facilities, including the highly skilled, professional staff who operate the facilities, to the mining industry within Australia."

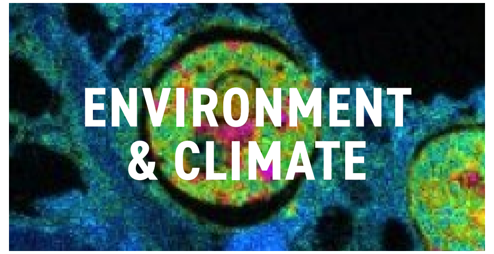
Our South Australian facilities work in collaboration with businesses in the local defence supply chain to study future battery technology for maritime applications, and to also carry out failure analysis on components from the existing submarine fleet. They use microanalysis to quantify the chemistry of experimental responsive chameleon-like camouflage devices for military vehicles.

Microscopy is crucial for creating better crops, soils, fertilisers and pesticides (see page 42). For example, as part of the C4 Rice Project, our microscopes were used to understand how C4 plants retain carbon dioxide in their leaf cells. This information will help researchers to engineer more productive rice crops for greater food security.

Our microscopes help to improve satellites. Projects include development of 3D printed thermal management devices, new mechanical computers that withstand solar flares, and, in a project funded by the Defence Innovation Partnership Scheme, freeform optical devices for improved imaging and surveillance capabilities in small satellites (see page 40).



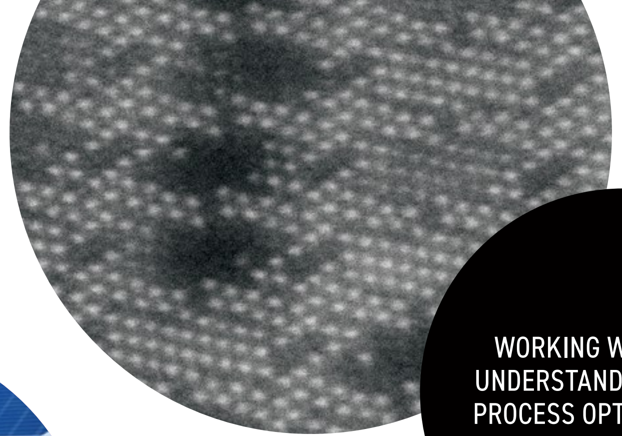
Our facilities have been used in the development of several bio-compatible synthetic bone graft products. The most significant of these is a 3D printable bone scaffold that can both regenerate bone and support load-bearing bones such as the spine. It is the only synthetic bone product that can do both, and is currently being commercialised by Allegra.



Microscopy Australia's NanoSIMS, a high sensitivity analytical tool, is being used to understand how microbial inhabitants of larger marine organisms, such as corals and anemones, contribute to ecosystem health and phenomena such as coral bleaching, global sulfur cycling, atmospheric chemistry, cloud formation and associated cooling effects.

In the last two years Microscopy Australia's users have achieved five solar efficiency world records for emerging solar cell technologies including perovskite, quantum dots (transparent and flexible) and non-toxic kesterite solar cells (see page 32). A range of high-end microscopy techniques are crucial in the development of these technologies.

Microscopy Australia enables research into a wide range of hydrogen production and storage technologies. From hydrogen-embrittlement resistant steels for storage, through to the Hazer process, now operating commercially to convert methane from Perth's sewage into clean hydrogen fuel.

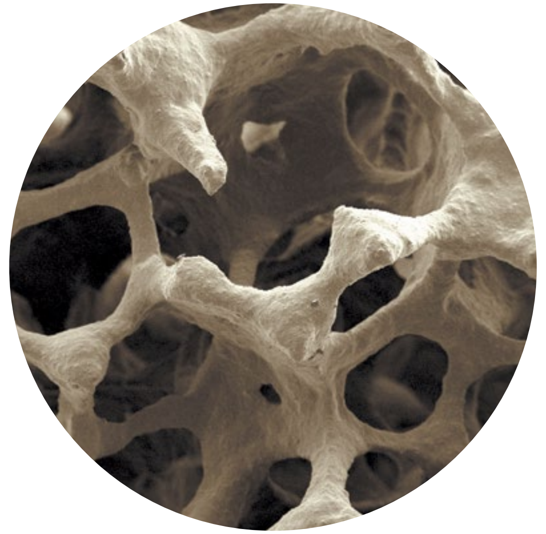


WORKING WITH BHP TO UNDERSTAND ORIGINS AND PROCESS OPTIMISATION OF THEIR ORE DEPOSITS

RECORD-BREAKING SOLAR CELL TECHNOLOGIES

See next page

3D-PRINTED, SUPER-STRONG, SAFE BONE SCAFFOLDS BEING COMMERCIALISED



GELION IS DEVELOPING ROBUST AND SAFE BATTERIES USING ABUNDANT MATERIALS

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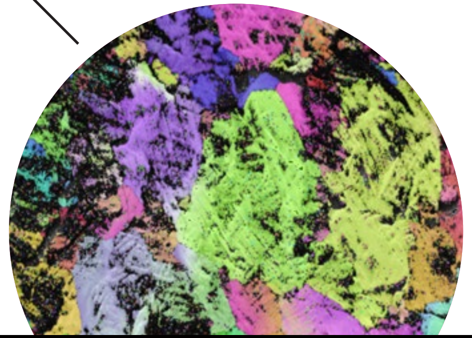
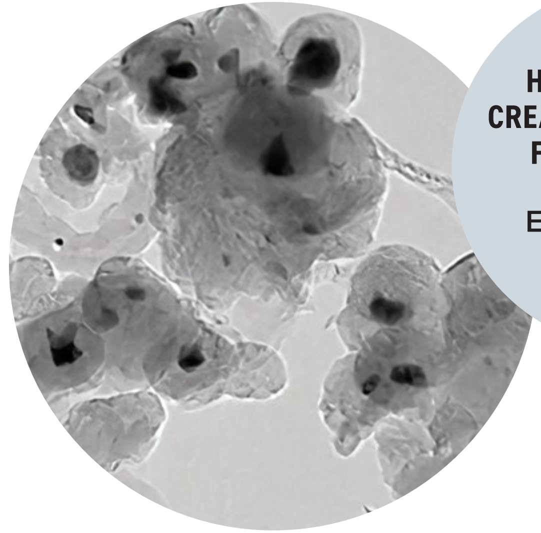


NEW SPINOUT USING BIOMIMETIC SURFACES TO HARVEST WATER FROM AIR



HAZER GROUP IS CREATING CLEAN FUEL FROM METHANE

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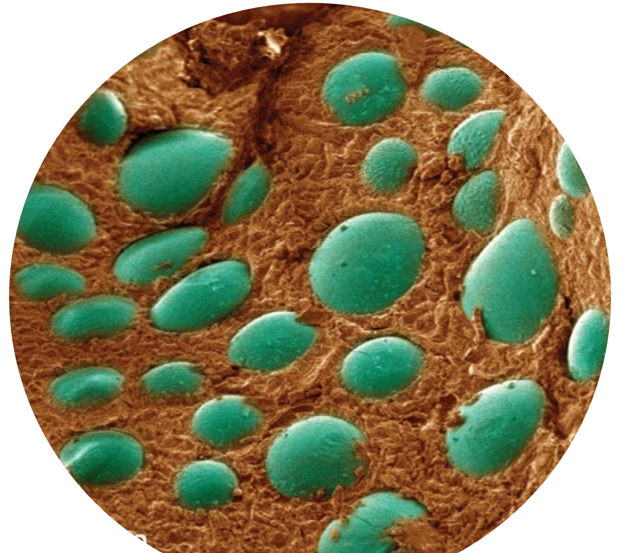
Expanded story on the next page

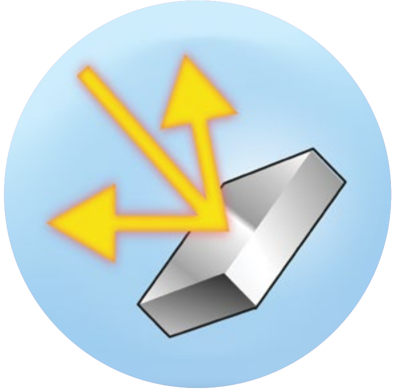
ENABLING IMPACT FOR OVER 15 YEARS

DEVELOPMENT OF INNOVATIVE MICRO-CT NOW BEING SOLD AROUND THE WORLD.

See next page

CLEANING UP THE PLANET WITH INNOVATIVE NEW POLYMERS FROM WASTE





TWELVE MODULES IN MYSCOPE, OUR ONLINE TRAINING ENVIRONMENT

MICRO-X ARE CREATING PORTABLE X-RAY DEVICES WITH NANOTECH

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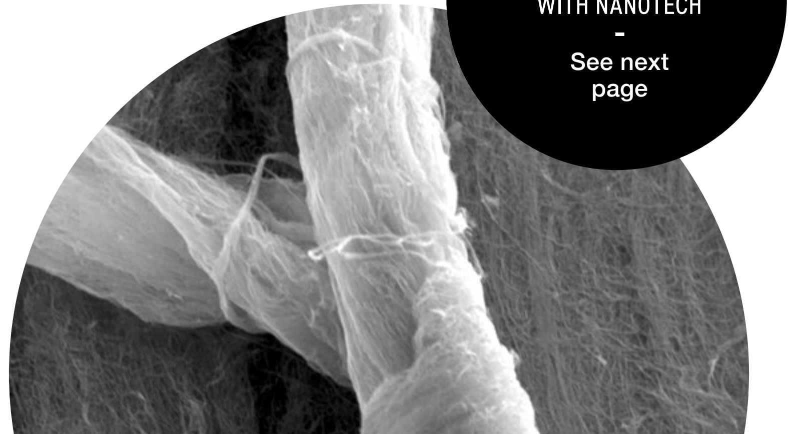
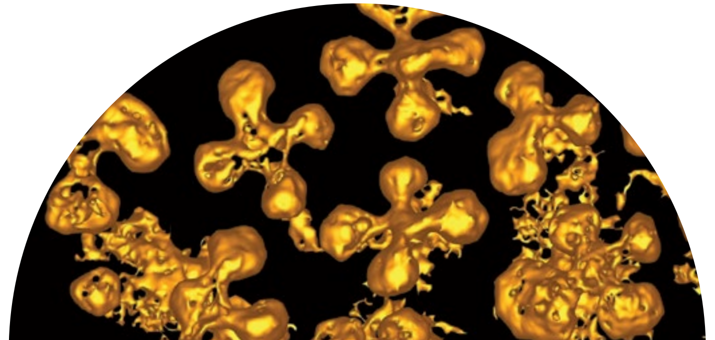
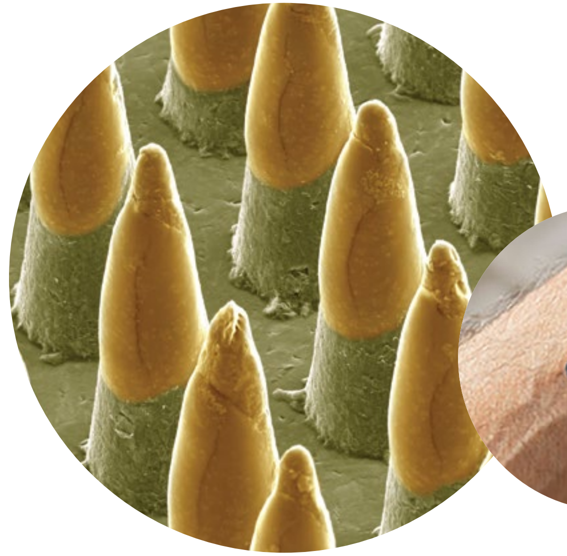
See next page



RESEARCH. MICROSCOPY. INNOVATION. CHANGE.



REVEALING DETAILS OF THE CELL SURFACE IN HEALTH AND DISEASE



REVOLUTIONARY VACCINE DELIVERY AND HEALTH SENSING SKIN PATCHES

IDEAS TO IMPACT

EMPOWERING INNOVATION FOR OVER 15 YEARS

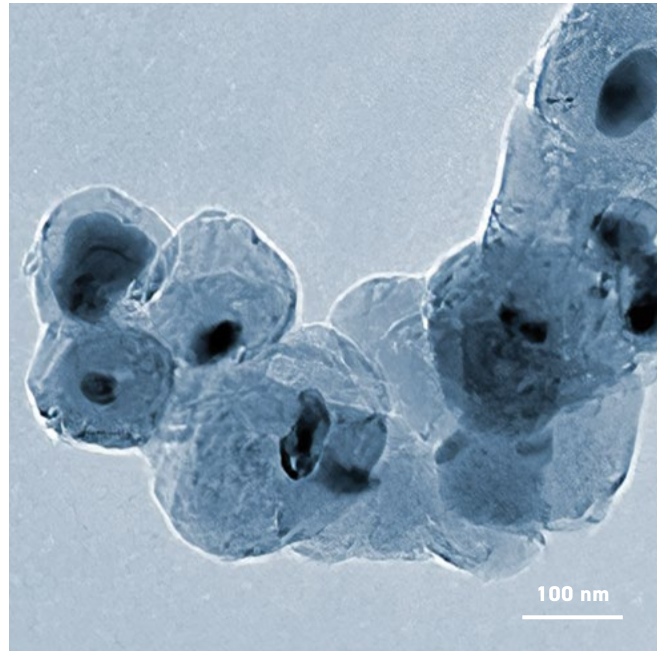
Microscopy Australia has enabled some fantastic innovations. Some of the stories from the previous page are highlighted here in more detail.

GELION

Microscopy Australia has supported renewable-energy storage firm Gelion as they've developed their innovative and safe Endure™ energy storage system.

Endure batteries use abundant, inexpensive, recyclable, non-toxic materials to make abuse-tolerant batteries. This makes them ideal stationary storage to provide grid stability for wind and solar energy farms. They will also have applications for large-scale commercial and industrial customers.

They have recently partnered with Sydney-based, lead-acid battery maker, Battery Energy Power Solutions to make Gelion's batteries in Australia. They have also signed an MOU with Mayur Renewables in Papua New Guinea, to supply 100MWh of energy storage over the next five years. Coupled with large-scale solar energy this could provide remote PNG communities with an affordable, renewable and robust solution for their energy needs.



HAZER GROUP

Spun out of UWA in 2010 and listed on the ASX, Hazer Group is commercialising their low-emission process to convert methane into hydrogen and graphite.

Microscopy was fundamental in the technology development stage of this work. In 2020, after a successful feasibility study, Hazer attracted A$9.4 million in government funding and partnered with the WA state government to convert methane from wastewater into fuel-grade hydrogen and graphite.

The company has now signed an MOU with FortisBC and Suncor Energy to develop a hydrogen production facility in Canada. Suncor and FortisBC will have exclusive rights to deploy the Hazer Process™ in Canada and Colorado, USA, in return for a royalty payment scheme. The feasibility study began in February 2022, with a target date for final investment decision by 2023, and operations commencing in 2025.

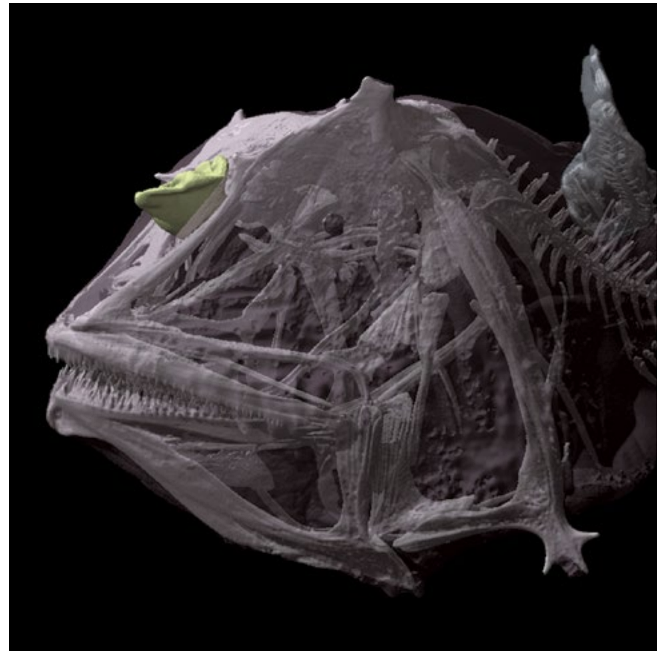
MICRO-X

Micro-X has developed and patented an innovative X-ray emitter that uses carbon nanotubes (CNTs). The use of CNTs is the key to reducing size, weight, heat and power for truly portable X-ray machines.

This award-winning CNT emitter is the basis of Micro-X's portable X-ray machines, which are manufactured in Adelaide. These machines are now installed in an increasing number of Australian and international hospitals. Their development was supported by both Microscopy Australia and Australian National Fabrication Facility.

Micro-X are also developing portable brain scanners for ambulances and aircraft, small baggage scanners for airports and an IED-detecting X-ray camera for military use.

12 OF MICRO-X'S MOBILE UNITS ARE NOW SUPPORTING MEDICS IN UKRAINE



HELISCAN

Research collaborators at the Australian National University (ANU) and UNSW Sydney developed and patented a new type of X-ray micro-CT instrument and analysis system called the Heliscan™.

This award-winning intellectual property has supported industry sectors from large energy and mining, aerospace and medical devices to important Australian museum collections. Microscopy Australia enabled the development of this technology.

This success led to their spin-out company Digitalcore, formed in 2009, providing rock analysis for the global oil and gas industry. The company was sold for A$76 million to Thermo Fisher Scientific (formerly FEI) in 2014. The Heliscan is now commercially available to the international imaging community. While the technology has been sold, the instruments and expertise still reside at Microscopy Australia's ANU facility.

SOLAR TECHNOLOGIES

Prof. Martin Green, Director of the Australian Centre for Advanced Photovoltaics (ACAP), with its headquarters at UNSW Sydney, developed the Passivated Emitter and Rear Cell solar technology back in 1983. This technology was the basis for 91% of worldwide silicon solar module production in 2021.

His research group has held the record for silicon solar cell efficiency for 30 of the last 39 years. He and the ACAP researchers continue to build on this success. Prof. Green is the first Australian to win the prestigious Millennium Technology Prize for transforming the production of solar energy. His large team and collaborators are developing a range of new types of solar cells to push efficiency boundaries, make use of easily available materials and improve recyclability. Microscopy Australia has been supporting this work since our inception. One example of this is ACAP researcher Prof. Xiaojing Hao's innovative kesterite solar cells. Read more on page 32.

INDUSTRY

Microscopy Australia is committed to supporting Australian industry. Here are some of our recent initiatives.

CURRENT FOCUS: ADVANCED MANUFACTURING

Seven Industry Application Scientists have been employed to engage with, and provide microscopy support to, industry clients. They are making new connections and have already delivered results to clients from graphene producers to packaging manufacturers.

We are working together with Australian National Fabrication Facility and Innovations Connections staff to deliver better solutions to industry.

A booth at Australian Manufacturing Week in Sydney (left) allowed us to meet manufacturers and discuss their challenges. With a benchtop SEM on site, we impressed visitors with the ability of microscopy to address a wide range of questions. As a result, new clients are now engaged.

Working with the Advanced Manufacturing Growth Centre, our UWA facility held an industry session for local manufacturers to demonstrate the value of microscopy to their businesses. Guests discovered what microscopy can reveal about their products and processes. There was a hugely positive response and projects are already emerging from the interactions.

Importantly, our industry subsidy scheme is attracting and supporting new industry clients.

Monash Centre for Electron Microscopy

NEW MICROSCOPY FOR FUTURE MATERIALS

Materials for our future industries are being developed today and, on the horizon, are even more sensitive microscopes that can reveal greater detail about the atomic structure of these materials.

Prof. Joanne Etheridge (left), Director of our Monash University facility, was awarded the prestigious 2022 Georgina Sweet Australian Laureate Fellowship from the ARC to develop new forms of electron microscopy.

To understand how materials behave, it can be critical to understand the type and arrangement of their atoms. Transmission electron microscopy is an extremely powerful tool to reveal the atomic structure of materials. However, there are still structures in some materials that can't be identified with existing techniques. Prof. Etheridge's Laureate project aims to re-imagine the fundamental concepts behind an electron microscope. This includes the development and integration of new ways to control, scatter and detect electrons to capture the relevant atomic information. She anticipates that this will achieve an entirely new level of sensitivity to analyse crucial atomic-scale features. This higher sensitivity will enable new insights into materials being engineered for energy storage and production, computing, communications, lighting and drug delivery, as just a few examples.

Using the Georgina Sweet Award, Prof. Etheridge will also establish programs to support early- and mid-career researchers within the electron microscopy and imaging physics communities. She will work through entities such as the Australian Academy of Science and the International Science Council's Standing Committee for Gender Equality in Science to develop and advocate for employment structures and funding mechanisms that facilitate diverse career pathways in scientific research.

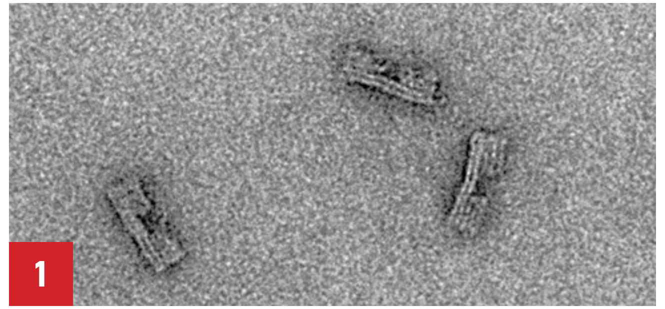
THINK SMALL TO THINK BIG

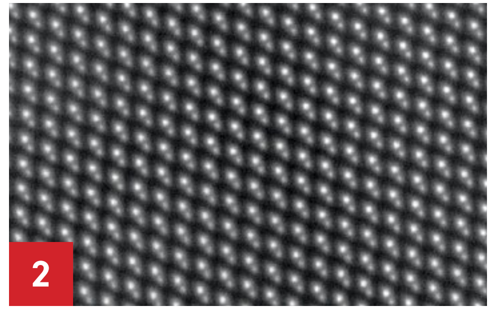
SCANNING ELECTRON MICROGRAPH OF MICROSPHERES IN AN INNOVATIVE NEW PEROVSKITE SOLAR CELL MATERIAL BY SIQI DENG, MONASH CENTRE FOR ELECTRON MICROSCOPY

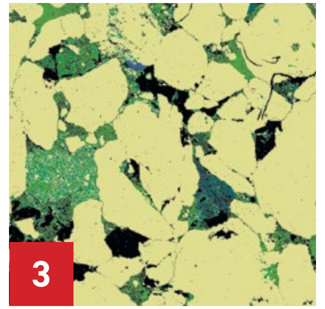
RESEARCH OUTCOMES & IMPACT

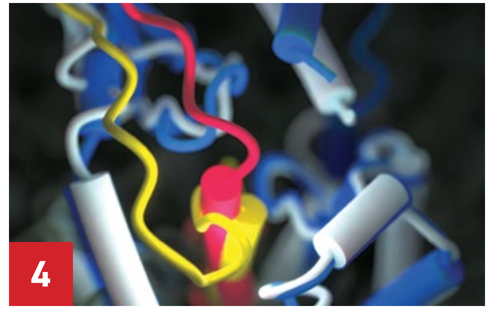
2022

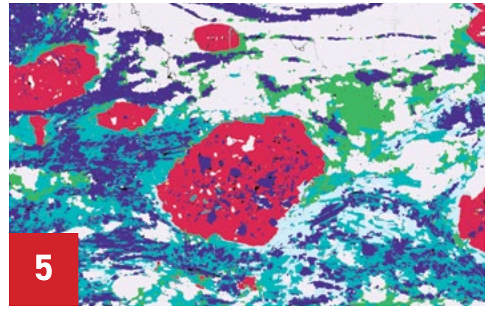
Take a closer look at this year's research highlights – all enabled by Microscopy Australia. With over 3,000 researchers accessing our facilities annually, here are just a few of their recent research highlights.


1 SYNTHETIC MOLECULAR MACHINES WITH DNA ORIGAMI

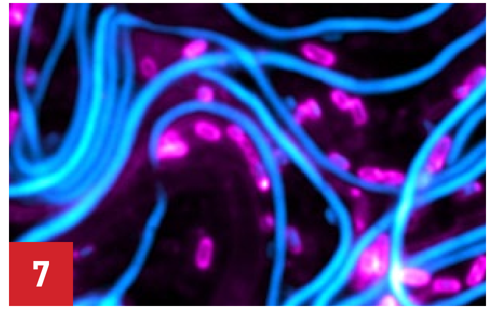

2 ATOMIC-SCALE SOLUTIONS FOR MICROSOFT

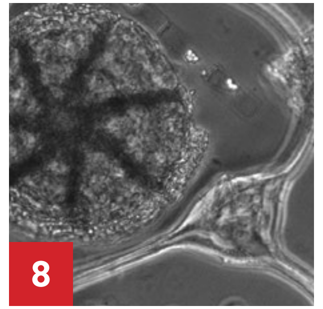

3 STORING CARBON AS MINERALS

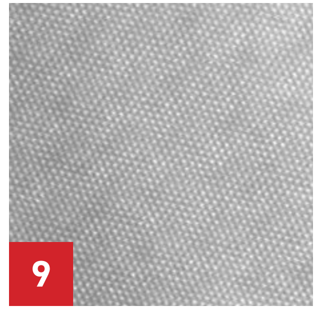

4 STRUCTURAL STUDIES FOR BETTER OBESITY DRUGS

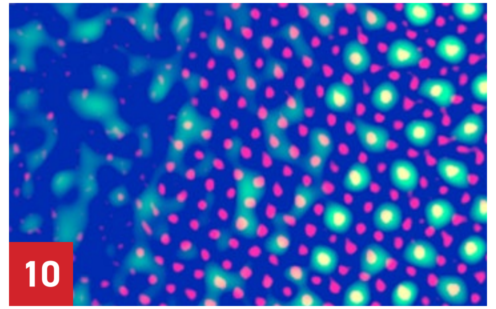

5 INNOVATIVE TECHNIQUES FOR MINERAL DATING


6 ECO-FRIENDLY RNA PESTICIDE

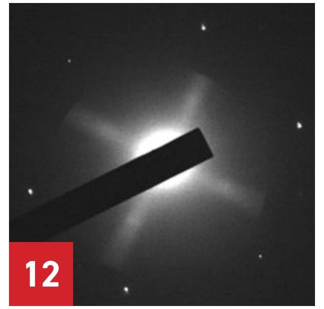

7 SHAPE-SHIFTING BACTERIA: UNDERSTANDING UTIs

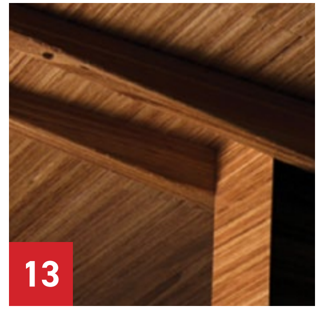

8 BLOOMING COLLABORATION

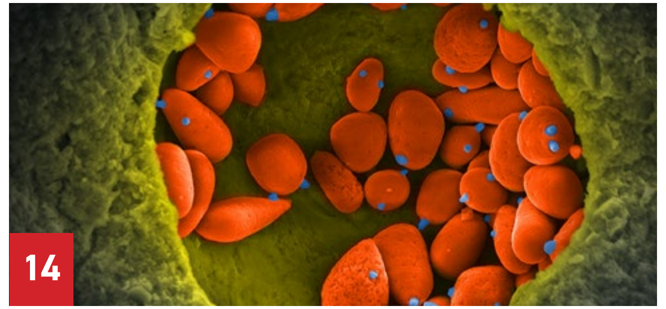

9 DURABLE METAL-SULFUR BATTERIES

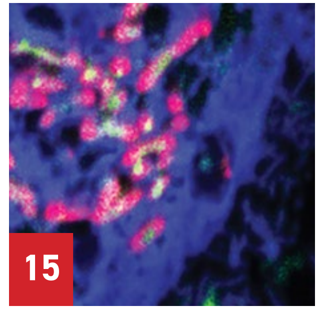

10 CHEAPER, SAFER, THIN-FILM SOLAR


11 WHO WAS SHE? MUMMY UNDER THE MICROSCOPE

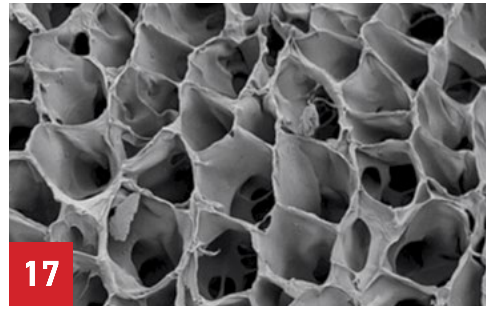

12 WORLD'S THINNEST X-RAY DETECTOR


13 SUSTAINABLE HARDWOOD


14 UNPRECEDENTED GLIMPSE INTO 15 MILLION YEAR OLD RAINFOREST

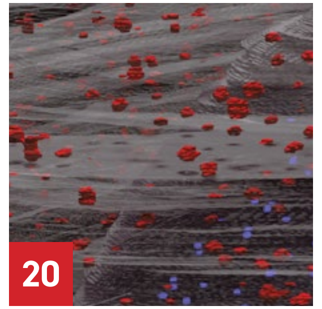

15 IMPROVING TB TREATMENTS

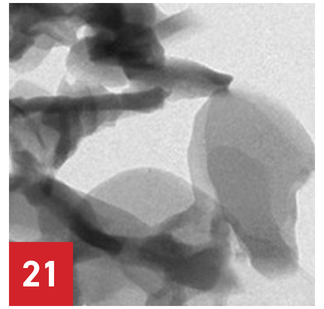

16 BETTER SATELLITES


17 SILVER IN BANDAGES TO TREAT INFECTION

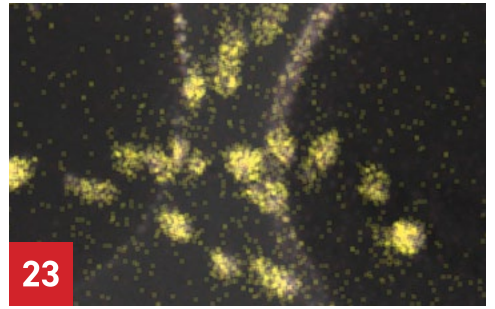

18 MINING WITH PLANTS

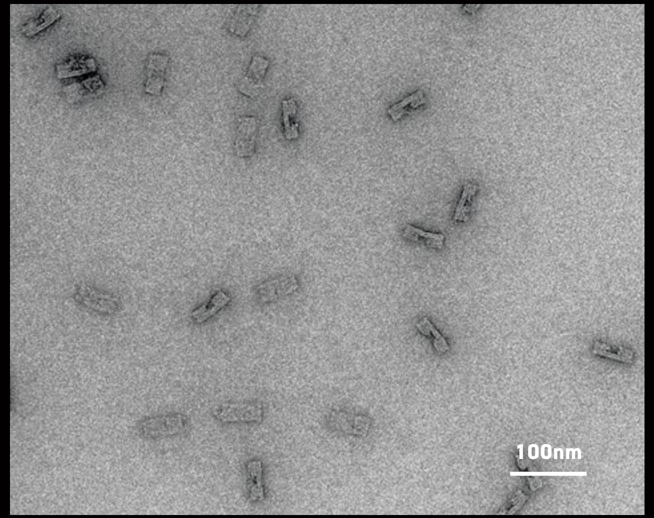

19 CARBON-NEUTRAL AMMONIA SPIN-OUT

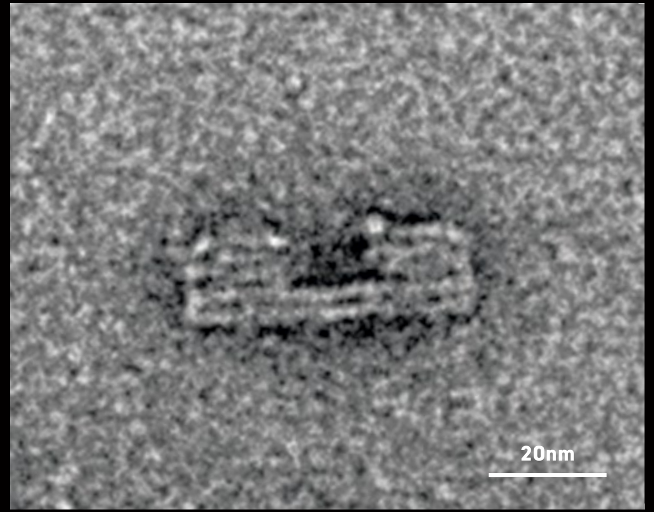

20 DEEP LEARNING FOR IMAGE ANALYSIS

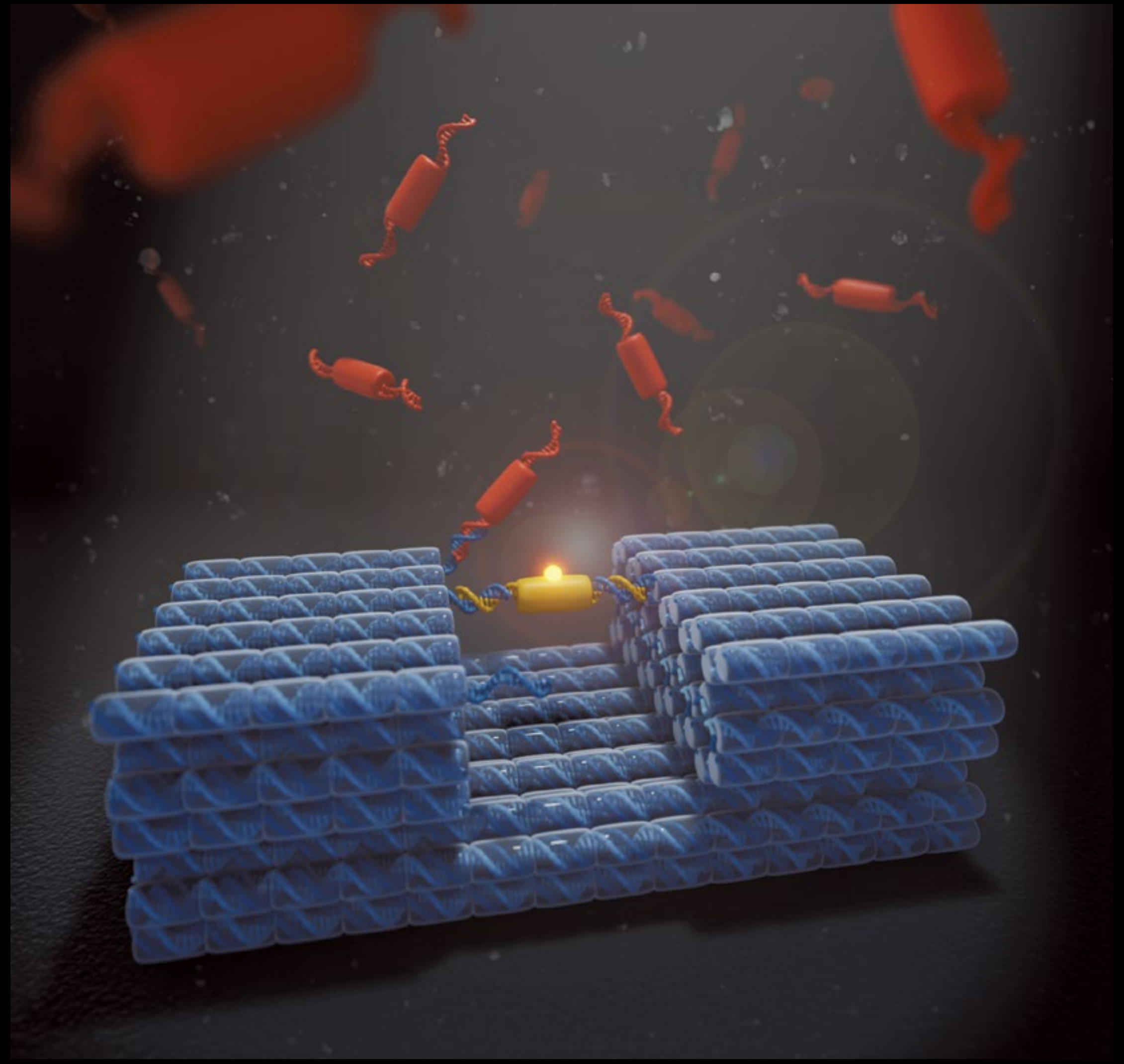

21 MILK SENSOR TO INDICATE SPOILAGE


22 UNDERSTANDING MALE PREGNANCY IN SEAHORSES


23 NANOPARTICLES REVEAL HIGH-GRADE GOLD DEPOSITS







Left images: TEM images of DNA origami transporters. The transporters have a thin central 'cargo bay' and thicker end blocks where the attachment sites are located.
Right image: Illustration of DNA transporter with protein cargo, surrounded by other protein subunits in solution. Illustration by Dr Jonathan Berengut, UNSW Sydney.

1

SYNTHETIC MOLECULAR MACHINES WITH DNA ORIGAMI

CHALLENGE

Synthetic biology is an emerging area of science that applies engineering principles to biological systems in order to give them new and useful abilities. This area is usually approached by understanding how natural biological molecules work and then using those principles to design large synthetic molecules, or molecular machines for a range of applications. Designing these molecular machines is one of the core challenges of synthetic biology.

DNA is one tool being used by synthetic biologists to build innovative molecular machines using what is called DNA origami. Through its specific base pairing, DNA can now be designed to fold up into modular blocks that in turn can be put together into many different structures. Researchers can control the behaviours of these machines by controlling the arrangement of the blocks.

RESEARCH

A/Prof. Lawrence Lee and his team at UNSW Sydney are designing a range of molecular machines using DNA origami, based on known biochemical and biophysical principles. One of these is a prototype synthetic DNA origami transporter that can carry protein and DNA cargo, picking up, carrying and dropping off proteins and pieces of DNA. To make cargo bind securely and yet come off when necessary, the team has developed their system using the biochemical principles of DNA base pairing and chemical competition.

They have also generated a polymer of DNA origami bricks, the length of which is automatically controlled through a process called strain accumulation. Distortions gradually accumulate as each block is added until the last block is so distorted that the next block would have to distort beyond its physical capacity and therefore doesn't bind. The length of the polymer can be controlled by slightly altering the shape of the blocks so that different amounts of strain are introduced.

The team relies on transmission electron microscopy (TEM) at our UNSW facility to visualise and validate their structures.

IMPACT

Although the field of DNA nanotechnology and synthetic biology is still in its infancy, by tapping into nature's blueprints, these researchers are creating exciting new opportunities in the development of bioinspired 'smart molecules' that can act autonomously and adapt to changes in their environment. It is easy to foresee applications in molecular diagnostics, targeted drug delivery, vaccine design and agriculture, as well as in many areas that have not yet been imagined.

J. Brown et al., ACS Nano 2022
DOI: 10.1021/acsnano.2c00699

2 ATOMIC-SCALE SOLUTIONS FOR MICROSOFT

Silicon-based computer chips are reaching their physical limit for size and speed. Microsoft is funding researchers at Microscopy Australia's University of Sydney facility to understand the behaviour of a potential new material for making computer chips.

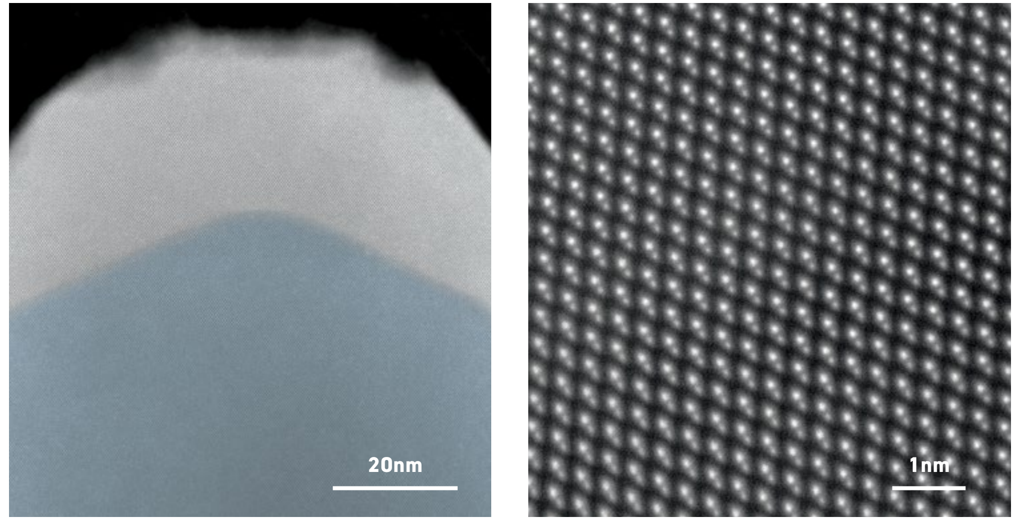
Silicon, which has been used since the beginning of modern computing, is currently etched into layers of interconnecting silicon nanowires processed so that electrons only need to travel approximately three nanometres to carry signals around the chip. As this is the thickness of only a few atoms, it leaves hardly any room to manoeuvre: silicon chips are approaching their minimum possible size.

To overcome this problem, a new material called indium arsenide (InAs) is being explored. Even though indium and arsenic atoms are larger than silicon atoms, electrons can flow faster through them than through silicon.

Research collaborators in Denmark have grown nanowires made of InAs. These need to be grown at high temperatures around an indium gallium arsenide (InGaAs) core (blue in image below). However, at these high temperatures, indium and gallium diffuse easily. When the gallium diffuses from the core into the outer InAs layer, it compromises the purity of that layer, reducing its electron-carrying capacity. Microsoft wanted to know how they can visualise the extent of that diffusion.

By using atom probe tomography and atomic-resolution scanning transmission electron microscopy at Microscopy Australia's University of Sydney facility, the researchers were able to accurately measure how much diffusion had occurred during nanowire growth to help inform the design of these nanowires into the future.

J. Qu et al., Applied Materials & Interfaces 2022
DOI: 10.1021/acsami.2c09594



Scanning transmission electron micrographs of the atomic structure of the nanowire.

3 CONVERTING CARBON DIOXIDE INTO MINERALS FOR LONG-TERM STORAGE

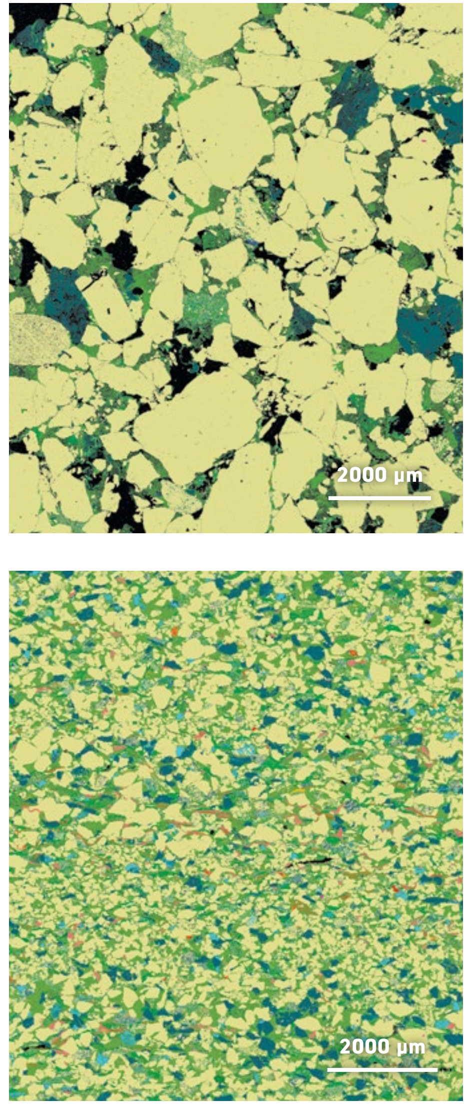
Carbon dioxide (CO_2) released from burning fossil fuels is one of the most significant drivers of global climate change. Strategies to capture and store this CO_2 are of great interest.

One proposed solution is pumping this CO_2 into emptied oil reservoirs deep in the earth. Oil reservoirs are generally made up of an oil-filled porous rock, like sandstone, surrounded by an impermeable rock, called a cap-rock, that traps the oil. This cap-rock can also trap CO_2. Once in the reservoir, CO_2 can dissolve into ground water to form an acidic solution that over thousands of years, will crystallise into carbonate minerals, trapping the CO_2 in a solid form.

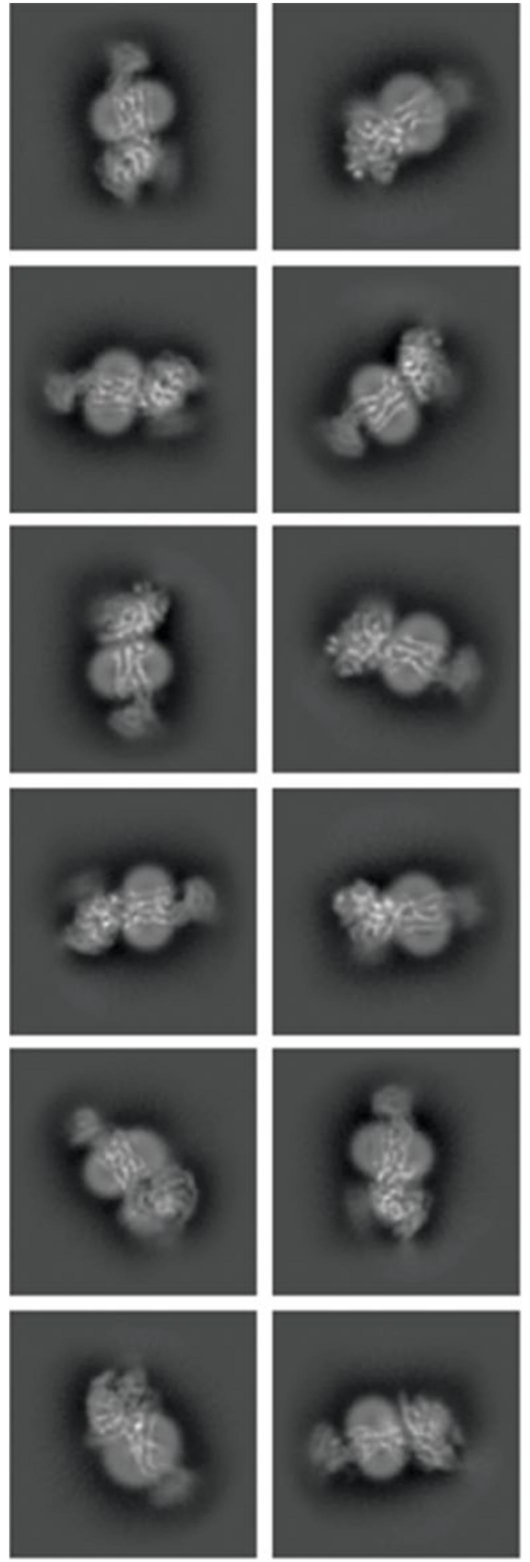
Dr Julie Pearce and her team from the University of Queensland along with collaborators at the Australian Synchrotron and the Microscopy Australia facility at the Australian National University (ANU), have studied the Precipice Sandstone and Evergreen Formation in the Surat Basin in eastern Australia to evaluate its suitability as a CO_2 injection site. QEMSCAN mineral mapping at Microscopy Australia's ANU facility, as well as scanning electron microscopy and elemental microanalysis at our University of Queensland facility, were used to provide a detailed picture of the porosity, mineralogy and composition of these rocks. This data was used to produce a model showing that several sites could potentially trap and convert CO_2 into minerals for long-term storage.

The Moonie Oil Field is in this region of south-east Queensland and has been proposed as a site for carbon capture. Operators at the site are already considering pumping CO_2 under pressure into oil reservoirs, to squeeze more oil out. If they can then trap this pumped-in CO_2 it would hit two birds with one stone, helping to mitigate climate change.

J. K. Pearce et al., International Journal of Coal Geology 2022 DOI: 10.1016/j.coal.2021.103911



Images of thin sections from a reservoir sandstone (top) and a cap-rock that prevents CO_2 migration (bottom) taken using QEMSCAN.



4 STRUCTURAL STUDIES FOR BETTER OBESITY DRUGS

Obesity and its associated diseases are a major problem in developed countries worldwide. In 2018, 8.4% of the total disease burden in Australia was due to patients being overweight or obese, costing the Australian economy around A$8.6 billion/year.

Amylin is a hormone that acts to signal satiety, reduce food intake, decrease fat deposition, and increase energy expenditure. This makes amylin receptors (AMYRs) important targets for potential obesity drugs. Even though drugs that mimic amylin and calcitonin are being produced to treat obesity, it is unknown how their different effects are generated at a molecular level, meaning that drug developers are effectively 'working in the dark'.

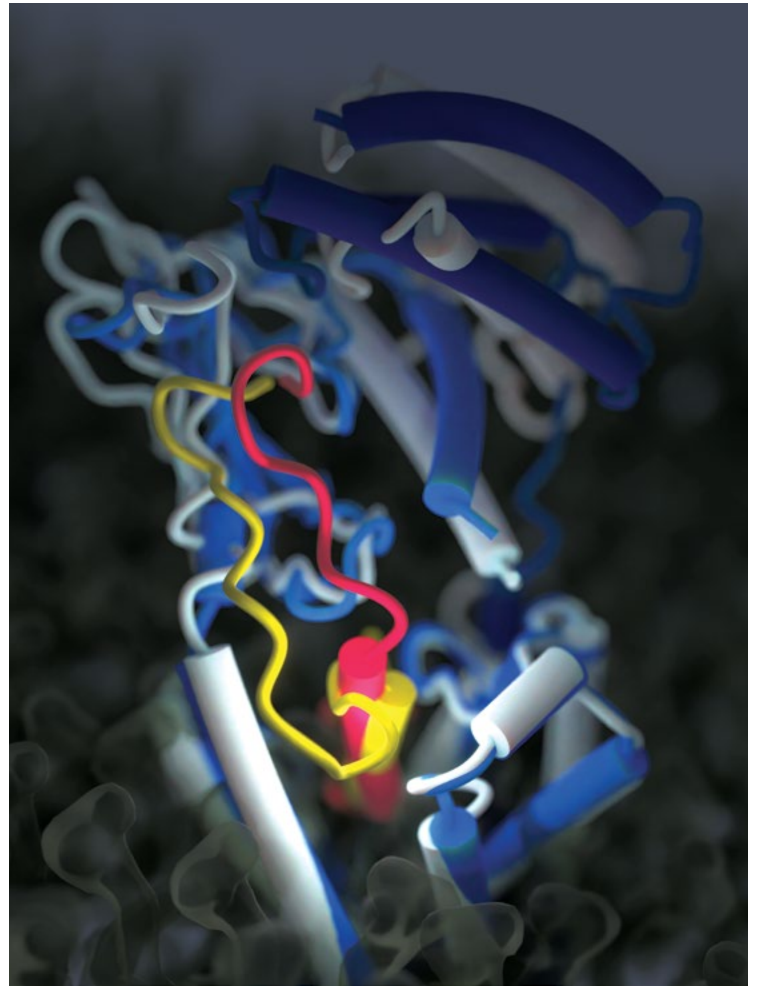
Amylin receptors are made up of two components: the calcitonin receptor, and one of three possible receptor activity-modifying proteins (RAMPs). Each of these RAMPs changes how amylin and calcitonin bind to the complete AMYR.

In an international collaboration led out of Monash University as part of the ARC Industrial Transformation Training Centre for Cryo-electron Microscopy of Membrane Proteins by Profs Patrick Sexton and Denise Wootten, cryo-electron microscopy has been used to understand the structural basis for the binding and the selective action of calcitonin and amylin with the various AMYRs.

Their detailed study, published in *Science*, has shown how molecules with an amylin structure activate the various receptors differently from molecules with a calcitonin structure. These findings explain some of the unexpected effects seen when newly developed obesity drugs are translated from animal studies to clinical trials. The structural details of hormone binding will enable a much more informed approach to the design of new obesity drugs.

J. Cao et al., Science 2022
DOI: 10.1126/science.abm9609

Left image: Each square shows an assembly of cryo-EM images of the AMYR grouped together by orientation, part of the structure reconstruction process. The reconstruction is shown in the right image.



Two overlaid cryo-EM structures showing the differences when amylin-like peptides (yellow) are bound to the receptor (blue) and when calcitonin-like peptides (red) bind to the receptor (light grey). Each receptor is approximately 25nm long. Image created by Dr Sarah Piper @PiperProteins

"ADELAIDE MICROSCOPY WAS KEY RESEARCH INFRASTRUCTURE THAT DROVE A PARADIGM SHIFT IN HOW WE NEEDED TO SAMPLE."

– Prof. Richard Hillis, CEO of DET CRC (now MinEX CRC)

5

INNOVATIVE TECHNIQUES FOR MINERAL DATING

CHALLENGE

Critical mineral and energy resources are found in ancient geological deposits. Dating these rocks to understand how and when they formed is vital to discover and utilise these resources. Many important minerals can't be dated using traditional methods based on uranium–lead decay because they don't contain these elements. There is therefore a need for alternative and complementary dating techniques to expand our 'tool box' for resource exploration.

Left: Mineral map identifying the location of garnets (red) for dating with the new techniques. Image collected by Samantha March.

Above: Dr Sarah Gilbert at Adelaide Microscopy at the instrument used to develop the techniques.

RESEARCH

Dr Sarah Gilbert from Microscopy Australia's University of Adelaide facility has been working with University researchers and the MinEx Cooperative Research Centre (CRC) to develop innovative techniques for dating 'difficult-to-date' minerals such as garnet (red in right image), apatite, carbonate, micas, feldspars and some clays. It also allows the dating of minerals present as a result of earlier fluid transport in rocks. This is important knowledge for finding gold and other metal ores.

The new laser ablation collision cell ICP mass spectrometer techniques Dr Gilbert has developed, are the first to date non-uranium bearing minerals where they sit within the rock. Minerals are first identified within a slice of rock using the NCRIS-supported Automated Mineralogy scanning electron microscope (left image). They are then dated using either the ratio of rubidium to strontium (Rb–Sr) or lutetium to hafnium (Lu–Hf). Dating using these isotopes normally requires rock samples to be ground up and the mixture of minerals dated using solution mass spectroscopy techniques. Seeing where minerals, with potentially different ages, are located within the rock sample, provides a more detailed understanding of its geological history.

Industry partners include the MinEx CRC, Geological Surveys of NT and WA, SA Department of Energy and Mines, and many mining companies including BHP, Teck and Santos. Companies from around the world are now also reaching out to our Adelaide facility to access this exciting new technology.

IMPACT

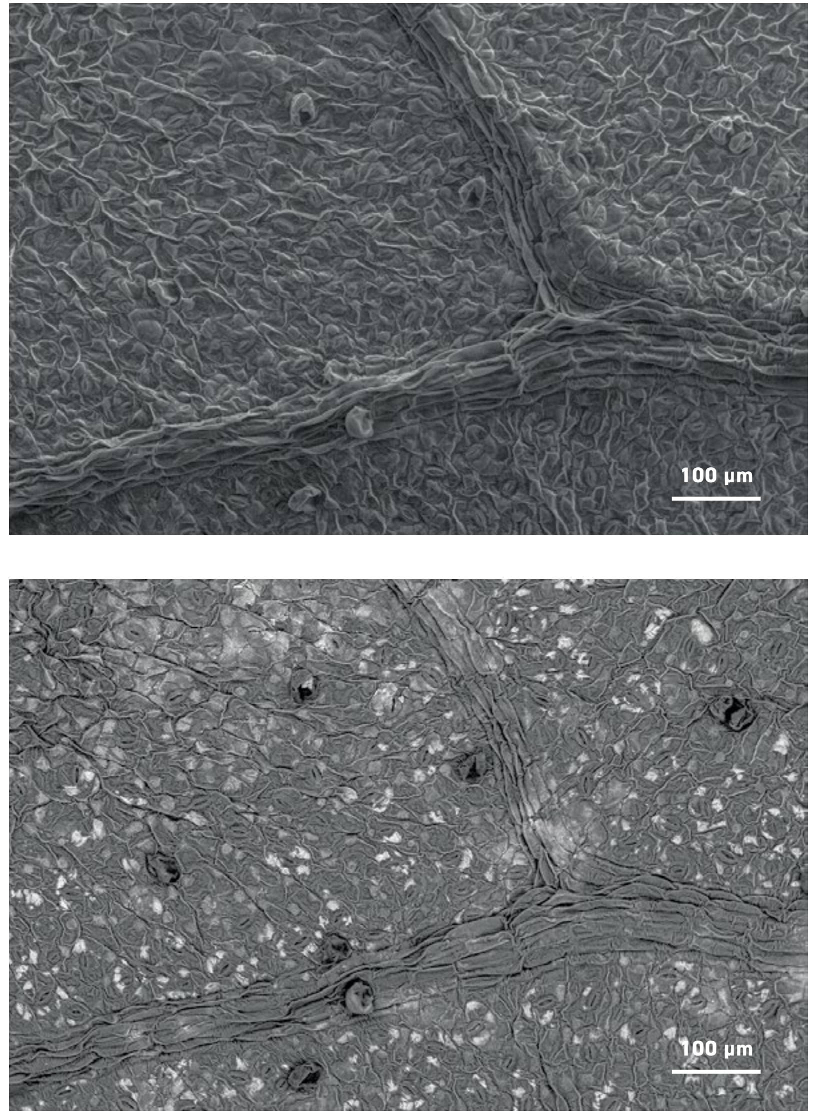
Australian and international exploration companies now have a practical, fast and cost-effective approach to finding the age of ore deposits and associated sedimentary, igneous and metamorphic rocks.

The data generated by this new technique is providing companies with extremely valuable information, building a picture not seen before. This will allow a far greater understanding of existing deposits and help to explore new deposits in a more informed and targeted way.

These developments support exploration and the urgent need to discover critical minerals required both for electric vehicles and advanced manufacturing as we transition to a more sustainable future.

6

ECO-FRIENDLY RNA PESTICIDE



Two images of the same cotton leaf sample under different scanning electron microscope modes. In the ultra-variable detector mode (top) it is hard to distinguish the pesticide from the surface of the cotton leaf. In backscatter electron mode (bottom) the small particles of pesticide are clearly visible (white).

CHALLENGE

Plant pests and pathogens are a major challenge for agricultural productivity, resulting in annual crop losses of up to 40% worldwide. The whitefly is one of these pests, responsible for more than US$430 million in annual global damage. They carry and transmit over 200 different plant viruses, injecting toxic saliva, and producing a sticky substance, known as honeydew, that causes sooty mould to develop on crops.

Treating a whitefly infestation is a unique challenge. Insecticides are only effective on adult whitefly and have been shown to have little long-term impact on infestations, usually only aggravating the problem by wiping out competition and predators such as wasps. Due to this, the Queensland government currently advises against the use of insecticides to control whitefly despite the significant damage they cause to vegetable, cotton and grain crops.

RESEARCH

A research team based at the University of Queensland has harnessed RNA to create an environmentally friendly pesticide that only targets whitefly and is effective at all life stages. Once ingested, the RNA pesticide "silences" target genes within the whitefly resulting in death or an inability to reproduce.

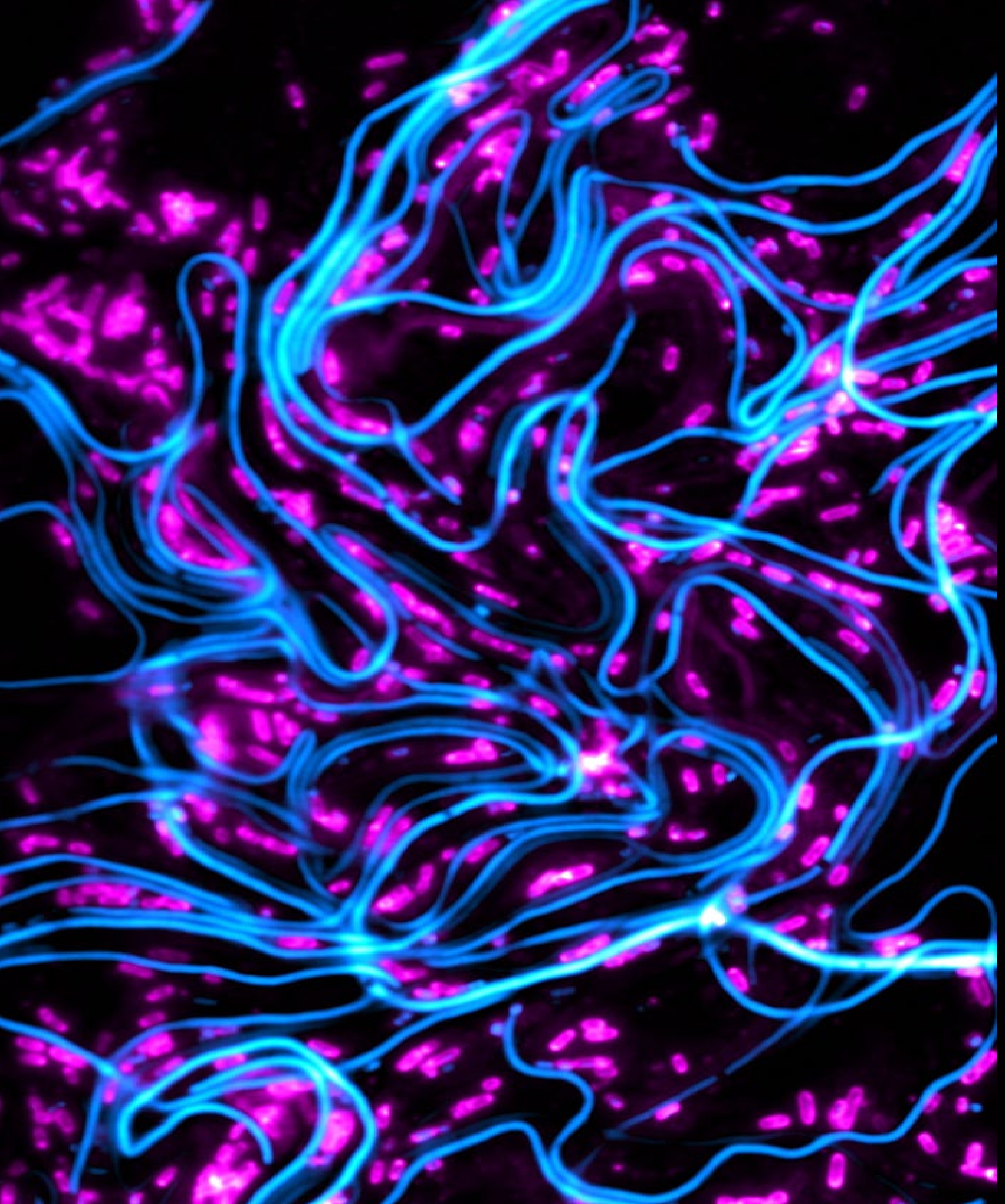
While RNA-based pesticides have been in development for over a decade, a significant challenge has been holding them back. They are very fragile and breakdown too quickly to be effective. In order to deliver the RNA to the whitefly, it needs to be stable enough to persist until it can be consumed. The team found that by combining the RNA with a special clay, called BioClay, it significantly improved the RNA's stability, resulting in the uptake required to make the pesticide a viable solution for growers.

The team, led by Prof. Neena Mitter (right) and Ritesh Jain, used scanning and transmission electron microscopes, along with elemental analysis, at our University of Queensland facility to better understand the components that make up the BioClay, and assess their ability to load and release the RNA pesticide. Microscopy was also used to demonstrate the longevity of the pesticide coating.

IMPACT

- The targeted elimination of a significant invasive agricultural pest with no impact on the surrounding environment, protecting bees and waterways.
- Increased agricultural productivity, improving food security.
- Creation of a valuable commercial product.
- A new method to tackle other sap-sucking pests.

R. Jain et al., Nature Plants 2022
DOI: 10.1038/s41477-022-01152-8



7 SHAPE-SHIFTING BACTERIA: UNDERSTANDING UTIs

Urinary tract infections (UTIs) are the most common bacterial infections worldwide and cost the Australian health care system around $909 million per year. Disease-causing strains of *E. coli* account for around 70% of cases.

E. coli are normally rod-shaped but change shape when they infect bladder cells. At first, they become rounder and clump together inside the cells, continuing to divide until they fill the cell. As the cell fills up and bursts open, some of the bacteria revert to a rod shape and disperse to infect more cells, while others grow into very long filaments that can't directly infect cells. The length of these filaments is variable, but they can reach up to 50–100 times the length of a rod before cell division is switched back on and the filaments pinch off to form infectious rods.

So why are the filaments formed? Possibly to evade the immune system: long filaments are hard to engulf. As they emerge from the bursting cell, they could help attach the soon-to-be daughter rod cells to the surface of nearby uninfected bladder cells, ready to infect once cell division generates more rods.

Dr Bill Söderström and his team at the University of Technology Sydney (UTS) work to understand how and why these shape changes happen and how they are controlled. By using a range of super-resolution and fluorescence microscopy techniques at Microscopy Australia's linked lab at UTS, they showed that when the filament divides into rods the bacteria use the same machinery as normal division, but it is controlled differently. The researchers hope to harness this understanding to develop new therapies for UTIs.

B. Söderström et al., Nature Communications 2022
DOI:10.1038/s41467-022-31378-1

Image: Fluorescence microscopy image showing E. coli filaments (blue) and rods (pink). Rods are 2–4μm long. Imaged by Dr Bill Söderström.

8 MONITORING ALGAL BLOOMS IN A CHANGING CLIMATE

South West Western Australia experienced an exceptionally wet winter in 2021, with significantly higher than average rainfall causing an increased outflow of water from many rivers along the south west coast during the period from August to October. High levels of chlorophyll in the ocean had been seen on satellite images of the area, although these observations can be difficult to interpret in coastal areas.

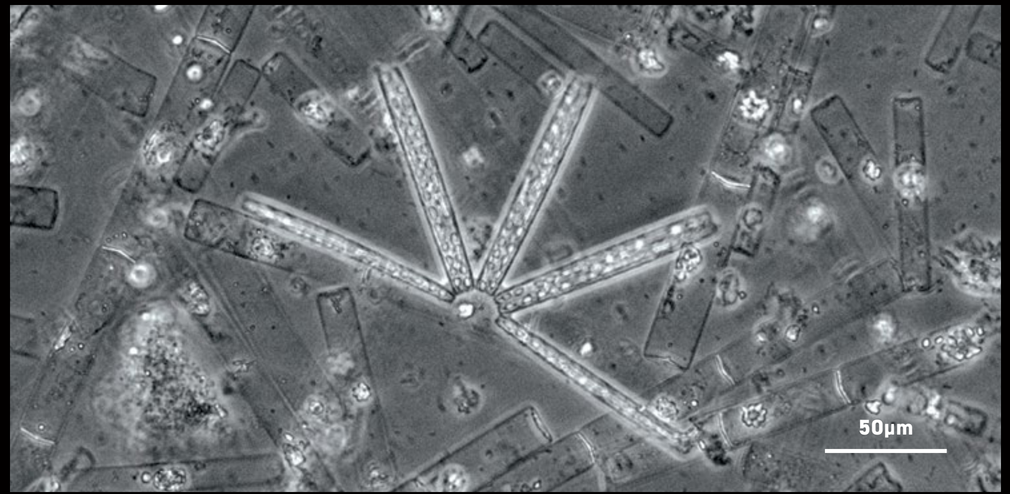
University of Western Australia (UWA) researchers, Prof. Chari Pattiaratchi and Dr Paul Thomson from the Integrated Marine Observing System, wanted to investigate further and gathered data on salinity and chlorophyll concentration from their autonomous Ocean Gliders operating at multiple sites in the ocean near Perth. The researchers also collected water samples at selected locations for more detailed analysis, observing water clarity as well as nutrients such as nitrates, phosphorus and ammonia. Microscopy Australia's facility at UWA imaged microscopic marine algae in the water samples, allowing the researchers to identify and quantify the species of algae at different sites and correlate the species found at each site with other measurements.

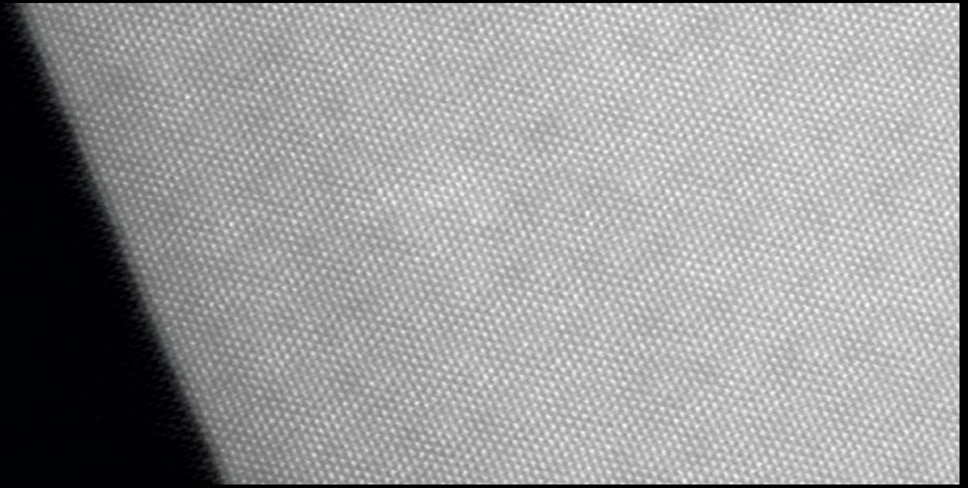
They were able to confirm that sustained discharge of freshwater into the coastal system stimulated algal blooms that are rare in these waters.

A bloom of an unidentified alga was found at all sites within Cockburn Sound, along with other types of algae, and a species of small crustacean. The bloom was not evident at the Rottnest Island site and nutrients at all sites were very low, indicating that the algal bloom had already drawn down nutrients from the river outflow.

The presence of the particular types of algae found would have provided a boost to the food chain, feeding tiny aquatic animals (zooplankton) which feed the fish, which in turn feed fairy penguins, dolphins and many other species.

Image: Light micrograph of the new type of algae (diatom) found in the bloom.





9 MORE DURABLE METAL-SULFUR BATTERIES

Sulfur is an attractive electrode material for next-generation batteries because of its low cost and ability to carry a lot of electrons per gram. However, metal-sulfur batteries have a significant drawback: they generally suffer from poor cycling durability, meaning they cannot be recharged many times.

A team led by Prof. Shizhang Qiao at the University of Adelaide has overcome this limitation. "We have designed a highly efficient electrode material to catalyse the battery reaction and improve the durability of metal–sulfur batteries," said Prof. Qiao. "Our new sulfur–metal battery can be charged and discharged at least 10,000 times," he added.

The researchers have optimised the atomic structure for molybdenum nitride anodes to significantly increase the cycling durability of metal–sulfur batteries.

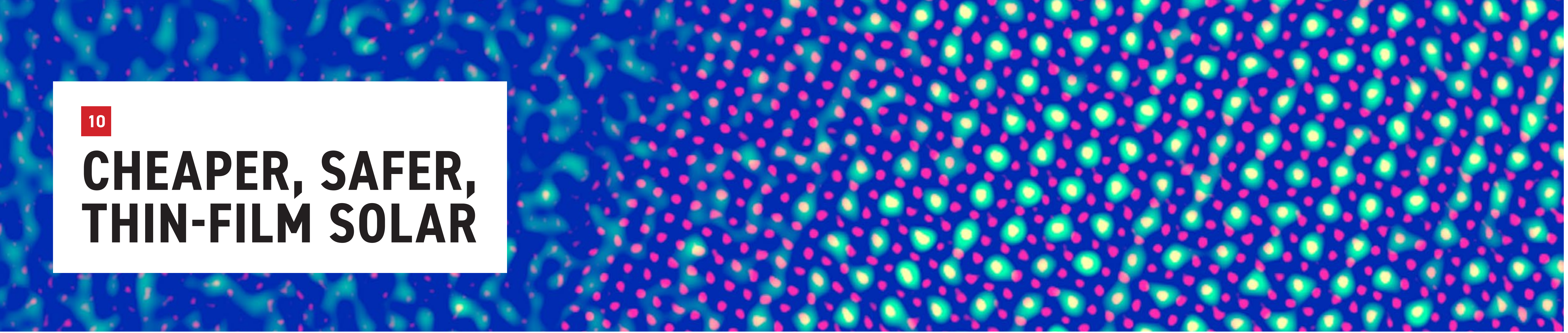
In their demonstration, the research team used atomic-resolution scanning transmission electron microscopy (STEM) at our University of Adelaide facility to observe how changes in the atomic structure of different molybdenum nitride anode materials (Mo_5N_6, MoN, and Mo_2N) impacted the performance of room temperature sodium–sulfur batteries.

They found that despite containing the same elements, the changes in atomic structure between the different molybdenum nitrides had a significant impact on battery efficiency. By choosing the most compatible molybdenum nitride structure, the team created a sodium–sulfur battery that could be cycled over 10,000 times.

This new methodology can now be applied to other metal–sulfur battery types, opening the door to the next-generation of lighter and cheaper batteries, providing long-term storage to help mitigate climate change.

C. Ye et al., Nature Communications 2022
DOI: 10.1038/s41467-021-27551-7

Image: Atomic resolution STEM image of the new electrode material.



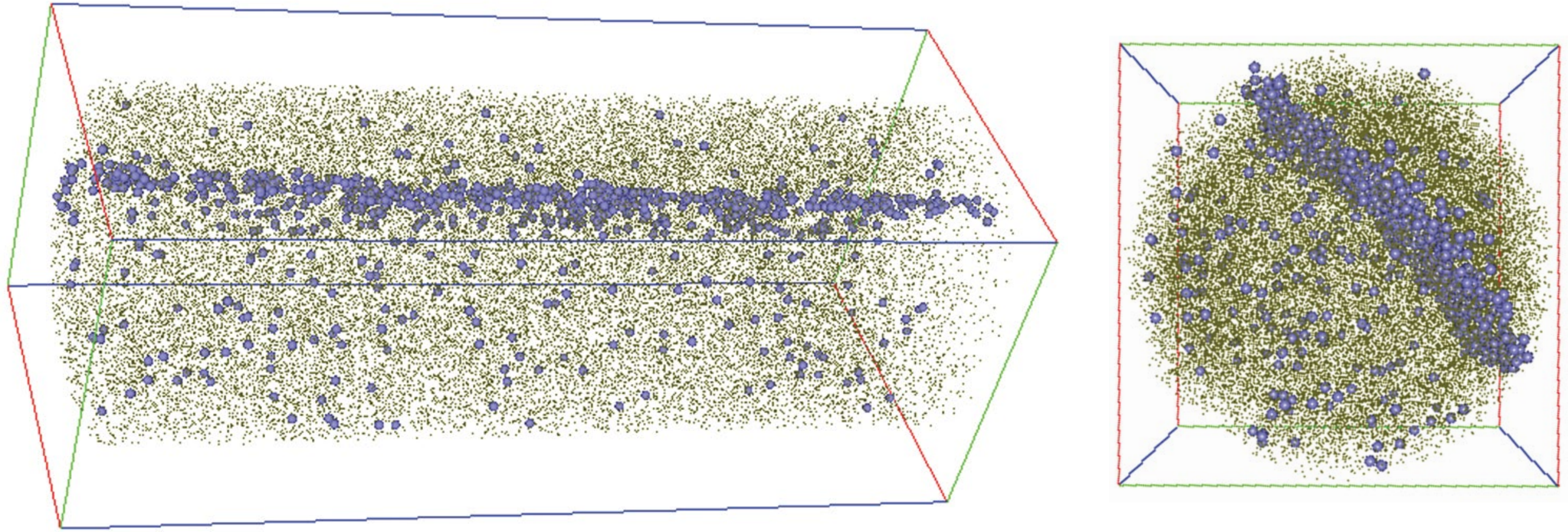
10

CHEAPER, SAFER, THIN-FILM SOLAR

Below: Side and top view of atom probe data of CZTSSe showing zinc atoms (green) and sodium oxide atoms (blue) highlighting a grain boundary.

Above: An atomic-scale electron microscope image of CZTS showing the tin atoms in green.

Above: Prof. Hao has been recognised for her pioneering work in thin-film photovoltaics.



CHALLENGE

Australia has the highest per capita uptake of rooftop solar in the world. This reflects a growing demand for cheap and renewable energy. However, there are many drawbacks to current silicon wafer-based solar technologies. They are expensive to produce and difficult to recycle. They are also inflexible and must be installed on a flat surface, severely limiting the locations in which they can be used.

One solution to this is flexible thin-film solar cells which can be installed as coatings on a range of surfaces, from car bodies to buildings. However, commercially available thin-film solar options, CIGS and CdTe, use scarce and toxic materials, making them expensive to produce and recycle. Cheaper, non-toxic, thin-film alternatives are needed in order to scale up their adoption.

RESEARCH

Prof. Xaiojing Hao and her team at UNSW Sydney have broken four world records in their quest to create cheap and 'green' thin-film solar cells. In the process, Prof. Hao has emerged as a world leader in the area, recognised in both the 2020 Prime Minister's and 2018 NSW Premier's Prizes for Science.

Her team is developing an alternative to CIGS and CdTE called sulfide kesterite (Cu_2ZnSnS_4), also referred to as CZTS, that uses non-toxic and abundant elements. It can also be manufactured using existing equipment that is already in use to produce CIGS. Another benefit of CZTS is it captures a different spectrum of light than silicon solar cells. This means they can be combined into a 'tandem' solar cell that can capture more energy than silicon or CZTS alone.

Prof. Hao's team have already achieved two energy efficiency world records for CZTS, breaking the 10% energy conversion efficiency barrier for this promising new material. To achieve this result the researchers used a range of high-end microscopy techniques across three of our NSW facilities: UNSW Sydney, the University of Sydney, and the University of Wollongong.

Her team is also investigating a related kesterite material CZTSSe ($Cu_2ZnSn(S,Se)_4$), where some of the sulfur is replaced with selenium. Prof. Hao's team have achieved 12.5% efficiency with this material and, by using our microscopy, have recently identified some factors that are limiting its performance, clearing the way for further improvements.

IMPACT

More efficient CZTS/Se will reduce emissions and environmental impact through:

- increasing the range of surfaces that can be used for generating electricity
- cheap and efficient solar energy options
- non-toxic components that are safe and easy to recycle contributing to a circular economy.

J. Li et al., Adv Materials 2020
DOI: 10.1002/adma.202005268

J. Li et al., Nature Energy 2022
DOI: 10.1038/s41560-022-01078-7

11 WHO WAS SHE? MUMMY UNDER THE MICROSCOPE

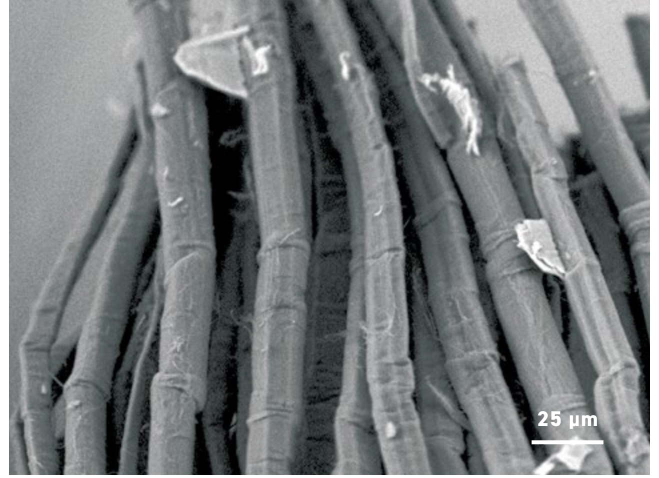
A cedar coffin in the Chau Chak Wing Museum at the University of Sydney, belonging to a high priestess named Mer-Neith-it-es, is stylistically dated to the Egyptian 26th Dynasty (664-525 BC). Gifted to the Museum by Sir Charles Nicholson in 1860, it was long thought to be empty. However, in an astonishing discovery in 2017, the coffin was found to contain the heavily disturbed remains of a individual along with linen bandages, hardened resin and thousands of small beads from a degraded beadnet. To learn more about the individual inside, and discover if it is Mer-Neith-it-es, researchers carefully recorded and removed the contents and used a suite of scientific techniques for their analysis.

Dr Karen Privat from the Microscopy Australia facility at UNSW Sydney examined the structure and composition of fragments of the mummy wrappings by using variable-pressure scanning electron microscopy (VP-SEM) and elemental analysis (EDS). This allows precious non-electrically conductive materials such as textiles, paint, glass and wood, to be imaged without needing to be made conductive with gold or platinum beforehand.

Results clearly showed that the threads are linen. They had a plain weave and although they were of good quality, they were not the finest seen in this period. The EDS results showed the presence of sand and mineral salts on the inner wrappings, which, coupled with examination by textile expert Dr Glennda Marsh-Letts, suggested that the linen had been used previously before becoming mummy wrappings.

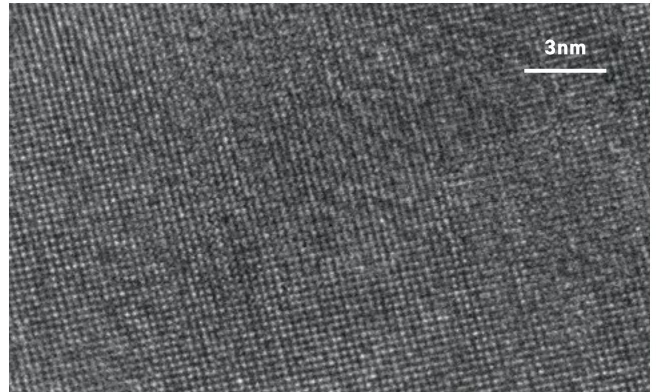
In ancient Egypt, it was usual for household linen and clothing to be used for burial wrappings to save on mummification costs. This is typical of a non-royal burial. The results above, viewed together with carbon dating that showed the contemporaneous dates of the coffin and its contents, and the historical analyses, are consistent with the remains belonging to Mer-Neith-it-es.

G. Marsh-Letts, 2022, Speak my Name, Sydney University Press, ISBN:9781743328460



Top: SEM image of mummy wrappings. Above: Microscopy Australia expert Dr Karen Privat with the coffin of Mer-Neith-it-es.

Atomic resolution TEM image of a tin mono-sulfide nanosheet.



12 WORLD'S THINNEST X-RAY DETECTOR

Researchers at the ARC Centre of Excellence for Exciton Science at Monash and RMIT Universities have developed a new fabrication process to make the world's thinnest X-ray detector. At less than 10 nanometers thick, it more than halves the previous record.

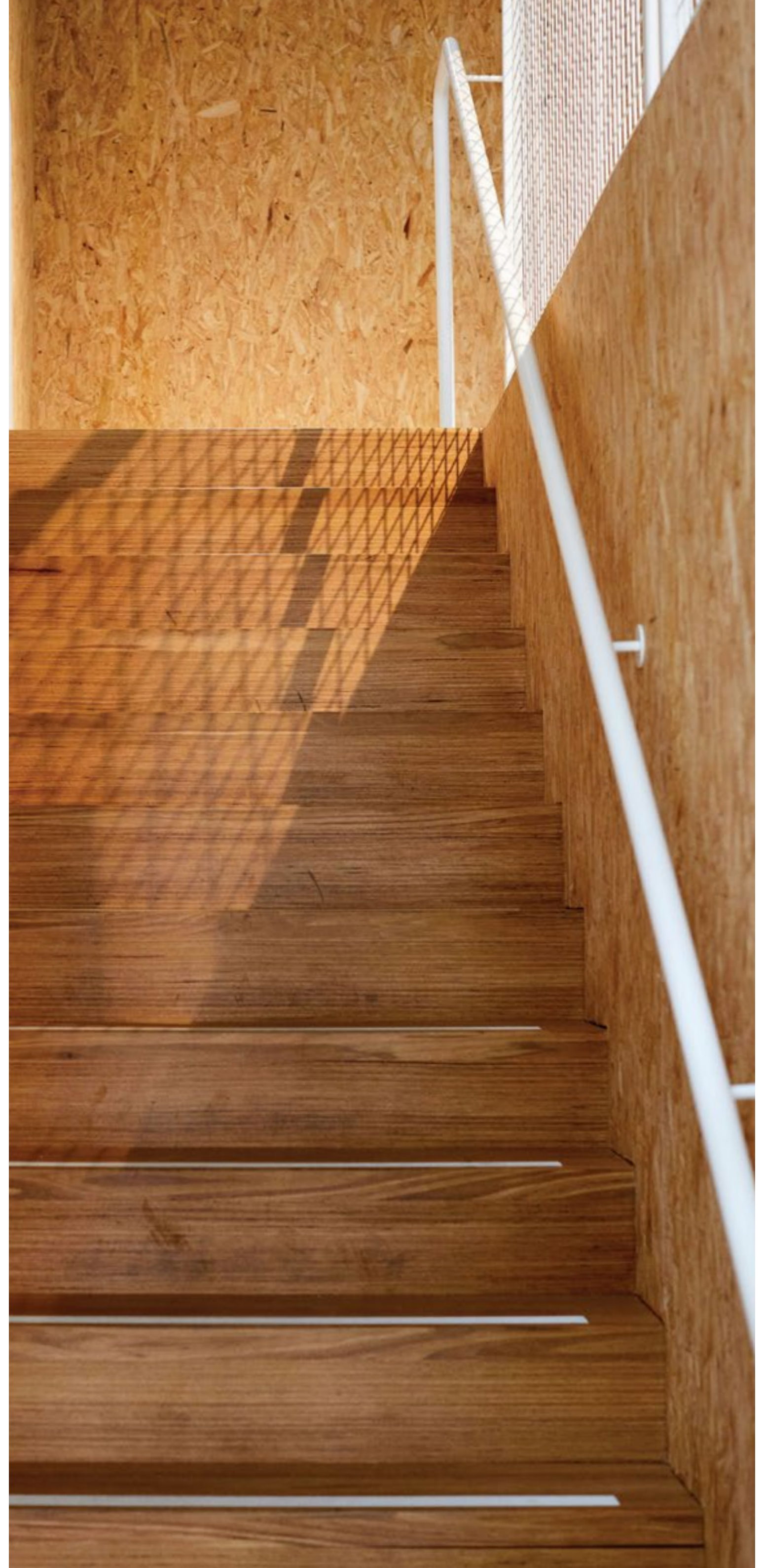
X-rays can be broadly divided into two types: 'hard' X-rays are the kind used by hospitals to scan the body and 'soft' X-rays have a lower energy and can be used to study wet proteins and living cells. Soft X-ray detection can be done in a synchrotron, but this is very expensive and access is difficult to secure. New non-synchrotron soft X-ray laser sources could provide a cheap and accessible alternative, however, they need an ultra-sensitive detector

Tin mono-sulfide (SnS) nanosheets are a promising new detector material but there are no standard SnS nanosheet fabrication methods that allow precise control over thickness and area, the two most important variables for detector sensitivity.

To overcome this challenge, a team led by Dr Nasir Mahmood at RMIT University developed a new technique that uses liquid metal as an exfoliant to precisely control the area and thickness of SnS nanosheets. A Monash University team led by Babar Shabbir and Prof. Jacek Jasieniak then used these sheets to create the ultra-sensitive detector. They demonstrated that it could efficiently detect soft X-rays even from a region of the electromagnetic spectrum that is normally difficult to image using X-rays and which is important for biological applications. The detector's ultra-fast response time also opens up the possibility of real-time imaging of cells.

The researchers used a combination of ultra-high resolution microscopy techniques at Microscopy Australia's linked lab at RMIT and the Monash facility to confirm the structural integrity of the nanosheets.

B. Shabbir et al., Adv. Functional Materials 2022
DOI: 10.1002/adfm.202105038



13 SUSTAINABLE HARDWOOD INNOVATION

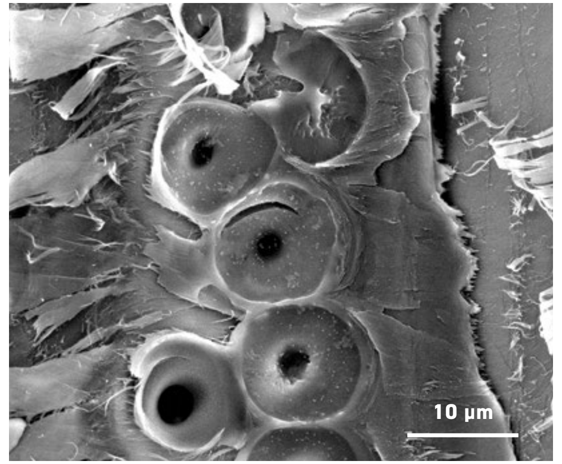
Natural hardwoods are in great demand for beautiful architectural interiors and high-end furniture. Traditionally, hardwoods are sourced from mature native forests. However, these old-growth forests renew themselves more slowly than they are being consumed. This has led to concerns around the sustainability of the native hardwood industry. With businesses and politicians coming under increasing pressure to protect forests, alternatives to native hardwood need to be found.

3RT was established in 2014 in conjunction with Flinders University. Two of its founders, Prof. David Lewis and A/Prof. Jonathan Campbell, developed a patented laminating process that turns forest and plantation residue into a novel engineered wood product with the look, feel and properties of 100-year-old native hardwoods. This adds value to an under-utilised resource. The process uses a carefully developed combination of heat, water, pressure and a water-based nano-glue in a specially designed, automated workflow to produce a wide range of Designer Hardwood™. The Microscopy Australia facility at Flinders University helped the team in their process development, visualising the structures within the engineered wood.

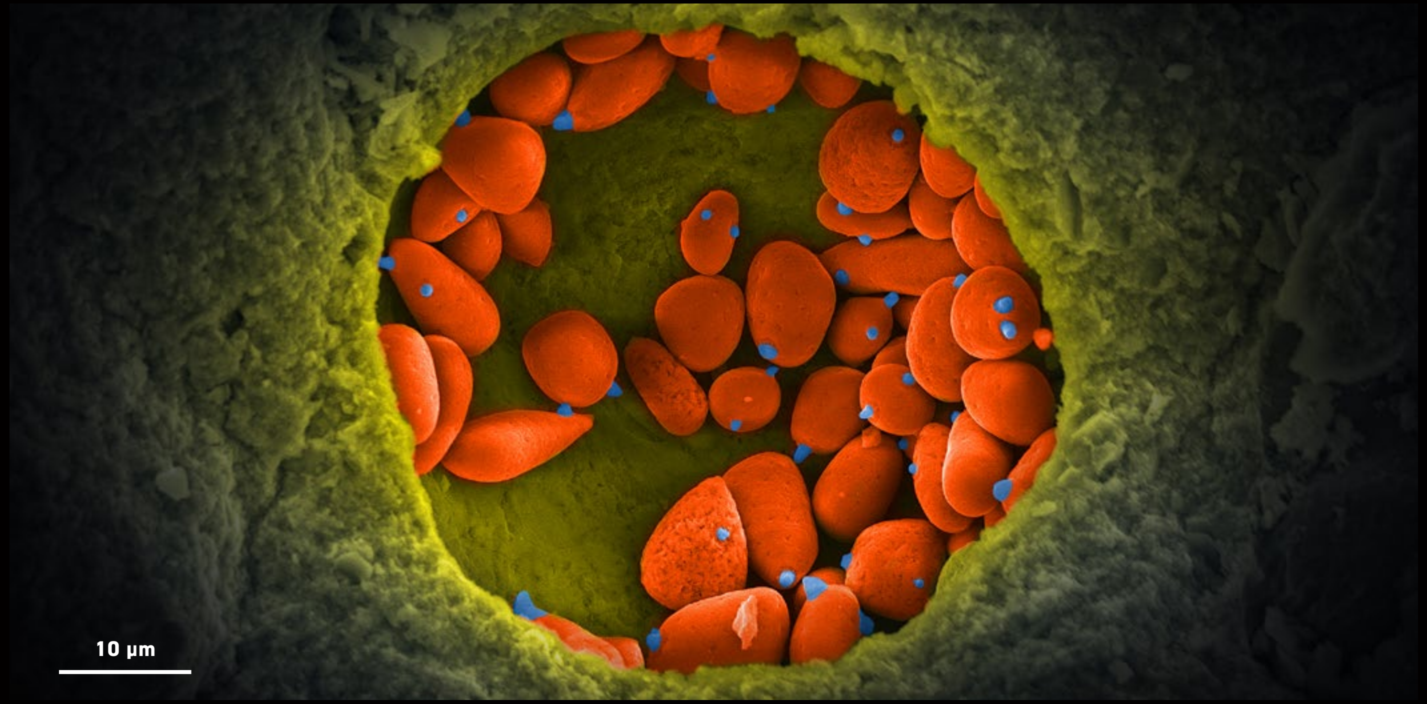
"3RT is focused on continuous improvement both in the fields of new material properties and methods of production to help address the significant environmental and supply challenges relating to old growth forests," says Peter Torreele, Managing Director of 3RT.

The company uses advanced robotics and smart automation that allow for efficient and fast manufacturing anywhere on Earth using local wood species. Their technology licensing model includes a Bosch-made plug-and-play production unit that can be set up quickly to provide local solutions to local markets. These facilities remain connected to the Adelaide Innovation Centre for bespoke product development, quality control, upgrades and technical support.

3RT has recently undertaken successful Australia-wide product sales trials with Bunnings and continues to grow their range of products and manufacturing technologies. 3RT's success has been recognised by becoming one of three finalists in the South Australia Innovator of the Year awards 2022.



Micrograph of the cell structure of Araucaria cunninghamii in 3RT Designer Hardwood™



SEM image of fossilised yeast from a 15 million year old rainforest, taken by A/Prof. Michael Frese and coloured by Mike Cheeseman.

14

UNPRECEDENTED GLIMPSE INTO 15 MILLION YEAR OLD RAINFOREST

CHALLENGE

The Miocene is a period where reduced rainfall triggered the retreat of rainforests around the world. In Australia, this led to a rapid transition from wet, humid rainforests to the shrublands, grasslands, and deserts of today. This transition resulted in the middle-Miocene extinction event, where many species died out. The Miocene period therefore provides important insights into how species adapt or perish in a changing climate.

In Australia, there are very few well-preserved Miocene fossil sites. The two known sites mostly contain the skeletons of larger animals, with very few insects, fish, and plants. This leaves a significant gap in understanding what our local Miocene ecosystem looked like.

RESEARCH

A new Miocene fossil site with unprecedented preservation, dated to around 15 million years ago, has been uncovered at McGraths Flat in Western NSW. This site is unique in the world, with soft tissue preservation so exceptional that even pigment-storing sub-cellular structures can be seen, allowing researchers to reconstruct the colours and patterns of these creatures. It has been described as a 'Rosetta Stone' for this middle Miocene environment.

A diverse team, led by Dr Matthew McCurry from the Australian Museum and A/Prof. Michael Frese from the University of Canberra, have spent the last three years excavating and cataloguing over 2,000 fossils including rainforest plants, insects, spiders, and fish that haven't yet been identified.

A/Prof. Frese used a scanning electron microscope (SEM) at Microscopy Australia's Australian National University facility to reveal microfossils including individual plant and animal cells and even very small sub-cellular structures.

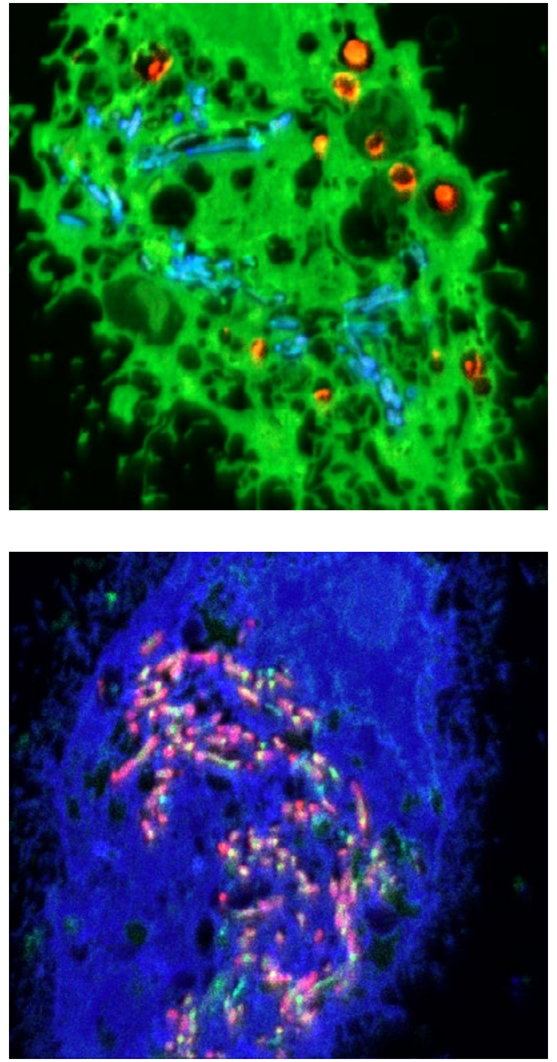
"The fossils also preserve evidence of interactions between species. For instance, we have stomach contents preserved in the fish, meaning that we can figure out what they were eating. We have also found examples of pollen preserved on the bodies of insects so we can tell which species were pollinating which plants," Dr Frese said.

IMPACT

"The McGraths Flat plant fossils give us a window into the vegetation and ecosystems of a warmer world, one that we are likely to experience in the future. The preservation of the plant fossils is unique and provides important insights into a time period for which the fossil record in Australia is rather poor." David Cantrill, botanist, Royal Botanic Gardens Victoria.

M. McCurry et al. Science Advances, 2022
DOI: 10.1126/sciadv.abm1406

Above: Photo of Dr Matthew McCurry at the McGraths Flat site in Western NSW. Right: Fossil samples show the extremely high level of preservation found at the site.



NanoSIMS images of two TB-infected cells from the study. Top: pyrazinamide (blue) accumulated in TB-bacteria and bedaquiline (orange). Bottom: pyrazinamide (pink) accumulated in TB-bacteria and more disperse bedaquiline (green).

15

CORRELATIVE MICROSCOPY FOR IMPROVED TB TREATMENTS

CHALLENGE

Tuberculosis may not be the curse it was before the era of antibiotics, but treatment is still long and tedious and, with the emergence of antibiotic-resistant strains, the TB threat is rising again, killing 1.6 million people worldwide in 2021.

Current treatment regimes involve taking a cocktail of four antibiotics for six months. This long time frame and toxicity of the drugs reduce patient compliance leading to failed treatment, relapse and the emergence of drug-resistant bacteria. Because of this, better treatment options are needed.

However, to create better treatments, researchers need to understand how current antibiotics kill TB. TB bacteria, *Mycobacterium tuberculosis*, live inside the patient's cells. However, cells have many compartments. It is currently unknown whether the bacteria and the antibiotics occupy the same compartments and how those compartments could affect drug effectiveness. Understanding this is critical to optimising the effectiveness of these drugs.

RESEARCH

Researchers from the University of Western Australia, Hong Kong, the UK and Switzerland, have developed a new method that combines correlative light, electron and ion (nanoSIMS) imaging that allows researchers, for the first time, to see where the bacteria and antibiotics are located in the cells. They have also been able to decipher how different intracellular micro-environments affect the action of the TB drugs.

Different cellular compartments have different properties, such as acidity or the presence of enzymes, that could degrade or enhance the drugs. Researchers revealed that pyrazinamide, one of the antibiotics used in TB treatment, could more effectively target and kill the bacteria inside acidic cellular compartments. They also found that another of the antibiotics, bedaquiline, accumulates in the fat droplets used as a food source by TB bacteria, potentially facilitating drug uptake. Bedaquiline's effectiveness was found to be influenced by the fat metabolism of host cells. The team also revealed that the two antibiotics work synergistically, with bedaquiline improving the ability of pyrazinamide to target TB bacteria.

The researchers found considerable variability in where the bacteria reside, even in adjacent cells. They were also surprised to find that pyrazinamide is not distributed consistently within cellular compartments but, rather, it accumulates within specific intracellular bacteria, being present in one bacteria but not in its neighbour.

These differences in drug accumulation highlighted that antibiotic targeting of intracellular pathogens remains a complex puzzle, one that correlative microscopy is helping to solve.

IMPACT

This new correlative microscopy method combined with research findings opens the door to further work into how antibiotics act inside the cell. It also opens avenues for the development and implementation of efficient, short and more patient-friendly therapeutic alternatives for tuberculosis, which are desperately needed worldwide.

D. Greenwood et al., Science 2019
DOI: 10.1126/science.aat9689

P. Santucci et al., Nature Communications 2021
DOI: 10.1038/s41467-021-24127-3

16 BETTER SATELLITE TECHNOLOGIES FOR THE AUSTRALIAN SPACE INDUSTRY

Microscopy Australia's facilities are helping to build a sovereign space industry in Australia by enabling collaborative research into new technology for satellites.

At the University of Queensland, Prof. Warwick Bowen's research team has used Microscopy Australia's facilities in the development of a nanomechanical logic gate, a key component in making ultra-low-energy computer chips that can withstand the harsh environment of space.

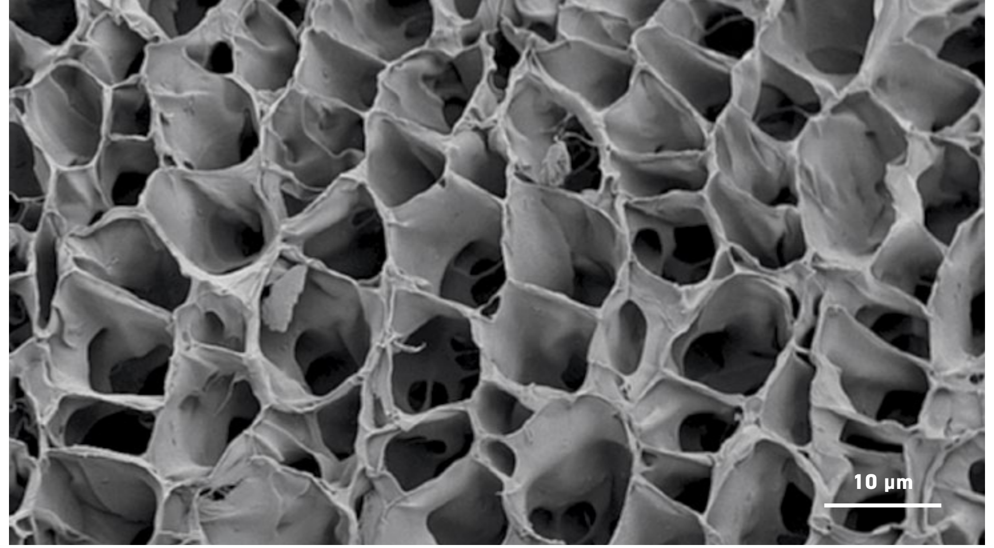
The majority of computer chips today use electrons travelling through semiconductors to transmit information. Nanomechanical chips rely on vibrations instead. This has significant advantages for satellites and spacecraft as nanomechanical chips do not have sensitive electrical components and can withstand much harsher conditions, such as solar flares, without losing information. They also use a fraction of the energy of a semiconductor-based computer.

At our University of South Australia facility, Prof. Kamil Zuber and team are collaborating with industry partners in the local defense supply chain to develop freeform optics for small satellites. This new optics system will expand Australia's current intelligence, surveillance and reconnaissance capabilities.

Freeform optics do not require a symmetrical mirror like traditional optics systems but, instead, can be manipulated into any shape needed for peak optical performance. This allows them to be more compact, while producing better image quality. Microscopy Australia's University of South Australia facility has been key in enabling the development of this device.

The UniSA team has partnered with specialist additive manufacturing company, Amaero, to develop a durable coating that will protect the optical system from radiation and other damage in the harsh low-Earth-orbit environment.

Both of these technologies pave the way to better satellites and support Australia's growing space industry.



Scanning electron micrograph of the hydrogel in the bandages.

17 SILVER NANOPARTICLES IN BANDAGES TO TREAT INFECTION

Infected wounds pose a serious risk to patients, often resulting in chronic infection, significant discomfort and even death. In Australia, chronic wound infection adds $2.85 billion annually to the healthcare burden. Increasing emergence of antibiotic resistance demands new approaches to address this problem.

Silver is effective at killing many types of bacteria, and, as silver attacks many bacterial processes at once, resistance is unlikely to develop. However, too much silver can damage human cells and prevent healing. This can be a particular problem with wound dressings impregnated with traditional silver nitrate that release large amounts of silver into the wound. Silver nanoparticles are a step forward, presenting silver to wounds at lower concentrations, helping to protect tissue while retaining strong antibacterial activity.

Dr Zlatko Kopecki and colleagues at the University of South Australia (UniSA) and Flinders University, have gone a step further, recently developing bandages that release silver nanoparticles into a wound only as they are needed. This bandage is based on a biocompatible hydrogel containing pores that hold the tiny silver nanoparticles. Our facilities at UniSA provided scanning electron microscopy (SEM) for this research.

Infected wounds are more alkaline (higher pH) than healthy wounds and typically also have a higher temperature. The responsive hydrogel developed by the team changes its structure as temperature and pH increase during bacterial infection to release the silver nanoparticles only into infected areas of the wound. When tested on *Staphlococcus aureus*-infected wounds, the hydrogel bandages cleared the infection effectively and promoted wound healing.

This combination of targeted release, antibacterial action and improved wound-healing in a single platform could facilitate better treatment for those suffering wounds caused by burns, trauma, surgery or skin disorders and all wounds that are prone to serious infection.

H. Haidari et al., ACS Appl. Mater. Interfaces 2022
DOI: 10.1021/acsami.2c15659

18 MINING AND REMEDIATION WITH PLANTS

A few rare plants can concentrate unusually high levels of particular metals in their cells. Harnessing this property to remove toxic metals from the ground to produce a 'bio-ore' is an exciting approach to remediating contaminated soils and mine sites.

Metals can be recovered from bio-ore in a process known as phytomining. Battery metals are an important target for phytomining and a number of plants are now being tested for their ability to concentrate them. Farming for nickel, cobalt, and manganese is currently within reach, with nickel being one of the most commonly accumulated metals.

Dr Antony Van der Ent at the University of Queensland (UQ) studies the physiology of these metal-accumulating plants from around the world and explores their potential for phytomining. He uses micro X-ray fluorescence (XRF) at Microscopy Australia's UQ facility to visualise the distribution of the metals in plant structures.

An example is the Australian native *Neptunia amplexicaulis*, one of the strongest selenium hyperaccumulators, capable of holding more than 10 g/kg selenium in its leaves. They can be a source of both selenium metal and organic selenium compounds for pharmaceuticals. The team has developed a way to propagate these plants in culture for research and phytomining. Another is the macadamia. Dr Van der Ent correlated leaf-scale studies undertaken at UQ, with cellular-level imaging from the Australian Synchrotron revealing that manganese accumulates in specific leaf structures and not in the nuts. This could provide a foundation to guide development of macadamias as a dual-purpose crop, providing both luxury food and battery metals.

Recently, a proof-of-concept trial using a mix of plants that each accumulates a particular metal, successfully extracted multiple metals from mine tailings at the Dugald River and Mt Isa zinc–lead–copper–silver mines, paving the way for practical development of phytomining of toxic mining waste, bringing new meaning to 'green mining'.

P. N. Nkrumah et al., Plant Soil 2022
DOI: 10.1007/s11104-022-05586-z

Image: XRF image of a whole Neptunia amplexicaulis plant showing calcium in red, selenium in green and potassium in blue.

AMMONIA PRODUCTION EMITS MORE CO_2 THAN ANY OTHER INDUSTRIAL CHEMICAL

19

CARBON-NEUTRAL AMMONIA SPIN-OUT

CHALLENGE

Ammonia is the source of most modern fertilisers with 50% of global food production relying on it. However, it's production emits more CO_2 than any other industrial chemical reaction. This is because it relies both on natural gas as a feed stock, and uses huge amount of electricity, accounting for 2% of global energy use and 1% of global greenhouse gas emissions. Finding a way to make ammonia without natural gas and with renewable energy would eliminate two major global sources of emissions, while still providing the fertilisers that billions of people around the world rely on for food. When ammonia is made using renewable energy, it is also an excellent way to transport that energy. At its destination, it can then be converted into hydrogen or used directly as a fuel source.

RESEARCH

Monash University researchers, Prof. Douglas MacFarlane and Dr Alexandr Simonov and their team, have developed an electrochemical process that makes ammonia using only nitrogen from the air and water as the source materials. Inside an electrochemical cell, hydrogen ions from the water are sequentially added to nitrogen from the air without producing any greenhouse gases. The unique chemistry inside the cell allows a continuous cycle to generate hydrogen ions at one electrode and deliver them to the nitrogen at the other electrode, where they react to form ammonia.

Scanning electron microscopy carried out at the Microscopy Australia facility at Monash University has allowed the researchers to develop, optimise and monitor their electrodes.

IMPACT

In 2021, Prof. MacFarlane and Dr Simonov founded spin-out company Jupiter Ionics to commercialise their patented technology. Since then, it has raised over $5 million of funding to transition their technology from the lab to a scalable commercial device. They are a winner in the Science Start-ups category in the international Falling Walls Science Breakthroughs of the Year 2022 as one of the top projects that will shape the future of science and society.

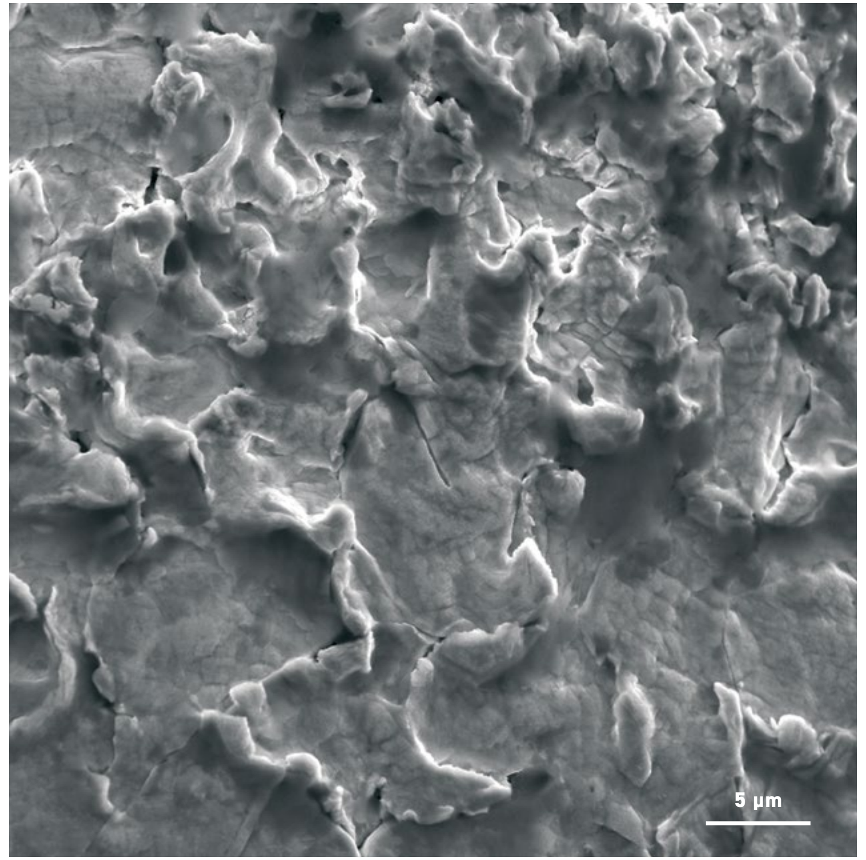
Impacts of this work will be felt through:

- significant reduction of greenhouse gas emissions
- small-scale modular facilities to localise ammonia production providing local control, jobs, food security, reduced transport costs and risks of explosion (as happened in Beirut in 2020).

H. L. Du et al., Nature 2022
DOI: 10.1038/s41586-022-05108-y

B. Suryanto et al., Science 2021
DOI: 10.1126/science.abg2371

PUBLISHED IN NATURE AND SCIENCE

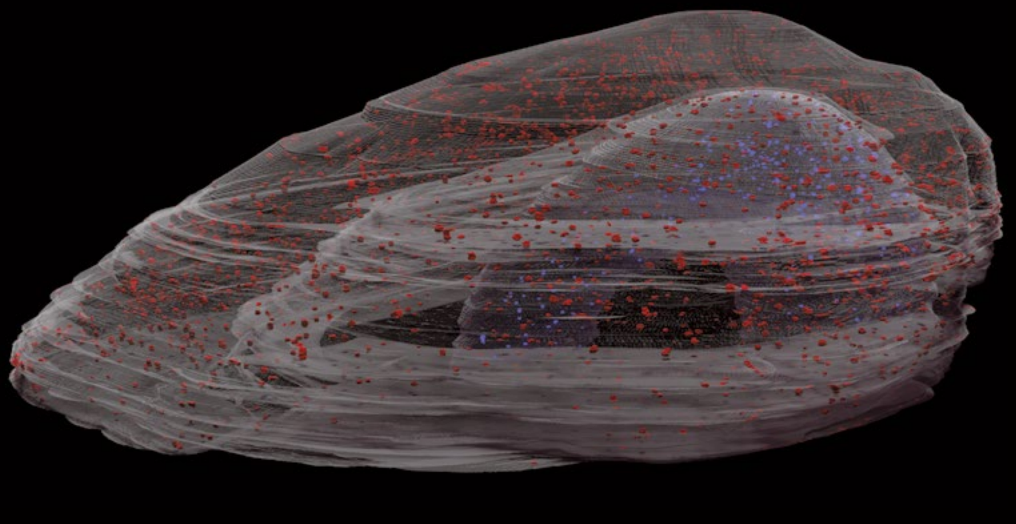


Scanning electron micrograph of an electrode used in the electrochemical cell.

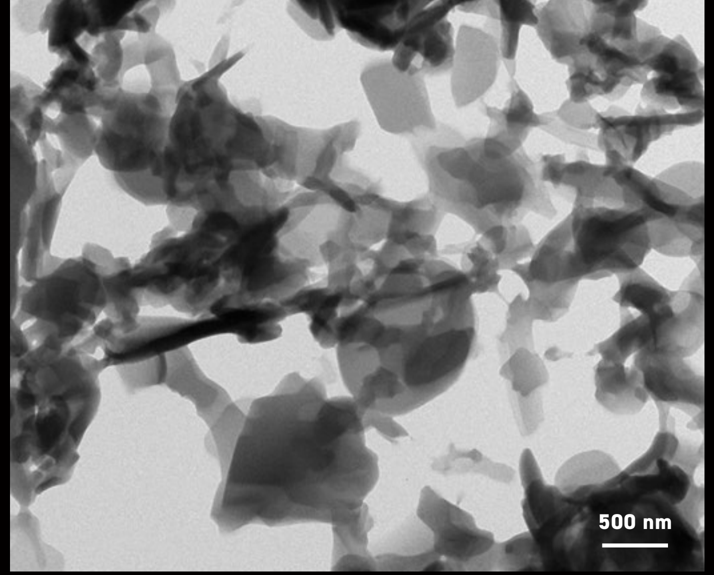
20 DEEP LEARNING FOR IMAGE ANALYSIS

3D microscopy is extremely powerful, generating enormous quantities of data. However, analysis and interpretation can be very time consuming. Identifying and separating out features within an extensive image set requires expertise but is very tedious, often taking months or even years. Although there are processes that will select certain features based on a specific threshold, they don't always get it right.

Sydney University PhD student, Veronika Valova is studying amyloid plaques in Alzheimer's disease. She acquired 3D images of amyloid in mouse brains by light sheet microscopy. However, as each sample contained thousands of plaques of variable size, it was impossible to set thresholding levels that identified plaques reliably. Enter deep learning. This is a type of machine learning that imitates the way humans gain certain types of knowledge. It enables a computer to be trained to do time-consuming and laborious tasks. Ms Valova worked closely with Microscopy Australia's Sydney Data Specialist to harness deep learning to analyse her data. A model was trained to select plaques based on their shape. Although this approach, did not give perfect results, it sparked a "close enough–good enough" conversation regarding large data: how much error can be present and still allow meaningful conclusions to be drawn? After considering the results in their biological context and comparing them to other studies, Ms Valova confirmed that the plaque selection was "good enough" to be useful to her research. Her work also demonstrates the issues, value and potential of deep learning to image analysis of microscopy data.



Amyloid plaques (blue: hippocampal, red: cortical) in a mouse brain, identified by deep learning.



Transmission electron microscopy image of the milk sensing composite.

21 MILK SENSOR TO INDICATE SPOILAGE

Balancing food waste with risks to human health could be made easier with a new built-in sensor for milk packaging that indicates if the milk has spoiled. Researchers at UNSW Sydney, led by A/Prof. Rona Chandrawati, have developed a chemical sensor that changes colour as the milk spoils. This is based on the fact that milk becomes more acidic as bacteria convert the lactose to lactic acid.

After testing a range of compositions, the best is a combination of a polydiacetylene polymer and zinc oxide (PDA/ZnO). By altering the chemistry of the sensing molecules used, the team was able to adjust the sensor so it works over the precise acidity range needed to see the change from fresh milk to spoiled milk. Fresh milk turns the sensor blue, ageing milk shows as purple and spoiled milk shows as pink. Transmission electron microscopy (TEM) was used to visualise and monitor structures formed by the different chemical combinations tested for the sensor.

In other previous studies, the colour stability of the PDA/ZnO sensor in food was seen to be unstable. The researchers' new method stabilises the nanocomposite by pre-exposure to the food matrix prior to locking together the structure of the composite. Hopefully this new sensor technology will be in milk packaging in the not-too-distant future.

M. Weston et al., Colloid and Interface Sci. 2020
DOI: 10.1016/j.jcis.2020.03.040

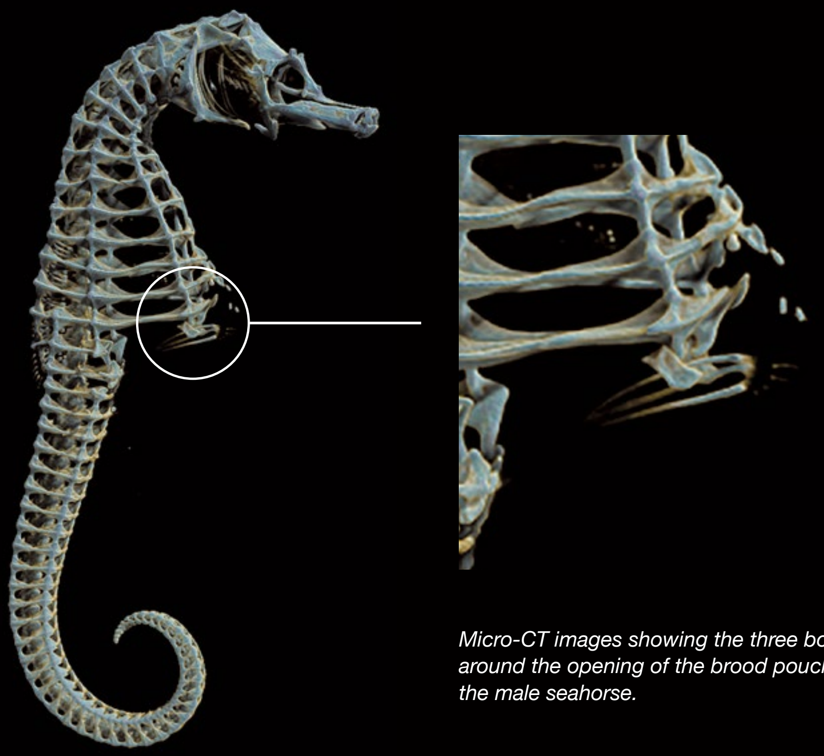
22 UNCOVERING THE SECRETS OF MALE PREGNANCY IN SEAHORSES

Male pregnancy and live birth is a feature of all seahorses, pipefish and seadragons. Instead of a uterus, some species of male seahorse have a brood pouch and even a placenta to provide nutrients to the embryos.

In a mammalian uterus, labour is initiated by oxytocin, which causes the smooth muscles of the uterus to contract. For a long time this was thought to be the case in the brood pouch of seahorses too. However, researchers at the Universities of Sydney and Newcastle, led by Dr Camilla Whittington, have revealed that this is not the case. Instead of smooth muscle contractions, the males have a unique anatomy and perform elaborate movements to expel their babies.

X-ray micro-CT at Microscopy Australia's University of Sydney facility, showed that there are large skeletal muscles attached to three bones around the opening to the brood pouch. Skeletal muscle, unlike smooth muscle, can be consciously contracted. In other fish these three bones are associated with the anal fin but in the seahorse they have evolved a new use, controlling the opening of the brood pouch. These results suggest that seahorse fathers can consciously expel their young at the end of pregnancy. They reveal a significant evolutionary divergence of both the anatomy and control of the birth process across the animal kingdom.

J. S. Dudley et al., Placenta 2022
DOI: 10.1016/j.placenta.2022.07.015



Micro-CT images showing the three bones around the opening of the brood pouch in the male seahorse.

Photo by Rudie H. Kuiter, marine life photographer

UNIVERSITY, GOVERNMENT & INDUSTRY COLLABORATION

IMPROVING MINERAL EXPLORATION IN AUSTRALIA

23

NANOPARTICLES REVEAL HIGH-GRADE GOLD DEPOSITS

CHALLENGE

Increasing efficiency and sustainability of gold exploration and mining is a challenge when the overall quality of many ore bodies is declining.

The unique properties of gold – inert, malleable, and beautiful – have made it a valuable resource for over 7,000 years. Today, 75% of gold is mined from orogenic deposits. These form when hot fluids from deep within the earth travel up to near the surface through fractures in the rock. Once near the surface they cool and dissolved metals and minerals solidify into veins that can then be mined. Despite most high-grade gold being found in this type of deposit, gold isn't very soluble and doesn't travel easily in fluids. How large quantities of gold came to be in the fluid has long puzzled researchers – until now.

RESEARCH

Atomic resolution microscopy at Microscopy Australia's University of Western Australia (UWA) facility has helped to reveal, for the first time, the role of carbon in concentrating precious metals into fluids to create exceptionally high-grade deposits.

Dr Laura Petrella, with a team from the Centre for Exploration Targeting and the Geological Survey of Western Australia, along with platform scientist Dr Alexandra Suvorova, used a range of high-end microscopy and microanalysis techniques to examine specimens of ultra-high-grade gold-bearing quartz veins from five mines around the globe.

A specific carbon-rich fluid chemistry deep within the earth causes single atoms of gold, and other precious metals, to be surrounded by molecules to form a nanoparticle. While gold itself is not very soluble, the larger nanoparticles can be carried along easily by fluids near to the surface. As it approaches the surface, changes in temperature cause the fluid chemistry to change and the nanoparticle to break apart releasing the gold to form a deposit.

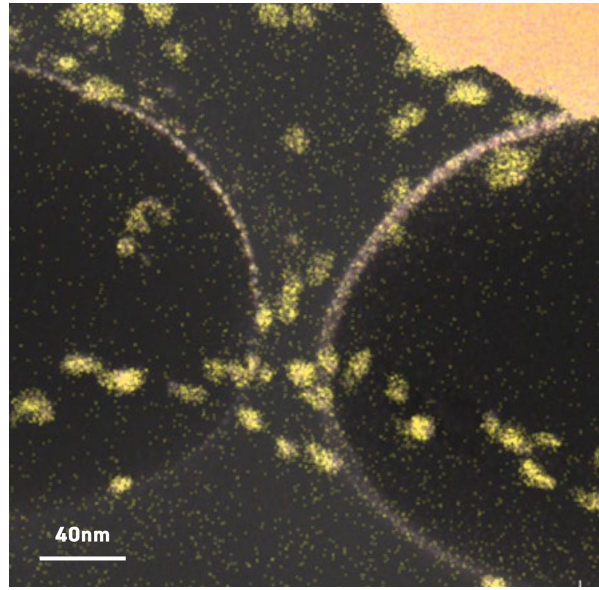
IMPACT

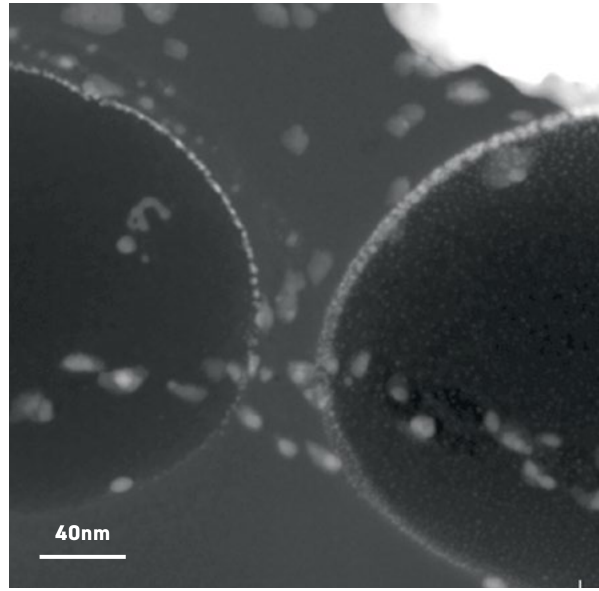
By uncovering the chemical make-up of fluids that result in high-grade gold deposits, the research team has provided mining operations around the world with valuable information on how to better find and target ultra-high-grade gold deposits. Mining high-grade deposits is both more energy efficient and has a lower environmental footprint – crucial to developing a more sustainable mining sector.

"Our work aims at further understanding the formation of high-grade, high-tonnage ore bodies so that mineral explorers may develop the tools for a more efficient targeting of these deposits," Dr Petrella said.

L. Petrella et al., Nature Communications 2022
DOI: 10.1038/s41467-022-31447-5

Images: Scanning transmission electron microscopy images of precious metal nanoparticles in a quartz vein. The top image has an overlaid elemental map (EDS) highlighting the gold (orange) and silver (yellow) atoms clumped together into nanoparticles.





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Right: Transmission electron microscope image of cellular structures called rough endoplasmic reticulum. Imaged by Simon Crawford at the Ramaciotti Centre for Cryo-EM, Monash University.

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