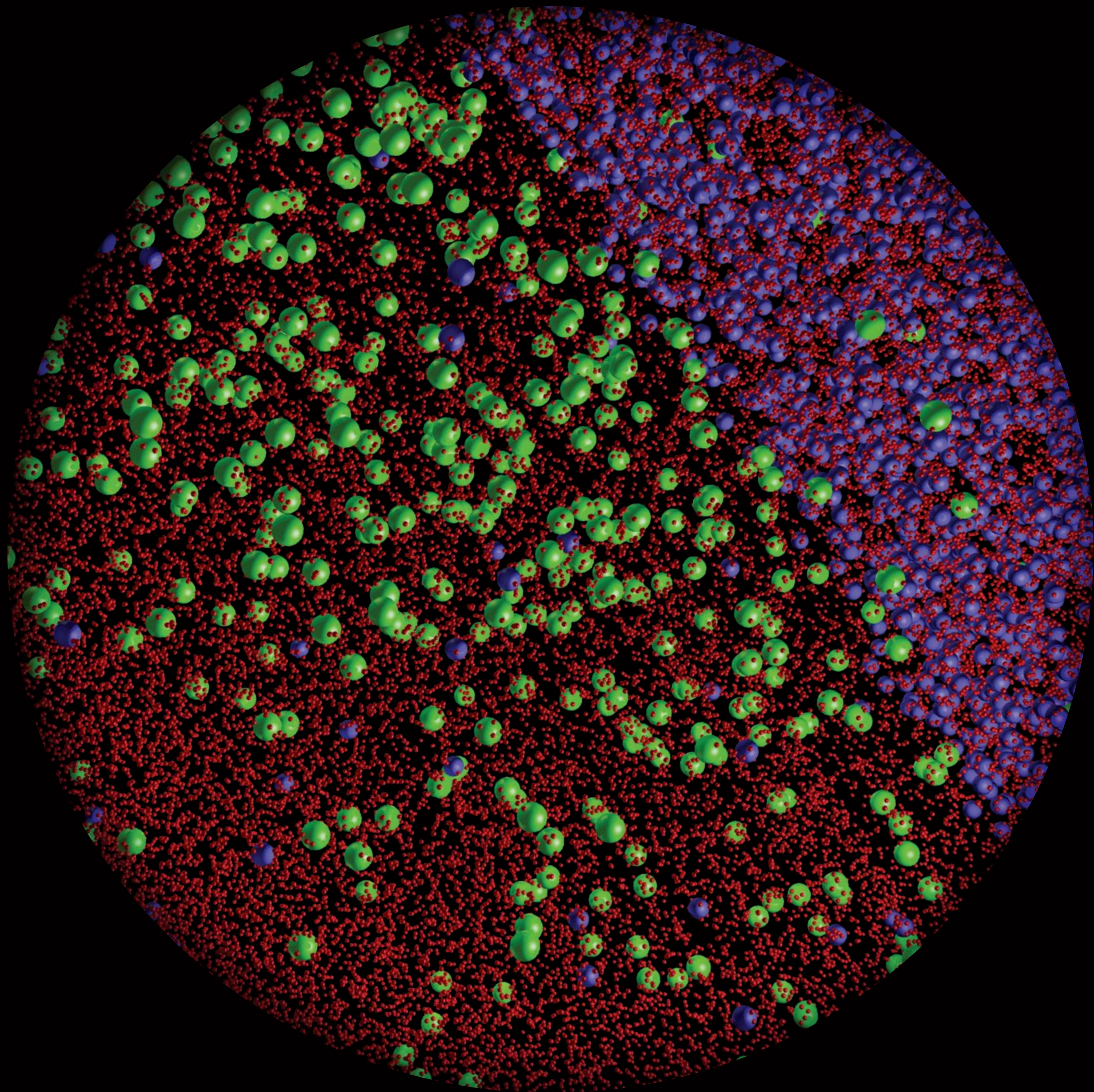
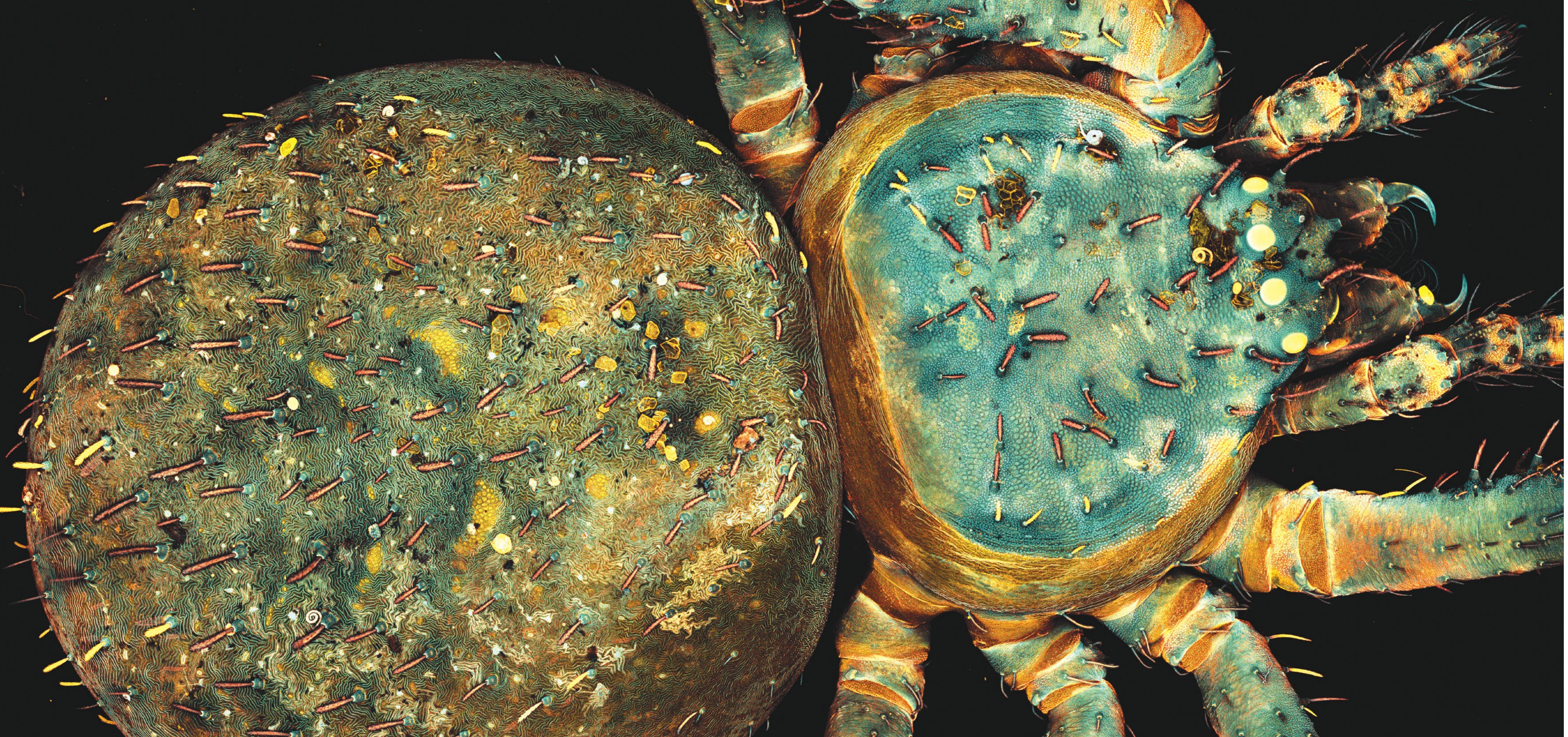
MICROSCOPY AUSTRALIA RESEARCH HIGHLIGHTS 2023





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

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Cover: Atom probe tomography map of atoms in a 3D printed titanium alloy recorded at Sydney Microscopy and Microanalysis. The 3D printing breakthrough allows the strength and ductility of the alloy to be finely tuned depending on its end use. Read more on p24.

Left: A confocal image of a native Diamond Comb-Footed Spider, Cryptachaea veruculata, taken by Angus Rae at the Centre for Advanced Microscopy, Australian National University.

LEADERSHIP REFLECTIONS

Left page: Scanning electron micrograph of a carnivorous plant, Drosera sp. sundew, with a partially digested meal (can you spot the faceted eye?) taken by A/Prof. Peta Clode at Microscopy Australia's University of Western Australia facility.

CHAIR

Dr Gregory R. Smith
Chair of Board

Microscopy Australia is geographically dispersed and operates across multiple facilities in Australia. Each facility has strategically invested in microscopy instrumentation, expertise and technologies. Extensive collaboration between the geographical nodes of the facility is used to optimise capital investment, productivity and human resources in order to deliver a national open-access microscopy capability.

Recently, the Microscopy Australia Board has welcomed the federal government's support of Australia's national microscopy research infrastructure for an additional five years until mid 2028.

At the close of 2022, Microscopy Australia's leadership structure changed. Prof. Julie Cairney moved on from her role as CEO into a newly established Chief Scientific Advisor role. Meanwhile, Dr Lisa Yen was appointed as the CEO. The Board is confident that this new structure will serve the organisation, while ensuring that the knowledge and expertise of the organisation's leadership is retained. Microscopy Australia's leadership and governance has been further strengthened, with the recent appointment of Dr Kath Smith as an additional independent board member.

Microscopy Australia is committed to continuous improvement across the delivery of its services, its international connections, its industry engagement and governance. Early in 2023, a self-initiated Independent External Review was conducted that sought to benchmark Microscopy Australia against international standards. An illustrious panel of world-leading experts visited Microscopy Australia's facilities and later provided a comprehensive report that is proving to be incredibly valuable for the organisation. The report certainly recognised the successes of Microscopy Australia. It also provided encouragement that the Australian national microscopy research infrastructure is achieving at a level above world-standard status, with excellence in organisational structure and output. The panel also encouraged Microscopy Australia to develop a comprehensive strategic plan with a 10-year outlook that identifies the evolving research needs to guide Australian strategic future investment in cutting-edge microscopy. This will be critical for improved fundamental understanding and advances in critical minerals, biotechnologies, and advanced materials.

CEO

Dr Lisa Yen
Chief Executive Officer

Reflecting on this past year, Microscopy Australia has been focussed on re-connecting and forward planning. Researchers and staff were able to participate in in-person conferences including the major International Microscopy Congress IMC20 and Australian Conference in Microscopy and Microanalysis, ACMM 27.

Microscopy Australia supported nearly 3800 researchers this year, enabling them to produce over 1500 publications. Some of these incredible discoveries are featured in this Research Highlights, starting from p18. The range of stories never ceases to amaze me, such as the infection resistant implants inspired by nature, ongoing advances in 3D printing technologies, the potential to convert air into electricity, and so many more. These stories demonstrate the underpinning role of microscopy in Australian research outcomes, and I hope they are an inspiration for future breakthroughs as well.

Over the last five years, Microscopy Australia has implemented its five-year investment plan, significantly uplifting the advanced microscopes and expertise available to public and private researchers across Australia. This national plan focussed on increasing access to cryo-electron microscopy, the importance of which was recognised with the 2017 Nobel Prize awarded to the key developers of this technique. We have also reinvigorated our approach to industry engagement, and I would like to acknowledge and thank the Industry Engagement Committee and staff members who have worked hard to increase Microscopy Australia's support to industry.

Microscopy Australia remains committed to underpinning Australia's future research achievements. We have secured funding for the next five years that will ensure Australian researchers are supported with strategically placed, high-quality instruments and experts to enable advances in priority research areas.

THINK SMALL TO THINK BIG

We are Australia's 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.

WHY IS MICROSCOPY SO IMPORTANT?

Microscopy is a fundamental scientific technique. It reveals the structure and properties of materials and living systems at unimaginably tiny scales, down as far as individual atoms.

Microscopy is fundamental to the creation of new knowledge in many fields from medicine and engineering to art and archaeology: without microscopy, scientific knowledge as we know it would not be possible.

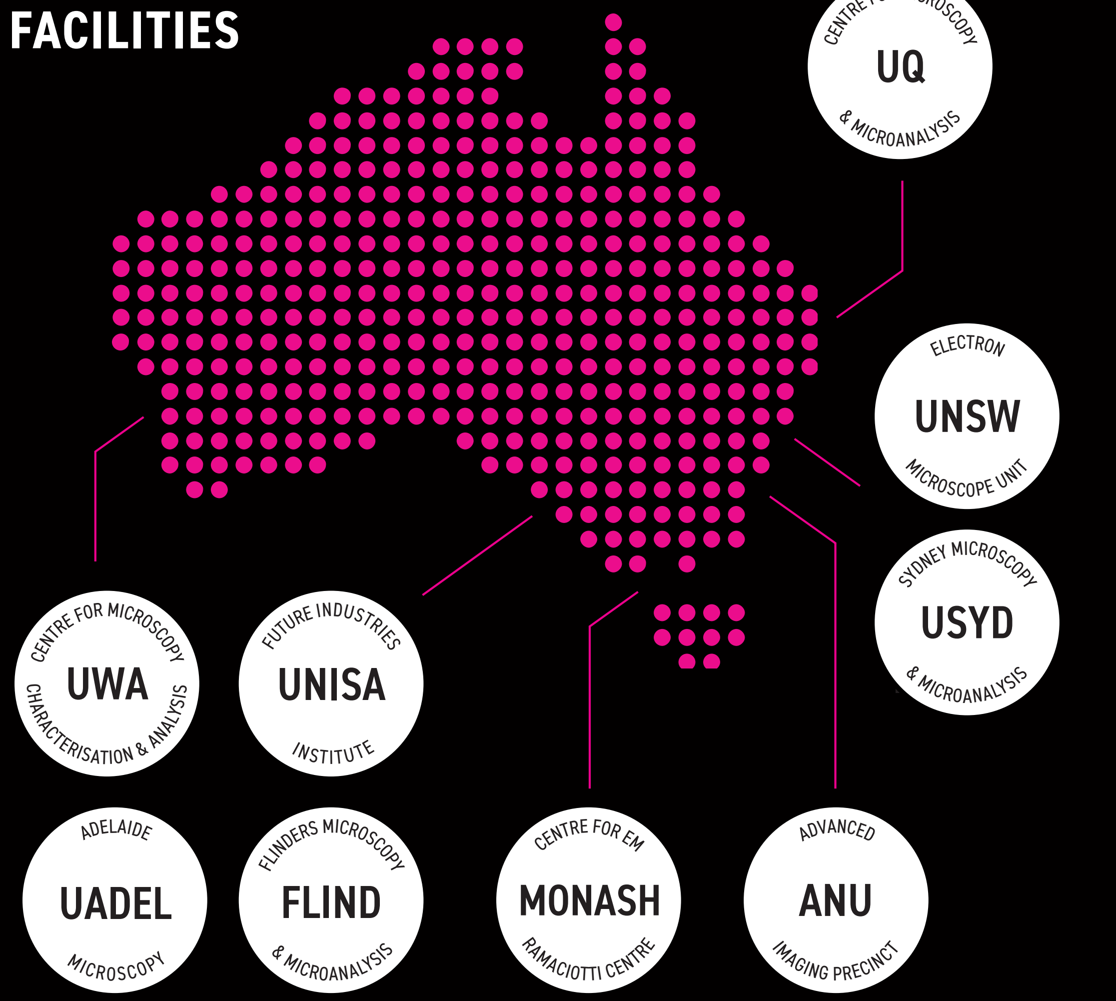
"Without microscopy, there is no modern science – end of story."

– Dr Alan Finkel, former Chief Scientist of Australia, Opening Address at IMC19.

Scanning electron micrograph of radiating crystals taken at Microscopy Australia's University of Queensland Facility by Ping Cheng from the AIBN.

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 2022 (2023 collection). Left: The atomic structure of a nanowire, developed for computing, showing a defect called a twin, imaged using an atomic scale transmission electron microscope by Dr Jiangtao Qu at Microscopy Australia's University of Sydney facility.

291
INSTRUMENTS

180
EXPERTS

3,792
USERS

263
INDUSTRY CLIENTS

360,474
HRS BEAMTIME

1,514
PUBLICATIONS

68,000
VIEWS ON YOUTUBE

47% MATERIALS & ENGINEERING
41% BIOLOGICAL & MEDICAL
12% GEOSCIENCE & ENVIRONMENT

36% MANUFACTURING
21% BIOMEDICAL
36% RESOURCES & ENVIRONMENT
% OTHER

99%
OF USERS REPORT OUR FACILITIES WERE VALUABLE TO THEIR RESEARCH

98%
OF USERS WOULD RECOMMEND OUR FACILITIES TO A COLLEAGUE

33%
OF PUBLICATIONS WE ENABLE ARE IN THE TOP 10% MOST CITED JOURNALS

MYSCOPE
MICROSCOPY TRAINING

MYSCOPE UPDATE: 2023

Microscopy Australia's educational website, MyScope, helps train new microscopists all around the world.

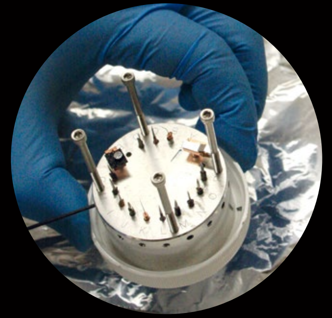
This year we have greatly expanded the range of techniques available in the Light and Fluorescence simulator to include the super-resolution technique of stimulated emission depletion microscopy to complement single molecule localisation microscopy that went live late in 2022. We have also added phase contrast, differential interference contrast, darkfield and polarised light microscopy modes. A new Secondary Ion Mass Spectrometry module has also been added covering ToF-SIMS, large geometry and nanoSIMS.

A panel of international microscopy experts conducting a review of Microscopy Australia (see p10) said:

"The MyScope microscope simulators and online training modules are one of Microscopy Australia's most internationally visible and cost-effective investments... There is no comparable resource to MyScope anywhere else in the world."

EQUIPMENT & EXPERTISE

TAKE A CLOSER LOOK



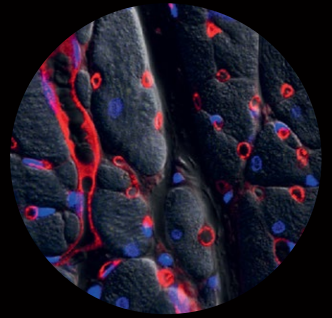
SPECIMEN PREPARATION

Biological & Materials

Cell Culturing & Molecular Preparation

Thermomechanical Processing

Ion Milling, Machining & Implantation



LIGHT & LASER MICROSCOPY

Confocal, Fluorescence & Optical Microscopy

Super-resolution Microscopy

Live-cell Imaging

Bioluminesence

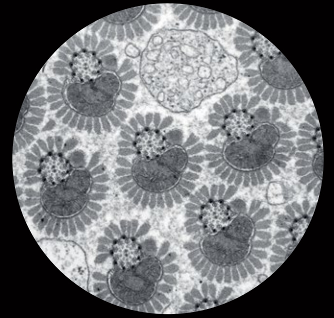
SCANNING ELECTRON MICROSCOPY

Imaging & Analytical Spectroscopy

In-situ Imaging & Testing

Cathodoluminescence

Electron Backscatter Diffraction



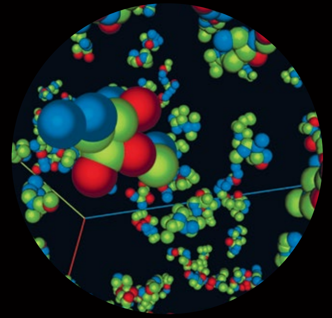
TRANSMISSION ELECTRON MICROSCOPY

Imaging & Analytical Spectroscopy

Cryo-techniques & Tomography

Phase & Z-contrast Imaging

Electron Diffraction



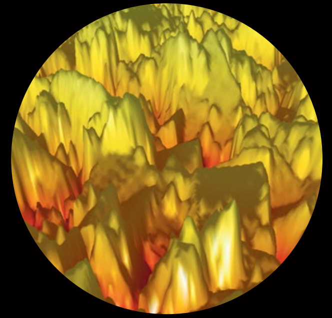
MASS SPECTROMETRY & SPECTROSCOPY

Secondary Ion & Imaging Mass Spectrometry

LA-ICP-MS

Atom Probe Tomography

Raman, Vibrational & Laser Spectroscopy

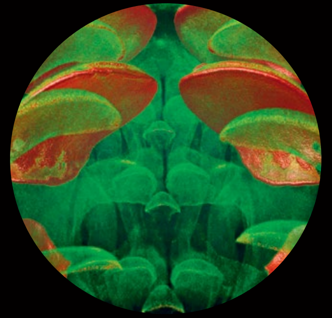


SCANNED PROBE TECHNIQUES

Atomic Force Microscopy

Scanning Tunnelling Microscopy

Near-field Scanning Optical Microscopy



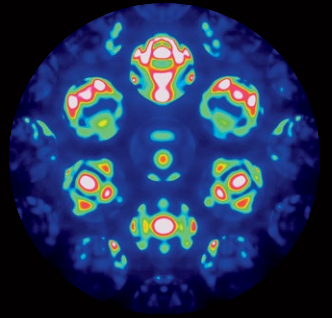
X-RAY TECHNOLOGIES

X-ray Diffraction

X-ray Fluorescence

X-ray Micro-CT

NanoESCA III



DATA ANLYSIS & VISUALISATION

Data analysis

Data visualisation

Data Simulation & Modelling

Computed Spectroscopy & Diffraction

WHAT WE'VE ACHIEVED SINCE 2018

Over the last National Research Infrastructure Roadmap period we delivered the following outcomes...

23 NEW INSTRUMENTS

142 EXPERTS

LEVERAGED FUNDS — **$1** AWARDED BY NCRIS = **$1.27** ADDITIONAL CO-INVESTMENT

PROGRAM AVG. $1 NCRIS = $0.34 RETURN (2020 CENSUS)

3500 USERS PER YEAR

1.44M HOURS BEAMTIME

>375 INDUSTRY CLIENTS

>635 PATENTS GRANTED

7491 PAPERS & BOOKS

6 MYSCOPE MODULES

KEY TECHNOLOGIES SUPPORTING AREAS OF NEED

CRYO-ELECTRON MICROSCOPY

Reveals the nanoscale structure of polymers, sub-cellular components, viruses, enzymes and other proteins, including their interactions with small molecules.

8 NEW INSTRUMENTS

IMPACT AREAS

- Understanding disease
- Drugs & biotech
- Agriculture, forestry & fisheries
- Renewables & low emissions technologies

CASE STUDY

Used to understand and optimise an enzyme that can convert air into electricity, published in *Nature*. More on p28.

ATOMIC SCALE MICROSCOPY

Reveals the atomic scale structure and makeup of materials. This capability is important for the development of batteries, solar cells and quantum technology.

4 NEW INSTRUMENTS

IMPACT AREAS

- Renewables & low emissions technologies
- Transport, defence & space research
- Medical devices
- Quantum technology

CASE STUDY

Enabled a ground-breaking titanium alloy manufacturing technique, published in *Nature*. More on p22.

HIGH-SENSITIVITY MICROANALYSIS

Reveals fine-scale variations in elements, compounds and isotopes, along with identifying presence and distribution of different phases, within materials and minerals.

7 NEW INSTRUMENTS

IMPACT AREAS

- Earth science & mining
- Renewables & low emissions technologies
- Transport, defence & space research
- Agriculture, forestry & fisheries

CASE STUDY

Isotopic analysis led to a fundamental change in our understanding of how the continents formed, published in *Nature* (2021).

CORRELATIVE MICROSCOPY

Combines different light, electron and microanalytical techniques on one sample to provide both structural and functional information simultaneously.

4 NEW INSTRUMENTS

IMPACT AREAS

- Understanding disease
- Drugs & biotech
- Agriculture, forestry & fisheries
- Renewables & low emissions technologies

CASE STUDY

Showed how a suite of engineered bacteria-killing peptides work within our cells to kill the invading bacteria. More on p26.

INTERNATIONAL BENCHMARKING

Early in 2023, Microscopy Australia conducted a self-initiated review of our operations and outcomes based on international research infrastructure standards and best practice.

The aim of the review was to consider the achievements, challenges and barriers in delivering a national research infrastructure, as well as to assess the quality of cooperation and support within and between the facilities, and with external research partners.

This panel consisted of five highly-regarded experts in microscopy research infrastructure from around the world who spent a week touring our facilities and talking to staff, users, industry clients and key government stakeholders. They included Prof. Odile Stéphan (second from the left), Prof. Kazuhiro Hono, Prof. Rafal Dunin-Borkowski, Prof. Paul Verkade and Prof. Rhonda Stroud (centre to right).

KEY FINDING 1: Microscopy Australia achieves an excellent balance between more standard characterisation and state-of-the-art research for the benefit of scientists and engineers… Its activities in methodology and instrumentation development are internationally leading. The online training tools that it has developed and made available internationally are a particular highlight.

KEY FINDING 2: Microscopy Australia… provides immeasurable added value to academic and commercial research in Australia… and is a shining example of how a national research infrastructure should be designed, managed and operated.

COMING TOGETHER WITH THE MICROSCOPY COMMUNITY

With borders open and international visits on the table, 2023 has been a year for reaching out. Here are some examples of how we are engaging with the local and international microscopy community.

VISITS AND VISITORS

Our University of Western Australia facility hosted representatives from the **International Atomic Energy Agency (IAEA)** and the Director General of the Australian Safeguards and Non-Proliferation Office. Our Ion Probe Facility is the only university-based facility within the IAEA's Network of Analytical Laboratories. It plays a key role in Australia's contribution to global nuclear safeguards, analysing samples from around the world for evidence of illicit nuclear activity.

The **NCRIS Advisory Group,** established to provide the Australian Government with independent strategic advice on research infrastructure, toured our University of Queensland facilities.

As part of our participation in **Global BioImaging**, we attended and presented at the Facility Management Course in Mexico and the Exchange of Experience in South Africa.

STAFF SHADOWING

With borders open, our experts are finally able to travel internationally on our staff shadowing program to visit leading labs around the world to bring back new techniques and best practice, which they can implement here in Australia. This year our **staff have visited labs in the UK, Sweden, and Germany**.

CONFERENCES

Over the last year Microscopy Australia has participated in **eight conferences**, from industry focused events like Advanced Manufacturing Week and the Quantum Australia showcase, to academic meetings like eResearch Australia and ComBio. For the first time since 2019 both the **Australian and the International Microscopy Congresses** could be held. These were a fantastic opportunity to re-engage with the local and international microscopy community, promote MyScope, and forge new, international connections.

MASTERCLASSES & WORKSHOPS

Our staff around Australia have been busy hosting and organising masterclasses, inviting internationally renowned microscopists to Australia to teach. These include the **Electron Crystallography School** at Monash, with attendees from 13 different countries, a **Cryo-CLEM masterclass** at the University of Queensland and our UNSW facility hosted an **advanced in-situ transmission electron microscopy masterclass**.

PUBLIC ENGAGEMENT

Staff from a number of our facilities took part in activities aimed at engaging the public and sharing the joy of microscopy. These included the 'SmART Science' activities and exhibition as part of Adelaide Fringe Festival, a booth at the Indigenous Science Experience and the display of our exhibition *Stories & Structures* in the Charles Perkins Centre, both in Sydney.


STAFF SHADOWING



MASTERCLASSES & WORKSHOPS



NETWORKING

From a visit to our University of Western Australia facility by the International Atomic Energy Agency, to the first post-COVID Australian and international microscopy meetings, 2023 has been a year for reaching out and reconnecting.





CONFERENCES





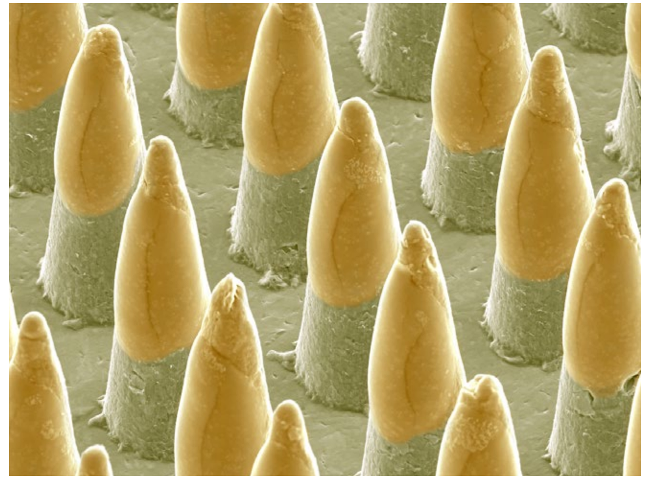
INTERNATIONAL VISITS

INDUSTRY

Microscopy Australia is committed to supporting Australian business. Here are some of our recent outcomes.

TECHNOLOGY READINESS LEVEL & COMMERCIALISATION READINESS INDEX (TRL & CRI)

TRL1	TRL2/CRI1	TRL3	TRL4	TRL5	TRL6	TRL7	TRL8	CRI2	TRL9	CRI3	TRL10	CRI4	CRI5	CRI6
FUNDAMENTAL RESEARCH	TECHNOLOGY CONCEPT	PROOF OF CONCEPT	TECHNOLOGY DEMO	PROTOTYPE DEMO	PROTOTYPE VALIDATION	PILOT PRODUCT	SYSTEM TEST	COMMERCIAL TRIALS	SYSTEM OPERATIONAL	COMMERCIAL SCALE-UP	WELL PROVEN OPERATIONS	BROADENED APPLICATIONS	MARKET INTEGRATION	COMMERCIALLY COMPETITIVE



Vaccine (yellow) on the HD-MAP (green) imaged using SEM.

TRL CONFIDENTIAL: VAXXAS

Vaxxas, a spin-out company commercialising a needle-free vaccine patch, the HD-MAP, used our facility at the University of Queensland throughout the technology's development, and continues to access our facilities for ongoing clinical and pre-clinical trials.

Vaxxas recently opened a $5,500m^2$ first-of-its-kind manufacturing site to support the scale-up of the HD-MAP production for late-stage clinical trials and first commercial products. Vaxxas' R&D and manufacturing teams are working side-by-side to streamline the translation of research to commercialisation. The company plans to expand to over 200 employees in the coming years.

Founders Prof. Michael Kassiou and A/Prof. Michael Bowen.

TRL6: KINOXIS THERAPEUTICS

Kinoxis Therapeutics is an Australian spin-out company developing KNX100: a drug candidate to treat substance use disorders, and agitation and aggression in dementia.

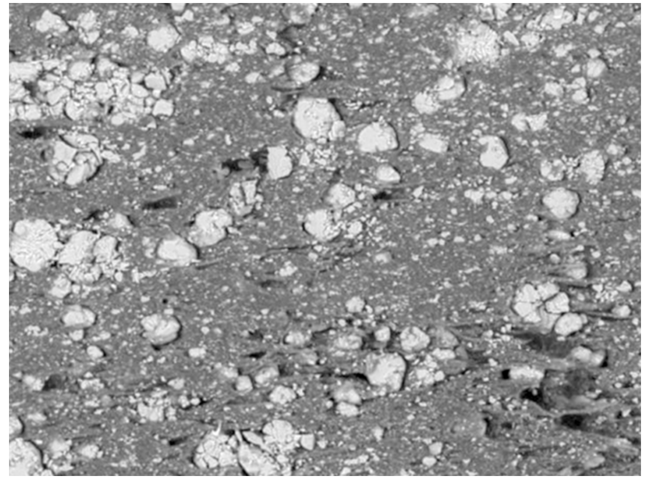
Our University of Sydney facility was used to help develop the drug and understand how it works in the brain. Kinoxis has received grants totalling over US$6M million from the US National Institutes of Health to support the development of KNX100, including the recently completed phase 1 clinical trial. In 2021 Kinoxis Chief Scientific Officer, A/Prof Michael Bowen was recognised with the New Innovators award at the Prime Minister's Prizes for Science for the development of KNX100.

Lithium crystals imaged using scanning electron microscopy.

TRL CONFIDENTIAL: NOVALITH

Spun out of the University of Sydney, Novalith is commercialising their low-cost, sustainable process to convert lithium bearing ores to battery grade lithium chemicals. Microscopy Australia's UNSW facility, was fundamental in the development of this technology.

After a successful feasibility study and demonstrations at lab scale, Novalith attracted ~US$15 million in Venture Capital funding. The company has since started the construction of their Pilot Plant Facility in Alexandria, Sydney. The Pilot Plant is expected to be running at real-world scale producing kilograms of lithium chemicals per day by 2024.

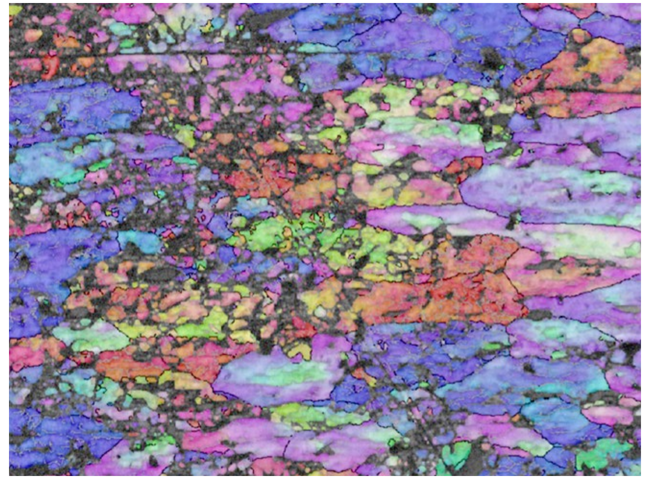


Aluminium cladding imaged using scanning electron microscopy.

CRI5-6: SAFER CLADDING

In the wake of the Grenfell Tower fire, the Australian construction industry wrestles with assessing the flammability of aluminium composite panel cladding on Australian buildings.

Staff of the Microscopy Australia facility at the University of Queensland have developed a method that uses scanning electron microscopy to identify flame retardants and analyse the flammability of different cladding. They are applying this method to help clients across the industry make informed choices and create safer buildings.

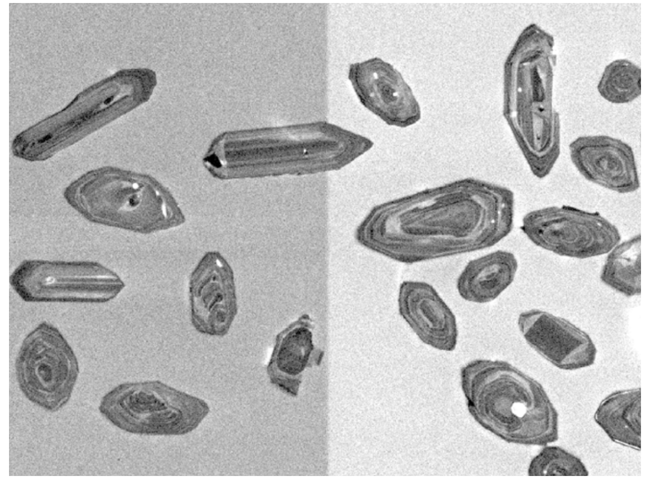


Grain structure of sheet metal imaged visualised using EBSD.

CRI6: BETTER PACKAGING

A client in the packaging industry had been encountering unpredictable failures in the metal sheeting from one of its two suppliers.

Our University of Sydney facility conducted analysis to examine the grain structure of the two products. They discovered that the product that was failing was not meeting the required specifications, which accounted for the observed failures. The packaging company was then able to present these findings to the suppliers who admitted their shortcomings, saving time and money for our client.



Cathodoluminesence image of zircon grains.

CRI6: STRIKING GOLD

A mining client needed to identify the age of a rock package to update geological models and better target rock units of interest.

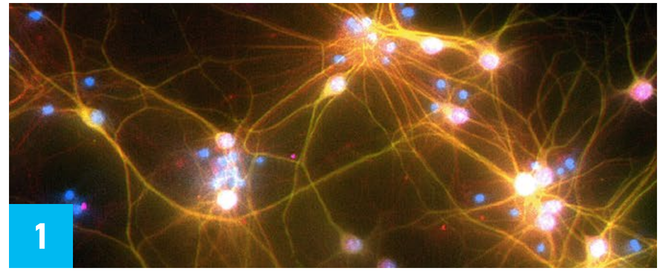
Our University of Western Australia facility conducted U–Pb dating on zircon grains from two intrusive rock samples. The dating of these samples improved the understanding of when the gold deposit formed and provided further insights into its structure. The mining company was then able to use these findings to better target their gold mining activities.

THINK SMALL TO THINK BIG

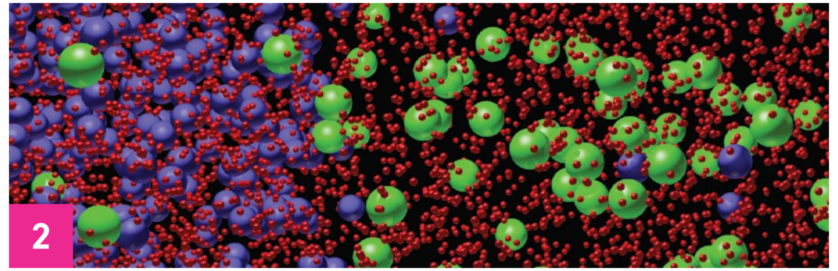
SCANNING ELECTRON MICROSCOPE IMAGE OF MOLYBDENUM(IV) DISULFIDE (MoS_2) CRYSTALS
BY DR ANDREW SULLIVAN, INSTITUTE FOR FRONTIER MATERIALS, DEAKIN UNIVERSITY

RESEARCH OUTCOMES & IMPACT

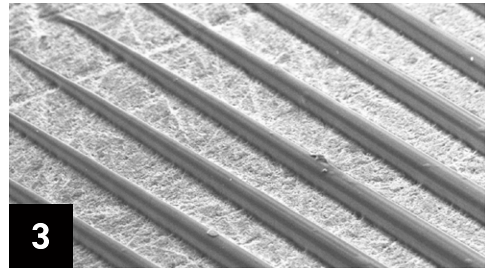
Take a closer look at this year's research highlights – all enabled by Microscopy Australia. With over 3,500 researchers accessing our facilities annually, here are just a few of their recent findings.



1 ARE PONG-PLAYING NEURONS THE FUTURE OF AI?

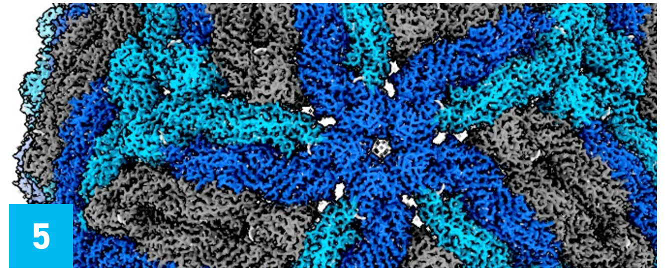


2 SEEING ATOMS TO CREATE ADVANCED ALLOYS

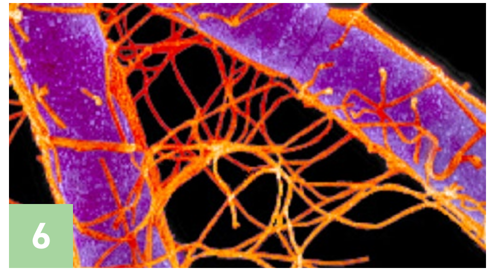


3 MICROTAU: REDUCING DRAG TO SAVE FUEL

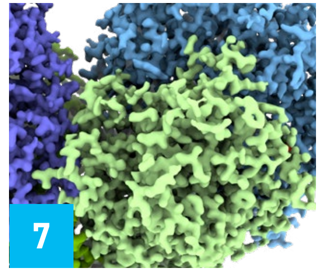
4 FUNGI FOR FIRE SAFETY



5 VACCINE DEVELOPMENT PLATFORM SUPPORTS AGRIBUSINESS

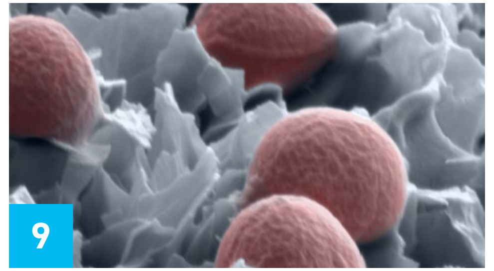


6 KILLER PEPTIDES TO TACKLE SUPERBUGS

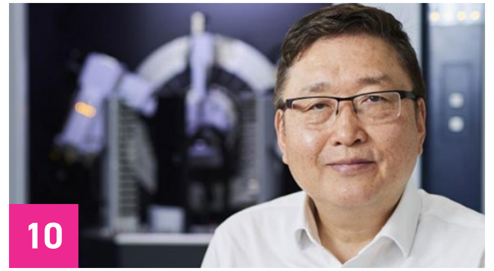


7 ELECTRICITY FROM THIN AIR

8 'OILY GUNK' A RED-HERRING FOR EARLY LIFE ON EARTH?

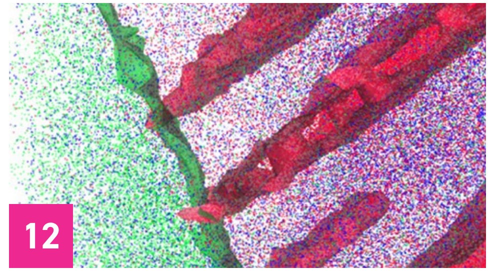


9 ANISOP: INFECTION RESISTANT DENTAL IMPLANTS INSPIRED BY NATURE

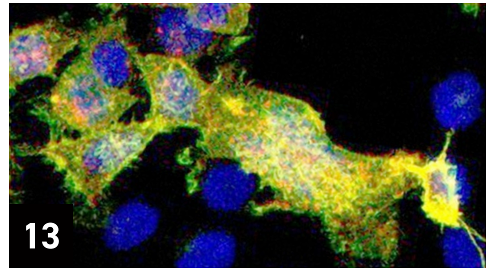


10 3D-PRINTED CATALYSTS FOR SUSTAINABLE CHEMICALS

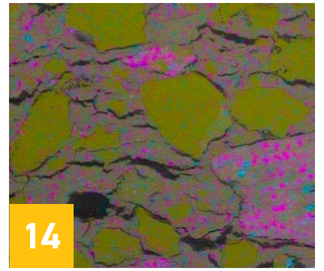
11 ALPACAS JOIN FIGHT AGAINST COVID-19



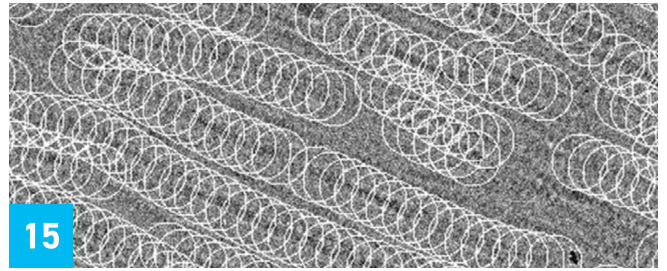
12 ANALYSING ASTEROIDS TO PREVENT COLLISIONS



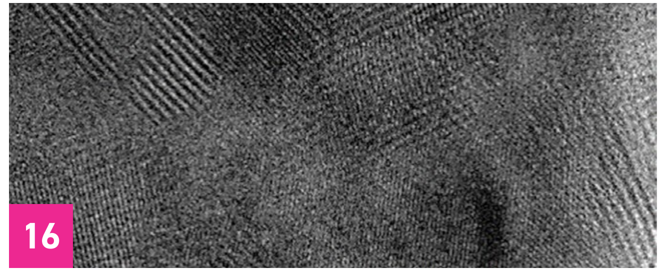
13 DEFENDING OURSELVES AGAINST COVID-19



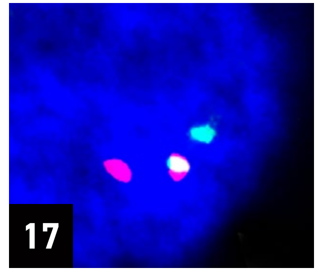
14 A MULTICULTURAL TAPESTRY



15 MOLECULES OF DEFENCE AND ATTACK



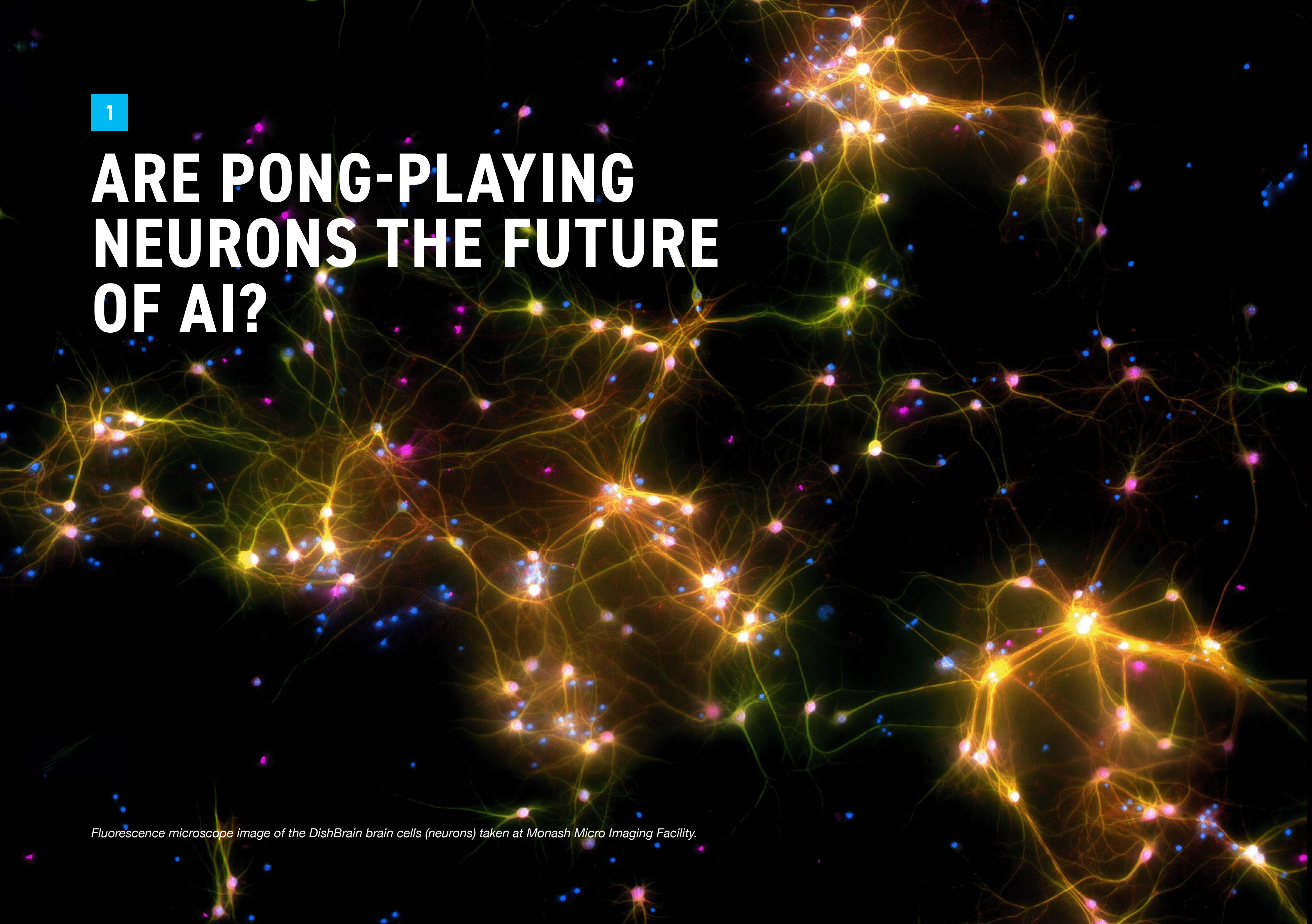
16 SOLAR CELL DREAM TEAM BREAK OWN WORLD RECORD



17 LINK BETWEEN 'STICKY' RNA AND CANCER REVEALED

KEY TECHNOLOGIES

- CRYOGENIC ELECTRON MICROSCOPY
- ATOMIC-SCALE MICROSCOPY
- HIGH-SENSITIVITY MICROANALYTICAL TOOLS
- CORRELATIVE TECHNIQUES



1

ARE PONG-PLAYING NEURONS THE FUTURE OF AI?

Fluorescence microscope image of the DishBrain brain cells (neurons) taken at Monash Micro Imaging Facility.

CHALLENGE

Neurons are incredibly space and energy efficient. The human brain is thought to be able to perform an exaflop – one quintillion (10^{18}) operations per second – using only 20 watts of power. The Oakridge Frontier, one of the most advanced supercomputers in the world, requires 1 million times more power and over 680 square metres of space to do the same. If neurons could be harnessed for computing, it could revolutionise the industry.

Additionally, researchers working in neuroscience face a common challenge: the best model for research is the human brain, however, it's rarely ethical to perform experiments on living humans. This means much research into neurological disorders and consciousness rely on animals and limited computer models. A human–neuron based model could open up new pathways for neurological research.

RESEARCH

An international team of scientists, led by Dr Brett Kagan from Melbourne-based start-up, Cortical Labs, have embarked on a project called DishBrain. The goal is to develop a biological computer that can outperform traditional electronic computers in specific applications while consuming significantly less energy.

Mouse and human neurons were placed on an electrode array that could stimulate the cells and record their activity. The neurons were connected to a game of Pong where they received electrical feedback about the position of the ball and paddle via the electrode array. In just under five minutes of gameplay brain cells coordinated their activity to successfully hit the ball, demonstrating a learning response.

The "free energy principle" suggests that neurons strive to reduce the unpredictability of their environment. In Pong, by hitting the ball the neurons learned to avoid uncertainty and organised their signalling activity to play the game effectively.

Scanning electron microscopy at Microscopy Australia's Monash University facility, the Ramaciotti Centre for Cryo-EM, was used to examine the integration of neurons into the high-density multi-electrode array.

Next, they plan to explore the brain cells' behaviour under the influence of alcohol, to observe how they organise themselves when "drunk." This new avenue of research could help us understand the adaptability of neurons to altered environments.

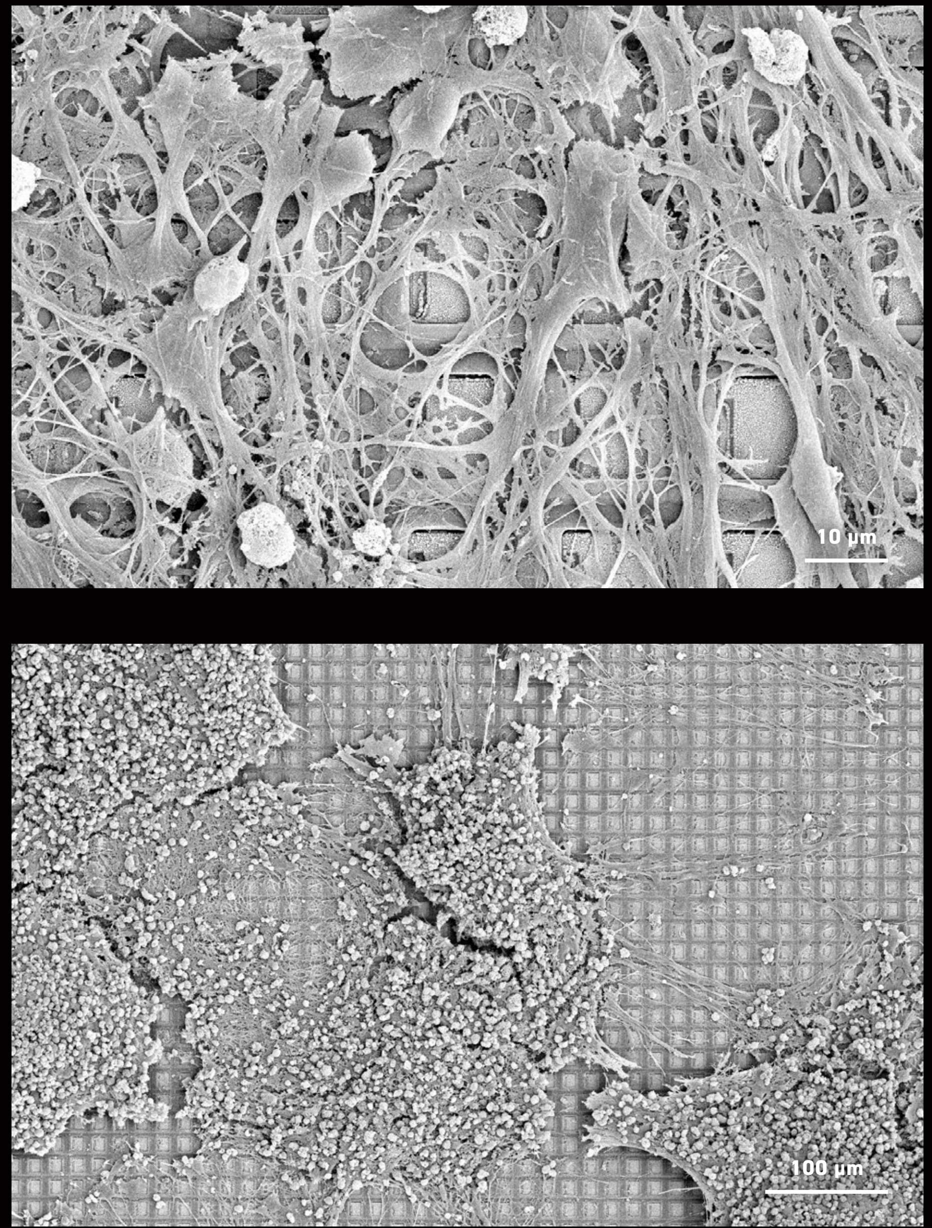
IMPACT

DishBrain's "synthetic biological intelligence" model is a significant step forward in our understanding of intelligence and consciousness. It has not only demonstrated potential as biological intelligence for more efficient computing, but also for advancing consciousness research and disease modelling. it offers an alternative to animal testing and imperfect computational models, potentially leading to more effective treatments and interventions.

Researcher A/Prof. Adeel Razi of Monash University said "This new technology capability in future may eventually surpass the performance of existing, purely silicon-based hardware. The outcomes of such research would have significant implications."

The team recently received a $600,000 grant from the Australian Office of National Intelligence to create a DishBrain-based AI with new continual learning capabilities. Continual lifelong learning is something current AI cannot do.

B. Kagan et al., Neuron 2022
DOI: 10.1016/j.neuron.2022.09.001



Cryogenic scanning electron microscopy of the neurons growing on a multi-electrode array.

2

SEEING ATOMS TO CREATE ADVANCED ALLOYS

CHALLENGE

Titanium alloys are crucial for aerospace, biomedical, and chemical engineering applications due to their strength, lightweight nature, and corrosion resistance. However, their brittleness at room temperature poses a challenge. To increase pliability while maintaining strength, researchers are developing high-performance titanium alloys.

Many titanium alloys incorporate aluminum and vanadium within the atomic structure to enhance ductility. Replacing aluminum with oxygen could boost strength by 20 times. The drawback of oxygen with current production methods is that the atoms escape their intended locations and move through the atomic structure of the alloy, collecting to form weak points, causing embrittlement. Iron is a cheaper vanadium alternative, but high iron content has previously led to undesirable mechanical properties. A new production method is needed to realise the value of oxygen and iron as alloying elements in titanium.

RESEARCH

Researchers from the University of Sydney, RMIT University, Hong Kong Polytechnic University and Melbourne company Hexagon Manufacturing Intelligence have published a breakthrough study in *Nature*. They used Laser Directed Energy Deposition (L-DED), an additive manufacturing technique that is ideal for large and intricate objects, to control and lock-in the locations of oxygen and iron in the alloy. The process allows the creation of alloy segments with high oxygen content for strength and segments with low oxygen content for ductility. These segments can be tuned to make the alloy stronger, or more ductile, depending on its intended end use.

Advanced atomic-scale microscopy called atom probe tomography (right) at Microscopy Australia's University of Sydney facility was used to confirm the 3D locations of iron and oxygen atoms within the alloy. Our linked laboratory at RMIT provided critical insights for the multi-scale characterisation.

IMPACT

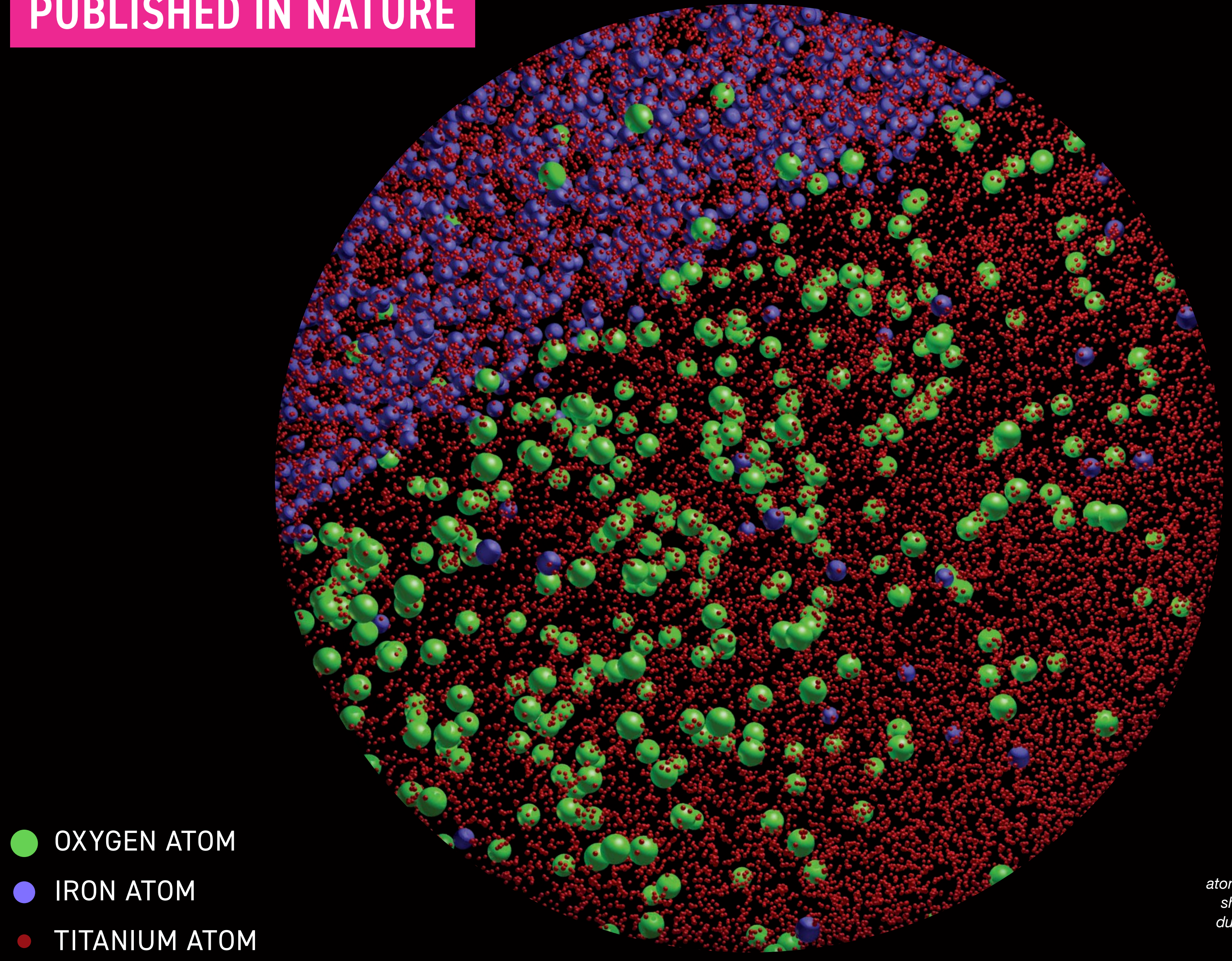
This new design will provide lighter, stronger, cheaper, and more ductile titanium alloys for applications in aerospace, defence, transport, medical implants, and more. It also presents an opportunity to utilise iron- and oxygen- rich sponge titanium as a feedstock, a waste product of mainstream titanium production, reducing the titanium industry's carbon footprint. This breakthrough offers tremendous potential to reduce waste and environmental impact while delivering superior performance.

Senior authors Profs Ma Qian (RMIT) and Simon Ringer (Sydney) are excited about the wider potential beyond titanium of this design approach, and the implications for other critical metals like zirconium, niobium, and molybdenum. Australia's collaborative research infrastructure strategy played a vital role in this work, with the potential for future advancements in advanced manufacturing.

"In many ways, this work showcases the power of Australia's national collaborative research infrastructure strategy and sets the scene for extending this strategy into advanced manufacturing,"said lead researcher Zibin Chen.

T. Song et al., Nature 2023
DOI: 10.1038/s41586-023-05952-6

PUBLISHED IN NATURE



Atom probe tomography map of atoms in the 3D-printed titanium alloy showing two distinct segments: the ductile low oxygen segment and the stronger high oxygen segment.

3 MICROTAU: SAVING FUEL WITH MICROSTRUCTURES

Australian start-up MicroTau's sharkskin-inspired coating and novel manufacturing technique, both developed with the help of Microscopy Australia's microscopes, could save commercial aviation and shipping over US$34 billion in fuel costs and 225 million tonnes of CO_2 emissions annually.

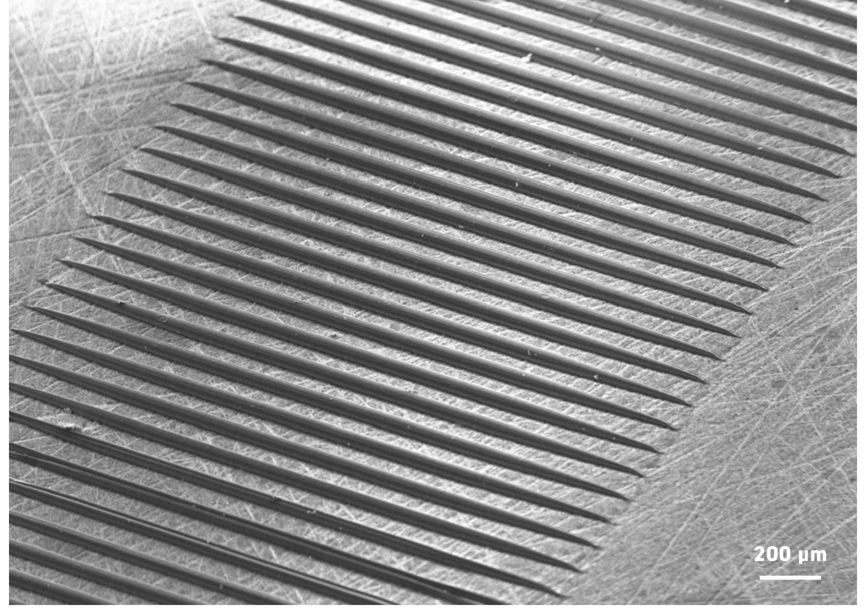
Microscopic patterns found on many plants and animals have functional properties that have evolved over millions of years. For example, sharks have thousands of microscopic overlapping 'scales' structured in a way that reduces drag, allowing them to glide swiftly and silently through the water.

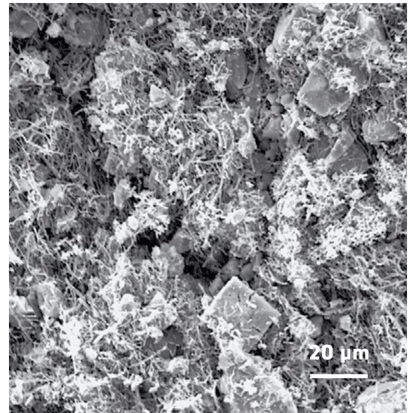
Inspired by these structures, MicroTau is creating drag-reducing coatings. It is hoped that these will reduce the tens of billions of dollars spent each year on fuel in aviation and shipping. They have developed an innovative ultraviolet curable coating that allows these microstructures to be applied to many surfaces.

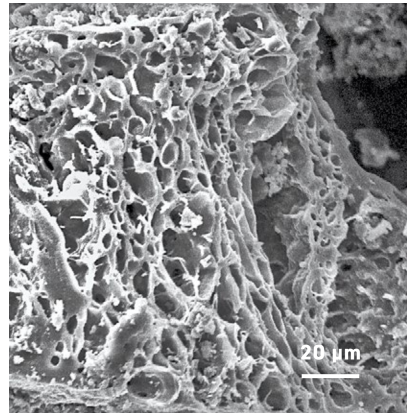
Microscopy Australia's University of Sydney facility has played a key role in the development of this technology, and they continue to play a role as MicroTau develops new microstructures and techniques. The Australian National Fabrication Facility, another NCRIS funded project, has also been instrumental in development of this technology.

Moving forward, MicroTau is also investigating new anti-fouling, anti-bacterial, and optical structures. Our University of Sydney facility is being used in a collaboration with Prof. Chiara Neto's team and MicroTau to test new microstructures for anti-fouling of ships. Anti-fouling involves inhibiting the growth of marine life, such as barnacles, that increase drag and therefore fuel costs. Scanning electron microscopy is being used to examine and compare different hydrophobic structures and their ability to reduce the attachment of marine bacteria. In 2023, a full time PhD student was engaged to enable this ongoing collaboration.

Top: scanning electron micrograph of MicroTau's drag reducing microstructural coating.







4 FUNGI FOR FIRE SAFETY

A hot, dry climate and regular bushfires makes fireproofing a high priority in Australia. Historically, industries have relied on bromide- or chlorine-based chemical flame retardants to safeguard electronics, furniture, and building materials from fire. While effective, these chemicals have been linked to significant health risks. Even modern phosphorus and nitrogen-based flame retardants have been linked to issues with bone and brain development. A safe, non-toxic solution is needed.

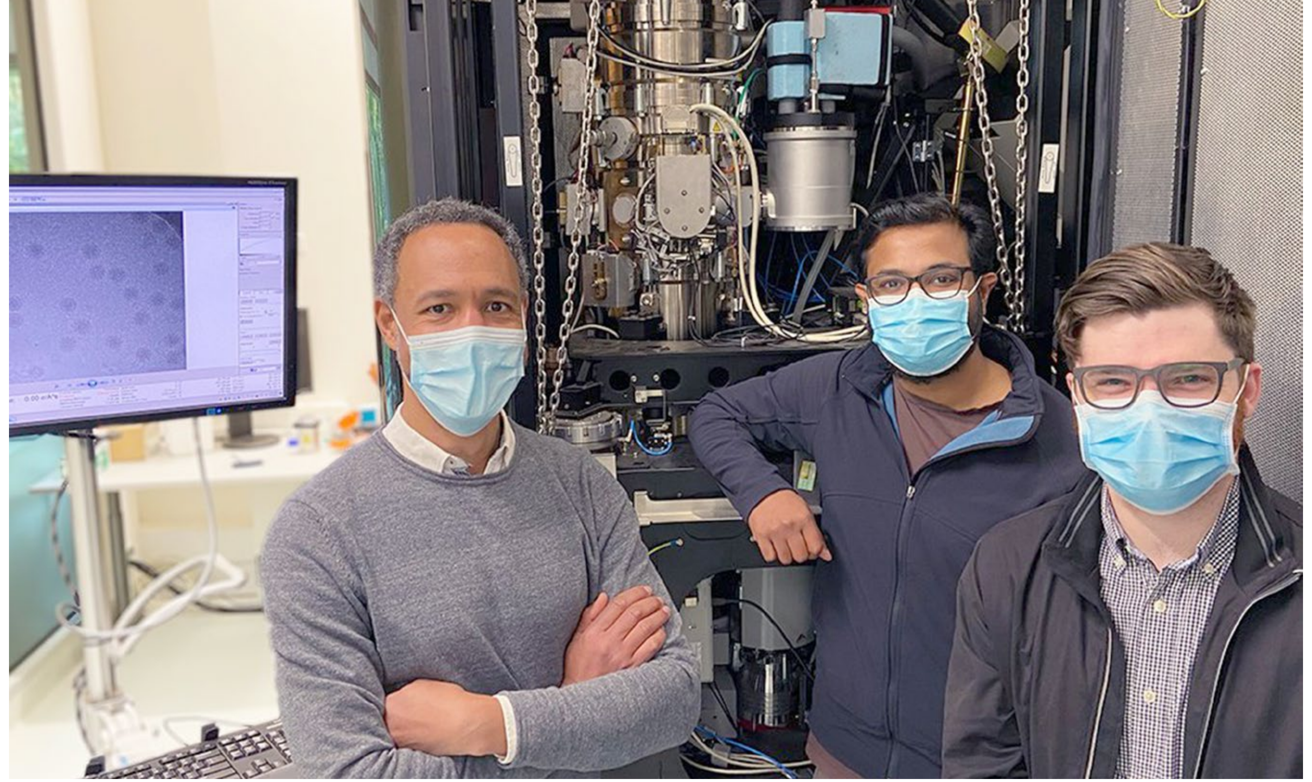
In response, researchers at RMIT, led by A/Profs Everson Kandare and Tien Huynh, are harnessing the properties of mycelium – a fine network of filaments that acts like a root system for fungi. The cell walls of these filaments are made of a polymer called chitin. When exposed to intense heat or fire, the chitin chars to form a protective layer similar to wood charcoal. This layer acts as a shield, protecting the underlying material from heat, preventing combustion. The team found that they could increase the amount of char produced, and improve the thermal insulation provided by the mycelium by treating it with an alkaline substance.

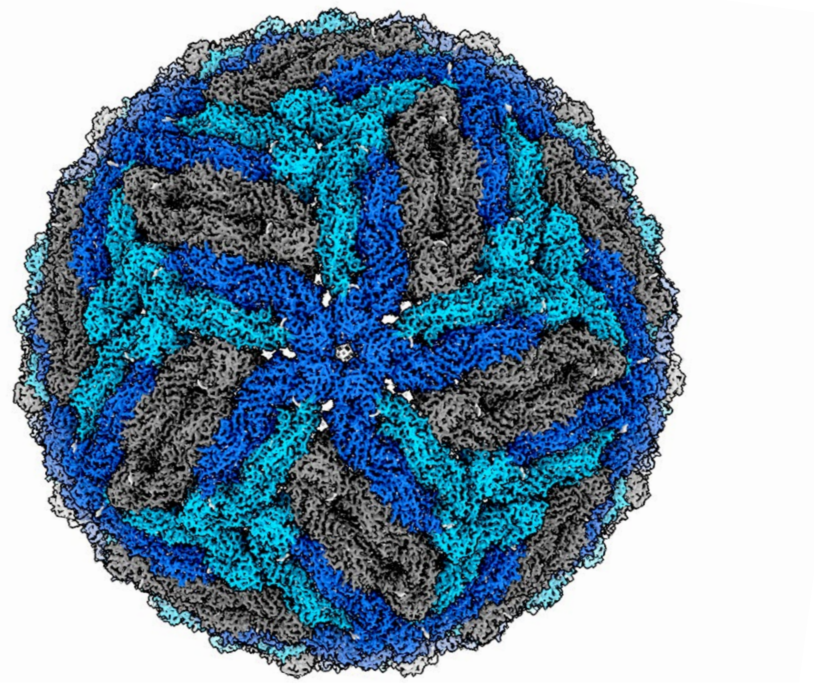
Scanning electron microscopy at Microscopy Australia's RMIT linked lab was used to better understand both the alkaline treatment and the charring process. The team then developed a method to grow the mycelium in paper-thin sheets (centre image) without soil so it can be engineered for different uses – from flat panels for fire proofing buildings to materials for fashion and furnishings.

The researchers are now looking to reinforce the fungal mats with engineering fibres to delay ignition, reduce the flaming intensity and improve fire safety ranking. This research paves the way for safer and more sustainable fireproofing, with potential to export worldwide.

N. Chulikavit et al., Polymer Degr. & Stab. 2023
DOI: 10.1016/j.polymdegradstab.2023.110419

Left: scanning electron micrographs of the untreated (left) and the more consolidated alkaline treated (right) mycellium char.





5 VACCINE TECHNOLOGY SUPPORTING AGRIBUSINESS

A recently developed and patented vaccine platform from the University of Queensland (UQ) is enabling effective vaccines and diagnostics to be made against mosquito-borne diseases known as flaviviruses.

The vaccine development platform is based on a flavivirus, called Binjari, discovered by Dr Jody Hobson-Peters and her team at UQ. It only reproduces in mosquito cells but not in mammals (including humans).

Proteins on the surface of viruses are important in generating an immune response and are often used as vaccines. The Binjari virus is very tolerant to having its surface proteins replaced by those from a disease-causing flavivirus to make a hybrid virus for use as a vaccine. These vaccines have worked well to protect mice against dengue, Zika, West Nile and yellow fever.

One outcome of this research is a new vaccine for Japanese encephalitis virus (JEV) for pigs, developed in collaboration with the Elizabeth Macarthur Agriculture Institute and QIMR Berghofer. JEV is a mosquito-borne disease that infects both pigs and humans, but can only be transmitted between the two by mosquito. The team plans to use the new vaccine to interrupt the transmission of JEV from pigs to mosquitoes, reducing the risk of infection for humans. Recent trials showed that more than 90% of young pigs were protected. The researchers are collaborating with veterinary company Treidlia Biovet to roll out the vaccine commercially in 2023.

Another significant development is a vaccine to protect farmed saltwater crocodiles from West Nile virus (WNV). Crocodile farming faces a considerable threat from WNV. It causes skin lesions in crocodiles, rendering their hides unsellable and costing the industry millions of dollars each year. Vaccinated crocodiles show a good immune response and long-term protection is now being assessed. The researchers are working with the Centre for Crocodile Research in Darwin to commercialise the vaccine.

The hybrid Binjari viruses are also being used in lateral flow tests (like COVID-19 RATs) for flaviviral diseases. This suite of vaccines and diagnostics has the potential to make a significant impact on public health and Australian agribusiness.

Dr Daniel Watterson at UQ and Dr Fasséli Coulibaly at Monash University, in collaboration with Dr Hobson-Peters, used cryo-electron microscopy at Microscopy Australia's UQ and Monash facilities to validate the structures of these hybrid viruses.

J. Hobson-Peters et al., Science Trans. Medi. 2019
DOI: 10.1126/scitranslmed.aax7888

N. D. Newton & J. Hardy et al., Science Adv. 2021
DOI: 10.1126/sciadv.abe4507

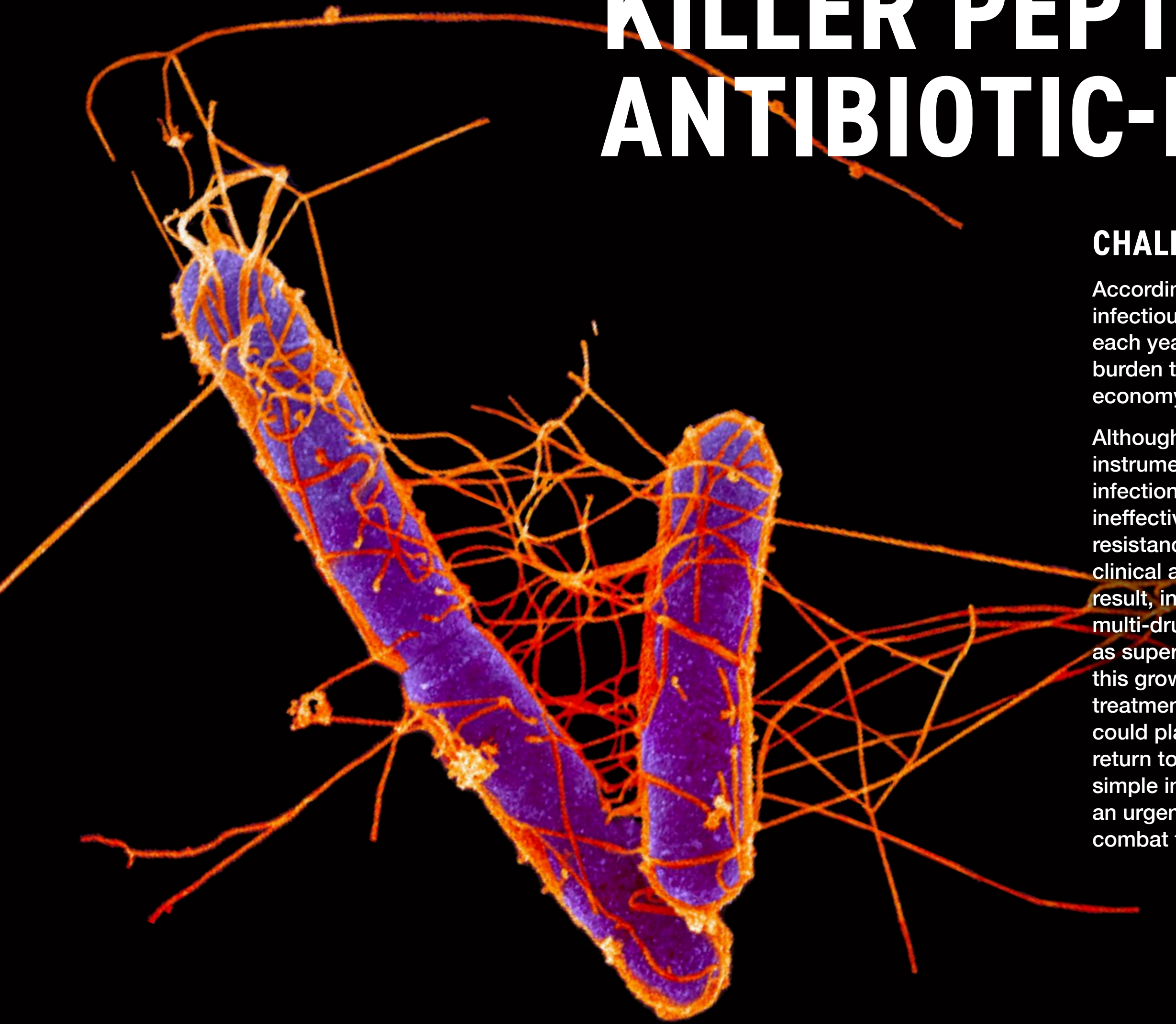
G. Habarugira et al., npj Vaccines 2023
DOI: 10.1038/s41541-023-00688-w

Left: A/Prof. Fasséli Coulibaly, platform scientist Dr Hariprasad Venugopal, and Dr Joshua Hardy from the Biomedicine Discovery Institute, at our Monash Facility.

Right: Reconstruction of a hybrid Binjari virus (~50nm) from cryo-electron microscopy data acquired at our Monash facility, the Ramaciotti Centre for CryoEM.

6

KILLER PEPTIDES TO TACKLE ANTIBIOTIC-RESISTANCE



CHALLENGE

According to the World Health Organisation, infectious diseases kill 17 million people each year, posing a significant economic burden to the Australian and global economy.

Although antibiotics have long been instrumental in the treatment of bacterial infections, many are rapidly becoming ineffective. This is due to rising antibiotic resistance driven by their overuse in clinical and agricultural settings. As a result, infections from difficult-to-treat, multi-drug-resistant bacteria (also known as superbugs) are increasing. Despite this growing threat the number of new treatments available has flatlined. This could place us dangerously close to a return to the pre-antibiotic era, when even simple infections can cause death. There is an urgent need to identify new therapies to combat these bacteria.

RESEARCH

A research team led by Prof. Si Ming Man at the Australian National University has engineered a suite of bacteria-killing peptides derived from guanylate-binding proteins (GBPs), a family of proteins that help our immune system defend us from bacteria. They found that these synthetic peptides can kill bacteria that are prone to antibiotic resistance. These include *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, which are leading causes of hospital-acquired urinary tract, lung, and blood infections; *Neisseria meningitidis*, a primary cause of bacterial meningitis; *Moraxella catarrhalis*, a major cause of ear, nose and throat infections in children; *Francisella novicida*; and *Yersinia pestis*, which causes the plague.

To reveal the mechanisms by which the GBPs target bacteria and the synthetic peptides kill various bacterial species, the team used a combination of fluorescence microscopy, scanning and transmission electron microscopy (left), and correlative light and electron microscopy (right) at Microscopy Australia's Australian National University facility. This microscopy showed that the GBPs and synthetic peptides rupture the bacterial membrane causing it to explode – similar to a balloon bursting.

IMPACT

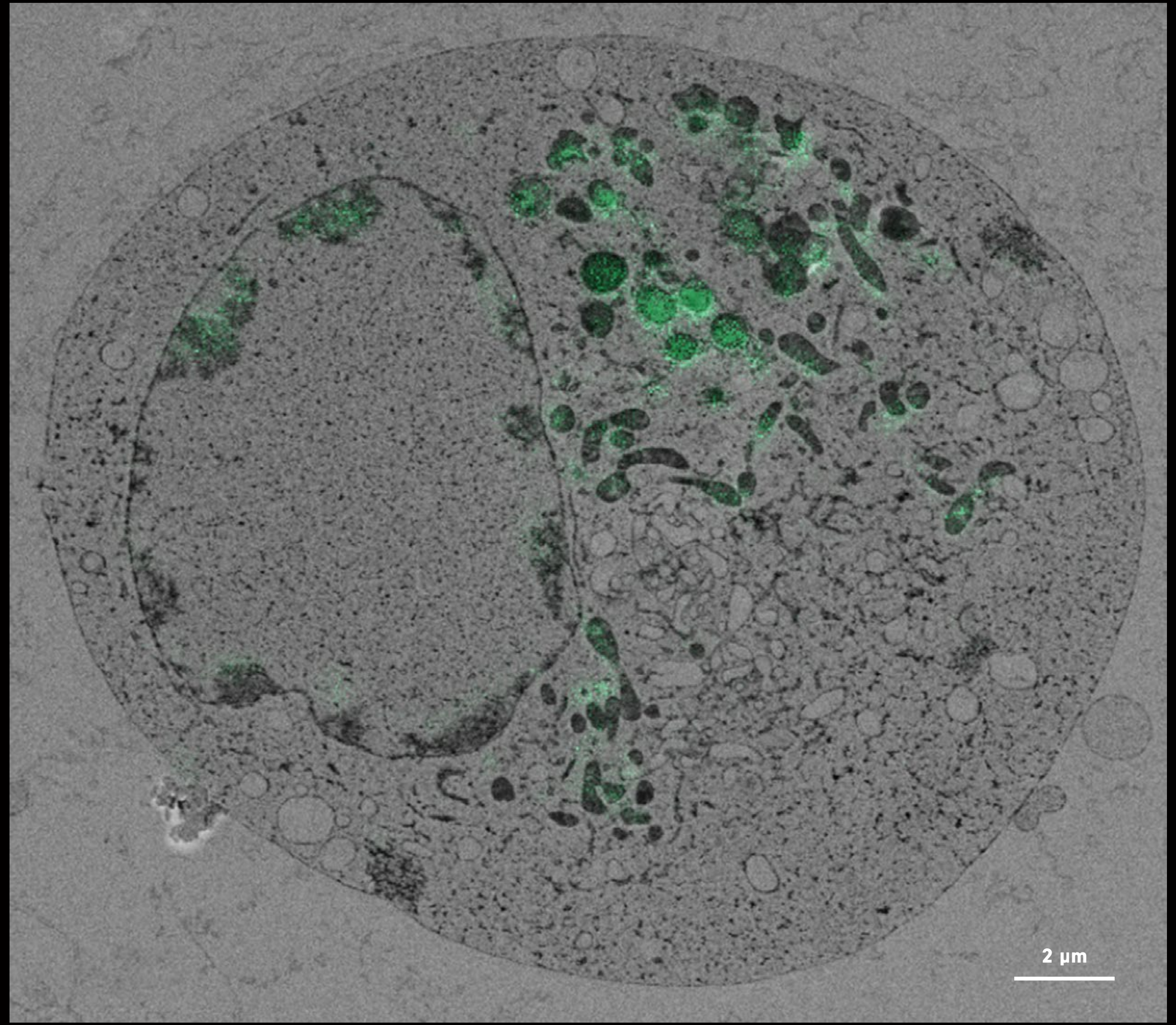
By 2025 antibiotic-resistant bacteria are expected to kill 10 million people every year. This research harnesses the bacterial-killing capacity of our own immune system to combat these bacteria. The new synthetic peptides developed by Prof. Man's team could be translated into therapies for antibiotic-resistant infections, potentially providing an important new tool in the fight against one of the greatest health threats of the 21st century.

S. Feng et al., Nature Communications 2022
DOI: 10.1038/s41467-022-32127-0

D. Enosi Tuipulotu et al., EMBO Journal 2023
DOI: 10.15252/embj.2022112558

Left: Scanning electron microscope image of sepsis causing bacteria.

Right: Correlative light (GBP fluorescence in green) and scanning electron microscope image (grey; inverted contrast) of a macrophage infected with the bacterium species Moraxella catarrhalis, showing GBP targeting the bacteria.



7

ELECTRICITY FROM THIN AIR

Two of the project leads, Ashleigh Kropp and Dr Rhys Grinter, in the Grinter Lab at Monash University.

CHALLENGE

Finding alternative and sustainable energy sources to power future technologies is an ongoing challenge. In nature, many biological systems have developed efficient ways of converting chemicals into energy using enzymes. Human engineering is yet to come close to achieving this level of efficiency. Harnessing these biological systems could allow us to benefit from what evolution has already achieved.

By seeking to understand how bacteria survive in their environments, Monash researchers have made an exciting discovery that could lead to a new source of power.

RESEARCH

Scientists from Monash University, led by Dr Rhys Grinter and Prof. Chris Greening, discovered that an enzyme produced by a common bacterium found in soil, naturally converts hydrogen in the air into electricity. Their discovery is now published in Nature.

Many bacteria use enzymes to convert hydrogen from the environment into energy. However, the soil bacterium *Mycobacterium smegmatis* has an enzyme called Huc, which is different. When isolated, it is very stable and can tolerate temperatures from –80°C to 80°C.

The team's experiments showed that Huc can generate an electrical current from hydrogen in the air and that this current was enough to power a small electrical circuit. Huc can generate this current at very low levels of hydrogen: much lower than other enzymes, although it does produce more current when more hydrogen is available. Unlike other hydrogen-converting enzymes, Huc isn't hindered by oxygen. While Huc couldn't generate large-scale electricity, it could be used to develop small hydrogen-powered devices, such as watches and smartphones.

To work out how the enzyme converts hydrogen into electricity, the team used cryogenic transmission electron microscopy (cryo-TEM) in our Monash University facility to understand the structure of the enzyme.

By understanding the structure of Huc, the researchers can link its structural features with its ability to convert hydrogen to electricity. This can be used to improve the efficiency of this conversion, or even design other enzymes for a variety of useful chemical reactions.

The cryo-TEM revealed a four-lobed structure (right) that sits on a supporting stalk. It contains clusters of nickel, iron and sulfur that facilitate the chemical conversion of hydrogen into electricity and a nanowire made of iron and sulfur clusters that transfer it out of the enzyme. In *M. smegmatis*, this electricity is used to power the bacterial cell. However, it can also be used to power an electrical circuit.

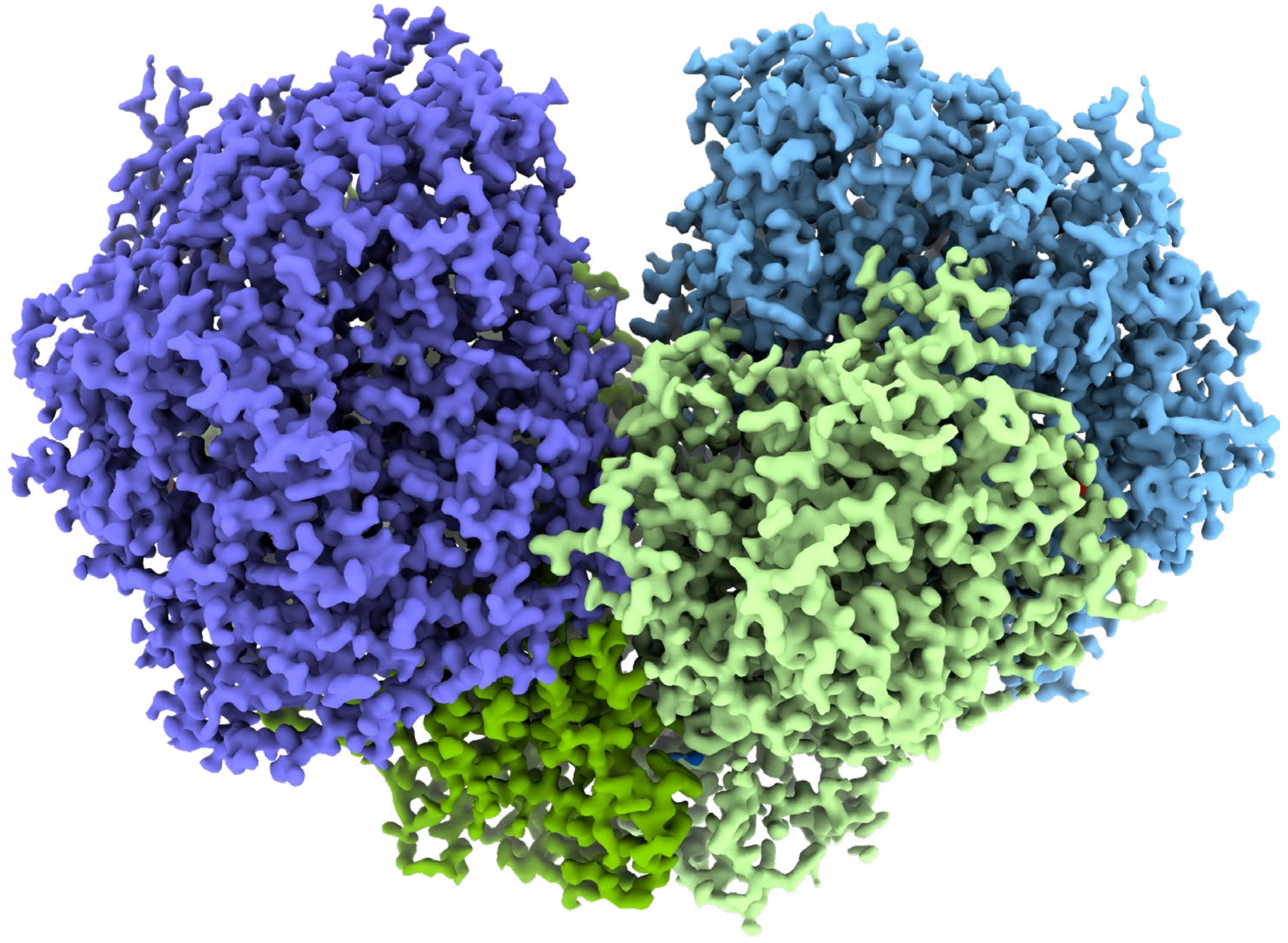
Fuel cells built to use purified Huc could, in theory, continue generating power from the air indefinitely, or at least as long as the enzyme lasts. The team will explore this further.

IMPACT

This enzyme shows potential for generating clean electricity that only requires air as fuel. When commercialised, Huc fuel cells should be ideal for many small devices, especially those where a solar power would not be feasible but ongoing power is essential, such as in underground sensors or implanted medical devices. It also links to Australia's major push towards hydrogen as a fuel source.

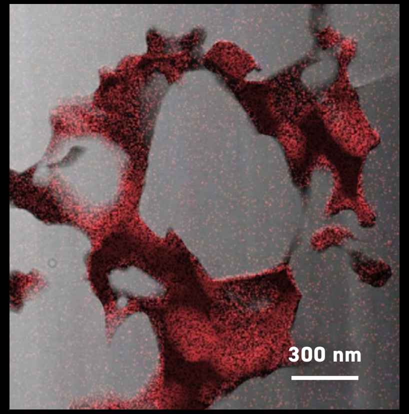
More broadly, the detailed knowledge of Huc's structure and functionality could inform the development of new, synthetic biology approaches to catalysis.

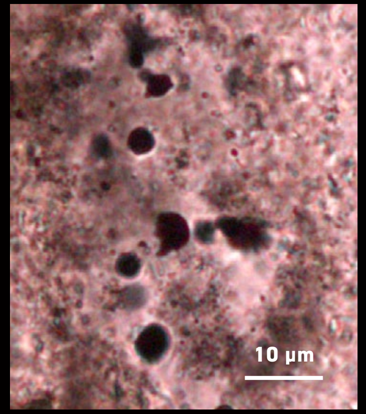
R. Ginter et al., Nature 2023
DOI: 10.1038/s41586-023-05781-7



A Cryo-EM map showing the Huc core catalytic complex at near atomic resolution.

PUBLISHED IN NATURE





Top: Photo of the study site near Marble Bar, Western Australia, by Steve Sheppard. Left: Elemental map of carbon (red) overlaid on a transmission electron micrograph of the organic compounds by Dr Janet Muhling. Centre: the 3.5 billion year old fossilised oil droplets. Right: a sample of the rock, a chert, in which the oil was found by A/Prof. Birger Rasmussen.

8 'OILY GUNK' A RED-HERRING FOR EARLY LIFE ON EARTH?

Researchers from the University of Western Australia (UWA) have unveiled new insights into what was thought to be the fossilised remains of early life on Earth.

The Pilbara region in Western Australia contains some of the world's oldest rock formations and fossils, providing an ideal window into early Earth. These rocks contain trapped oily organic compounds, some as old as 3.48 billion years. Many believe they are fossilised remnants of early microbial life, potentially the precursors of all life. However, a ground-breaking study challenges this view.

Led by A/Prof. Birger Rasmussen and Dr Janet Muhling from UWA, the research suggests that these carbon compounds were not from fossils at all. Using high-resolution microscopy and microanalysis at Microscopy Australia's UWA facility, the team found the carbon was likely to be from an oily solution that had migrated into the rock rather than from fossilised bacteria.

They posit that as seawater interacted with lava on the ocean floor, the water and carbon dioxide could react with mineral surfaces to form organic compounds. These fluids could have then moved through the rock, crystalising into 'oily biomorph' structures resembling fossils. While not ruling out a biological origin entirely, the lack of typical mineral indicators for fossils in these rocks raises questions.

Beyond Earth, the study also sheds light on Mars. Meteorites from the red planet contain similar organic carbon compounds, hinting at comparable chemical processes in Mars' early oceans. The findings highlight potential parallel paths that researchers should consider when investigating development of life on Earth and Mars.

This discovery challenges the idea that carbon unequivocally equals life and adds essential pieces to the puzzle of life's origins.

B. Rasmussen et al., Science Adv. 2023
DOI: 10.1126/sciadv.add7925

9 ANISOP: INFECTION RESISTANT IMPLANTS INSPIRED BY NATURE

Medical and dental implants and devices are central to modern medicine. However, their performance is often compromised by bacterial infections or rejection by the patient's immune system.

Researchers at the University of South Australia led by Prof. Krasimir Vasilev (now at Flinders University), under their spin-out ANISOP, have been striving to replicate unique nano-structures found in nature that are resistant to bacteria and other microbes and apply them to medical devices and implants. The sharp, spiky nano-surface they have developed mechanically kills the same broad range of bacteria known to cause orthopaedic and dental implant infections, and which can lead to the failure of the procedure. This nanotechnology opens up new ways of preventing infections before they become a serious or potentially life-threatening problem.

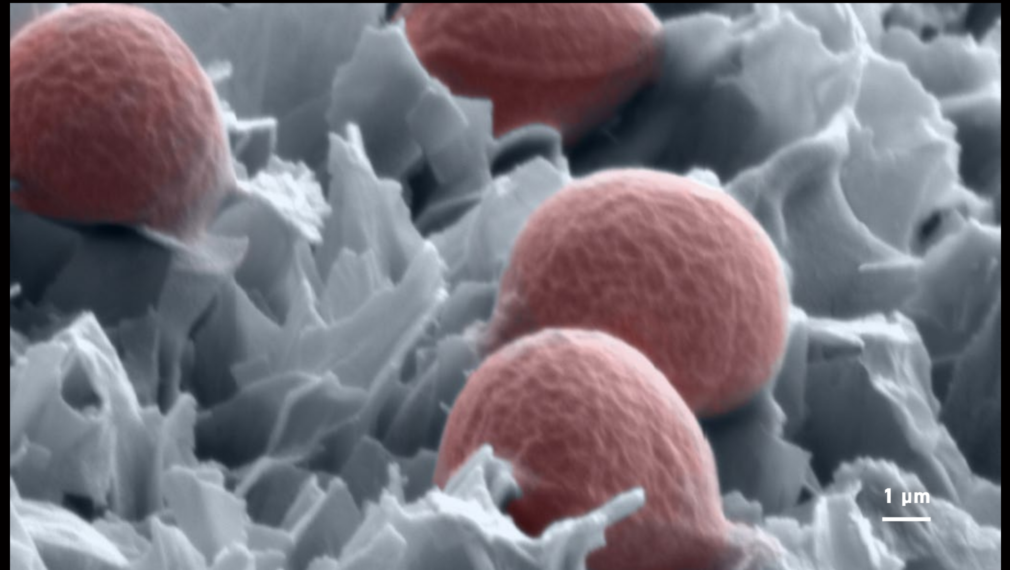
Further research by the team revealed that this spiky nanostructure interacts with blood proteins and immune cells to reduce the inflammation response and enhance healing. Additionally, host cells grow as well, or better, on the spiky surfaces than on flat titanium. These structures can therefore create implant surfaces that are both anti-bacterial and anti-inflammatory, providing solutions to two of the key reasons for implant rejection.

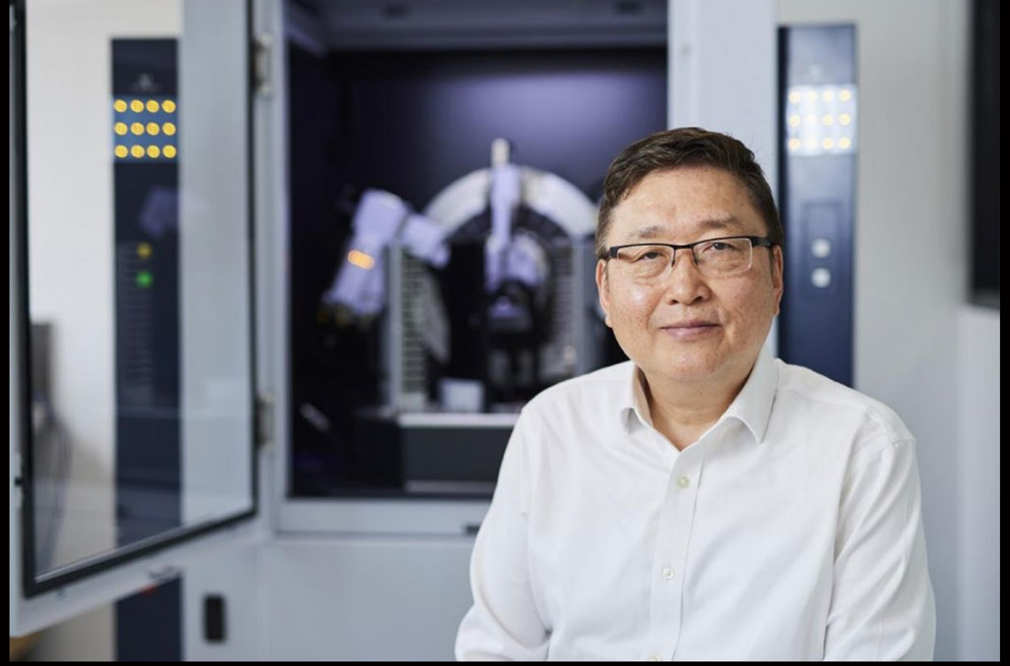
Years of ongoing atomic force microscopy, transmission and scanning electron microscopy and confocal microscopy at Microscopy Australia's University of South Australia, Flinders University and University of Adelaide facilities have made this research possible.

The nano-structural surfaces have been patented in both Australia and the US by spinout company ANISOP Holdings, which plans to apply the anti-microbial and inflammatory surfaces to advanced titanium dental implants. This will lead to:

- fewer infections resulting in reduced economic and health burden associated with implant rejection
- the potential for licensing to other biomedical implants and device applications.

Below: Scanning electron micrograph of bacteria on the nano-structured surface.





The University of Adelaide's Prof. Shizhang Qiao, Director, Centre for Materials in Energy and Catalysis.

10 3D-PRINTED CATALYSTS FOR SUSTAINABLE CHEMICALS

Chemical reactions are at the centre of modern industry, from converting wastewater to hydrogen fuel through to turning vegetable oils into margarine. Catalysts make these chemical reactions faster and more energy efficient. New single atom catalysts act faster and are more energy efficient than traditional catalysts, making them an exciting prospect. However, their adoption has been hindered by the complexity and cost of production.

Now, an international team led by Prof. Shizhang Qiao at the University of Adelaide, has developed a simple, low-cost technique for 3D-printing single-atom catalysts. These catalysts are made up of many individual metal atoms dispersed in a scaffold, creating space between the atoms to allow maximum reaction efficiency. Prof. Qiao's team found they could use a 3D bioprinter with cheap and readily available materials to print a polymer scaffold with the metal atoms embedded within it.

Atomic scale microscopy and elemental mapping at our University of Adelaide facility, along with X-ray spectroscopy at the Australian Synchrotron, were used to confirm the even dispersal of metal atoms within the polymer.

To test the printing system, the team printed a single atom catalyst designed to convert nitrates in wastewater into ammonia – the world's most important fertiliser and one of the most energy intensive industrial chemical processes. Excitingly, this test demonstrated highly efficient ammonia production.

Moving forward, the team are exploring the potential of 3D-printed single-atom catalysts for other critical chemical reactions used in industry. They hope to make these catalysts technically and economically viable within ten years.

F. Xie et al., Nature Synthesis 2023
DOI: 10.1038/s44160-022-00193-3

11

ALPACAS JOIN FIGHT AGAINST COVID-19

CHALLENGE

The COVID-19 virus, SARS-CoV-2, and particularly the Omicron variants, have spread rapidly around the world putting many people at risk. While vaccines can reduce severity, many people are still vulnerable to severe disease from emergent strains and would benefit from effective treatments. Antibodies to the virus can provide this benefit.

Antibodies are large and complex proteins that recognise and stick to invading pathogens, such as viruses, bacteria and parasites. Once the invader is covered with antibodies, other parts of the immune system then dispose of it, protecting you from disease. Alpacas, camels and llamas have unusually small and simple antibodies compared to those in other animals. They are still very effective but are about one tenth the size of most antibodies, hence the name 'nanobody'. Due to their small size, the genes for particular 'nanobodies' can be easily isolated and prepared in the lab in large quantities.

RESEARCH

Researchers at the University of Queensland (UQ), led by Dr Naphak Modhiran, Dr Yu Shang Low and A/Prof. Daniel Watterson have identified a nanobody (W25) that neutralises Omicron sub-variants of the SARS-CoV-2 virus very effectively, even better than it neutralises the Wuhan strain. When tested with live virus in mice, it protected them against infection from both Wuhan and Omicron variants. An alpaca called Budda was the nanobody donor.

The researchers used cryogenic transmission electron microscopy (cryo-TEM) at our UQ facility to identify that W25 binds to a part of the spike protein that doesn't change between the Omicron variants. Collaborators in Germany also used cryo-TEM to show how W25 binds to the same region of the Wuhan spike protein.

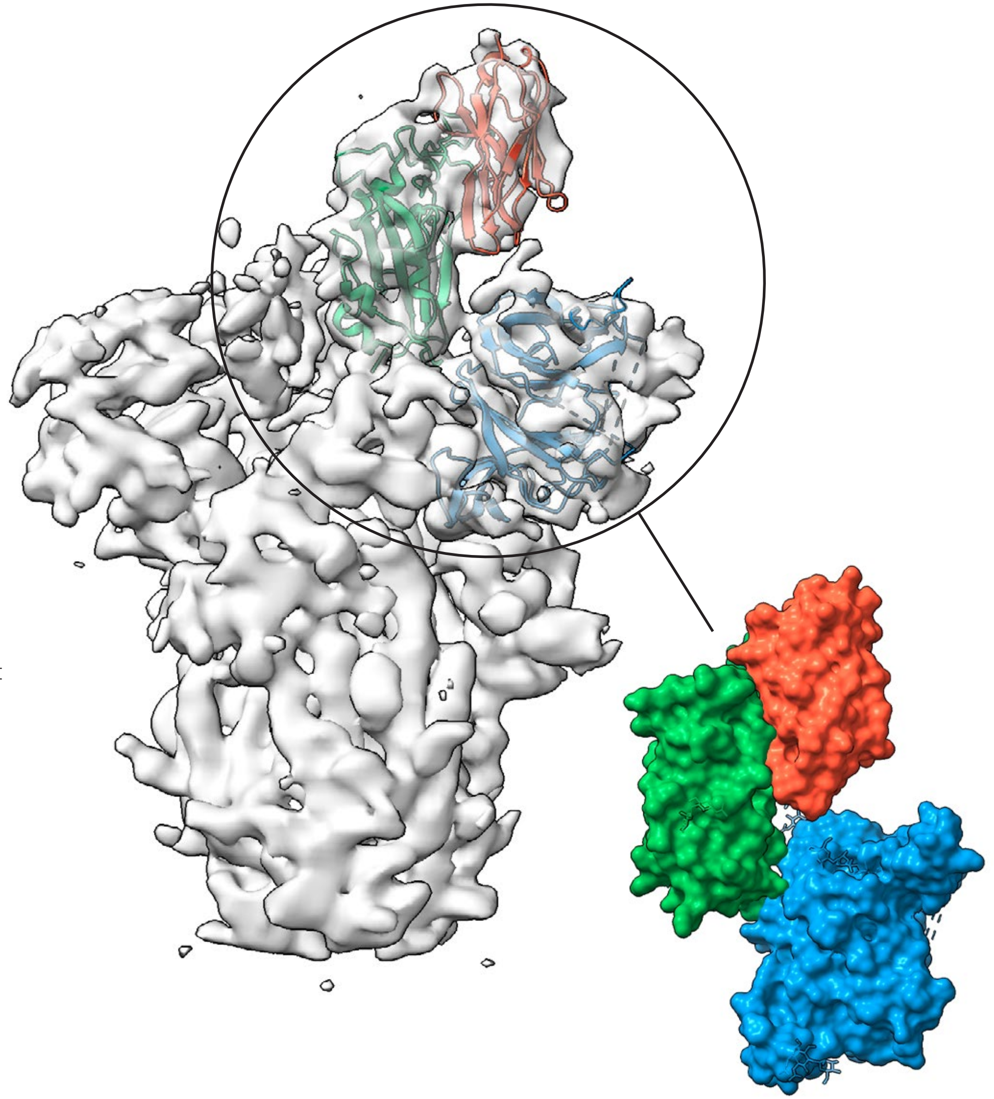
The team also showed that by joining two nanobody molecules together, the strength with which the nanobodies bind to the spike proteins was greatly enhanced. In mice, this made it more effective at neutralising the virus. Nanobodies, including W25, also have the advantage that their small size and stability makes them particularly effective when delivered intranasally, ideally by nebulisation, directly to the lungs.

IMPACT

With SARS-CoV-2 constantly evolving, it is likely that new variants of concern will drive a resurgence of infections. Although vaccination is the main measure against the pandemic, it is not suitable for, or effective in, all patients. Therefore, we still urgently need to provide other means to prevent infection and/or treat high-risk patients. Because of its high efficiency, remarkable stability, and resilience to nebulisation, W25 has high therapeutic potential in SARS-CoV-2-infected individuals.

Working with partners in Brazil, the team is now at the point of moving their research to clinical trials in humans, a further step on the road to using W25 as a COVID-19 treatment.

N. Modhiran et al., iScience 2023
DOI: 10.1016/j.isci.2023.107085



Cryo-TEM reconstruction of a Receptor Binding Domain of the SARS-CoV-2 Spike protein (blue) bound to two neutralising alpaca nanobodies (red and green).

12 ANALYSING ASTEROIDS TO PREVENT COLLISIONS

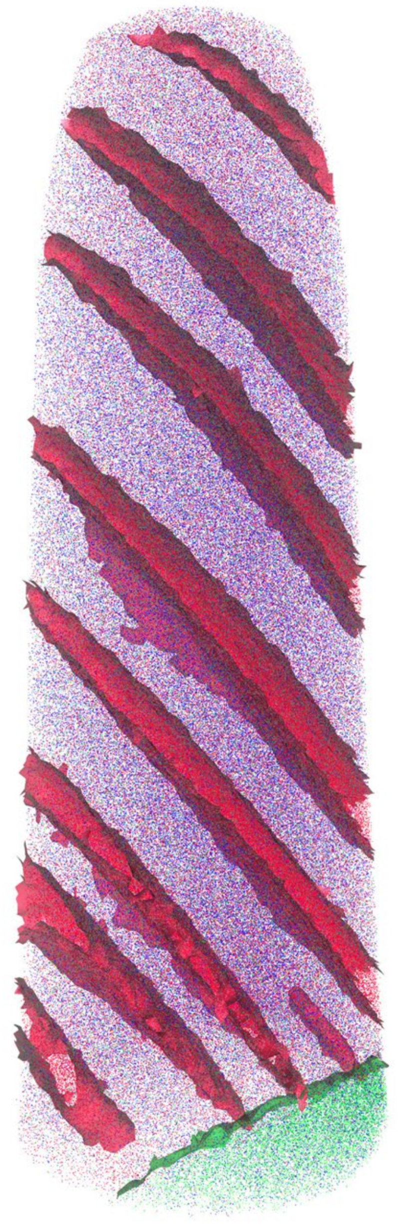
Researchers have used advanced microscopy at the Curtin University linked laboratory to understand the longevity of rubble pile asteroids, revealing important findings for planetary defence.

Rubble pile asteroids are made up of the rubble left behind after a single, giant asteroid, called a monolithic asteroid, is broken apart by a collision. Evidence points to monolithic asteroids having a life span of around 100 million years, however, the life span of rubble pile asteroids is unknown. Because they are entirely made up of loose boulders and rocks it was predicted that they would be less durable, with a life span of only several hundreds of thousands of years in the asteroid belt. However, recent analysis of dust particles from a 500-metre-long rubble pile asteroid, Itokawa, has revealed the opposite.

The new results from an international collaboration led by Curtin University have revealed that the Itokawa rubble pile asteroid is almost as old as the solar system itself. Lead author Prof. Fred Jourdan explained, "The huge impact that destroyed Itokawa's monolithic parent asteroid and formed Itokawa happened at least 4.2 billion years ago. Such an astonishingly long survival time for an asteroid the size of Itokawa is attributed to the shock-absorbent nature of rubble pile material." The findings suggest that rubble pile asteroids are both hard to destroy, and more abundant that previously thought. This knowledge is important for developing mitigation strategies to prevent asteroid collisions with Earth.

The particles from the Itokawa asteroid, returned to Earth by the Japanese Space Agency's Hayabusa 1 probe (left), were analysed at our Curtin University linked lab, the John de Laeter Centre by co-authors and facility leaders, A/Prof. William Rickard and Dr David Saxey, using a range of techniques including atom probe tomography (right). Dating was performed by Prof. Jourdan at the Western Australian Argon Isotope Facility within the same centre. These facilities are supported by another NCRIS project, AuScope.

Co-author A/Prof. Nick Timms said "[Rubble pile asteroids] must be more abundant in the asteroid belt than previously thought, so there is more chance that if a big asteroid is hurtling toward Earth, it will be a rubble pile. The good news is that we can also use this information to our advantage—if an asteroid is detected too late for a kinetic push, we can then potentially use a more aggressive approach like using the shockwave of a close-by nuclear blast to push a rubble-pile asteroid off course without destroying it."



Atom probe tomography data showing the iron-rich layers (red) in a sample from the Itokawa asteroid. Each dot represents an atom.

13 DEFENDING OURSELVES AGAINST COVID-19

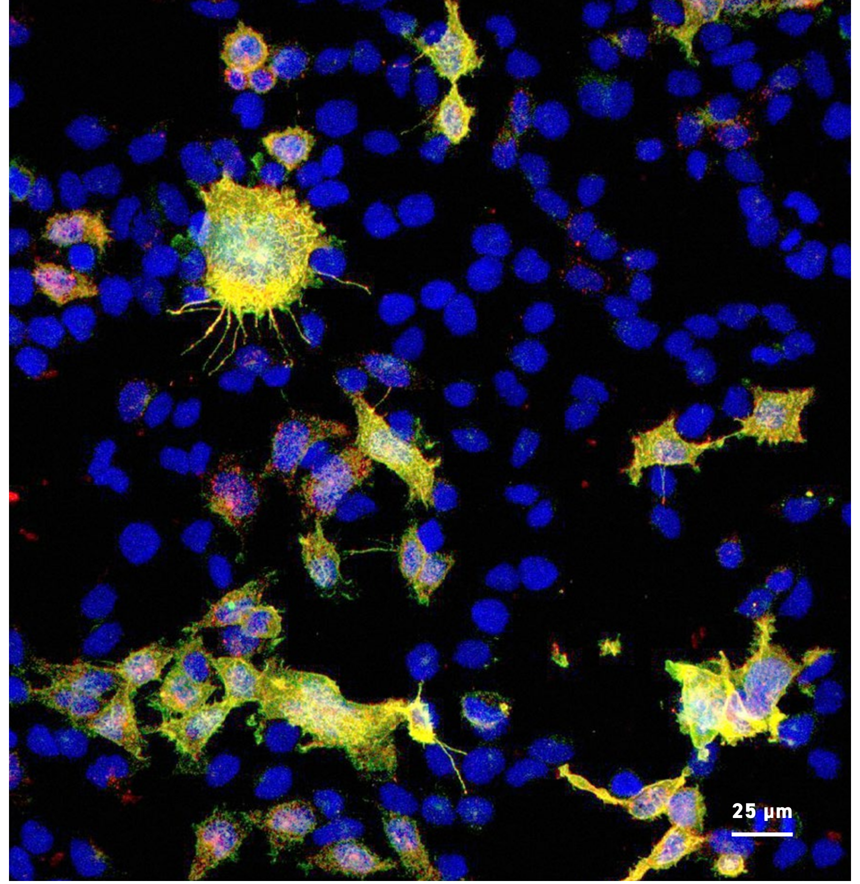
University of Sydney researchers have discovered that a naturally occurring protein helps the body fight off COVID-19.
The protein, called LRRC15, sticks to the viruses and creates a barrier, preventing them from entering and infecting cells. It forms part of the body's innate defense system and could be a target for future anti-COVID treatments.

When SARS-CoV-2, the virus that causes COVID-19, enters the body, the first step in the infection process is for the spike protein on the surface of the virus to attach to a protein called ACE2 on the outside of a host cell. This enables it to enter the cell. However, LRRC15 also binds to the virus, stopping it from binding to ACE2 and taking it out of the infection cycle. LRRC15 is typically found in many protective immune barriers, such as placenta, skin, mouth, throat, and lymph nodes, but only in lungs when they become infected. When lung cells turn on the LRRC15 gene, this also turns up the production of other antiviral molecules while switching off the production of collagen. Switching off collagen helps prevent scarring (fibrosis), as occurs during long COVID. The team and others also found that high levels of LRRC15 in the blood predict less severe COVID-19.

The researchers, led by Prof. Greg Neely, used confocal microscopy at Microscopy Australia's University of Sydney facility to help demonstrate LRRC15–virus binding. Prof. Neely said, "We can now use this new receptor to design broad-acting drugs to block viral infection or even suppress lung fibrosis: there are currently no good treatments for lung fibrosis".

L. Loo et al., Plos Biology 2023
DOI: 10.1371/journal.pbio.3001967

Top: Confocal image from the project showing cultured cells with LCCR15 in yellow and green and the SARS-CoV-2 spike protein in red taken by Dr Cesar Moreno



14 A MULTICULTURAL TAPESTRY

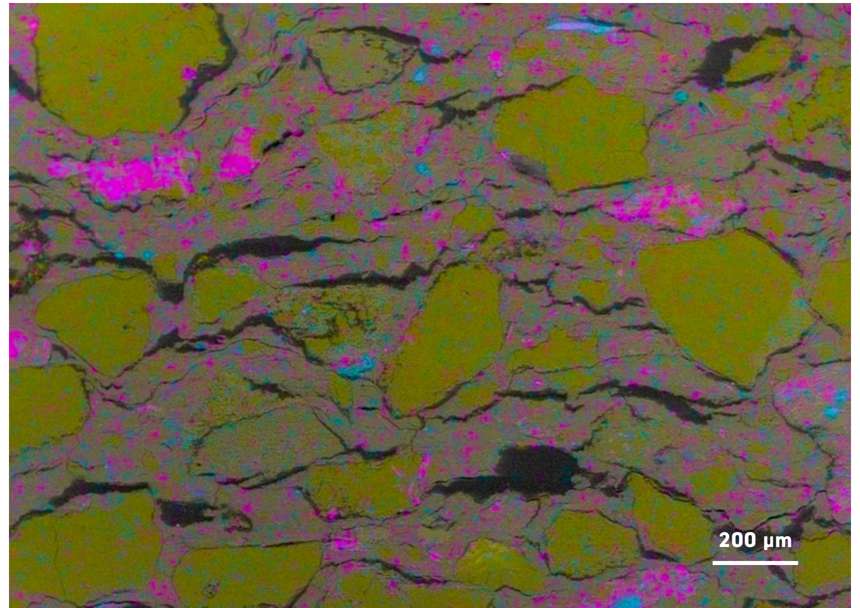
The colonisation of the remote Pacific Islands is one of humankind's largest migrations. Lapita cultural groups migrated from Southeast Asia via Papua New Guinea over the course of several centuries, bringing with them pottery and animals new to the region. By studying the archaeological record, researchers at the Australian National University and UNSW Sydney, led by Dr Ben Shaw, have found clues to discovering new sites of early Lapita occupation on islands off southern Papua New Guinea.

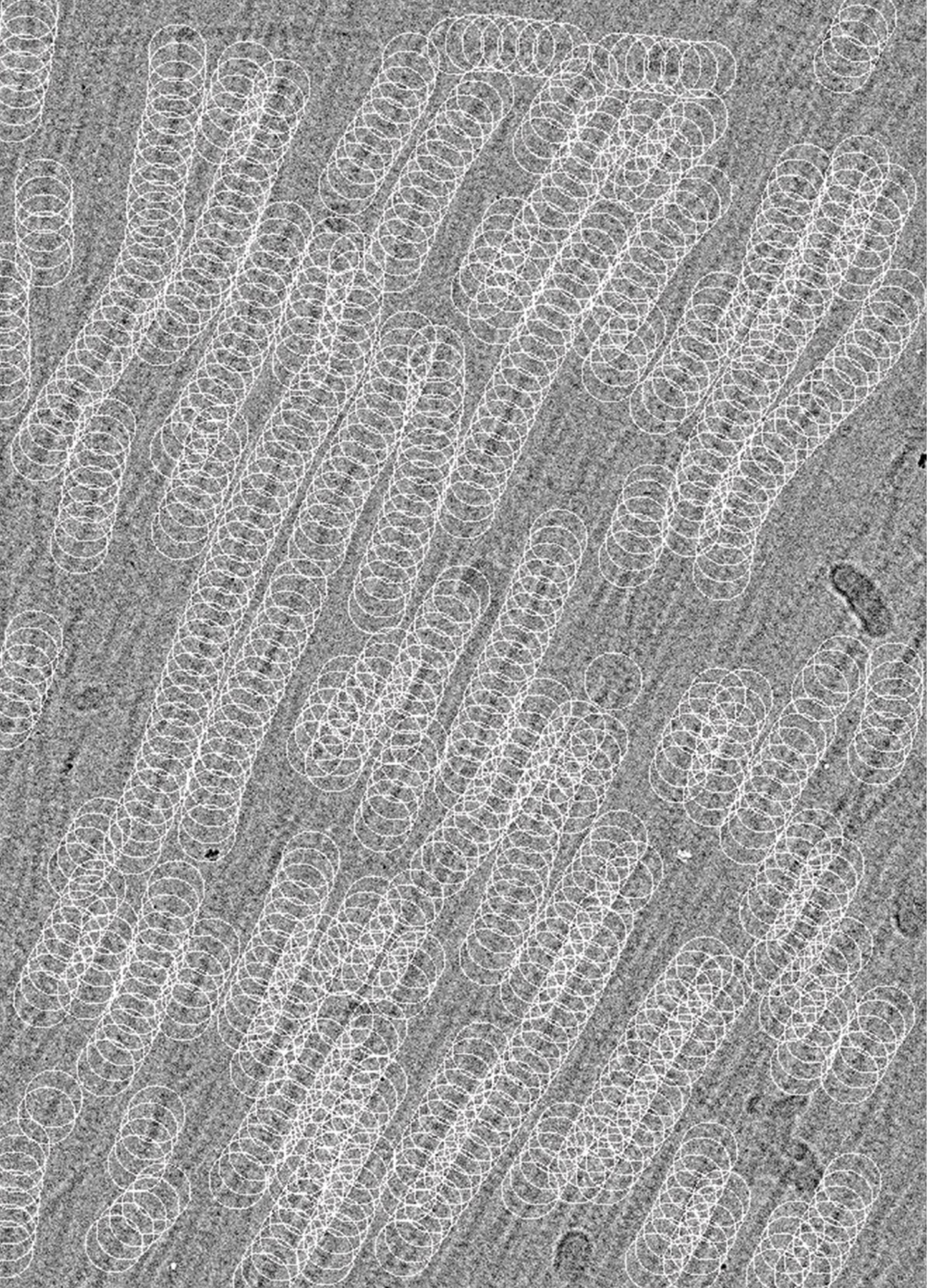
One of these islands revealed human occupation from 4,400 years ago. In the oldest layer they found volcanic glass for tools that originated from an island 300km away, and in slightly younger layers (3,480–3,060 years ago) dog and pig bones: animals only ever found in Lapita sites. Distinctive pottery has previously been used to identify Lapita sites but this was not found in the older layers of the dig, although it was found in younger layers representing periods of more sustained Lapita settlement (from 2,500 years ago) .

Microanalysis at Microscopy Australia's UNSW Sydney facility was used by co-author, Dr Karen Privat, to determine the composition of this early Lapita pottery. Dr Privat found that some of the pottery was made locally and some on nearby islands that had not previously been identified as Lapita sites. This shows both that Lapita potters very quickly adapted to using high quality local clay sources and that this sustained Lapita settlement was supported by a network of Lapita communities on surrounding islands, which can be identified by the minerals used to make the pots. These sites will be investigated soon.

B. Shaw et al., Nature Ecology & Evolution 2022
DOI: 10.1038/s41559-022-01735-w

Bottom: Elemental analysis of one of the pottery fragments showing silicon in green, iron in pink and titanium in blue. This provided a mineral signature that allowed the source of the clay to be identified.

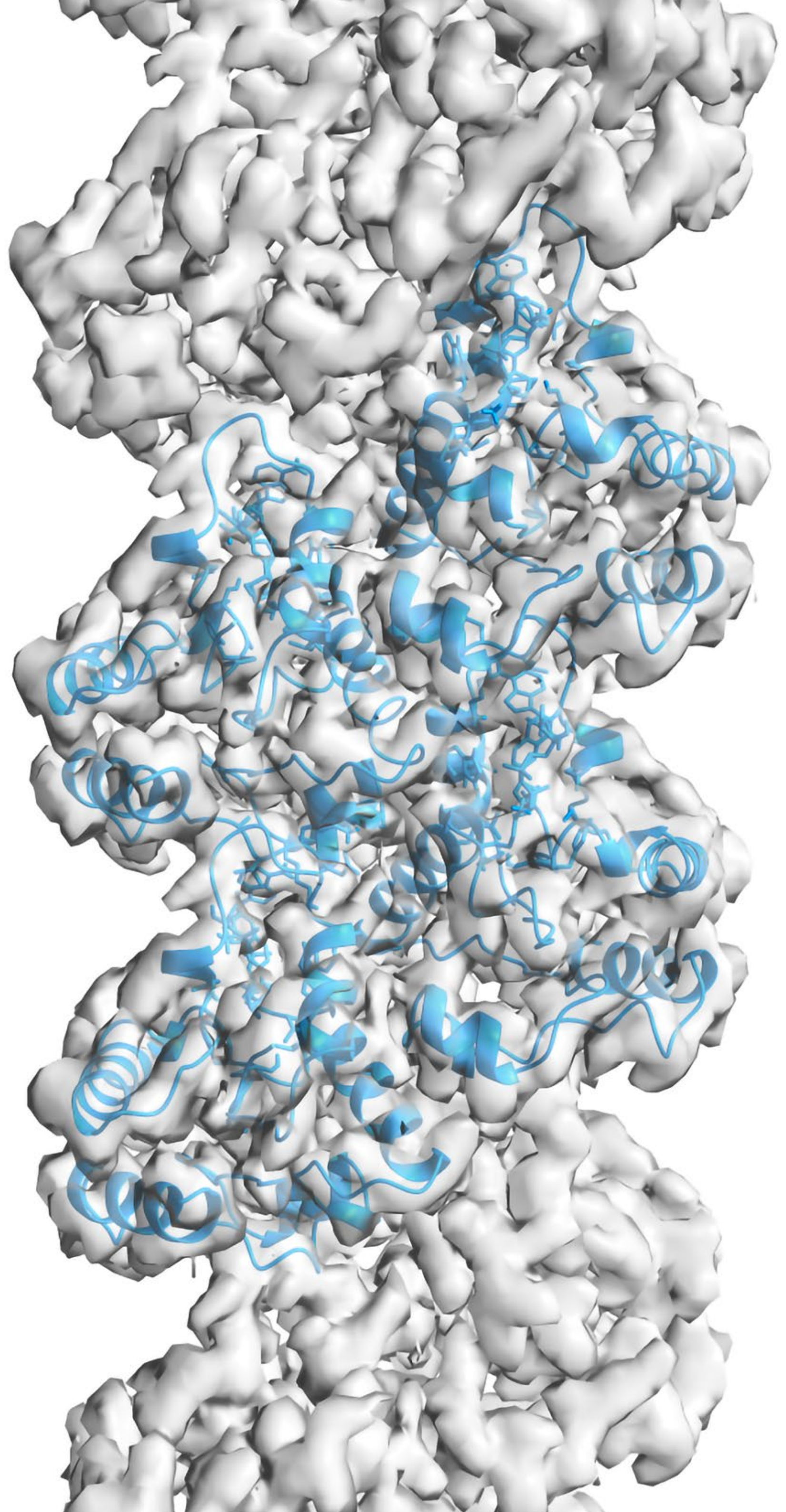




Cryo-transmission electron microscope image of multiple copies of the bacterial enzyme. The circles show individual molecules that were selected for image processing to reveal the final structure that can be seen on the next page.

"THIS STUDY, PUBLISHED IN THE WORLD-LEADING JOURNAL SCIENCE, PROVIDES ATOMIC LEVEL DETAIL OF AN INTRICATE BIOLOGICAL PROCESS."

– Prof. Mark von Itzstein AO



6

MOLECULES OF DEFENCE & ATTACK

CHALLENGE

Understanding how bacteria, plants and animals defend themselves against disease-causing organisms is essential to developing better treatments for disease.

Bacteria need to protect themselves from viruses known as bacteriophages, and plants and animals from viruses, bacteria, fungi and parasites. Many different approaches have evolved in different species, so there is much to discover and harness.

RESEARCH

A major international study, led by Prof. Bostjan Kobe from the University of Queensland (UQ) and A/Prof. Thomas Ve from Griffith University has been published in the journal *Science*. It examined how bacteria use a small molecule called nicotinamide adenine dinucleotide (NAD) to protect themselves against bacteriophages.

Using a wide range of techniques, the team investigated an enzyme that changes the structure of NAD into two circular forms. This conversion happens when a bacteriophage infects the bacterium. Once formed, the circular NADs activate the bacterium's immune system to help it fight off the bacteriophage.

Left: The structure of the bacterial enzyme generated from cryo-electron microscopy data at 0.274 nm resolution.

The team worked out how NAD is converted to the circular forms and, by using cryo-electron microscopy at Microscopy Australia's UQ facility, could identify exactly which bits of the enzyme are responsible for the conversion. Using X-ray crystallography they also showed that the circular NAD activates a crucial bacterial defence protein by changing its shape.

Surprisingly, the researchers found that one of these circular NADs (3′cADPR) helps bacteria to infect plants. *Pseudomonas syringae* is a bacteria that infects a wide range of plants and can cause severe economic losses. *P. syringae's* enzyme has developed extra functions that help the bacteria infect the plant. The enzyme is transferred into the plant as the bacterial infection takes hold. This then produces the circular NADs in the plant, which suppresses that plants immune system.

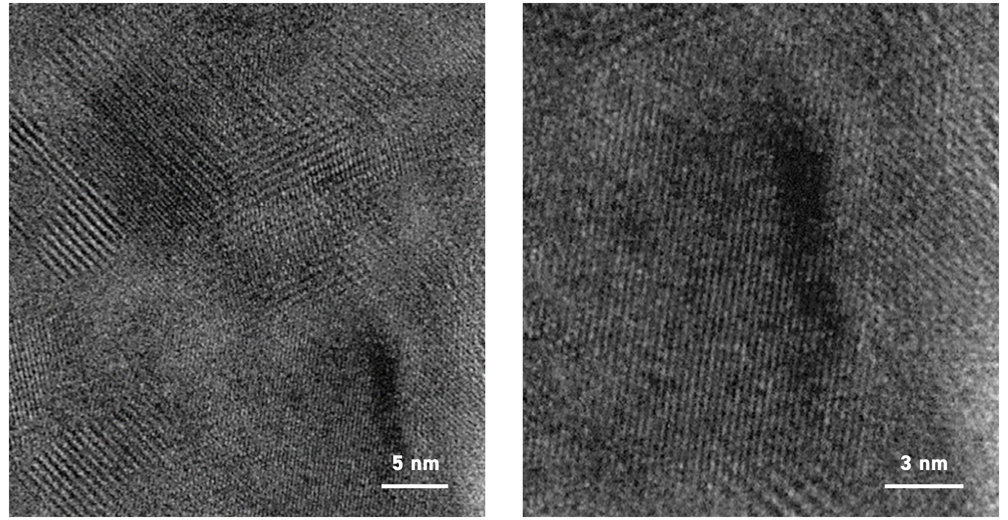
IMPACT

This fundamental research brings substantial new understanding of the complex biology of infection and defence mechanisms, opening up areas of endeavour. This will ultimately inform design of new drugs to target important diseases of plants, animals and humans.

M. Manik et al., Science 2022
DOI: 10.1126/science.adc8969

Dr Jun Peng and A/Prof. Tom White with their record breaking solar cells. Credit: Lannon Harley/ANU.

PUBLISHED IN NATURE & SCIENCE



Atomic scale transmission electron microscope images demonstrating two different atomic structures of perovskite (2D left, 3D right). The lines in these images are rows of atoms in the perovskite structure.

17 SOLAR CELL DREAM TEAM BREAK OWN WORLD RECORD

A team at the Australian National University who are developing a new, ultra-high efficiency solar cell have broken their own world record in what they hope will be an important step in bringing down the cost of solar energy.

The 'tandem' solar cells are created by stacking a perovskite cell – made from a family of materials with a specific crystal structure – on top of a silicon cell. Together they absorb a much wider spectrum of light, producing significantly more energy from sunlight than each individual device could alone. The team achieved an efficiency of 30.3% – meaning 30.3% of sunlight is converted into energy. In comparison, commercial silicon solar cells have an efficiency of around 20%.

Their new technique not only improves efficiency but enhances the operational stability of the solar cells. "Surpassing the 30% mark is significant," said lead author Dr The Duong. "That's currently considered the efficiency threshold for the commercialisation of tandem technology like that used in our study." The researchers also say the solar cells are easier to manufacture as they use a standard fabrication technique, applied to a new material.

The achievement also meets the first of three 2030 'stretch goals' set by the Australian government in 2021 under its 'Solar 30 30 30' target, aiming to reach 30% module efficiency and 30 cents per installed watt at utility scale by 2030.

"The current predictions are that tandem solar technology will be in mass production by 2026. However, more work is still needed to upscale and ensure the technology can be stable in the field over 25 to 30 years," said Dr Duong.

Microscopy Australia's Australian National University facility has been supporting Prof. Kylie Catchpole's research team and the development of these solar cells for over a decade.

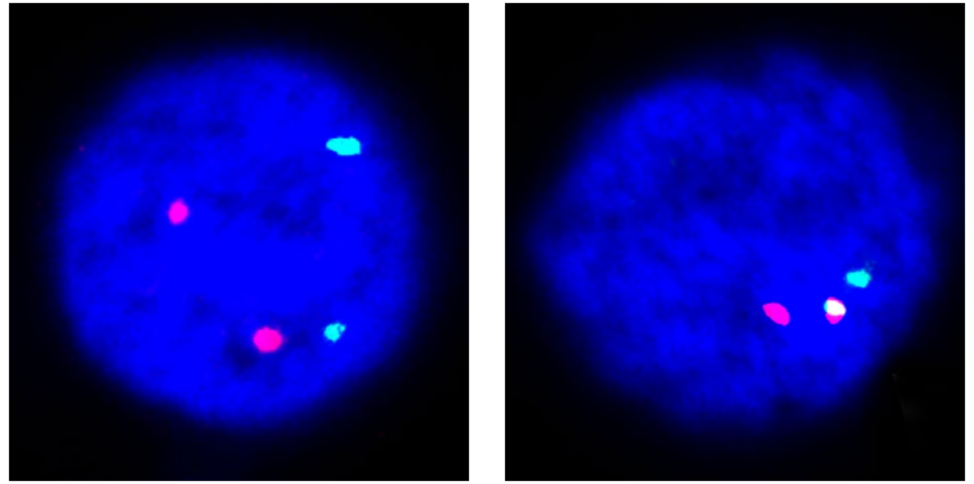
The team is now working to further improve the efficiency and stability of the solar cells. The work has been financially supported by ARENA through the Australian Centre for Advanced Photovoltaics.

T. Duong et al., Adv. Energy materials 2023
DOI: 10.1002/aenm.202203607

J. Peng et al., Nature 2022
DOI: 10.1038/s41586-021-04216-5

J. Peng et al., Science 2021
DOI: 10.1126/science.abb8687

Prof. Simon Conn and Dr Vanessa Conn's team has been researching the role of circular RNAs in DNA damage and cancer genes. Credit: Jonathan Barge, Flinders Foundation.



Two cell nuclei (blue) each showing two genes (pink and turquoise). The nuclei on the right has high levels of circular RNAs causing two of these genes to rearrange so they are now next to each other, overlapping in the image. The rearrangement of these two genes can cause the cell to become cancerous.

17 LINK BETWEEN 'STICKY' RNA AND CANCER REVEALED

Australia has the highest incidence of leukaemia in the world – around 35,000 Australians currently live with the disease.

It has long been known that some changes within a specific set of genes are associated with leukaemia. However, it hasn't been known how these changes come about.

A team of Flinders University researchers, led by Prof. Simon and Dr Vanessa Conn, have made an important new connection between these changes and the actions of circular RNAs, a recently discovered family of genetic fragments present within our cells.

The researchers showed that these circular RNAs stick to the DNA of genes that are commonly damaged and rearranged in cancers, particularly in childhood leukaemias. Prof. Conn said, "This opens the door to using these molecules as new therapeutic targets and markers of disease at a very early stage, when the likelihood of curing cancers is much higher."

The researchers compared blood from newborns (from their heel prick test) who went on to develop acute leukaemia as infants with children without any blood disorders.

They found that one specific circular RNA was present at much higher levels at birth, prior to onset of the symptoms of leukaemia.

The findings suggest that the abundance of the circular RNA molecules is a major determinant for why some people develop these specific cancer-causing changes and other do not.

The team demonstrated that when the circular RNA sticks to DNA it tends to cause breakages that need to be repaired. However, this repair process is not always completely accurate, allowing errors to creep in. Sometimes these are small mistakes, and sometimes they can be catastrophic rearrangements of the genetic material. These rearrangements can convert a cell from a normal cell into a cancerous cell.

By using fluorescent microscopy (left) at Microscopy Australia's University of Adelaide and Flinders University facilities the researchers showed that this process was happening in two different cell types and drove the rapid onset of aggressive leukaemia.

V. M. Conn et al., Cancer Cell 2023
DOI: 10.1016/j.ccell.2023.05.002

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Right: EBSD map of an alloy produced using an energy-efficient, large-scale Additive Manufacturing Technique being developed at the University of Sydney for recycled aluminium. By Halsey Ostergaard.

FUNDED BY

NCRIS National Research Infrastructure for Australia – An Australian Government Initiative
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