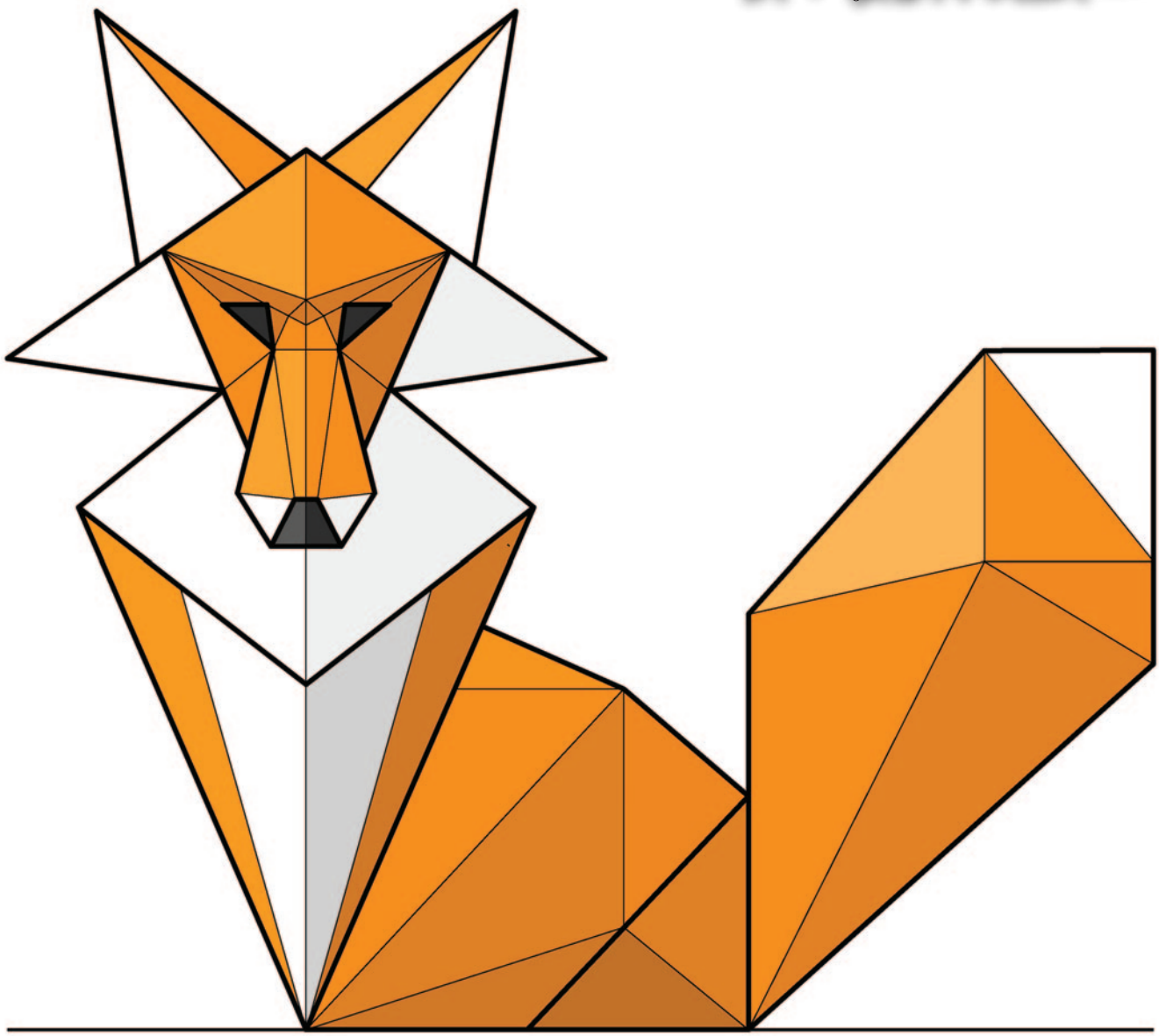
chemistry in Australia
March–May 2022



Controlling the wily fox: a new chemical angle

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March–May 2022


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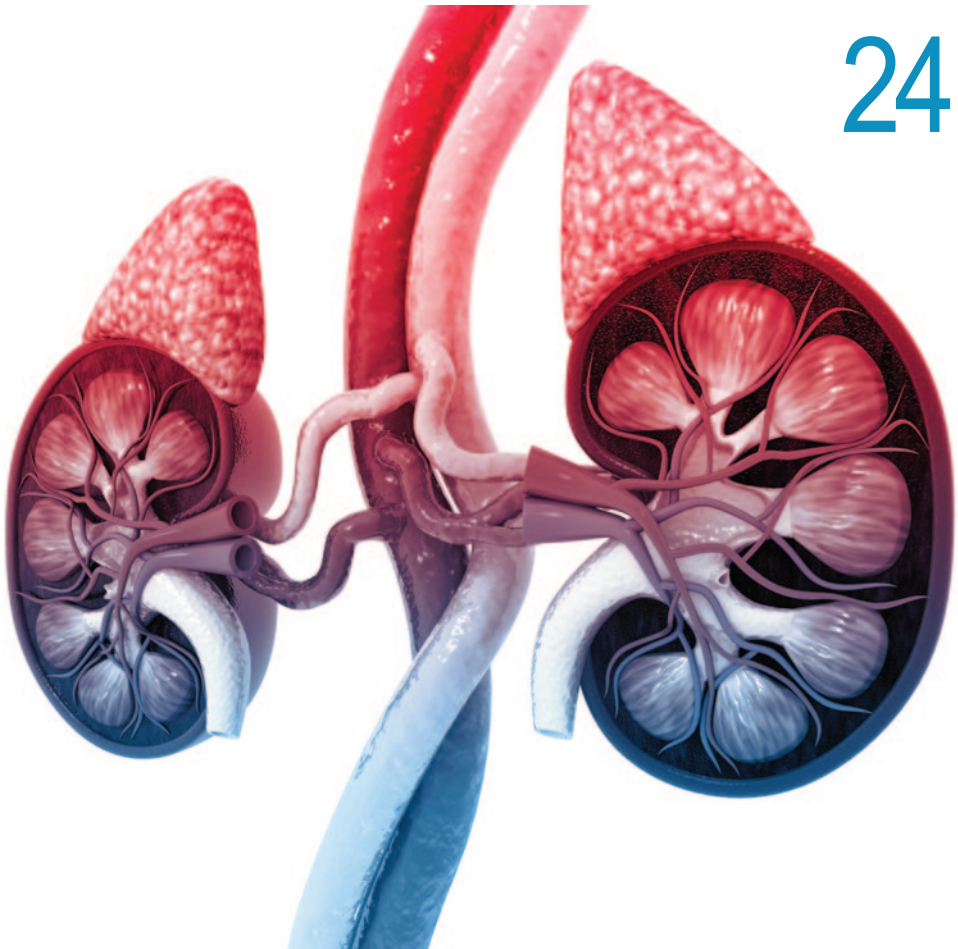
cover story

Towards outsmarting the wily fox: the chemistry of odours

20

As efforts to keep foxes out of Tasmania continue, local researchers are looking at the chemistry of fox secretions as a potential method of control.



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Big vaccine news that didn't go viral

Amidst all the news about COVID vaccination last year, it would have been easy to miss an important announcement on 6 October – and it wasn't the one about the Nobel Prize in Chemistry. In a milestone for vaccine development, the World Health Organization released its first recommendation for a malaria vaccine.

The WHO global advisory bodies for immunisation and malaria recommend RTS,S/AS01 (RTS,S) for use in young children in sub-Saharan Africa and in other regions where transmission of the *Plasmodium falciparum* parasite, which causes the disease, is moderate to high. In sub-Saharan Africa alone, more than quarter of a million children under five are estimated to die from malaria each year.

The other protozoans that can infect us with this disease (although not as severely) are *P. vivax*, *P. malariae* and *P. ovale*. All are transmitted between people by *Anopheles* mosquitoes. This genus comprises about 500 species, but less than 10% of those transmit plasmodia well enough to cause public health problems.

Of course, RTS,S was not a 'breakthrough'. The design of this recombinant-protein-based vaccine arose from extensive academic research and has been several decades in the making. Marketed by GlaxoSmithKline as Mosquirix, it is part of a partnership with the non-profit PATH Malaria Vaccine Initiative, and has support from a network of African research centres.

The genetics and life cycle of malaria parasites are complex, and the human immune response to infection has also proved tricky to unravel. These factors and a non-traditional market for such a vaccine have been barriers to vaccine development.

The latter challenge has been surmounted by sharing risk and cost through public–private partnerships. Gavi, the Vaccine Alliance; the Global Fund to Fight AIDS, Tuberculosis and Malaria; and Unitaid have collaborated to finance the pilot program.

The controversial use of the antimalarials chloroquine and hydroxychloroquine for the treatment of COVID-19 has been much publicised during the pandemic. Senior author of a Cochrane Review assessing evidence on this practice (bit.ly/3rJSKet) commented early last year, 'This review certainly should put a line under using this drug to treat COVID-19, but some countries and health providers are still caught up in the earlier hype and prescribing the drug. We hope this review will help these practices end soon.'

Chloroquine was first synthesised by Johann 'Hans' Andersag at Bayer in Germany in the 1930s as a substitute for quinine. Although it is still in use for malaria, effectiveness varies with *Plasmodium* species and geographical region. Papua New Guinea (where malaria transmission rates are second only to those in sub-Saharan Africa) no longer includes chloroquine in its official malaria treatment protocol because of significant parasite resistance. (For an interesting read on why many in PNG feel resistance of a different kind to the COVID vaccine in particular, see Fraser Macdonald's article at The Conversation, bit.ly/3KGlVrx.)

Collaborating with the WHO Global Malaria Programme is the Malaria Atlas Project, which curates case surveillance, cross-sectional survey data and satellite imagery to support malaria research, intervention and treatment. The project's interactive world map (malariaatlas.org/explorer) can be manipulated to show malaria risk, prevalence and many other data layers. The map clearly shows the regions in Africa, PNG, South and South-East Asia and South America where men, women and children battle daily with mosquitoes and malaria.

GSK has committed to making Mosquirix a not-for-profit vaccine. Before his retirement, Dr Joe Cohen headed up GSK's malaria vaccine research project. Speaking to *The Guardian* about his visit to the children's ward of a local hospital in The Gambia in the late 1990s, he said:

> *… the 20 or so beds were each often occupied by two or three tiny children – most of them seriously ill with malaria. Their mothers sat beside them, clearly despondent and almost resigned: many told us they had already lost a child to this dreadful disease. The visit starkly illustrated what malaria meant for the local population and gave even more meaning and urgency to our work.*

RTS,S was one of more than a dozen antimalarial vaccine candidates in clinical development. Australia has a strong and active malaria research community across several medical research institutes and universities, including research on vaccines, new drugs, diagnostics, and other prevention strategies and clinical trials.

I spoke with Professor James Beeson, Head of the Malaria Immunity and Vaccines Laboratory at the Burnet Institute, about the development and implementation of RTS,S. One aim of his research group is to develop vaccines and public health programs to reduce malaria. 'The vaccine is an important new tool in combating malaria, especially in children', he said. 'Adequate funding and resourcing are essential to ensure the vaccine is available for all children at high risk of malaria.'

The RTS,S pilot program preceding WHO's recommendation has been running in Kenya, Ghana and Malawi. It has found that the vaccine has a strong safety profile and is cost-effective. It is reducing severe malaria and is not causing a decline in bednet use or in people seeking help for illness with fever. It will continue so that the value of the fourth of the four recommended doses can be better understood. More broadly, further research is continuing to build on RTS,S to achieve vaccines with higher levels of protection.

Sally Woollett
(editor@raci.org.au)

From isoprene to limonene

As I drank my breakfast lemon juice, I contemplated the connection between two articles in the December 2021 – February 2022 issue. The first detailed the 2021 Ig Nobel prize for the measurement of isoprene exhalations in cinema audiences ('Tongue in cheek award with cult status for cinema air study', p. 10). The second mentioned limonene in the article 'An ingenious tool for building molecules' (p. 6), a brief description of Benjamin List and David MacMillan's 2021 Nobel Prize in Chemistry award for the development of organocatalysts.

The monoterpene limonene (the principal oil in citrus peel) is biosynthesised from isoprene, and isoprene may be cracked from limonene at elevated temperatures. Yearly bio-emissions of isoprene, principally from trees and shrubs, are estimated at around 600 million tonnes, accounting for about one-third of all hydrocarbons released into the atmosphere. Synthetic isoprene from petroleum napthas is the monomer in the production of *cis*-1,4-polyisoprene – synthetic rubber.

My breakfast juice is squeezed from the fruit of our 'lemonade' tree, an Australian mandarin–lemon hybrid. It makes a delightful naturally sweet drink, requiring no additional sugar. Unfortunately, our cool (often cold) climate in the New South Wales Southern Highlands permits only one crop per year, so it is a pre-Christmas treat at our place. Do both enantiomers of limonene exist in the peel of our mandarin–lemon hybrid fruit?

Tom Smith FRACI CChem

'Your say' guidelines

We will consider letters of up to 400 words in response to material published in *Chemistry in Australia* or about novel or topical issues relevant to chemistry. Letters accepted for publication will be edited (no proof supplied) for clarity, space or legal reasons and published in print and online. Full name and RACI membership type will be published. Please supply a daytime contact telephone number (not for publication).

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Send letters to wools@westnet.com.au.

Dorothy Hodgkin and insulin

I was interested to read the article by Dave Sammut and Chantelle Craig on diabetes and insulin in the December 2021 – February 2022 issue (p. 22). It informs us of the award of the 1923 Nobel Prize in Physiology or Medicine to Frederick Banting and John Macleod for their discovery of insulin. Readers of a journal such as *Chemistry in Australia* will also have an interest in the determination of the chemical structure of insulin over 40 years later by Dorothy Hodgkin OM FRS (1910–1994). An X-ray crystallographer, Hodgkin received the 1964 Nobel Prize in Chemistry for determining the structure of vitamin B12. She went on to report the structure of insulin in 1969.

She was born Dorothy Crowfoot and married into the very gifted Hodgkin family, who include the physician Thomas Hodgkin (1798–1866) after whom Hodgkin's disease is named. Dorothy's husband, also Thomas, was a historian of note. He specialised in African history and spent a good deal of time in Africa. The 1963 Nobel Prize for Physiology or Medicine went to Alan Lloyd Hodgkin, who is described in the biography of Dorothy Hodgkin by Georgina Ferry (*Dorothy Hodgkin: a life*, Granta Books, 1999) as Dorothy's 'cousin by marriage'.

It is also recounted in the biography that when in the early 1960s Dorothy was offered a chair at Oxford, Thomas was away in Ghana. She naturally wanted to discuss it with him before committing herself to accepting, and telephoned him there. He was not immediately available to take the call and had to be tracked down. Afterwards, the telephone operator, who had unavoidably overheard most of the conversation between Dorothy and Thomas, was heard to remark: 'What a fuss about a chair. Now you are to have it I hope you will find it comfortable'.

Clifford Jones FRACI CChem

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TGA approves novel COVID-19 oral treatment

Pfizer

The Therapeutic Goods Administration (TGA) has granted provisional approval for the supply and use in Australia of PAXLOVID™ (nirmatrelvir [PF-07321332]) tablets and ritonavir tablets. PAXLOVID has provisional approval for the treatment of COVID-19 in adults 18 years of age and older who do not require initiation of supplemental oxygen due to COVID-19 and are at increased risk of progression to hospitalisation or death.

PAXLOVID is the first oral antiviral of its kind; it includes nirmatrelvir, a 3CL protease (also known as Main protease or Mpro) inhibitor that was specifically developed in Pfizer's laboratories to combat SARS-CoV-2. Under this authorisation, PAXLOVID can be prescribed as an oral treatment to certain high-risk adults within the first five days of symptomatic infection, potentially helping patients avoid severe illness that can lead to hospitalisation or death.

'This milestone in Australia is an important moment in our continued fight against COVID-19, paving the way for use of PAXLOVID as cases continue to rise and we address the threat of a new variant of concern, Omicron', said Anne Harris, Pfizer Australia and New Zealand Managing Director.

'This at-oral therapy, developed to reduce hospitalisations and save lives, has the potential to transform COVID-19 treatment and help lessen the devastating impact of the virus that has now taken over 5 million lives globally.'

The TGA based its decision on positive results from the phase 2/3 EPIC-HR (Evaluation of Protease Inhibition for COVID-19 in High-Risk Patients) interim analysis, which enrolled non-hospitalised adults with confirmed COVID-19 who were at increased risk of progressing to severe illness. The data demonstrated an 89% reduction in risk of COVID-19-related hospitalisation or death from any cause in adults treated with PAXLOVID compared with placebo in those treated within three days of symptom onset, with no deaths in the treatment group. Similar results were seen in those treated within five days of symptom onset. Treatment-emergent adverse events were comparable between PAXLOVID (19%) and placebo (21%), most of which were mild in intensity. Pfizer recently announced that results from the final analysis of the primary endpoint from all patients enrolled in EPIC-HR were consistent with the interim analysis, confirming efficacy with a similar safety profile. Additional phase 2/3 clinical trials are ongoing in adults at standard risk of progressing to severe illness, and in those who have been exposed to the virus through household contacts.

In October 2021, Pfizer announced an agreement with the Australian Government to supply 500 000 treatment courses of PAXLOVID over 2022. With the oral treatment now approved for supply and use by the TGA, Pfizer will begin delivering the first treatment courses from the first quarter of 2022.

For more information on the EPIC phase 2/3 clinical trials for PAXLOVID, visit clinicaltrials.gov.

Pfizer Australia

Wearable air sampler assesses personal exposure to SARS-CoV-2

A wearable air sampler clip can monitor personal exposure to SARS-CoV-2.

Adapted from *Environmental Science & Technology Letters* (doi.org/10.1021/acs.estlett.1c00877)

Masks, social distancing, proper hygiene and ventilation can help reduce the transmission of COVID-19 in public places, but even with these measures, scientists have detected airborne SARS-CoV-2 in indoor settings. Now, researchers reporting in *Environmental Science & Technology Letters* have developed a passive air sampler clip that can help assess personal exposure to SARS-CoV-2, which could be especially helpful for workers in high-risk settings, such as restaurants or healthcare facilities.

COVID-19 is primarily transmitted by inhaling virus-laden aerosols and respiratory droplets that infected individuals expel by coughing, sneezing, speaking or breathing. Researchers have used active air sampling devices to detect airborne SARS-CoV-2 in indoor settings; however, these monitors are typically large, expensive and non-portable and require electricity. To better understand personal exposures to the virus, Krystal Pollitt and colleagues wanted to develop a small, lightweight, inexpensive and wearable device that doesn't require a power source.

The researchers developed a wearable passive air sampler, known as the Fresh Air Clip, that continually adsorbs virus-laden aerosols on a polydimethylsiloxane (PDMS) surface. The team tested the air sampler in a rotating drum in which they generated aerosols containing a surrogate virus, a bacteriophage with similar properties to SARS-CoV-2. They detected virus on the PDMS sampler using the polymerase chain reaction (PCR), showing that the device could be used to reliably estimate airborne virus concentrations. Then, the researchers distributed Fresh Air Clips to 62 volunteers, who wore the monitors for five days. PCR analysis of the clips detected SARS-CoV-2 RNA in five of the clips: four were worn by restaurant servers and one by a worker in a homeless shelter. The highest viral loads (more than 100 RNA copies per clip) were detected in two badges from restaurant servers. Although the Fresh Air Clip has not yet been commercialised, these results indicate that it could serve as a semiquantitative screening tool for assessing personal exposure to SARS-CoV-2, as well as help identify high-risk areas for indoor exposure, the researchers say.

American Chemical Society

Superabsorption unlocks key to next-gen quantum batteries

Researchers at the University of Adelaide and their overseas partners have taken a key step in making quantum batteries a reality. They have successfully proved the concept of superabsorption, a crucial idea underpinning quantum batteries.

'Quantum batteries, which use quantum mechanical principles to enhance their capabilities, require less charging time the bigger they get', said Dr James Quach, who is a Ramsay Fellow in the School of Physical Sciences and the Institute for Photonics and Advanced Sensing, at the University of Adelaide.

'It is theoretically possible that the charging power of quantum batteries increases faster than the size of the battery, which could allow new ways to speed charging.'

To prove the concept of superabsorption, the team – who published their findings in *Science Advances* (doi.org/10.1126/sciadv.abk3160) – built several wafer-like microcavities of different sizes that contained different numbers of organic molecules. Each was charged using a laser.

'The active layer of the microcavity contains organic semiconductor materials that store the energy. Underlying the superabsorbing effect of the quantum batteries is the idea that all the molecules act collectively through a property known as quantum superposition', said Quach.

As the microcavity size and number of molecules increased, the charging time decreased.

The idea of the quantum battery has the potential to significantly affect energy capture and storage in renewable energy and in miniature electronic devices.

By 2040, energy consumed by people is expected to have increased by 28% from 2015 levels. Most energy will still come from fossil fuels at great cost to the environment. A battery that is capable of harvesting and storing light energy simultaneously would provide significant cost reduction while reducing the unpredictability of energy from solar technologies.

A new vista in battery technology, driven by the power of quantum mechanics, could become a reality by applying the team's work. The next step is to develop a fully functioning quantum battery prototype.

University of Adelaide

STA: time to 'double down' on our science investment

The 2022 Budget should 'double down' on Australia's return-generating investments in science to prepare for new complex challenges after the pandemic, fast-track our economic recovery and smooth the nation's climate transition, says Science & Technology Australia (STA).

This would start with boosting direct R&D investments to shift Australia closer to the top ten OECD countries to seize economic opportunities for our nation.

The first major stride towards that goal would be a $2.4 billion Research Translation Fund to secure Australia's science future and generate strong returns on investment.

'Australia should use the next federal Budget to fund science like our lives and our economy depend on it – because they do', said STA CEO Misha Schubert.

'We should heed the lessons of the pandemic and "double down' on our investments in science to see off major threats and seize new economic opportunities for Australia.'

'As we enter the third year of the COVID-19 pandemic, it's never been clearer that Australia needs the deep expertise of scientists to navigate this historic challenge – and many others.'

'Science has given us diagnostic testing, respirators, medical equipment, epidemiological expertise, and – crucially – life-saving vaccines.'

'Those vaccines have saved lives from COVID-19, and could open the door to a host of potential new vaccines against cancers – and create tens of thousands of Australian jobs.'

STA President Professor Mark Hutchinson urged the Government to use the 2022 Budget to safeguard the future of our science talent, institutions and infrastructure.

'The lessons of the past few years are clear. We must invest deeply in science and scientists. The success of science is crucial to our safety.'

The pre-Budget submission sets out fiscally responsible initiatives to deliver strong returns on investment to both tax revenue and the economy.

They include:

- Boost direct R&D investment to shift Australia closer towards investment levels in the top ten OECD countries.
- Create a new $2.4 billion Research Translation Fund to turn more of Australia's science into applications that will generate returns on investment.
- Safeguard the next wave of science breakthroughs by lifting ARC and NHMRC research grants budgets to $1 billion/year for each agency.
- Secure the future of science and research infrastructure with long-term funding certainty for the National Collaborative Research Infrastructure Strategy.
- Deepen investment in climate science and low-emission technologies, including extending the proposed Patent Box initiative to include clean energy tech.
- Avert a disastrous exodus of science talent by shifting to longer-term grants, employing researchers on longer-term contracts, adopting fixed timelines for grant applications and announcements, and slashing red tape in grant applications.
- Invest $3 million in an STA Bench to Boardroom program to turbo charge commercialisation training for scientists.
- Access Australia's full STEM talent pool by investing $2.3 million to advance women in STEM through STA's ground-breaking Superstars of STEM program, and $4 million to establish an Indigenous STEM Network.
- Secure Science meets Parliament for the decade with a $2.3 million endowment.
- Resource the promised review of the Job-Ready Graduates legislation and top up funding for STEM degrees if they have fallen under the new model.

Science & Technology Australia

C&EN's chemical outlook for 2022

In 2022, the global chemical industry hopes to recover from the ongoing pandemic, despite challenges posed by shifting consumer preferences, pollution reduction measures, and supply chain and labour shortages. A cover story in *Chemical & Engineering News* analyses the key policies, market trends and economic forces that will affect chemistry around the world in the coming year.

The chemical industry is eyeing several measures to slash emissions and pollution by, for example, reducing greenhouse gas emissions up and down the value chain, investing in carbon capture and clean technology, and rethinking packaging and manufacturing methods.

The United Nations will tackle pollution with the Stockholm+50 meeting and a possible global agreement to keep discarded plastics out of the environment. Meanwhile, the European Green Deal will challenge the chemical industry, with a potential $80 billion decrease in chemical sales from the new legislation. In the US, the Environment Protection Authority (EPA) will struggle to meet deadlines imposed by the *Toxic Substances Control Act*, such as completing risk evaluations for high-priority chemicals and proposing rules to mitigate risks. EPA also plans to propose enforceable limits on the flame retardants PFOA and PFOS in drinking water. Driven by strong consumer demand, the US chemical industry will experience an estimated 4.3% growth in 2022, despite continued inflation and supply chain shortages, predicts the American Chemistry Council.

The full article is available at https://cen.acs.org/policy/CENs-World-Chemical-Outlook-2022/100/i2.

American Chemical Society

Are scientists contaminating their own samples?

Researchers at Staffordshire University, UK, and Rozalia Project, USA, are investigating procedural contamination when sampling for microparticles in aquatic environments. The study, published in *Marine Pollution Bulletin* (doi.org/10.1016/j.marpolbul.2021.113095), shows that a significant amount of microplastics and microfibres from scientists' clothing and gear mixes with pollution in the water samples.

Claire Gwinnett, Professor in Forensic and Environmental Science at Staffordshire University, explained: 'In the field this can occur due to the dynamic nature of the environment such as wind or weather, actions required to obtain samples and the close proximity necessary for scientists to procure and secure samples whether in a medium-sized vessel, small boat or sampling from shore. In a mobile lab, this often occurs due to using small, multi-use spaces and similar requirements for scientists to be close to the samples while processing.'

Data was collected during an expedition along the Hudson River. The team tracked contamination by collecting fibres from every possible source of contamination on the vessel, including clothing worn by the science and boat teams, sail bags and tarps, sail and equipment control lines as well as interior textiles. By doing so, they created a catalogue to which every fibre and fragment found in environmental samples was first compared. If there was a match, that exact source of procedural contamination was noted. If there was not a match, that microparticle was considered pollution.

The research found that when robust anti-contamination protocols were not used when taking water samples (using a metal bucket for surface samples and a Niskin bottle for mid-water column samples), 71.4% of the microparticles in the samples were contamination. Similarly, when anti-contamination protocols were not used when processing water samples (using a vacuum filtration method), 68.4% of the microparticles in the samples were due to contamination.

Co-author Rachael Z. Miller, Founder of Rozalia Project for a Clean Ocean, said: 'This is a study that was designed to strengthen the scientific process and has revealed the extent to which our clothing sheds, not just in the washing machine or dryer, but as we wear it and conduct ourselves in our everyday lives.

'Some take-aways for everyday people from this study are to: take care of the clothes we have – that can be done by adapting laundry routines to reduce fibre-breakage such as washing in cold water and air drying when possible; being mindful of the clothing we choose – more and more information is coming out about how much various types of fabrics shed, and supporting brands and organisations who are aware of and addressing the problem by working to better understand our textiles and who are innovating to make them both more resilient and out of materials that exert less pressure on our natural world, while still maintaining their ability to protect us from the elements.'

The study also sets forth methods inspired by forensic science that could make a 37% reduction in the amount of procedural contamination mistakenly added to environmental samples during the collection phase of a study. This reduction can save research teams a significant amount of time by reducing the number of microparticles that must be analysed.

Solutions for future studies include outfitting the whole team in the same low-shed, unusually coloured garments ideally also with unusual fibre morphology. This would allow for rapid identification as contamination. It is important for the entire boat crew to be included in these quality control considerations since fibres from the captain and first mate were also found in samples during this study.

The researchers also describe a workflow using a polarising light microscope that can save research teams both time and money when microparticle, in particular microfibre, identifications must be made. When paired with Easylift® tape, an innovation used for sampling and fixing microparticles after vacuum filtration, this study found that a polarising light microscope could produce a high-confidence/correct material identification in 93.3% of the microfibres found in the water samples.

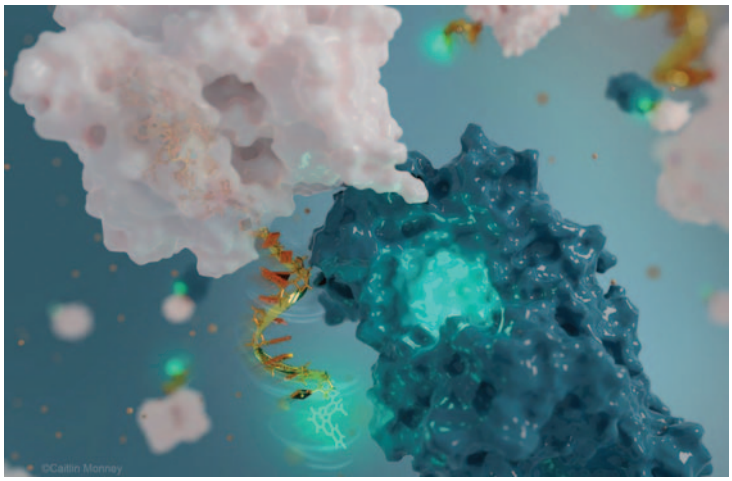
Some washing machine filters are designed to catch many of the microfibre particles from clothes. planetcare/Unsplash

Gwinnett added: 'Thinking like a forensic scientist during sampling for microplastics has its benefits as this study has shown. Forensic scientists are constantly thinking about how they might contaminate samples and how to prevent that. [They] also acknowledge that it is impossible to have zero contamination and instead focus on creating protocols to minimise and monitor.

'By using forensic analysis techniques, which aim to fully profile a particulate, including its morphological, optical and chemical characteristics then these "layers" of information allow much more confident conclusions to be made as to whether it is from the environment or from procedural contamination.'

Staffordshire University

Chemists use DNA to build world's tiniest antenna



One of the main innovations of the nanoantennas is that the receiver part of the antenna (bright green) is also used to sense the molecular surface of the protein studied via molecular interaction.
Caitlin Monney

Researchers at the University of Montreal, Canada, have created a nanoantenna to monitor the motions of proteins (*Nature Methods* (doi.org./10.1038/s41592-021-01355-5)).

One of the main innovations of these nanoantennas is that the receiver part of the antenna is also used to sense the molecular surface of the protein studied via molecular interaction.

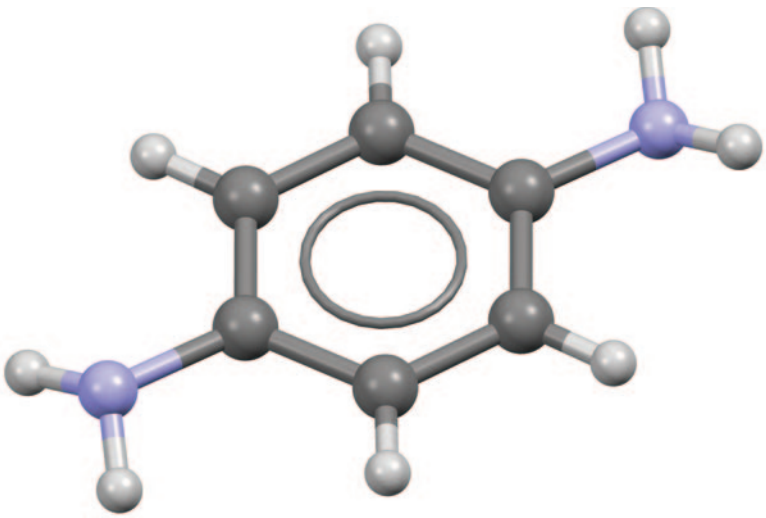
Fluorescent nanoantennas open many exciting avenues in biochemistry and nanotechnology, the scientists believe.

The scientists were able to detect the function of the enzyme alkaline phosphatase with a variety of biological molecules and drugs. This enzyme has been implicated in many diseases, including various cancers and intestinal inflammation.

'In addition to helping us understand how natural nanomachines function or malfunction, consequently leading to disease, this new method can also help chemists identify promising new drugs as well as guide nanoengineers to develop improved nanomachines', said co-author Dominic Lauzon.

University of Montreal

New hair dyes avoid allergic reactions



***para*-Phenylenediamine, a common ingredient in hair dyes, can trigger allergic responses.**
Ben Mills

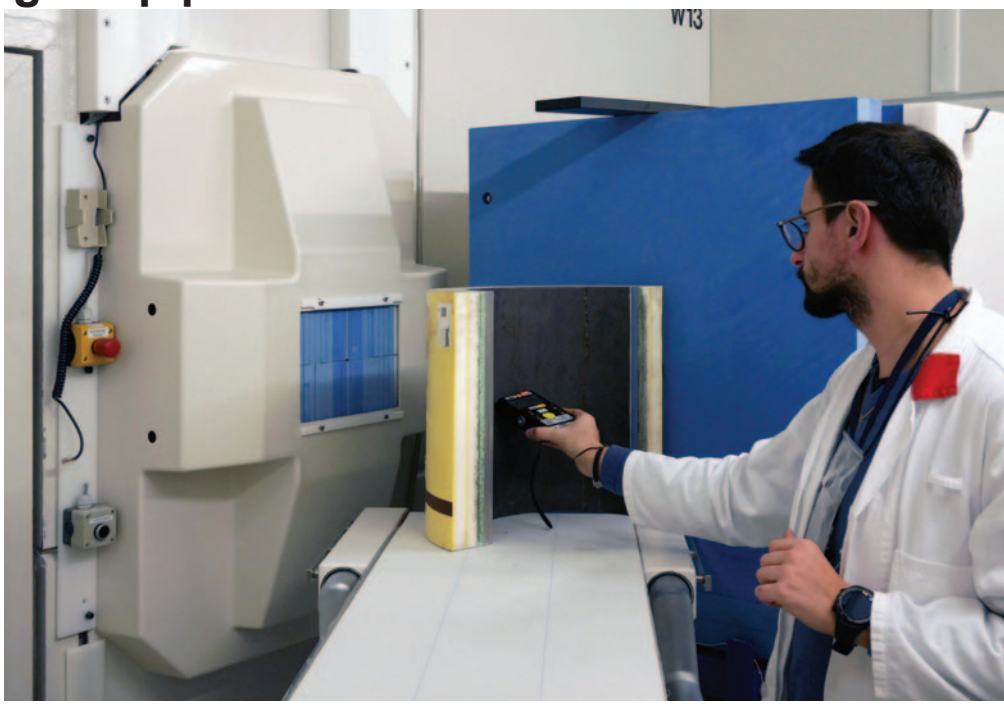
A bad dye job is bad enough on its own, but an itchy and irritating allergic reaction to it is even worse. And people who become allergic to hair dye can develop reactions to many other common substances, transforming a simple cosmetic treatment into a big problem. Now, researchers reporting in *ACS Sustainable Chemistry & Engineering* (doi.org/10.1021/acssuschemeng.1c06313) have developed a range of permanent hair dyes that avoid the allergenic properties of traditional formulations.

When applied as hair colour, *para*-phenylenediamine – a common ingredient in permanent dyes – undergoes a chemical reaction that turns the hair a dark colour that won't wash out over time. This reaction, however, can also produce compounds that bind proteins in the user's skin, causing allergic responses, such as eczema and facial swelling. *para*-Phenylenediamine can also sensitise users to other substances, including a compound commonly found in sunscreens and cosmetics, as well as common pigment and ink compounds. Alternatives have been proposed, but they generally are not water soluble, and the safety of some of the compounds are not well understood. Gopalakrishnan Venkatesan and colleagues wanted to create new alternatives that would avoid the problems of *para*-phenylenediamine while still providing permanent hair colouring.

The team prepared seven dyes based on *para*-phenylenediamine with modifications to the aromatic amine core. The modifications were chosen to potentially make the compounds less reactive toward proteins and less able to be absorbed into skin. All seven compounds permanently coloured hair samples, producing a range of hues from rosy pinks to deep blacks that did not fade, even after three weeks of daily washing. The team then examined the dyes in a test commonly used in the cosmetics industry to determine if a product is a skin sensitiser. Five of the modified dyes were 'weak' sensitisers, whereas *para*-phenylenediamine was 'moderate'. Another test showed that the new compounds generated a reduced inflammatory response in cells compared to *para*-phenylenediamine. These results suggest that the new dyes can effectively colour hair while also avoiding the potential allergenic and sensitisation risks of more traditional ones.

American Chemical Society

Neutrons detect clogs in pipelines



A scientist adjusting a pipe segment for one of the neutron experiments at the instrument FaNGAS.

Industry and private consumers alike depend on oil and gas pipelines that stretch thousands of kilometres under water. It is not uncommon for these pipelines to become clogged with deposits. Until now, there have been few means of identifying the formation of plugs in situ and non-destructively. Measurements at the Research Neutron Source Heinz Maier-Leibnitz (FRM II) at the Technical University of Munich (TUM) now show that neutrons may provide a solution.

It's not just supply bottlenecks that can lead to shortages. Under certain conditions, the mixture in the pipelines – typically gas, oil and water – can become very viscous and even form solid phases. Especially inconvenient for operators are solid hydrates that form from gas and water; for example, when the mixture cools down to the low temperatures of the seabed during longer pipeline shutdowns.

For a clog to be remediated in situ, the affected section of the pipeline must first be found. Localising clogs from the outside is challenging because they can form anywhere along the length of the pipeline. To date, thermal imaging cameras and gamma rays are used to detect the clogs. However, neither of these methods works under water. Ultrasound can penetrate water, but the hydrate blocks can only be detected at close range from outside the pipeline wall.

This constraint poses practical difficulties because underwater pipelines are laid at depths of up to 2000 metres and are often naturally covered by seabed materials such as sand or silt. Another technical challenge associated with acoustic methods arises from the lack of a clear difference between the acoustic impedances of the hydrate phase and other phases of the crude oil mixture, which makes discrimination difficult.

TechnipFMC, a company that specialises in subsea pipelines, was 'looking for a more efficient method to find the plugs in a non-contact, non-destructive and reliable way despite thick walls', said Dr Xavier Sebastian, a project manager at the company.

As suggested by Dr Sophie Bouat, CEO of Science-SAVED (Scientific Analysis Vitalises Enterprise Development), 'neutrons are the perfect probe for the task at hand.'

'Using prompt gamma neutron activation analysis, light atoms and hydrogen in particular can be detected very precisely.'

Since the hydrogen content of hydrates and normal oil or gas is considerably different, it should be possible to detect blockages by measuring the hydrogen concentration.

Dr Ralph Gilles, industry coordinator at the Research Neutron Source FRM II carried out a feasibility study on this topic together with other colleagues from the TUM and the Forschungszentrum Jülich, Germany. Using the prompt gamma activation analysis instrument, which uses cold neutrons from FRM II, the researchers established that this approach can be used to differentiate between oil and gas and the blockage.

At the NECTAR radiography and tomography facility and the FaNGAS (fast neutron-induced gamma ray spectroscopy) instrument, they used fast neutrons from FRM II to show that a sufficiently large number of neutrons penetrate the metal walls of the pipelines to facilitate the respective measurement, and that the measurement also works well underwater.

The results clearly demonstrate that neutrons are ideally suited for this application.

'Our experiments have shown that we can even distinguish an incipient blockage from a fully developed one', said Gilles. 'That's very beneficial, because then one can even preventatively heat a pipe segment to melt the blockage before it fully develops.'

In practice, a mobile detector with a small neutron source will move back and forth along the pipeline to look for plugs.

Technical University of Munich

Heavy hydrogen stabilises drugs

Illustrative experiment: the red cubes made of moulded water ice float to the top normally; the green cubes of heavy water sink.
Volker Lannert/University of Bonn

Deuterium has been the focus of pharmaceutical research for some years because it can ensure that drugs are broken down 5, 10 or even 50 times more slowly. 'We call this the kinetic isotope effect', explained Professor Dr Andreas Gansäuer of the Kekulé Institute for Organic Chemistry and Biochemistry at the University of Bonn (Germany).

'If you replace hydrogen with deuterium, the activation energy usually increases somewhat. As a result, reactions are slower. This also applies to the metabolism of pharmaceuticals in the liver.'

This means that introducing deuterium instead of protium into drugs causes them to have a longer effect. They can therefore be taken in lower doses or less frequently. However, deuterium is rare and thus comparatively expensive. Consequently, deuterium should ideally only be introduced at the points where metabolisation occurs primarily. This is where the new process comes in.

It is based on epoxides, which can now be produced almost at will in many different ways. 'We introduced epoxides into different test molecules and then opened the strained ring with our catalyst', said Gansäuer. 'This contains a titanium atom to which deuterium is bonded. This allows us to introduce a deuterium atom at a single location and with a very specific and desired spatial orientation.'

Another advantage of the method is that, for many complex molecules, there are two different ways of bonding that mirror each other. The new process can be used to create almost exclusively one of the two shapes. 'Since compounds of mirror-image molecules are very difficult to separate and, moreover, they often have different properties in the human body, such stereoselectivity is very important', commented Gansäuer.

The method developed has been used, for example, to produce deuterated precursors of the painkiller ibuprofen and the antidepressant venlafaxine. The scientists are confident that it will be applied to many more pharmaceuticals in the future.

University of Bonn

Self-powered liquid robots need salt to keep moving

Scientists at Berkeley Lab and the University of Massachusetts Amherst, USA, have demonstrated the first self-powered, aqueous robot that runs continuously without electricity. The technology has potential as an automated chemical synthesis or drug delivery system for pharmaceuticals.

As reported in *Nature Chemistry* (doi.org/10.1038/s41557-021-00837-5), the scientists have demonstrated 'water-walking' liquid robots that, like tiny submarines, dive below water to retrieve precious chemicals, and then surface to deliver chemicals 'ashore' again and again.

The technology is the first self-powered, aqueous robot that runs continuously without electricity. It has potential as an automated chemical synthesis or drug delivery system for pharmaceuticals.

The scientists said that the technology significantly advances a family of robotic devices called 'liquibots' so that they don't need electrical energy because they get their power or 'food' chemically from the surrounding media. The scientists learned that 'feeding' the liquibots salt makes the liquibots heavier or denser than the liquid solution surrounding them.

Additional experiments revealed how the liquibots transport chemicals back and forth. Because they are denser than the solution, the liquibots – which look like little open sacks, and are just 2 millimetres in diameter – cluster in the middle of the solution where they fill up with select chemicals. This triggers a reaction that generates oxygen bubbles, which like little balloons lift the liquibot up to the surface.

Another reaction pulls the liquibots to the rim of a container, where they 'land' and offload their cargo.

The liquibots go back and forth, like the pendulum of a clock, and can run continuously as long as there is 'food' in the system.

Depending on their formulation, an array of liquibots could carry out different tasks simultaneously. For example, some liquibots could detect different types of gas in the environment, while others react to specific types of chemicals. The technology may also enable autonomous, continuous robotic systems that screen small chemical samples for clinical applications, or drug discovery and drug synthesis applications.

Theresa Duque, DOE/Lawrence Berkeley National Laboratory

Cerium oxide nanozyme joins pesticide detection taskforce

The new electrochemical method using a cerium oxide nanozyme can detect pesticide contamination in plants for human consumption. LiuTao/Flickr

Monitoring pesticide concentrations constitutes an entire area of active research. In a recent study, scientists from China have successfully developed a sensitive electrochemical detection method based on bifunctional cerium oxide nanozyme to detect the organophosphate pesticide methyl-paraoxon, in plant extracts, adding to the ever-increasing pool of pesticide detection methods.

Organophosphates, like methyl-paraoxon, have grown in prominence as effective pest repellents for crops like cotton and legumes. Studies have shown that these pesticides remain in trace concentrations in the final produce, and cause severe ill effects in humans, including neuro-, embryo-, geno-, cyto- and immune-toxicity. Hence, detecting and removing even trace amounts of organophosphates in consumed plant products is imperative.

A group of scientists in China is looking to advance pharmaceutical analysis of organophosphates in plants, beginning with methyl-paraoxon. Considering the therapeutic potentials of indigenous herbs, the scientists were concerned if these plants could be contaminated by methyl-paraoxon.

Their research to find detection methods led them to cerium oxide nanozyme. Dr Peng Li (University of Macau, China) said, 'Under the optimised conditions, we achieved desirable recoveries for different herbal samples using cerium oxide nanozyme. We believe that our electrochemical method can be practically applied in the rapid detection of pesticide residues.' Their findings have been published in the *Journal of Pharmaceutical Analysis* (doi.org/10.1016/j.jpha.2020.09.002).

The scientists modified glassy carbon electrode using the cerium oxide nanozyme. Using methods like cyclic voltammetry, they confirmed that there is a significant signal enhancement owing to the presence of cerium oxide nanozyme.

Next, they used this electrode to detect methyl-paraoxon, degraded to *p*-nitrophenol using the same nanozyme. Their analysis showed that the developed electrochemical method provided an unprecedented wider linear range, from 0.1 to 100 mmol/L, and a detection limit of 0.06 mmol/L for methyl-paraoxon.

Further, they validated the proof of concept, which is electrochemical detection of methyl-paraoxon using bifunctional cerium oxide nanozyme, using three Chinese herb samples – *Coix lacryma-jobi*, *Adenophora stricta* and *Semen nelumbinis*.

Li and fellow scientists believe that the design can be further improved by supporting the cerium oxide nanozyme on porous materials, or on three-dimensional materials with a large surface area, to perform dual functions of catalysis and detection simultaneously, rather than in isolation.

Furthermore, they are hopeful about the extended application of the method.

Journal of Pharmaceutical Analysis

Too much heavy metal stops stars producing

The heart of the globular star cluster Messier 92 (M92), one of the oldest and brightest in the Milky Way. NASA/ESA

Stars produce most of the elements in the universe – including the elements in us, and in the Earth's metal deposits. But what stars produce changes over time.

Two papers published in *Monthly Notices of the Royal Astronomical Society* (doi.org/10.1093/mnras/stab3205 and /stab3379) shed light on how the youngest generation of stars will eventually stop contributing metals back to the universe.

The authors are all members of ASTRO 3D, the ARC Centre of Excellence for All Sky Astrophysics in 3 Dimensions. They are based at Monash University, the Australian National University and the Space Telescope Science Institute.

'We know the first two elements of the periodic table – hydrogen and helium – were created in the Big Bang', said Amanda Karakas, first author of a paper studying metal-rich stars.

'Over time, the stars that came after the Big Bang produce heavier elements.'

These 'metal-rich' stars, like our Sun, spew out their products into space, enriching the composition of the galaxy over time.

These objects affect us directly because around half of the carbon and all elements heavier than iron are synthesised by stars like our Sun. About 90% of all the lead on Earth, for example, was made in low-mass stars, which also produce elements such as strontium and barium.

But this ability to produce more metals changes depending on the composition of a star at its birth. 'Introducing just a tiny bit more metal into the stars' gas has really large implications on their evolution', said Giulia Cinquegrana. Her paper uses modelling from the earlier paper to study the chemical output of metal-rich stars.

'We discovered that, at a certain threshold of initial metal content in the gas, stars will stop sending more metals into the universe over their lifetime', Cinquegrana said.

The Sun, born about 4.5 billion years ago, is a typical 'middle-aged' star. It is 'metal-rich' compared to the first stellar generations and has a heavy element content similar to that of many other stars in the centre of the Milky Way.

'Our papers predict the evolution of younger stars (most-recent generations) which are up to seven times more metal-rich than the Sun', said Karakas.

'My simulations show that this really high level of chemical enrichment causes these stars to act quite weirdly, compared to what we believe is happening in the Sun', said Cinquegrana.

'Our models of super metal-rich stars show that they still expand to become red giants and go on to end their lives as white dwarfs, but by that time they are not expelling any heavy elements. The metals get locked up in the white dwarf remnant', she says.

'But the process of stars constantly adding elements to the universe means that the make-up of the universe is always changing. In the far distant future, the distribution of elements will look very different to what we see now in our solar system', said Karakas.

Monash University

Latest mass detector for biomolecule attribute monitoring

Biopharmaceutical laboratories can now benefit from high-quality mass information delivered by Thermo Fisher Scientific's Orbitrap technology for molecule attribute monitoring in development and quality control (QC). This offering is a part of a multi-attribute method (MAM) workflow that offers reduced down time and maintenance and provides seamless method transfers from development to QC.

The Thermo Scientific Orbitrap Exploris MX mass detector offers high-resolution accurate mass data for intact analysis of monoclonal antibodies, oligonucleotide mass determination and peptide mapping, making it ideal for biopharma process confirmation.

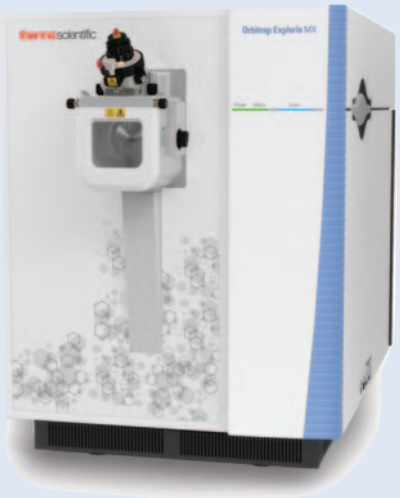
The offering enables accelerated drug characterisation processes in QC and productivity improvements by fully integrating the Orbitrap Exploris MX into the MAM 2.0 workflow, thereby replacing multiple assays into one information-rich mass spectrometric assay.

Furthermore, the hardware and software transition from using the Thermo Scientific Orbitrap Exploris 240 mass spectrometer in the development stage to using the Orbitrap Exploris MX mass detector in the QC stage is made seamless by the compliance-ready Thermo Scientific Chromeleon chromatography data system software.

The Orbitrap Exploris MX mass detector simplifies workflow operation and provides users with confidence in their results, exceeding their needs by offering built-for-purpose, user-friendly solutions that deliver high-quality and reliable data.

Other advantages of the Orbitrap Exploris MX are:

- easy adoption for contract research, development and manufacturing organisations enabled by rapid calibration procedures, built-in methods and reliable performance



- Orbitrap technology, which provides market-leading resolution, mass accuracy and sensitivity
- simplified implementation of MAM into QC.

Learn more about the Thermo Scientific Orbitrap Exploris MX mass detector at www.thermofisher.com/OrbitrapExplorisMX.

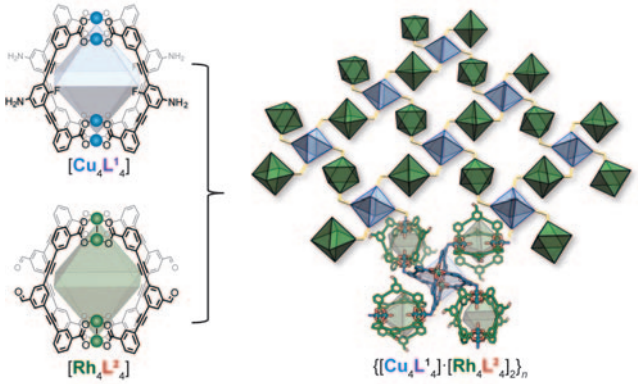
Ingenza and Johnson Matthey collaborate for efficient industrial enzyme synthesis

Biotechnology company Ingenza reports the successful conclusion to its recent six-month project with Johnson Matthey, a speciality chemicals and sustainable technologies supplier. Together, the companies have developed new, efficient approaches for the production of industrially relevant enzymes – including cytochrome P450 – through judicious selection of suitable microbial hosts.

Ingenza combined its comprehensive panel of microbial hosts, including Pichia pastoris, *Saccharomyces cerevisiae*, *Escherichia coli* and *Bacillus subtilis* with its visABLE® platform, and a proprietary predictive codon modification algorithm to select favourable genetic elements and significantly increase expression of the candidate enzymes. This approach was combined with automated high-throughput screening of thousands of colonies performed at the Edinburgh Genome Foundry, using highly sensitive functional enzyme assays designed by Ingenza to rapidly identify the optimally performing clones with the highest level of enzyme secretion and activity towards different substrates.

For more information, visit www.ingenza.com.

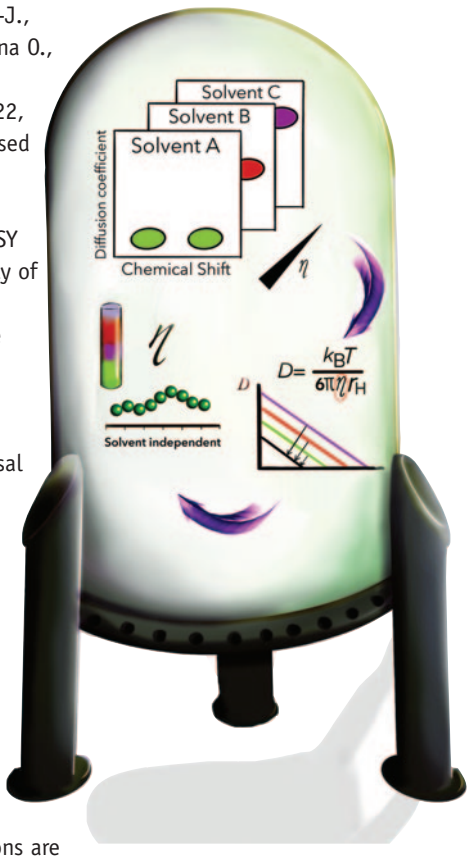
Designing multivariate MOFs from metal–organic cages



One of the defining challenges in the synthesis of metal–organic frameworks (MOFs) is the ability to rationally integrate a number of different chemical entities within a crystalline porous lattice. Such control opens up opportunities to prepare sophisticated materials for applications in gas separation, biomedicine and catalysis. However, the typical 'one-pot' synthesis that MOFs rely upon becomes more and more unpredictable as the number and type of components (metal ions and ligands) increase. Researchers at the University of Adelaide have overcome this challenge by developing a new synthetic approach to prepare chemically complex MOFs from metal–organic cages (MOCs) (Markwell-Heys A.W., Roemelt M., Slattery A.D., Linder-Patton O.M., Bloch W.M. *Chem. Sci.* 2022, **13**, 68–73). The approach exploits a finely tuned Rh(II)–aniline interaction and stoichiometric control to link $Cu_4L^1_4$ (L = ligand) and $Rh_4L^2_4$ MOCs into a 2D MOF. The checkerboard structure of the material is preserved upon desolvation, resulting in a significantly improved surface area compared with the two discrete MOC counterparts. This strategy is expected to open up new possibilities to design bespoke porous solids that incorporate two different types of metal ions and ligands with atomistic control over their location and coordination environment.

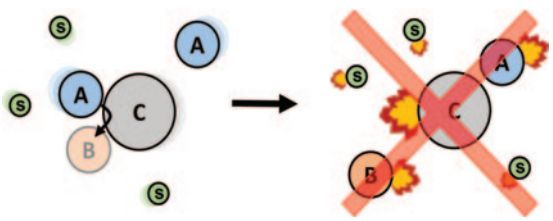
Accurate polymer molecular weights by NMR

Absolute average molecular weights of polymers are difficult to determine. Although routine methods are available, they often only yield relative results that are prone to calibration errors. Now, researchers led by Tanja Junkers from Monash University have shown that diffusion-ordered NMR spectroscopy (DOSY) can be used for accurate molecular weight calibration and determination (Voorter P.-J., McKay A., Dai J., Paravagna O., Cameron N.R., Junkers T. *Angew. Chem. Int. Ed.* 2022, **61**, e202114536). They used polystyrene and poly(ethylene glycol) standards to calibrate DOSY diffusion data for a variety of solvents, showing a high data correlation when the bulk viscosity (η) of the solvent was taken into account. Based on these findings, a type of universal calibration was proposed that enables average molecular weights to be determined with an accuracy on par with, if not better than, that of traditional methods such as size-exclusion chromatography. DOSY also reduces interlaboratory variation of results, since calibrations are instrument independent and globally applicable, raising the accuracy of measurements to a previously unmatched level.



Not so fast! Laws of thermodynamics safe for now

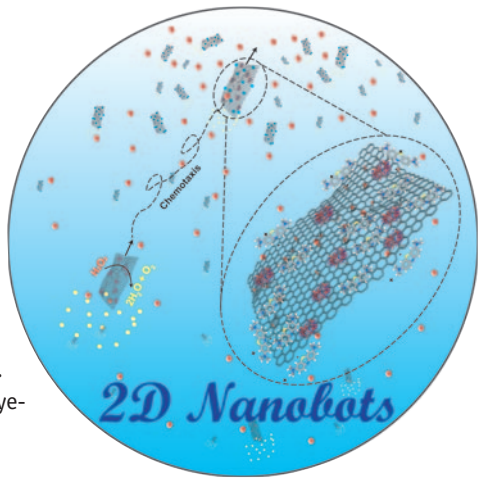
Molecular-level motion underpins our understanding of chemistry. Recently a high-profile paper claimed that reactants and solvents during catalysed reactions have 'boosted' diffusion, challenging the laws of thermodynamics (Wang H. et al. *Science* 2020, **369**, 537–541). The spectacular claim was based on diffusion NMR measurements that were ascribed to the propulsion of molecules by the energy released from chemical reactions. However, an international team of researchers in Australia, Germany and USA evaluated the NMR data and repeated the experiments to find the claims were unfounded and almost entirely based on known measurement artefacts (Fillbrook L.L., Günther J.-P., Majer G., O'Leary D.J., Price W.S., Van Ryswyk H., Fischer P., Beves J.E. *J. Am. Chem. Soc.* 2021, **143**, 20 884–90). While this study found no evidence of the claimed 'boosted mobility', it did discover a decrease in the rate of diffusion of one reactant during the copper(I)-catalysed alkyne–azide cycloaddition (CuAAC) reaction. The results for this reactant provide new insight into the well-studied CuAAC catalytic cycle.



Simple electrostatic parameter predicts specific ion effects

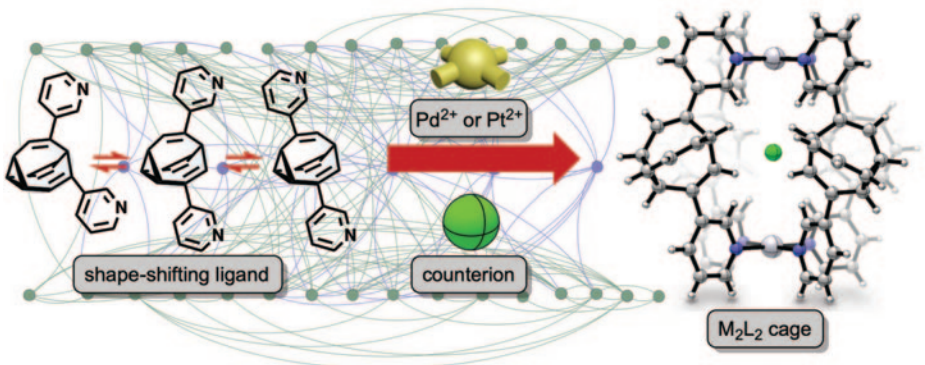
Specific ion effects are physicochemical phenomena caused by salts for which the *identity* of the ions is a determining factor, not just their charge or concentration. Specific ion effects have been observed in biological processes, such as viral and enzyme activities, protein precipitation, and cell permeability, as well as in chemical reactions, polymer morphology, and geophysical phenomena such as glacial stability. These effects and the recurring trends that are observed have been known for over 130 years. However, predicting when a specific ion effect will occur has proven challenging. A team of researchers from the University of Newcastle and Australian National University has revisited this problem by considering an ion's electrostatic interactions with its solvation environment (Gregory K.P., Wanless W.J., Webber G.B., Craig V.S.J., Page A.J. *Chem. Sci.* 2021, **12**, 15 007–15). They developed a new parameter based on ion-specific radial charge densities that approximates these interactions, and showed that it is able to quantify specific ion effects in an array of aqueous and non-aqueous systems. This new parameter will aid the development of more general predictive theories of the myriad specific ion effects that exist.

Enzyme-powered 2D chemotactic nanobots

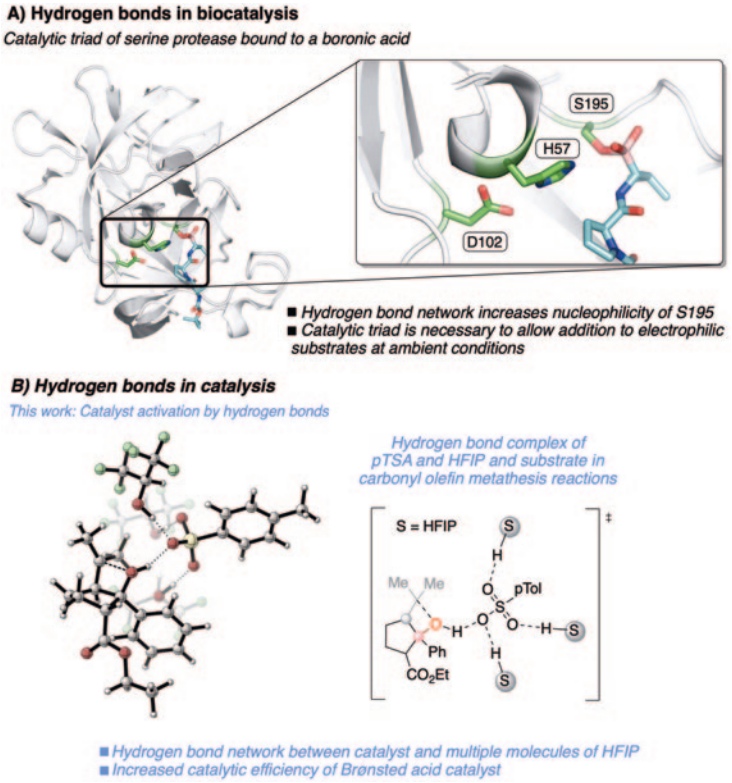


Autonomous nanoscale systems have received tremendous attention due to their diverse applications in areas ranging from biomedicine to environmental remediation. However, current designs mainly use complex three-dimensional architectures that have limited accessible surface area for catalytic sites, thus requiring a high fuel concentration to achieve active motion. A new strategy based on two-dimensional (2D) nanomotors would therefore have considerable benefits. Recently, a team from Deakin University developed a straightforward method to power 2D nanobots at an ultra-low fuel concentration based on a soft nanoarchitectonic approach using catalase (Mathesh M., Bhattarai E., Yang W.R. *Angew. Chem. Int. Ed.* 2022, **61**, e202113801). The 2D nanobots exhibited efficient positive chemotactic behaviour and the ability to swim against gravity by virtue of solutal buoyancy. Furthermore, a proof-of-concept study showed that 2D nanobots had excellent 'on-the-fly' dye-removal capabilities.

Shape-shifting metallosupramolecular cages



Bullvalene is the archetypal shape-shifting molecule that exists as an ensemble of isomers with no permanent carbon–carbon bonds. While this extraordinary hydrocarbon has been known since the 1960s, the synthesis of substituted derivatives has been fiendishly difficult. However, Thomas Fallon at the University of Adelaide has pioneered easy synthetic methods, opening up interesting possibilities. Now, the Fallon and Bloch groups at Adelaide have reported the first synthesis of metallo-supramolecular assemblies that employ a shape-shifting bis(pyridyl)-substituted bullvalene ligand (Birvé A.P., Patel H.D., Price J.R., Bloch W.M., Fallon T. *Angew. Chem. Int. Ed.* 2022, doi.org/10.1002/anie.202115468). Four ligands and two metal ions (Pd^{2+} and Pt^{2+}) self-assemble to form regular 'lantern' M_2L_4 cage complexes. In principle, each shape-shifting ligand may adopt one of 15 possible isomers, leading to a vast pool of possible isomeric M_2L_4 cages. However, in the presence of halide counterions, the system converged to employ only one bullvalene isomer, in rapid stereochemical exchange in solution. In the solid state, X-ray crystallography revealed the further convergence to a single cage diastereoisomer. This work paves the way for further exploration of shape-shifting ligands in organometallic and supramolecular chemistry.

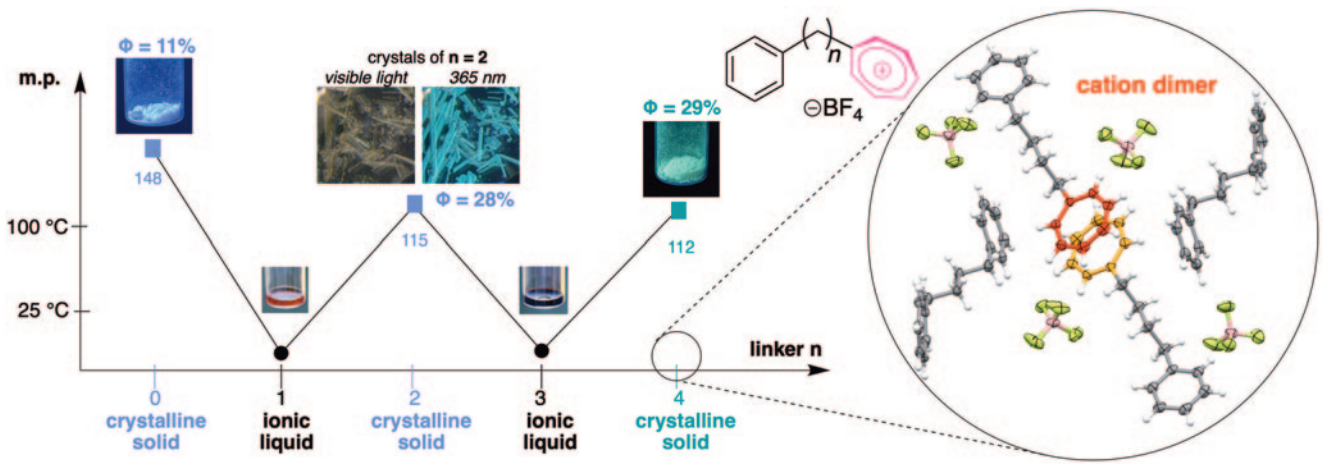


Activating catalysts using hydrogen bonds

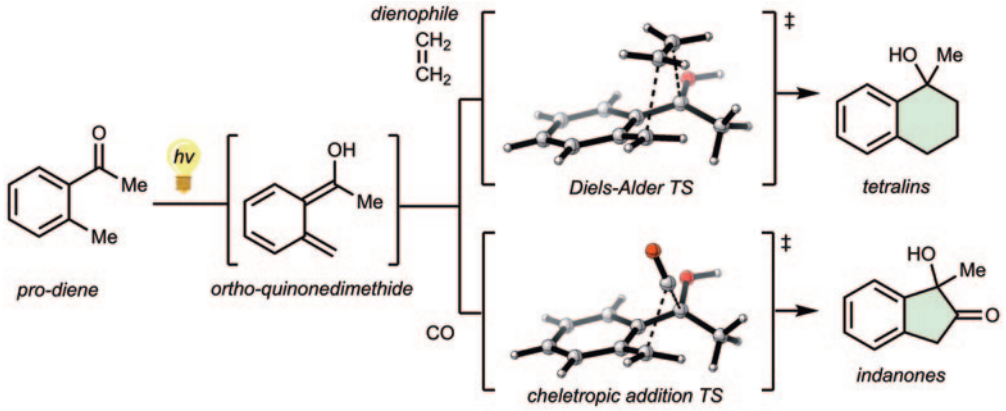
The activation of reactants via weak non-covalent interactions, especially hydrogen bonding, is one of the most frequently encountered paradigms in catalysis. However, the activation of a catalyst molecule itself by such interactions has not been widely studied, despite being common in naturally occurring chemical processes. For instance, hydrogen bonds between amino acid side chains play a key role in enhancing the catalytic activity of enzymes. A prominent example can be found in serine proteases, in which a hydrogen-bond network between three amino acid sites, the so-called catalytic triad, has been identified as vital to its catalytic function, enhancing the nucleophilicity of serine to enable scission of amide bonds. Researchers at the University of New South Wales have recently used hexafluoroisopropanol (HFIP), a very strong hydrogen-bonding solvent, as the reaction medium to activate a simple Brønsted acid so that it can in turn enable the carbonyl-olefin metathesis (COM) reaction (To T.A., Pei C., Koenigs R.M., Nguyen T.V. *Angew. Chem. Int. Ed.* 2022, doi.org/10.1002/anie.202117366). This work provides important new insight into homogeneous Brønsted acid-catalysed COM reactions specifically and lays the foundation for new biomimetic approaches to catalysis in general.

Turning on light emission by crystallisation of non-conjugated organic salts

Researchers at the University of New South Wales and the University of Melbourne have recently reported the synthesis of a series of novel ω-phenyl *n*-alkyl tropylium organic salts that display intriguing physical and photophysical properties (Crocker R.D., Pace D.P., Zhang B., Lyons D.J.M., Bhadbhade M.M., Wong W.W.H., Mai B.K., Nguyen T.V. *J. Am. Chem. Soc.* 2021, **143**, 20 384–94). The compounds with an odd number of carbons in the linker are room-temperature ionic liquids, whereas their counterparts with an even number of linker carbons are crystalline solids, as highlighted by melting point (m.p.) measurements. Despite the two terminal aromatic rings being non-conjugated, the even-linker molecules exhibit interesting photoluminescent properties in the solid state due to their ability to form through-space charge-transfer complexes. This phenomenon, called clusterisation-triggered emission (CTE), is an under-explored area but has enormous potential in the development of new optoelectronic materials. These simple molecular frameworks could be used as model systems to gain more insight into the mechanism of CTE. Most interestingly, the most photoluminescent compound in this series (as measured by the quantum yield φ) showed an unusual carbocationic dimer arrangement in the solid state, paving the way for novel approaches to developing future generations of ionic luminogens.



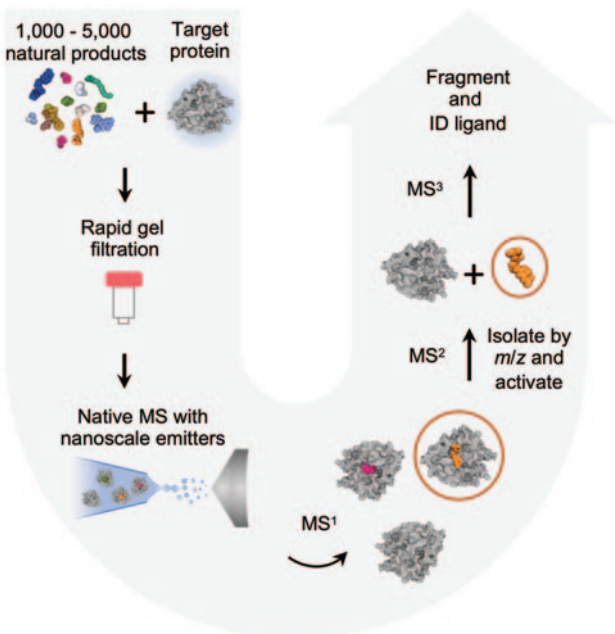
Light-driven carbonylation and cycloaddition



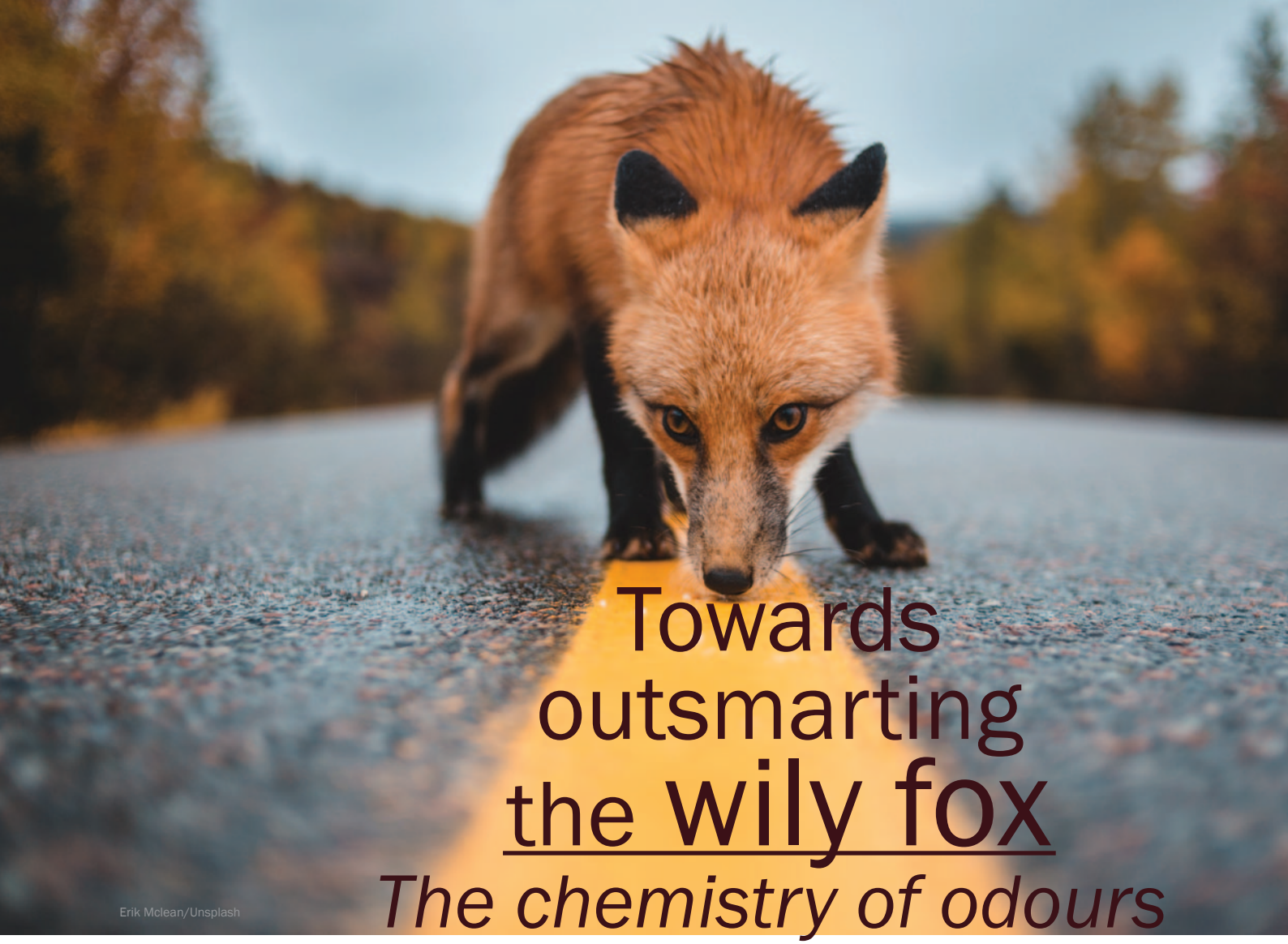
Photoenolisation of *ortho*-acetophenones and their derivatives is a powerful method for generating transient *ortho*-quinonedimethide intermediates that readily undergo [4+2]cycloadditions with dienophiles. The photoenolisation/Diels–Alder (PEDA) sequence is increasingly finding high-profile applications in -natural-product synthesis, CO_2 storage and photoligation, among others. However, to date these examples have been limited to carbonyl-containing aromatic ketones as pro-dienes. Now, researchers at the Australian National University have used theory, supported by experiment, to identify new opportunities for vastly expanding the synthetic scope of this sequence with respect to both the pro-diene and dienophile (Wang J.J., Blyth M.T., Sherburn M.S., Coote M.L. *J. Am. Chem. Soc.* 2022, **144**, 1023–33). Among their key findings, they uncovered a new mode of reactivity, in which CO is predicted to undergo a facile metal-free (4+1)cheletropic addition to the *ortho*-quinonemethide, thereby providing catalyst-free access to benzannelated cyclopentanones. The generation of carbocyclic five-membered rings through cycloaddition is considered a holy grail of pericyclic reactions, and the use of *ortho*-quinonemethides to solve this problem has been overlooked – until now. The study will serve as a useful guide for the intrepid chemist looking to apply the PEDA sequence to their own synthetic targets.

Rapid screening of natural-product drug leads by mass spectrometry

The structural diversity of natural products offers unique opportunities for drug discovery. However, the use of natural products as a source of lead compounds in drug discovery has significantly declined over the past 30 years, partly owing to the challenges associated with screening natural-product extracts to identify bioactive small molecules. The development of new methods for natural-product screening should promote a resurgence in natural-product drug discovery and facilitate the identification of novel small-molecule therapeutics. Recently researchers from the University of New South Wales reported a new approach for the rapid multiplexed screening of natural products for protein–ligand binding in native mass spectrometry (Nguyen G.T.H., Bennett J.L., Liu S., Hancock S.E., Winter D.L., Glover D.J., Donald W.A. *J. Am. Chem. Soc.* 2021, **143**, 21 379–87). The key was to use rapid, low-volume gel filtration and nanoscale ion emitters in native mass spectrometry to substantially increase measurement resolution and signal, facilitating the direct detection of intact protein–ligand complexes from mixtures containing about 5000 distinct small molecules. Unknown ligands can be identified by multistage mass spectrometry to obtain a fragment spectrum of the isolated ligand, which can then be matched to mass spectral databases. This workflow should significantly increase the efficiency of target-based natural-product drug discovery workflows.



Compiled by **David Huang** MRACI CChem (david.huang@adelaide.edu.au). This section showcases the very best research carried out primarily in Australia. RACI members whose recent work has been published in high-impact journals (e.g. *Nature*, *J. Am. Chem. Soc.*, *Angew. Chem. Int. Ed.*, *Chem. Sci.*) are encouraged to contribute general summaries, of no more than 200 words, and an image to David.



Erik Mclean/Unsplash

Towards outsmarting the wily fox

The chemistry of odours

BY **NOEL DAVIES, STUART MCLEAN** AND **DAVID NICHOLS**

As efforts to keep foxes out of Tasmania continue, local researchers are looking at the chemistry of fox secretions as a potential method of control.

Central to the typical nose-to-tail greeting of foxes is the 'violet' gland on the tail. This specialised organ, colloquially named for the distinctive floral scent it produces, is probably a significant source of chemical communication. The chemistry of this gland was first studied in the 1970s, and very little further work had been done until recently.

The red fox (*Vulpes vulpes*) is a major feral pest globally and nationally (see box p. 23); Tasmania is the only Australian state or territory that is fox free, because of its geographical isolation. Interest is increasing in the possibility of controlling foxes and other feral animals using the chemical secretions they use to communicate with each other.

Chemicals detected by olfaction (odorants or scents) are a primary source of information about the external environment for most animals. Scents include semiochemicals, which carry specific information between members of a species. Pheromones are a subset of semiochemicals that elicit innate responses, while other semiochemicals produce learned responses. Scents characteristic of a species can come from specialised glands, urine, faeces, general skin secretions and breath.

Chemical signals work between species as well as within members of the same species. There can be fatal consequences for any species not at the top of the food chain, because these signals alert predators to their presence. Dogs in a fox hunt can detect and track the characteristic scents from great distances. The signals can also alert prey to predators. Specific 'predator odours'

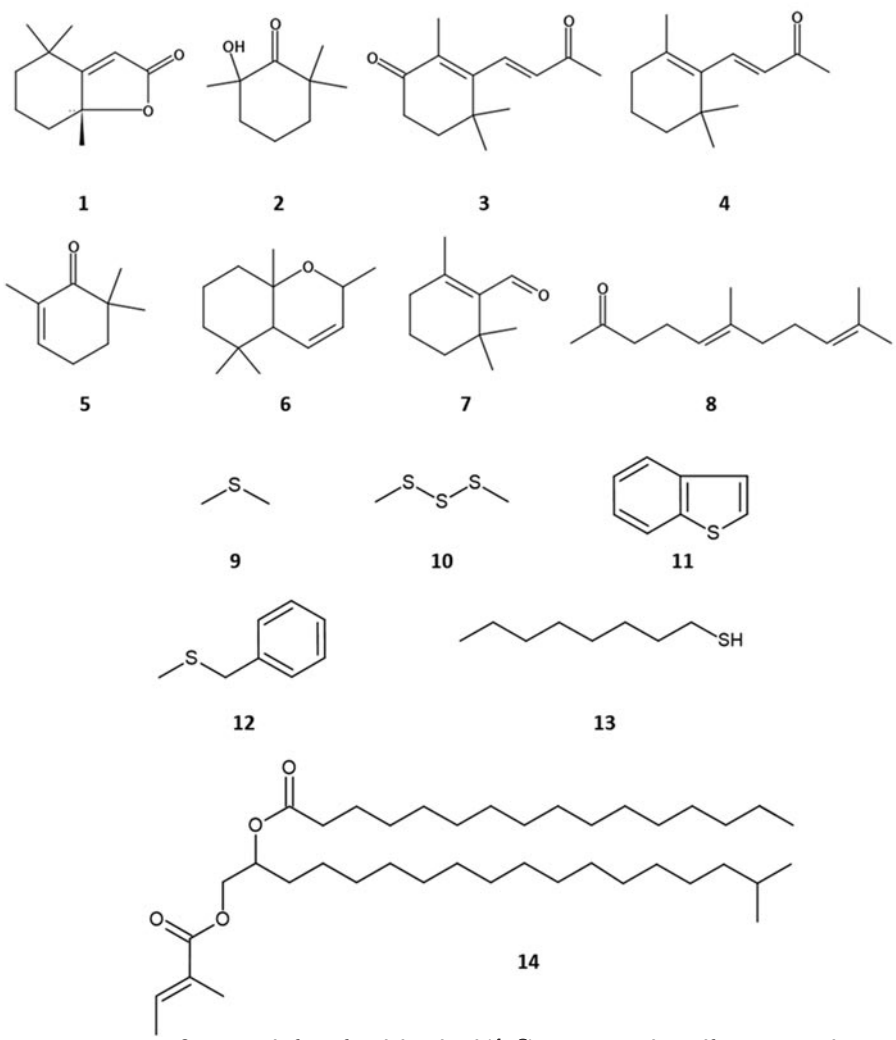
have been explored to deter prey species in both domestic and agricultural settings. At the Seventh International Symposium on Olfaction and Taste in London in 1980, E. Vernet-Maury reported identifying 2,4,5-trimethylthiazoline (TMT) as a specific fear-inducing odorant in fox faeces, and this compound became widely known as 'fox odour'. As a result, 71 behavioural studies have been carried out using TMT on prey species. However, more recent work using captive foxes (bit.ly/3r848jX) struggled to confirm the original finding and we were also not able to detect TMT in faeces of Australian feral foxes.

The identification of distinctive chemical secretions in an animal species suggests that they have a communication role, but confirmation requires behavioural studies, which can be a daunting task, especially as scents may act in combination. Much of the research in this area has been done on laboratory mice and rats, because of the relative ease of behavioural experimentation, whereas behavioural studies on larger animals are undertaken less frequently. Nevertheless, knowledge of animal scents may ultimately help in mitigating the problem of invasive feral species. For example, species-specific attractants can be added to poison baits, compounds indicating a dominant animal can be used to deter subordinate animals, and specific sex attractants could be used to disrupt mating behaviour. Pheromone-based methods are well established for insect pest control, and there is a case for developing additional, novel, methods of vertebrate pest control.

Scents other than pheromones may also provide effective methods of mitigating the damage caused by pest species. An indirect approach using false scents has been found to protect shorebirds from mammalian predators on Mackenzie Basin on New Zealand's South Island (bit.ly/3HX3ZH9).

Investigating the chemistry of the fox violet gland at the University of Bristol in the 1970s, E.S. Albone (go.nature.com/3GfXgYp) identified three ultimately plant-derived carotenoid breakdown products: dihydroactinidiolide (**1**), 2-hydroxy-2,6,6-trimethylcyclohexanone (**2**) and 4-oxo-β-ionone (**3**). These norisoprenoid compounds and/or their precursors can be derived directly by sequestering carotenoids through ingestion of plants, or indirectly through prey. The fox diet contains significant amounts of plant material, especially fruits, which are rich in carotenoids, essential for animal vision and general health. The expression of carotenoid-derived scents may act as

... species-specific attractants can be added to poison baits, compounds indicating a dominant animal can be used to deter subordinate animals, and specific sex attractants could be used to disrupt mating behaviour.



Compounds from fox violet gland (1–8), representative sulfur compounds from the urine (9–13) and an example of a skin wax ester (14).

Most mammals rely on pheromones to maintain their social structure and to locate potential mates, and foxes are no exception.
Jeremy Hynes/Unsplash

... a very minor component of the secretion may be a major component of the odour, making mammalian pheromone research very challenging.

a reliable signal of good nutrition, an important factor in mate choice. This phenomenon has been found to occur in birds in which dietary carotenoids provide the pigments that colour their skin and feathers. A good colouration enhances their attractiveness for mating (bit.ly/3tgEVH0).

At the University of Tasmania, we undertook a comprehensive analysis of the gland volatiles (bit.ly/3K2ptUD). This study confirmed the findings of Albone, and added a further 12 identified norisoprenoids and other carotenoid degradation products. These included β-ionone (**4**), 2,6,6-trimethyl-2-cyclohexen-1-one (**5**), cyclic β-ionone (**6**), β-cyclocitral (**7**), geranyl acetone (**8**), 6-methyl-5-hepten-2-one (sulcatone) and 3,3-dimethyl-2,7-octanedione. These mostly occur as floral volatiles, some are known as insect pheromones, but others have never been reported before from any animal or insect. 3,3-Dimethyl-2,7-octanedione is a particularly rare compound in nature, and was present in all samples in reasonable abundance. Other compound classes contributing to the violet gland chemistry profile are alkanes, alcohols, aldehydes, monoterpenoids, lactones, volatile fatty acids, longer chain fatty acids and their esters. In total, we identified about 100 compounds. Several of these have been reported as signalling compounds in other mammals. It is worth noting that odour perception thresholds of individual volatiles can vary by many orders of magnitude, so that a very minor component of the secretion may be a major component of the odour, making mammalian pheromone research very challenging.

Fox urine is an important part of a fox's territorial marking, and four urinary volatiles were identified more than four decades ago (bit.ly/3HPFITe); we have further investigated this source of volatile scents (bit.ly/3qeUQnl). We characterised more than 60 compounds by gas chromatography–mass spectrometry after headspace solid-phase microextraction of urine from 15 predominantly male foxes and stir-bar extraction of urine from four foxes. Sulfur compounds are known to generally have extremely low odour thresholds, and are common in mammalian urine. Sixteen organic sulfur compounds were found, but not all were detected in all animals. They include dimethyl sulfide (**9**), dimethyl trisulfide (**10**), benzothiophene (**11**), benzyl methyl sulfide (**12**), 1-octanethiol (**13**), 1-phenylethyl methyl sulfide, 2-phenylethyl methyl sulfide and 3-isopentenyl thiol. The last five of these had not been reported from any other mammal or previously from fox urine. Other compound classes in the urine were alcohols, aldehydes, amines, fatty acids, ketones, lactones and esters. Acetophenone was the only compound found in all urine samples, was a major component of most, and has been widely reported as a mammalian pheromone. There was an extremely wide variation in the presence and proportions of compounds in the different urine samples, but we were unable to differentiate between sexes because only two foxes were female.

Animal fur absorbs sebaceous skin gland secretions, so we also analysed fur extracts from different body areas to identify these (bit.ly/3HX4fWB). Skin waxes can moderate the release rate of the more volatile compounds, analogous to the inclusion of natural or synthetic 'fixatives' in perfume formulations. Through both gas and liquid chromatography coupled to mass spectrometry, the fox waxes were found to be dominated by alkane-1,2-diol esters. There were three distinct types: monoesters with a volatile C_5 acyl group at C1, diesters with a second longer chain acyl group at C2, and diesters where both hydroxyl groups were esterified to longer chain fatty acids. After hydrolysis, 34 diols were detected, ranging from 16 to 25 carbons, with iso- and anteiso-branching as well as unbranched chains; the branched chains were by far the most abundant, with C_{18}–C_{21} diols dominating the distribution.

About 100 fatty acids were detected in the hydrolysate, dominated by the volatile tiglic and isovaleric acids, and then mainly saturated C_{12}–C_{28} branched and straight-chain fatty acids. A quarter of these had seldom-reported dimethyl branching, several were novel fatty acids and others were unreported in animals. These diol and

fatty acid permutations create thousands of individual wax components, although the bulk of the wax can be assigned to a much smaller subset. The waxes in the tail fur over the violet gland differed significantly from the general body fur, with almost all of the former containing one C_5 acid.

A representative example is the tiglate/palmitate ester of isononadecane-1,2-diol (**14**). The presence of volatile fatty acids in the waxes raises the possibility of whether subsequent hydrolysis could ultimately release them as chemical signals. Alkane-1,2-diol esters are known in the sebaceous skin secretions of several animals, including dogs, and in humans in the vernix caseosa, the lipid film that protects the foetus. However, tiglate wax esters do not appear to have been reported from any other animals.

Our findings may lead to the development of novel methods of fox control. In contrast to those of insects, mammalian pheromones and scents generally are largely unexploited for management purposes. This is because mammalian olfactory responses are more complex, and are subject to many modifiers from the individual (age, sex, reproductive status) and social context (status, group). Mammalian responses are also affected by other sensory inputs (e.g. vision) and their experience and learning. For example, experiments with predator scents have found that prey species can actually be attracted to the area, perhaps an example of 'keeping your enemies closer'.

The exploitation of scent chemistry will require close collaboration between chemists and ecologists, especially those concerned with animal behaviour (ethologists). The rewards for successful control methods for foxes (and perhaps other invasive species) will be considerable.

Costs of invasive species control

Australia spends considerable amounts on managing invasive species, although detailed expenditure data is difficult to obtain. For vertebrates, the national total can be estimated at about $1.9 billion in 2011–12 (bit.ly/3HVwAMG). The recent mouse plague in New South Wales cost $1 billion.

Foxes prey on wildlife, livestock and domestic animals, and spread disease and weeds. They quickly adapt to urban environments and are well established in all mainland state capital cities – there are an estimated 16 foxes per square kilometre in Melbourne (bit.ly/3r7NzVj). The economic cost to Australia is more than $200 million annually. Populations are currently controlled by licensed hunters, trapping and the use of poison baits, typically '1080' (sodium fluoroacetate). Poisoning is the most effective control measure but has many problems, especially the unintended death of wildlife and domestic animals. The Victorian fox bounty scheme paid $10 each for almost a million fox scalps over 10 years from 2011, although shooting alone is unable to control the large fox population now present. Effective control of pest animals requires the integration of several methods using different approaches.

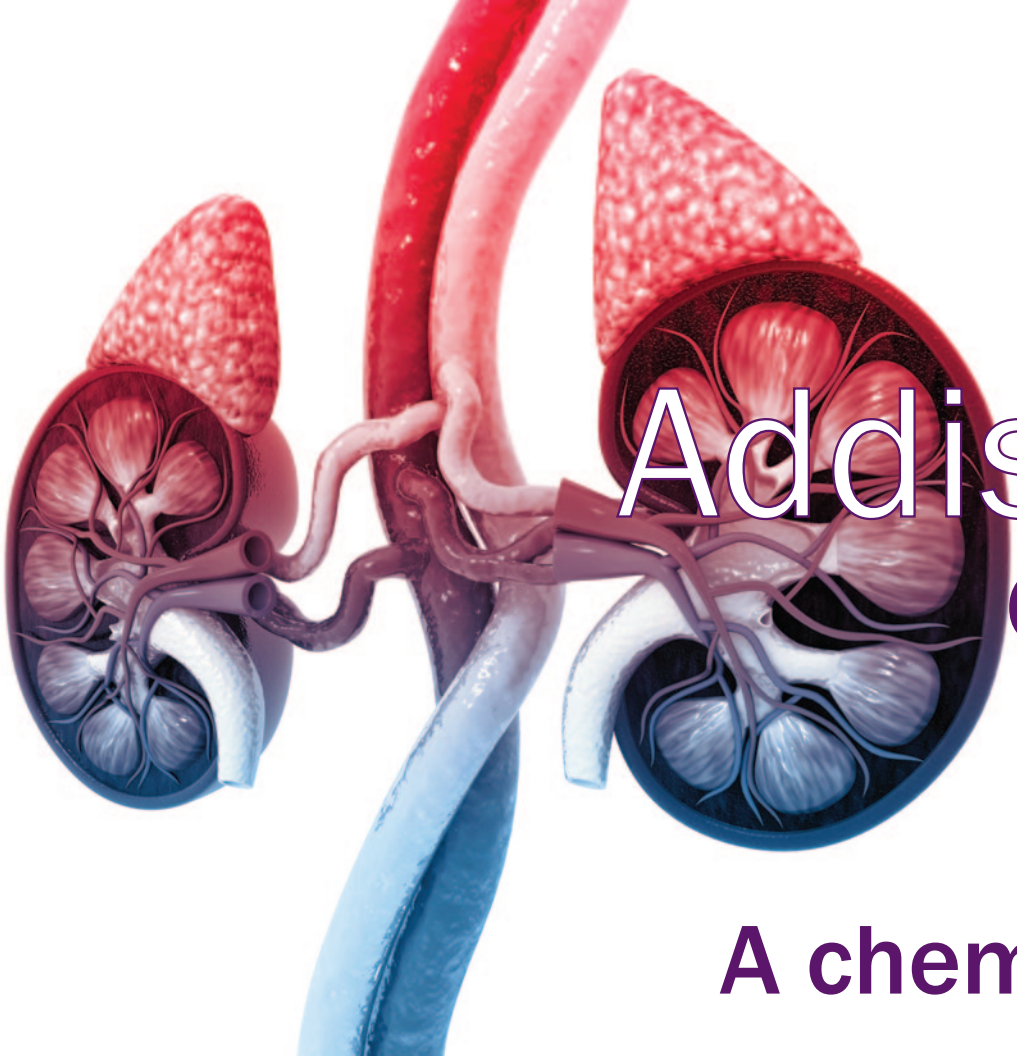
New Zealand is plagued by feral mammals, including rodents, stoats, ferrets, weasels, cats and brushtail possums, and in 2017 the NZ Department of Conservation released a 57-page report with more than 400 references on mammalian pheromones and the potential opportunities for their use in feral pest control (bit.ly/3HQttWv).

Workers fill a monsoon bucket on a helicopter with 1080 pellets to kill possums near Greymouth, New Zealand (c. 2009).
Lakeview_Images/iStockphoto

Further reading

Red Fox Senses (Wildlife Online): www.wildlifeonline.me.uk/animals/article/red-fox-senses
Why ARE foxes so smelly? (Part 2) (Wildlife Online): www.wildlifeonline.me.uk/questions/answer/why-are-foxes-so-smelly-part-2

Adjunct Professor Noel Davies FRACI CChem and **Dr David Nichols** MRACI CChem are at the Central Science Laboratory and **Emeritus Professor Stuart McLean** is at the School of Pharmacy and Pharmacology, University of Tasmania.



Mohammed Haneefa Nizamudeen/iStockphoto

Addison's disease

A chemical view

A friend's close call prompted Alf Larcher to investigate the causes, effects and treatment of Addison's disease.

This story begins with a close friend of mine, who had been unwell for some time. He became very weak, and his family insisted on taking him to hospital. A day of testing culminated in the diagnosis of Addison's disease. My friend was on the brink of a medical crisis, and his family probably saved his life.

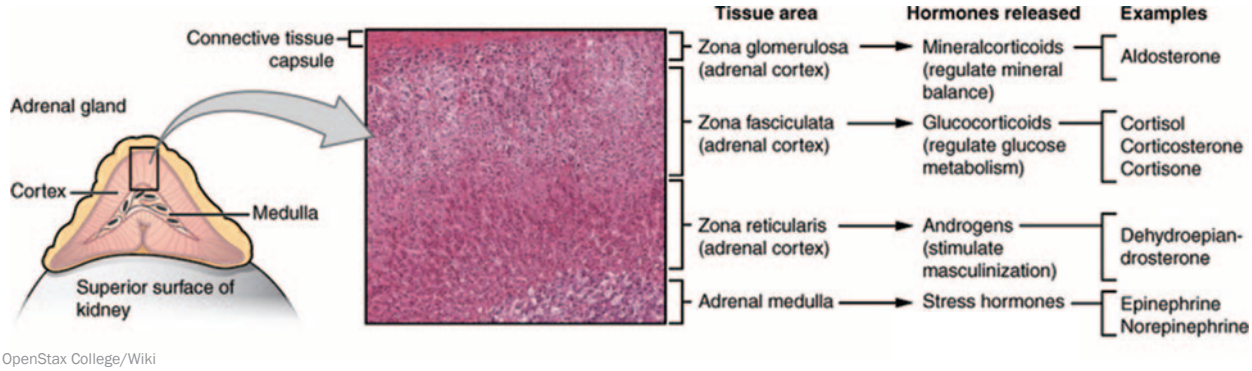
I would like to share with you what I have learned and now appreciate about Addison's disease and the powerful chemistry of the endocrine system.

Most medical sources classify Addison's disease as a rare condition, affecting 1 in 100 000 people, affecting males and females equally but more prevalent in the 30–50-year age group. It can go undetected for some time and is often suspected in people who fail to recover from minor illnesses easily or, more dramatically, have an adrenal (Addisonian) crisis (see below). Debilitating symptoms of the disease include nausea, fatigue, anorexia, anaemia, vomiting and low blood pressure.

Addison's disease is caused by the altered function or deterioration of the adrenal glands (see box p. 25). These two small glands – one 'capping' the top of each kidney and weighing 1.5–2.5 grams – are an important component of the body's endocrine system, which also includes the hypothalamus, pituitary, thyroid, parathyroid, pancreas and ovaries/testes.

The endocrine system regulates cellular and organ function to maintain a constant internal environment, which is critical for the body to operate.

Two of a kind: the adrenal glands



OpenStax College/Wiki

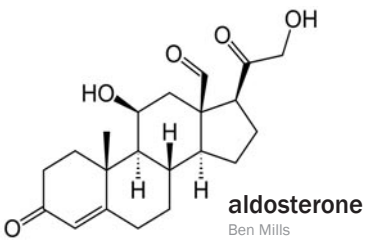
The adrenal glands are often called the 'fight-or-flight' glands because they secrete hormones necessary to maintain the body's constant internal environment under physical stress. An adrenal gland comprises two functional parts: the larger outer cortex (accounting for 90% of the weight) and the inner medulla. The adrenal glands are essential for life; if they are removed (e.g. by surgery to remove tumours) or destroyed (e.g. by disease), perpetual replacement therapies must be administered.

The adrenal cortex has three layers or zones, which make and secrete steroid hormones derived from cholesterol. The only other organs that synthesise steroids are the ovaries/testes, which make the sex steroids. The outermost layer, the zona glomerulosa, synthesises steroids such as aldosterone, a so-called mineralocorticoid because it stimulates renal retention of sodium and promotes secretion of potassium. As water retention/expulsion processes are involved, the processes affect blood volume and pressure.

The middle and thickest layer, the zona fasciculata, manufactures a group of glucocorticoids, the major one being cortisol (known as hydrocortisone when used as a medication). As their name suggests, these steroids help the body to maintain adequate glucose (energy) levels by regulating glucose synthesis and uptake. They are activated when the body is in a fasting state and in extreme cases can promote protein breakdown to provide the body energy. The zona fasciculata is part of a feedback loop. Its primary response is to adrenocorticotropic hormone (ACTH), which is a polypeptide of 39 amino acids secreted by the anterior pituitary gland. In response to ACTH, the zona fasciculata releases cortisol into the bloodstream so that the target concentration is reached. In times of stress (e.g. surgery, illness, strenuous exercise), the pituitary gland releases more ACTH, and the resulting release of cortisol stimulates metabolic pathways that increase the availability of glucose to the body. A significant physiological stress in women is pregnancy, where cortisol levels rise several times above normal. Mineralocorticoids and glucocorticoids can over overlap in biological activity by interacting with each other's receptors.

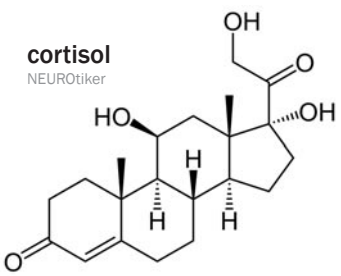
The innermost layer of the adrenal cortex, the zona reticularis, is the thinnest and makes adrenal androgen for both men and women. The predominant sex steroids produced are the weak androgens dehydroepiandrosterone and androstenedione, which can be converted to more potent androgens, such as oestrogen and testosterone, although in men this hormone is mainly made in the testes.

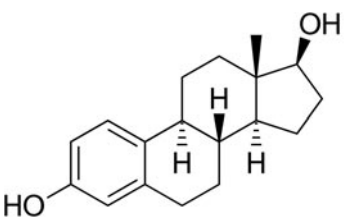
The inner portion of the adrenal gland, the medulla, synthesises catecholamines such as adrenaline, which is important in the body's response to stressful physiological situations. Catecholamines play an important role in the body's fight-or-flight response by, among other things, increasing heart rate, which increases blood flow to the muscles.



aldosterone
Ben Mills

adrenaline
Roland1952





oestradiol
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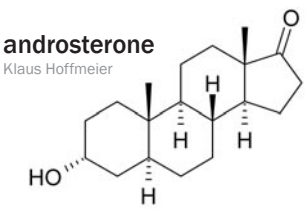
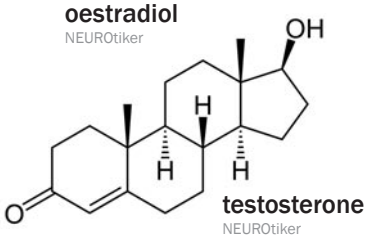




To achieve this environment, the endocrine system regulates and coordinates, among other things:

- sodium and water to control blood volume and pressure
- calcium and phosphate to maintain cell membrane integrity and intracellular signalling
- energy balance and optimisation of fuel utilisation
- haemodynamic (blood flow) and metabolic responses
- reproduction, development, growth and ageing.

The endocrine system affects distant target organs by secreting messenger molecules (hormones) directly into the bloodstream. Hormones have a wide variety of structures, in the form of proteins/peptides, steroids or amino acid derivatives.

Several diseases are related to the function of the adrenal glands. Addison's disease, or adrenal insufficiency, is a partial or complete failure of the adrenal glands to produce cortisol and, in some cases, aldosterone. Primary adrenal insufficiency can be caused when the adrenal glands are damaged by autoimmune disease, tuberculosis, infection or cancer. Secondary adrenal insufficiency can be caused by insufficient ACTH production by the pituitary gland, resulting in adrenal gland atrophication.

Cortisol is important for muscle function (including cardiovascular function), and a deficiency can result in muscle weakness. The lack of cortisol causes food to move more slowly through the gastrointestinal system, and reduces iron and vitamin B12 absorption. Appetite decreases, which, coupled with gastrointestinal dysfunction, often results in weight loss. Cortisol is important in glucose metabolism, so reduced levels disrupt several metabolic pathways, and blood glucose can become dangerously low (hypoglycaemia).

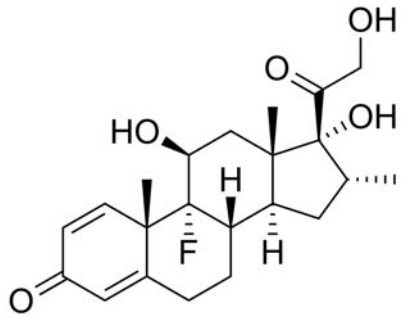
In primary adrenal insufficiency, both cortisol and aldosterone production are affected. This can increase potassium (hyperkalaemia) and decrease sodium (hyponatremia) in the blood. Coupled with the associated dehydration, and left untreated, these changes can have serious health consequences.

An Addisonian crisis may present as sudden loss of strength, pain in the lower back, abdomen or legs, vomiting and diarrhoea, low blood pressure and fainting. If untreated, it can lead to life-threatening shock, seizures and coma. In these cases, administering water too quickly may be harmful: 'water poisoning' can occur because the loss of cortisol impairs the ability of the body to expel water. It is understandable that people with Addison's disease, faced with so many health issues, are prone to mood changes and depression.

When adrenal cortex cortisol production is compromised, the pituitary gland, as part of a feedback loop, produces more ACTH to compensate. Another effect of these elevated levels is skin darkening because the body recognises the ACTH as melanocyte-stimulating hormone (MSH). This is because a 13-member amino acid sequence in ACTH's structure corresponds to that of MSH.

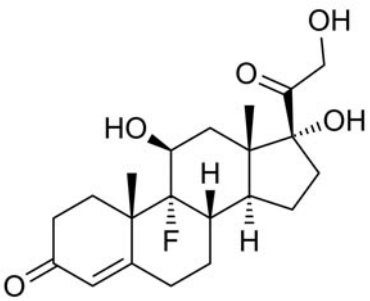
Melanocytes are melanin-producing cells and are the reason for the colour of moles, freckles and suntans. They have an important role in protecting the skin from ultraviolet radiation. Very high levels of ACTH in Addison's disease act like MSH, increasing melanin deposition and skin pigmentation. In fact, early in the disease people may actually be pleased because they lose weight and have a nice suntan, without any effort or the risks associated with excessive sun exposure. However, this is not a good way to get a tan because patients eventually become ill and may die if medical treatment is not sought.

The good news is that Addison's disease can be treated effectively and inexpensively. Cortisol was isolated in 1949 (see box p. 27) and it was deemed a wonder drug, although we know now that too much can be harmful.



dexamethasone

Ed



fludrocortisone

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Synthetic alternatives to cortisol such as dexamethasone can be used ... and a synthetic mineralocorticoid such as fludrocortisone must also be taken for secondary insufficiency, where aldosterone production has been compromised.

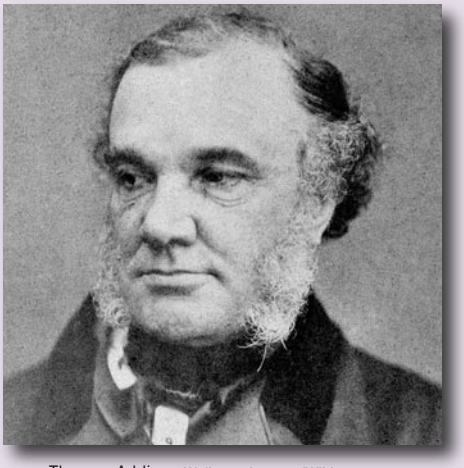
Either cortisol or cortisone can be taken orally (cortisone is biologically inactive and converted by the body to cortisol). Synthetic alternatives such as dexamethasone can be used, but since such compounds only have glucocorticoid activity, a synthetic mineralocorticoid such as fludrocortisone must also be taken for secondary insufficiency, where aldosterone production has been compromised. People with Addison's disease must increase their glucocorticoid dose accordingly (but not the mineralocorticoid) during stress to avoid severe illness.

My friend is following this medical regimen (basically two tablets a day) and the transformation has indeed been wondrous: he is regaining weight, energy and the zest for life.

Alf Larcher FRACI CChem (larcheralf@gmail.com) is a petroleum, environmental and industrial chemist with an occasional urge to write science articles. This is an overview of Addison's disease from a chemist's viewpoint and not should not be used as a basis for treatment of any medical issues. In such cases, consultation with a relevant medical professional is advised.

Research, rescue and reward

When anatomist and physician Andreas Vesalius published illustrations of the kidney in 1543, he omitted the adrenal glands. Twenty years later, Bartolomeo Eustachius re-examined the kidneys and published illustrations that included the adrenal glands. However, it would be three centuries before the function of the adrenals was elucidated.



Thomas Addison Wellcomeimages/Wiki

Thomas Addison received his medical degree from the University of Edinburgh and was appointed as a physician at Guy's Hospital, London, in 1817. Addison meticulously recorded all details of patients' symptoms during their illnesses, including detailed post-mortem examinations. His immediate interest on commencing at Guy's was to study skin disease, particularly in a group of patients with unusual skin darkening. Post-mortems on unfortunate individuals who had not survived the associated disease showed 'diseased suprarenal capsules'. These patients had displayed the symptoms that we now know are typical of Addison's disease.

Addison's findings promoted further interest in the adrenal glands, with Oliver and Schaefer discovering and isolating adrenaline (epinephrine) from the adrenal medulla. Oliver conducted experiments with animals and, unbelievably, his young son; he found that subjects injected with the new substance showed a rapid increase in blood pressure. These experiments led to the landmark experiments in 1927 of Stewart and Rogoff with (sometimes unfortunate) dogs. By administering canine adrenal gland extracts, they were able to extend the lives of dogs that had their adrenal glands removed, and otherwise would not have survived, showing the adrenals were vital to life.

Progress in adrenal gland function then progressed rapidly, culminating in the 1950 Nobel Prize for Physiology or Medicine for chemists Edward Kendall and Tadeusz Reichstein along with physician Philip Hench. Kendall and Reichstein's independent teams isolated and proved the structures of several steroids, including aldosterone. At the traditional Nobel Laureate speech, Hench richly acknowledged the contribution of his chemical co-laureates:

> *I, a physician, am delighted to stand here with two distinguished chemists, Drs. Reichstein and Kendall. Perhaps the ratio of one physician to two chemists is symbolic, since medicine is so firmly linked to chemistry by a double bond. For medicine, especially during the past twenty-five years, has been receiving its finest weapons from the hands of the chemists, and the chemist finds his richest reward as the fruits of his labor rescue countless thousands from the long shadows of the sickroom.*

John F. Kennedy was plagued with bad health for most of his life, and while in London in 1947 he once again became ill. He was rushed to hospital with fever and vomiting and was diagnosed with Addison's disease. Luckily for him, cortisone had just been discovered and he became a guinea pig for the new treatment.

The effect of JFK's health on his political career is much discussed – particularly his tanned skin, which gave him a healthy appearance and set him apart from his political adversaries. Whether this is due to his time in the sun – he was fond of sailing – or Addison's disease will probably never be known.

Research and the development of new treatments for Addison's disease is continuing with FDA approval being sought this year for an auto-injector platform (similar to an EpiPen) developed by Antares Pharma. It is designed to quickly deliver a liquid-stable formulation of hydrocortisone for immediate treatment during an adrenal crisis.

Vale Denis J. Hamilton

Distinguished pesticide chemist

Denis Hamilton passed away on 5 November in Brisbane after a short illness. He was an Honorary Life Member and Fellow of the RACI as well as a Fellow of IUPAC. He was a well-respected analytical chemist, highly regarded by his Queensland Department of Primary Industries (DPI) colleagues, but it was his outstanding international contributions to pesticide chemistry and associated regulatory systems that distinguished Denis from many of his peers.

Denis grew up on an apple orchard in Cottonvale, on Queensland's Granite Belt, near his grandparents and extended family. Denis was close to his grandfather, who instilled in Denis a love for woodwork. Later in life, at the Indooroopilly Men's Shed, Denis often recalled that his grandfather, a bush carpenter, would fix most things on the farm with just a hammer and screwdriver.

Denis excelled at school and was awarded an 'agriculture' bursary to board at Ipswich Grammar where he finished as dux in 1959. He also excelled at most school sports, particularly tennis. He graduated from the University of Queensland with a BSc and MSc in chemistry. In 1963, he joined Queensland's Department of Agriculture and Stock as an agricultural chemist, where he advanced to increasingly senior roles, including principal scientific advisor before his retirement in 2009.

In 1985, Denis was given responsibility for managing an Australian International Development Assistance Bureau project titled 'China Agrochemicals', whereby he began to develop his reputation as an international expert in 'pesticide chemistry'. His contributions towards the advancement of international regulations regarding acceptable levels of pesticide residues in food and feeds was significant and highly regarded. He represented Australia on the Collaborative International Pesticide Analytical Council and was involved in a number of WHO/FAO committees, including the Codex Committee on Pesticide Residues (CCPR), the Joint Meeting on Pesticide Residues and the Joint Meeting on Pesticide Specifications. The latter two are independent expert groups formed to provide advice and recommendations to CCPR and FAO/WHO. Both expert groups benefited from Denis's chairmanship for several years.

For a decade, Denis represented the states and territories on Australia's delegation to CCPR, which is responsible for establishing international standards (maximum residue limits) for pesticide residues in foods and feeds. Because of his knowledge and expertise, Denis substantially raised the profile and status of Australia within CCPR and the Codex Alimentarius Commission.

Denis was a member of the editorial board of *Pest Management Science* and the international advisory board for *Outlooks on Pest Management*. He edited or co-edited numerous international publications on pesticide residues and the safety assessment of pesticide residues in food and drinking water. Denis was also a member of the IUPAC Committee on Crop Protection Chemistry, where he led projects dealing with pesticide residues in food and water, which resulted in significant, influential publications. In recognition of this work, Denis was the recipient of the inaugural IUPAC International Award for Advances in Harmonised Approaches to Crop Protection Chemistry in 2010. Notwithstanding his formal retirement in 2009, Denis continued with his interest in pesticide chemistry, writing and reviewing scientific papers and consulting with Australian and international colleagues, many of whom continued to seek his advice.

Denis had a close and loving relationship with his family, including his wife Gloria, daughter Karen and grandchildren Stuart, Julia and Holly, on whom he doted.

I knew Denis by reputation, but I only met him personally after his retirement at RACI retired chemists outings and the Indooroopilly Men's Shed where he continued with his woodworking hobby, making native bee hotels with his favourite bamboo timber, which he cultivated at home. He retained all copies of *Chemistry in Australia* since his membership commenced in 1962 – all carefully bound with bamboo and fishing line. He was an active participant and contributor to the Men's Shed book club and the 'current affairs' discussion groups. He had a passion for historical books and frequenting the annual second-hand book fairs, he would often come to Men's Shed discussion groups with a last-century book to confirm that today's global problems were often a revisit on yesteryear's issues from which society still hadn't learned.

I would like to acknowledge the input from many of his past and present friends and colleagues in summarising Denis's distinguished career, his positive influence on the career development of younger scientists and his contributions to harmonising standards for pesticide residues in food. In recognition of his many colleagues worldwide and in testament to his national and international reputation, his funeral service was livestreamed nationally and to 15 other countries.

Pieter Scheelings FRACI CChem

National Congress to host a suite of symposia

Every five years, the RACI hosts its National Congress meeting, and the next Congress will be held in Brisbane in July this year. RACI is the oldest professional scientific society in Australia, and this meeting is an opportunity for chemists around the world to meet and to participate in the varied activities that the Congress has to offer. It is a chance to share research and build collaborative networks as well as make new friends during the social activities.

Spread over six days, the Congress will cover all areas of chemistry and will provide opportunity for delegates to move between parallel sessions to hear presentations across diverse topics or simply to immerse themselves in a given discipline. In addition, poster presentations will run during the Congress and ample opportunity will exist for delegates to view them.

We are pleased to announce the first five titles from our plenary speakers:

- 'Carbon in two and three dimensions' by Professor Rodney Ruoff
- 'Taking a scientific approach to science education' by Professor Carl Wieman
- 'Assembly line synthesis' by Professor Varinder Aggarwal
- 'Learning about carbohydrate recognition from functional glycomimetics' by Professor Thisbe Lindhorst
- 'Proton-coupled electron transfer in catalysis and energy conversion' by Professor Sharon Hammes-Schiffer

These eminent chemists will share their research and demonstrate how it is catalysing solutions to global challenges.

Symposia delivered by the RACI will include the following:

The **Medicinal Chemistry and Chemical Biology symposium** will take place over 3.5 days and offer an exciting and diverse program of keynote and invited speakers. The program will illustrate the best in our region's research, from tackling the search for new medicinal compounds to extraordinary advances in chemical probe development. We will also hear from the Division's award winners and editor-in-chief of *Journal of Medicinal Chemistry*.

The **Organic Chemistry symposium** will touch on the discipline's position as a driver of innovations in the sciences concerned with the generation and study of organic materials to address broad academic and societal problems. The symposium will highlight current and emerging activities within the Australian and international organic chemistry community. Themes relating to the design, discovery and execution of chemical synthesis are complemented by more multidisciplinary areas such as chemical biology, organometallics, green chemistry and medicinal chemistry.

The **Australasian Electrochemistry symposium** will provide a forum for the presentation and discussion of all aspects of electrochemistry research, from fundamental studies of electrode processes to their applications in energy, sensor and biomedical systems. The Electrochemistry Division's awards will also be presented during the symposium – or more broadly during the Congress – including the Bruno Breyer Medal, for internationally recognised contributions in the field of electrochemistry, the R.H. Stokes Medal, for distinguished research in the field of electrochemistry carried out mainly in Australasia, and the Bloom-Gutmann Prize, for the best student presentation at the symposium.

Universities across Australia are increasingly incorporating computational chemistry and programming (especially with Jupyter Python) into their teaching programs, particularly in high-year physical chemistry courses. The joint **Physical Chemistry and Chemistry Education symposium** is designed to:

- enhance the effectiveness of these teaching activities, improving the student experience and reducing the educator workload
- support educators design and efficiently evaluate lessons and courses.

These aims with be achieved by sharing case studies, chemistry education pedagogy and research design methodologies, technical knowledge, and resources.

The field of molecular electronics has matured and evolved over the past decades, growing from an initial focus on molecular mimics of solid-state electronic components to encompass a broad range of applications in molecular materials science. All of these endeavours are underpinned by theoretical concepts describing the most fundamental processes of charge transport and remarkable experimental work with electrode | molecule | electrode junctions formed from single-molecules, monolayers or thin-films. The **Molecular Electronics symposium** will integrate presentations describing the theoretical and experimental aspects of charge transport through molecules, molecular design and synthesis, and studies of the electrical properties of molecular junctions.

The Congress website www.raci2022.com is the place to go for all the latest information about the Congress as well as how to register to attend, or present. Over the next few months, the RACI will be promoting different aspects of the Congress in a series of articles, emails and social media posts – keep watching! We look forward to seeing you in Brisbane later this year.

Distinguished Fellowships for five RACI members

The 2021 recipients of Distinguished Fellowships were Professor Stephen Pyne, Dr Richard Thwaites, Professor Dave Winkler, Dr David Edmonds and Dr Pieter Scheelings.

Inaugurated in 1996, Distinguished Fellowships recognise highly distinguished contributions to the chemistry profession in academia, government or industry and the RACI.

The RACI congratulates all recipients and looks forward to presenting their awards in person at this year's National Congress in Brisbane.

Stephen Pyne has made important and significant advances in organic synthesis, medicinal chemistry and natural products chemistry. In recognition of these achievements he has received the University of Wollongong's Vice-Chancellor's Award for Research Partnerships (with Johnson & Johnson) (2009); the A.J. Birch Medal from the RACI Organic Chemistry Division (2012); and the RACI's Archibald Ollé Prize for chemical literature (2015). He has published 374 peer-reviewed journal articles, 11 book chapters and seven patents on drug development and discovery. He has had almost continuous Australian Research Council support since 1998 and has held six NHMRC grants for antibacterial drug development.

Stephen has served the RACI as Chair, NSW Organic Chemistry Group (1999–2001); Chair, National Organic Chemistry Group (2003–2008); member, executive committee (Past Chair), National Organic Chemistry Group (2009–2010); Chair, NSW Organic Chemistry Group One-Day Symposium (2008 and 2010); Chair, National Organic Conference in Hobart (2008); and Chair, NSW Natural Products Chemistry Group One-Day Symposium (2011).

Stephen has taught organic chemistry from first to fourth year at the University of Wollongong for 36 years. He has been Director of the Centre for Medicinal Chemistry and Deputy Director, Centre for Medical and Molecular Bioscience. He has been a member of Faculty Executive Committee, Faculty Research Committee, the Faculty Education Committee and the University Internationalisation Committee. He has served the Australian Research Council as a member of the College of Experts, 2016–2018.

Richard Thwaites graduated from Oxford and started working in London for Albright & Wilson Ltd in 1967. He arrived in Australia in 1970, initially on a two-year secondment but stayed.

His career with Albright & Wilson (Australia) Limited covered senior managerial roles in production, marketing, development and general management.

He joined the RACI in 1971 and was elected Fellow in 1994. In 2015, he was awarded an RACI Citation and he became an Honorary Life Member in 2021.

Richard was Chair of the RACI Qualifications and Accreditation Committee from 2003 to 2012. He has served as President, Secretary and Treasurer of the Victorian Branch and is now a member of the Branch Committee focusing inter alia on the titration competition and convening the Retirees' Group. He is a member of the *Chemistry in Australia* management committee, Chair of the Victorian Branch Health Safety and Environment Group, a member of the HS&E Division Committee, a member of the Food, Nutrition and Analytical Chemistry Group, and is part of the RACI mentoring program. He is Chair of the Australia Group of the Society of Chemical Industry.

His current interests outside chemistry include the Victorian Baptist Historical Society (Secretary), Ashburton Baptist Community Services Inc (Vice President), and the Oxford University Society in Victoria (Committee).

Dave Winkler had an unusually broad formal training in chemistry, physics, chemical engineering and radioastronomy. He is a professor of biochemistry and chemistry at La Trobe Institute for Molecular Science at La Trobe University, an adjunct professor of medicinal chemistry at the Monash Institute for Pharmaceutical Sciences, and a visiting professor in pharmacy at the University of Nottingham, UK.

Dave previously spent more than 30 years at CSIRO researching the application of computational chemistry, AI and machine learning methods to the

design of drugs, agrochemicals, nanomaterials and biomaterials.

He is ranked 227th out of 81 000 medicinal chemists, and 999th out of 520 000 chemists worldwide (Mendeley 2019). He has authored more than 250 refereed journal articles and book chapters, has an *H* index of 52, and is an inventor on 25 filed patents.

Dave has won several prestigious awards, including the CSIRO Medal for Business Excellence, RACI's Adrien Albert award for contributions to medicinal chemistry, the ACS Herman Skolnik award for excellence in cheminformatics, and a Royal Academy of Engineering (UK) Distinguished Fellowship (bioengineering). He is past President of the Federation of Asian Chemical Societies and of the Asian Federation for Medicinal Chemistry, and past Chairman and Director of the RACI Board.

In 1995, towards the latter part of his career, **David Edmonds** became a Fellow of the RACI. Before this, he worked for 35 years in the therapeutic goods industry in both the manufacture and quality assurance of medicines. In 1987, he joined therapeutic goods R&D company Peptech Limited and in 1989 joined the RACI New South Wales Pharmaceutical Science Group as a committee member.

At Peptech, he was appointed QA and regulatory manager. Peptech's animal research section, Peptech Animal Health, developed and eventually commercialised three products: Vaxstrate, a contraceptive vaccine for cows, intended to enhance meat quality; Ovuplant, to bring on ovulation in horses at a known time; and two strengths of Suprelorin, used to castrate male dogs for 6 or 12 months.

David also closely liaised with the Peptech Copenhagen plant, and, in the early 1990s, manufacture of Ovuplant was also set up in two sites in the US, necessitating regular supervising trips. The commercial manufacturing site was licensed by the FDA Center of Veterinary Medicine, involving considerable oversight from Sydney.

David left Peptech in 2008 and set up a part-time consultancy company to advise on chemical, manufacture and control processes. This consultancy specialised in advice for investigational drugs for initial clinical trial use.

David was RACI President in 2004 and RACI Board Treasurer 2014–2018.

David has been involved with the Pharmaceutical Science Group as Chair (1992–1999) and subsequently Treasurer, a position he retains. He has been heavily involved with the organisation of numerous seminars that the Group has presented. Since April 2020, the Group has organised eight webinars, mainly regarding aspects of the science of COVID-19.

David's wife, Barbara, has been highly supportive throughout his career. His other interests include live and recorded classical music, travel and photography.

Pieter Scheelings completed a PhD in organic chemistry at the University of Melbourne. His professional career included a contract post-doc followed by a research chemist and team leader position in the AGAL (NMI) Drug Research Laboratory in Melbourne and then an appointment as regional director and AGAL Board member in Adelaide. After an organisational restructure, Pieter joined QH Forensic and Scientific Services (FSS) as Principal Chemist, Food Chemistry before retiring in 2013. At FSS, he also took on the role of Director/Coordinator of the Asia Pacific Food Analysis Network (APFAN) from the founding coordinator, Dr Howard Bradbury, in 2001. APFAN commenced as a project under FACS, with a focus on providing 'hands-on' training for food analysts from the Asia–Pacific region, mostly at the FSS laboratories.

Pieter also undertook a number of training-based consultancies in developing countries, including Mozambique, Vietnam, PNG and Indonesia. Pieter is a past member of the editorial advisory board of *Managing the Modern Laboratory* and received a citation for 'exemplary contributions' to the AOAC Technical Division on Reference Materials. He has been a past member of the Australian delegation to FAO/WHO Codex Committee on Pesticide Residues meetings.

Pieter joined the RACI as a student in 1963, was admitted as a corporate member in 1968, appointed a Fellow in 2003 and an Honorary Life Member in 2018. He has received several citations for his service to a number of Institute committees, including the 14AC and 15AC conference organising committees and the RACI Policy Committee, and represented the Institute at annual NATA Council meetings for 10 years. He was co-opted as a member and eventually Chair of the Employment and Emoluments Committee for over 20 years and prepared many of the later salary survey reports in collaboration with APESMA for *Chemistry in Australia*.

Four newcomers to suite of RACI awards

Over several years, RACI members, the Board and the RACI Inclusion and Diversity Committee (RIDC) have voiced concerns about the RACI Awards. Many felt that the National Awards were not inclusive of all genders, employment sectors, career stages and backgrounds of RACI members.

In 2020, then President, Vicki Gardiner, instructed RIDC to prepare recommendations for an information proforma for awards, including the purpose of the award and the selection criteria. In early 2021, the General Secretary and Board representative on RIDC, Renate Griffith, undertook to champion changes to the National Awards. Consequently, the Board charged RIDC to undertake a survey of the existing National Awards with a view to identifying gaps, and checking existing award descriptions and the award webpage. A subcommittee consisting of Sally Hutchinson, Kathryn Fairfull-Smith and Renate Griffith undertook this review, and after further discussions within RIDC, the results were presented to the Board.

The Board agreed to some changes to the descriptions of existing awards straightaway, mostly to take opportunity into account when judging contributions of candidates and to use gender-neutral language. The Board decided to leave most existing awards otherwise substantially the same. The website also had a first overhaul, with the categories of awards organised so that they are now more inclusive of employment sectors and career stages.

The Board appointed a subcommittee consisting of Renate Griffith, Melanie MacGregor and David Springer to consider the National Awards further and to suggest new awards where gaps had been identified. These deliberations finally resulted in changes to the award previously known as 'Citation', now called the 'Service to Chemistry Award', and changes to the Distinguished Fellowship awards. Extensions and changes to the Centenary of Federation Teaching Awards have resulted in the Centenary of Federation Teaching Team Awards, and the Chemistry Educator of the Year Awards are now open at all education levels.

Four new awards have been created to encourage RACI members from previously underrepresented groups to apply. They are the:

- Ochre Award for candidates of Indigenous Australian or Torres Strait Islander descent
- Catalyst Award for early career chemists
- Welcome Award for senior chemists new to Australia
- Vicki Gardiner Advocacy Award.

For descriptions of the awards, visit raci.org.au/awards.

Renate Griffith FRACI CChem

Australia Day honours

RACI Fellows Dr Graeme Moad and Dr Graeme Batley have received Australia Day awards for their services to science.

Graeme Moad was honoured with a Companion of the Order of Australia (AC) 'for eminent service to science, particularly polymer design and synthesis and radical polymerisation, education through mentoring, and to professional scientific organisations.'

Graeme Batley received a Member of the Order of Australia (AM) 'for significant service to environmental toxicology and chemical science'.

Graeme Batley
CSIRO

Graeme Moad
CSIRO

Both award recipients are scientists at CSIRO. Moad is at CSIRO Manufacturing Clayton in Melbourne and is also an adjunct professor at Monash University and honorary professor at the Beijing University of Chemical Technology. Batley is Chief Research Scientist in the Environmental Contaminant Mitigation and Technologies research program at CSIRO Land and Water Lucas Heights labs in Sydney. He was granted Honorary Life Membership of the RACI in 2011.

In a CSIRO blog post about the awards, Moad said '… I am extremely proud of my efforts in collaborating with and enabling Australian business and industry, in helping to set international standards, while at the same time contributing to fundamental breakthroughs.'

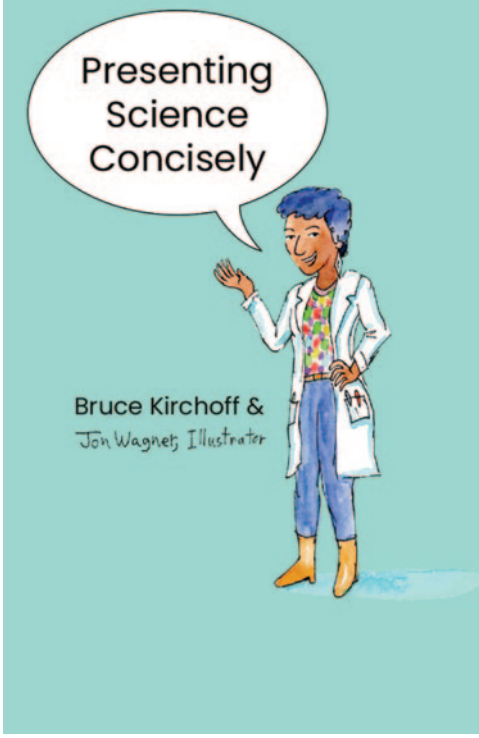
Encouraging diverse future scientists

To me, being a woman in science means opening doors to education and research for girls and women in STEM.

Debbie Silvester-Dean

Associate Professor **Debbie Silvester-Dean** FRACI CChem was speaking about what being a woman in science means to her ahead of International Day of Women and Girls in Science in February. She is an ARC Future Fellow at Curtin University. Her research includes electrochemical processes with a focus on sensing and room temperature ionic liquids. Secretary of RACI's Electrochemistry Division and the Australia/New Zealand representative for the International Society of Electrochemistry, she has received many awards for her contributions to science.

Curtin University



Presenting science concisely

Kirchoff B., Wagner J., CSIRO Publishing, 2021, paperback, ISBN 9781486314683, 134 pp., $44.99

The founding of Australian Science Communicators nearly 30 years ago encouraged scientists to communicate better with the general public. Since then, in Australia and elsewhere, there have been many books explaining how to do it. From its title you might think this was another, but it would profit from a subtitle such as 'A guide for research students', as that is clearly its focus.

Presenting science concisely starts by stressing the importance of telling a story with a look at narrative structure, and it develops, a little tortuously, a link between the scientific method and structures of both a three- and a five-act play. It uses published research papers as examples, but, while the theatrical structure suits these, it is harder to make it fit the work of others in applied science rather than experimental research. If you accept this more specialised niche, the guide has much to offer the young experimental researcher preparing to confront an academic audience.

The book's structure is one they will readily recognise, each chapter citing references listed at the end. This academic approach suits such an audience, but is uneven. One might question why obvious comments such as 'science is about changing the world' even require a reference, while sweeping statements such as 'society does not take our work seriously. It does not seem to value truth' receive none. The implication here and elsewhere is that the public and media are interested in the results but not the processes of science. That is belied by many hugely popular TV series (natural history, archaeology, astronomy etc.) and the CSIRO's own polling. There are other sweeping statements, such as 'All too often scientists have had to shut down their artistic, intuitive sides to complete their studies'. These, unsupported by any references, seem included only to strengthen the book's particular thesis.

The guide is peppered with small humorous cartoons that lift the tone, and there are exercises throughout where readers can put theory into practice. It develops more strongly as it goes along, using an 'and, but, therefore' model to show how to develop structure in talks of various lengths and becoming less theoretical while more practical. It really comes into its own in a substantial section on preparing posters, in which there is detailed advice on layout, colour (including colours suitable for those with colour vision deficiencies) and examples of eye-tracking data that show where observers actually looked.

The guide concludes with useful advice for those presenting at conferences. QR codes are embedded throughout so readers can scan and view online examples of various speakers. These work well. There are some omissions, such as how to use a laser pointer without maddening an audience by continually 'scribbling', and the arguable advice on how to gesture might better have been advice on how to not gesture unnecessarily. This would be appreciated by those irritated and distracted by the endlessly flapping hands of TV presenters and the speakers who copy them.

No guide can provide everything, and this is a slender volume. The author and much of the material are American but there is some important Australian content (such as the 3-Minute Thesis). Here, too, there are significant omissions. In discussing the importance of a good title, elevator and persuasive pitches, no mention is made of the '100 words for a general audience' increasingly required in grant applications. For the budding researcher, this requirement (often filled with an appallingly inappropriate cut-and-paste section from somewhere in the body of text) is arguably the most important section of an application. There is good advice in the guide that could apply to writing such a summary, but this important component of grant applications is not mentioned.

A puzzling omission is the media. Science and the media gets one and a half pages in which half a page makes rather negative sweeping generalisations about the media applicable to news only, while the remaining page is not really about the media at all. This is a pity, because much of the material dealing with short presentations, pitches and conference speaking could be applied to a media section, and postgraduate students need to be keenly aware of what not to do in their first exposures to media as much as what to do. A media section on scientific framing, the importance of a well-chosen grab or sound-bite, what not to say (political, social, institutional etc.), the different requirements of online, print, radio and TV, and journalists' own concise prompts such as 'What, when, where, why and how?' or 'How does this affect me or the people I love?' would show how closely the demands of journalism and science communication are, and would be a valuable addition. Surprisingly there is no mention of the Australian Science Media Centre and its valuable resources for a researcher, especially Science Media Savvy. In any reprint, a chapter on science and the media, prepared by an experienced science journalist, would be a welcome inclusion.

In summary, while one can argue with some content and question some omissions, this would be a useful guide and collection of reference material for postgraduate students, young researchers or others preparing early in their careers to present their work in conferences, posters, short or long talks or for publication.

Rob Morrison

How not to strike oil: Australia's science policy

The question of how to achieve the maximum return from the investment of public money in the funding of research is not new. It's a question that has occupied countries around the world for many decades. In a hearing before the US Congress into the authorisation of funding to the National Science Foundation in 1982, Dr F. Thomas Juster, Professor of Economics at the University of Michigan, likened research in both the natural and the social sciences to drilling for oil. He stated:

> *... a large number of explorations are expected to yield one or two big gushers, a couple of moderate-size producers, and a good many dry holes. The exploration program as a whole is worthwhile if the yield from the producing wells repays the investment in the dry holes, in addition to their own investment costs. Since no-one can predict in advance which idea will become a big gusher and which will be a dry hole, it is necessary to take risks – with the strong presumption that some projects will not (with the benefit of hindsight) have been worth undertaking.*

To make the discoveries that turn out to be the 'gushers', scientists must be allowed the freedom to explore many different avenues, and governments that provide the funding must be willing to take risks. Unfortunately, this is not the policy of the current Australian Government.

In an Open Letter of Expectation that the Acting Minister for Education, the Hon. Stuart Robert, sent to the CEO of the Australian Research Council (ARC) on 6 December 2021, the minister demanded immediate reforms to encourage research into priority areas chosen by the government and into topics that are in the national interest, in particular in the government's selected National Manufacturing Priorities, which are resources technology and critical minerals processing, food and beverages, medical products, recycling and clean energy, defence and space. This attempted railroading of Australia's researchers by the government represents an attack on the academic freedom of our country's scientists. In the opinion of the minister in his letter, 'It is my belief this approach will strengthen the quality of Australia's research endeavour'. I think the opposite is true; it will weaken Australia's scientific standing in the world and result in little or no lasting benefits to our country. Scientific discovery cannot be forced by political intervention. On the contrary, governments can only encourage scientific discovery by allowing scientists the freedom to follow their curiosity, with the hope, as Professor Juster explained, that one or more of them might strike oil. The policy of the government, as outlined by the minister, displays a fundamental lack of understanding of the process of scientific research. Of course, research discoveries must be translated into applications in industry for the benefit of society, but the first step is to make the discoveries, and this does not come from investing in applied research at the cost of basic research.

In an excellent commentary published in *Nature Reviews Chemistry* (2017, vol. 1, pp 1–3), Professor Helmut Schwarz, former president of the Alexander von Humboldt Foundation, Germany's leading funding organisation for the promotion of international academic research, stated that 'Basic research may or may not lead to new technologies. Our safest bet in this gamble is to give our brightest minds the funding and freedom to dream big'. One could only wish that Australia's politicians would read the entire article before making decisions on the direction of science policy. In this article, Professor Schwarz also tells a very relevant anecdote regarding an exchange between the 19th century British Prime Minister William Gladstone and the most famous physical chemist of the time Michael Faraday, the discoverer of electromagnetic induction, so important in electricity generation. When asked by Gladstone whether his research on electricity would ever be of any use, without missing a beat Faraday replied, 'One day, Sir, you may tax it'.

Helmut Schwarz, Honorary President of the Alexander von Humboldt Foundation. Humboldt Foundation/David Ausserhofer

In addition to the detrimental science policy proposed by the minister in his Letter of Expectation, a few weeks later, on Christmas Eve, the ARC published on its website the fact that the minister had vetoed six ARC-approved grant applications, all in the humanities. This was after he had held up the publication of grant outcomes for over a month, leaving researchers all around Australia who depend on grant funding for their salaries in doubt as to whether they still had a job in a week's time. This amounts not only to contempt of all researchers who invest their time and energy in the ARC's lengthy and meticulous peer-review process but also to heartless treatment of many of Australia's finest minds. Although the vetoed grants were all in the humanities, there is no reason why the same fate could not befall an application in the sciences. Such political interference in the approving of grant applications needs to stop.

Returning to the minister's Letter of Expectation, he requests that the CEO of the ARC 'develop clear guidance for researchers so that they use simple and easy-to-understand

language to identify in their applications the potential gains and practical outcomes from their proposed research and its likely contribution to the national interest'. Such a request would not be necessary if the minister left it to the ARC's chosen reviewers and its Colleges of Experts to assess the applications. However, he not only wishes to be able to veto approved grants; in his letter, he also asks that representatives from industry be included on the ARC's Colleges of Experts. Industry representatives are not qualified to assess applications in basic research. Research of the highest standard, worthy of funding by the ARC, is not always easy to understand. That is why the ARC recruits the help of experts.

In chemistry, Australia has only had a single Nobel Prize Winner, Sir John Cornforth, a graduate of the University of Sydney, who in 1975 won the prize for 'work on the stereochemistry of enzyme-catalysed reactions', although he carried out all the work for which he won the prize in the UK, not Australia. In their press release announcing the prize, the Nobel Foundation stated that 'This subject is difficult to explain to the layman'. Fortunately for Sir John, Minister Robert wasn't on the selection committee. The understanding of the mechanisms of enzyme-catalysed reactions, however, has been crucial to the development of modern drugs; for example, the statins, which inhibit the enzyme HMG-CoA reductase in the cholesterol biosynthetic pathway, are the most-commonly used drugs for the prevention of cardiovascular disease. In economic terms, the statins generate multi-billion-dollar sales each year for the pharmaceutical industry. It's hard to judge what scientific advances and economic benefits might be lost to Australia through political interference in the grant approval process. The minister needs to do an about-turn before he does irreparable damage to Australia's research efforts and to our standing internationally.

It's hard to judge what scientific advances and economic benefits might be lost to Australia through political interference in the grant approval process.

Ron Clarke FRACI CChem is Associate Professor at the School of Chemistry, University of Sydney

If an AI system can be an inventor, can it also be a person skilled in the art?

LuckyStep48/iStockphoto

Technology will always win. You can delay technology by legal interference, but technology will flow around legal barriers.

This is a quote from Andy Grove, former CEO of Intel Corporation, who also said: 'I was glad I liked Chemistry'.

The Federal Court of Australia has recently held that, for the purposes of the *Patents Act 1990*, an artificial intelligence (AI) system could be named as an inventor on a patent application (*Thaler v Commissioner of Patents* [2021] FCA 879). The Thaler decision has been appealed by the Commissioner of Patents to the Full Federal Court and only time will tell whether the initial Federal Court decision will stand. Perhaps the Full Federal Court will follow the trend in other jurisdictions, such as the UK, the US and Europe, and hold that AI cannot be an inventor.

While an inventor is a creator of an invention, any patent for the invention is usually viewed through the eyes of the person skilled in the [relevant] art (PSA).

One of the principal requirements for an invention to be patentable is that the invention is not obvious; that is, that it possesses an 'inventive step'. The *Patents Act 1990* (ss. 7(2)) states that an invention is to be taken to involve an inventive step when compared with the prior art base, unless the invention would have been obvious to the relevant PSA in light of the common general knowledge (CGK) as it existed (whether in or out of the patent area) before the priority date of the relevant claim. The CGK can be considered on its own or together with: (a) any single piece of prior art information; or (b) a combination of any two or more pieces of prior art information that the PSA could, before the priority date of the relevant claim, be reasonably expected to have combined.

Legal case law tells us that the PSA:

- is a skilled, but non-inventive, worker in the relevant field of technology
- knows the CGK in the art
- is well versed in the nature of the problem being addressed by the disclosure of the invention
- could be a team of relevant people.

Therefore, in brief, whether or not an invention is obvious is judged from the point of view of a PSA and in the light of a certain type of information that is already in the public domain at the priority date (the date of first filing) of the relevant patent.

Irrespective of whether or not AI can be an inventor, can AI be considered a PSA?

SYNTHIA™

AI and machine learning are being increasingly used in predictive chemistry and in the design of chemical syntheses. AI was initially used to design synthetic pathways, but its abilities have been expanded to navigate around patented syntheses.

Chematica was one such AI system that was developed in 2012 as a hybrid between a database and artificial intelligence,

containing about 60 000 reaction rules entered by scientists. It was renamed SYNTHIA™ after it was purchased by Merck KGaA in 2017 (bit.ly/3G12czs).

SYNTHIA can quickly identify viable routes for the synthesis of chemical targets from predetermined starting materials. SYNTHIA can also be used to circumvent chemical patents. The AI system can consider millions upon millions of synthetic pathways (that are considered to constitute prior art information) and find solutions that circumvent patented synthetic methods. The system looks at the key chemical structures and identifies which bonds must be disconnected in accord with the essential elements of the drug patent claims. The AI system then flags these bonds as not to be cut and refers to its database to find alternative synthetic routes.

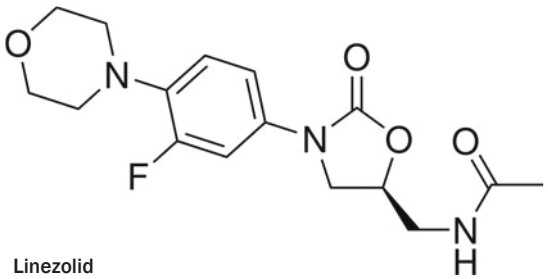
SYNTHIA's power has been illustrated by circumvention of patents granted for commercial drugs, such as Pfizer's antibiotic Linezolid, Merck's diabetes drug Januvia (sitagliptin), and Novartis' multiple myeloma drug Farydak (panobinostat). For example, for Linezolid, SYNTHIA identified formation of an ozaxolidinone ring as being essential and flagged that the ring should be preserved. Within five minutes, SYNTHIA designed several new synthetic pathways using different starting materials (Molga K., Dittwald P., Grzybowski B.A. *Chem* 2019, vol. 5(2), pp. 460–73).

Returning to the points outlined above, SYNTHIA would seem to have all four characteristics of the PSA. While its artificial intelligence is currently directed to finding ways *around* synthetic routes in existing patents, it could be directed to finding the synthetic route in the patent, based on publicly available data that was available at the priority date of the patent.

There are many tests applied by the courts to assessing the inventive step. A well-known test from the *Wellcome Case* is summarised as follows:

> *The test is whether the hypothetical addressee faced with the same problem would have taken as a matter of routine whatever steps might have led from the prior art to the invention, whether they be the steps of the inventor or not.*

(*Wellcome Foundation Ltd v VR Laboratories (Aust) Pty Ltd* (1981) Pty Ltd (1981) 148 CLR, 262 at p. 286)



Linezolid
Harbin

Is it fair to ask if SYNTHIA, given the problem that the inventor faced at the priority date, would have taken as a matter of routine whatever steps might have led from prior art databases to the invention?

This raises interesting questions for patent infringement or validity suits. SYNTHIA cannot appear in court, swear an oath and answer questions posed by a barrister (at least, not at the moment). However, SYNTHIA may be a key tool in the hands of expert witnesses. SYNTHIA could be notionally put in the place of the PSA, given publicly available data available at the patent priority date, and asked to generate synthetic routes that address the problem that is allegedly being solved by the patent-in-suit. The resultant output could provide evidence that the synthetic route claimed in the patent would be one that a PSA would find obvious and arrive at as a matter of routine.

Is it appropriate for AI to become a de facto PSA? If so, would a decision on the grounds of obviousness be justifiable based on a solution identified by AI – a solution that may have been beyond the abilities of a human being? Given the processing speed of AI, will any combination of information available in public databases now become obvious?

It is possible that SYNTHIA will one day be able to contribute her own comments in response to these questions.

Dr **Carolyn Rolls** MRACI and Dr **Jim Onishi** MRACI are at Houlihan2 Patent & Trade Mark Attorneys.

Minerals – we're just digging ourselves a hole

It's shortly after Australia Day, and a new invasion looms on the borders of Europe. Over recent years, world powers have appeased hostile foreign dictators while eastern lands have been invaded and annexed. And the heavy threat of conflict casts a pall over the entire Asia–Pacific, with Australia once again at risk of being dragged into someone else's war. It looks as though 1937 has returned, and we haven't learned a single damn lesson.

How does Australia stand in the face of that conflict? For that matter, how do we stand against the threat of just being cut off: by sanction, by pandemic, by natural disaster, even by simple accident? We're an *island*. Virtually every tonne of our exports (which are mostly composed of various types of dirt), virtually every tonne of the consumer goods that we need in return, go by ship. Ships that can sink. Ships that in the last two years alone have been blocked at the Suez Canal, by scarcity and by the outbreak of COVID among their crews.

During World War II, more than three million tonnes of US merchant shipping was sunk. Nearly 30 000 British sailors were lost. Thirty allied merchant ships were sunk in Australian waters, 19 of these off the coast of New South Wales. And while that war was fought by brave men and women in the field, with countless millions of civilians dying in the crossfire, it was won and lost on the basis of resources and production. The Allies had more of both.

According to the Reserve Bank of Australia, the Australian economy currently relies on mining (11.5% of GDP), mostly for export, and health and education (13.2%). How much will it suffer if material and people cannot move in or out? History tells us: 'The outbreak of war in August 1914 was disastrous for the Australian economy. Export industries were hit by the closing of markets and disruption of shipping, capital inflow slowed sharply, and vital imports were cut off'. (bit.ly/3IN2jj0)

Nearly a decade ago, Geoscience Australia conducted a review of strategic minerals. Its 2013 report was entitled 'Critical commodities for a high-tech world: Australia's potential to supply global demand'. In September 2021, the Morrison Government announced that it will (at some point) establish a $2 billion loan facility for Australian critical minerals projects '… to help secure the vital supplies of resources needed to drive the new energy economy and support the resources jobs of the future'. NSW followed in November, announcing its intent to (at some point) establish a Critical Minerals Hub in the Central West, to support projects such as the $1.3 billion Dubbo Zirconium Mine project. Every single one of these initiatives is focused on trade.

Our strategies need to urgently evolve. Instead of focusing on strategic minerals, we need to be expanding to strategic production.

Our federal and state governments talk. They announce. They engage in discussions such as the Quadrilateral Security Dialogue 'to develop a strategy to secure supply chains'. The world needs strategic minerals, they say. We have them. So they set up the Critical Minerals Facilitation Office to 'connect Australian critical minerals projects to investors and strategic partners to advance projects and provide midstream and downstream opportunities'.

But all of that does Australia precisely no good if we are just putting slightly more valuable dirt in boats and waiting for finished goods to come back to us. Rearranging the deck chairs didn't save the *Titanic*, which, if the analogy isn't obvious enough, sank.

Just 6.0% of our GDP comes from manufacturing. Cut off from the world, if we *make* nothing, then we will *have* nothing. No way to survive. Nothing to defend ourselves with but comparatively expensive rocks.

Our strategies need to urgently evolve. Instead of focusing on strategic minerals, we need to be expanding to strategic production.

I wrote an article in 2020 (September-November issue, p. 20), noting that Australia's supply of the critical chemicals needed to maintain our clean drinking water supplies have, in some cases, recently been increased from two to four weeks. The COVID crisis has left both our society and our very limited manufacturing short on all sorts of supplies. Critical to a country of our size, we are at the time of writing in desperate need of AdBlue (an additive to diesel), putting our entire transport supply chain at risk.

The world needs our critical minerals. As defined by the US, EU and Korea, that includes our platinum group metals (particularly Pt, Pd), rare earths, Ga, In, W, Co, Nb, Mg, Mo, Sb, Li, V, Ni, Ta, Te, Cr and Mn.

But we need our own strategic products. That is – all the chemicals, components (such as semiconductors) and ultimately the finished goods that make our society function. Even if we don't go to war, our inability to supply ourselves leaves us desperately vulnerable. We've seen it multiple times just in the last two years: after the *Ever Given* blocked the Suez; throughout COVID; and – importantly – when other countries diverted our supplies of vaccine 'because they needed them more'.

Somehow we haven't learned that lesson. When World War I broke out, we were fortunate that our troubled attempts to establish a steel industry gave us a single small smelter (at Lithgow). The Newcastle steelworks wasn't established until 1915. Port Kembla came in 1928, just in time for the Great Depression, and the Australian

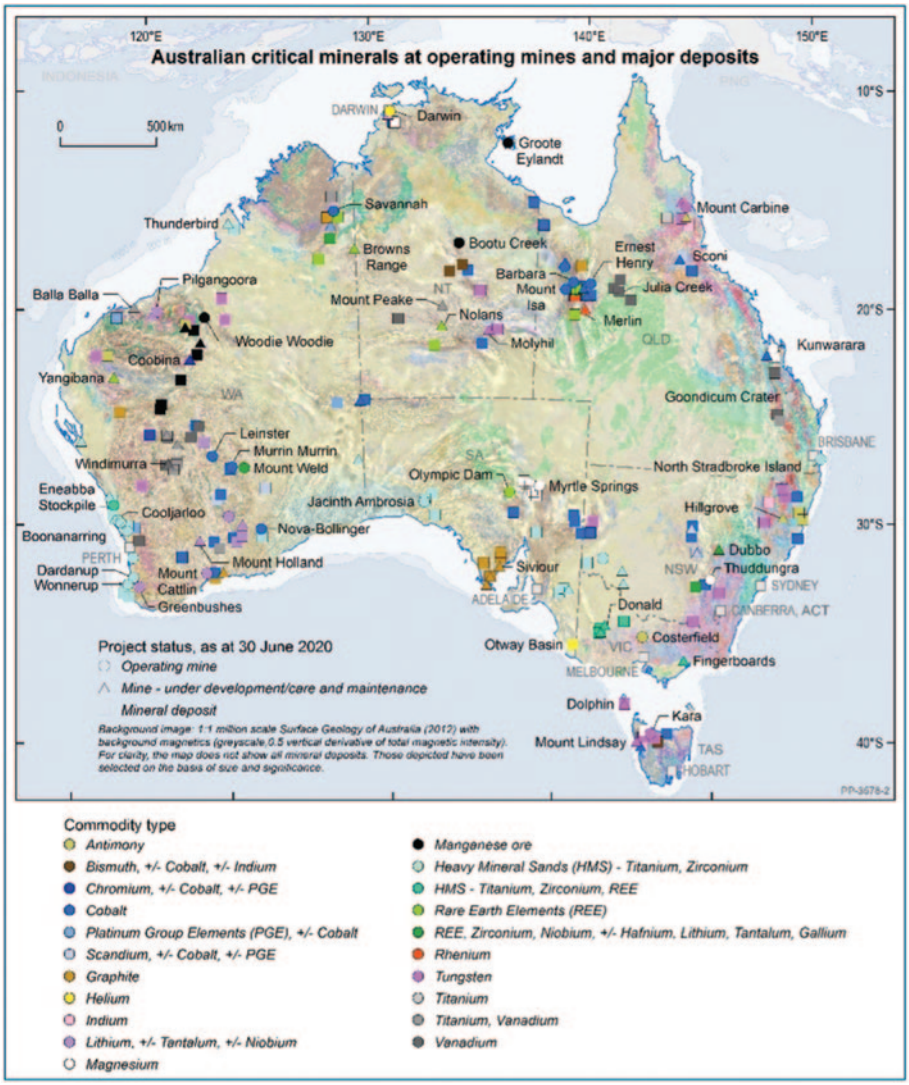
steel industry was barely saved by surging prices in 1937, just before the next global conflict broke out. Both times, Australia ended up with the production capacity base at the needed times. But both times, we just got lucky. Meanwhile, our steel production has halved in the last 20 years, while the value of iron ore exports has doubled in the last 10 years alone.

My late father told me a story about growing up poor in Malta in the 1930s. 'We used to collect all the scrap iron we could find for extra money. Sold it to the Germans. And then the bastards dropped it all right back on us.'

Just like us, Malta was an island that relied almost exclusively on maritime trade for its supply. Few people will know that the Luftwaffe dropped a greater tonnage of bombs on that tiny island in 1942 alone than it did on all of Britain in all of the Blitz. The total tonnage was four times more than everything the Allies dropped in the infamous attack on Dresden. Malta was the most bombed place on Earth. It was cut off and desperate. By August 1942, the fortnightly ration per adult was 400 grams of sugar, 200 grams of fat, 300 grams of bread and 400 grams of corned beef.

With supplies at critical levels, the people of Malta were within two weeks of surrender when the famous convoy of Operation Pedestal broke through. It's an incredible story of bravery that is worth reading about, but it involved terrible sacrifice and fewer than half of the civilian merchant ships in that convoy reached the island.

Our planning for the future can't rely on bravery. It can't rely on endurance or luck. It can't rely on the intervention of allies. And it can't rely just on resources. Our wealth of mineral resources is just half of the equation for our strategic success. If we want to remain a country 'one and free', we need to be uniting in the urgent creation of a new manufacturing base. The future we don't prepare for is one that we're not going to like at all.



Australia's critical minerals operations, 2020.

Dave Sammut FRACI CChem and **Chantelle Craig** are the principals of DCS Technical, a boutique scientific consultancy providing services to the Australian and international minerals, waste recycling and general scientific industries.

dkidpix/iStockphoto

The myth of a teaspoon

At a recent tasting, I was presenting some sparkling wines from the Limoux region of France, a region that was producing sparkling wines at least 100 years before wines from the Champagne region were well known. Towards the end of the tasting, I commented that if the bottle is not empty and you wish to keep it, seal the bottle with a sparkling wine-stopper and store the bottle in the refrigerator. The immediate response was 'Why bother to seal it – just put a spoon in the neck'.

I was somewhat surprised by this response as, although I had heard it suggested previously, I did not think that anyone took the idea seriously. From my years working on wine chemistry and wine oxidation, I know that making every attempt to minimise contact between wine and oxygen is vital for stopping the onset of oxidative spoilage. Thus, sealing the bottle is essential.

The source of bubbles in sparkling wine is the carbon dioxide released during the secondary fermentation. Carbon dioxide is more soluble in wine at a lower temperature, so storing the wine in the refrigerator is also beneficial to the opened bottle.

Searching the literature, I was amazed to see the number of claims that have been made for the 'success' of a teaspoon placed in the neck of the bottle. Some even claim that the teaspoon must be silver and not stainless steel, although the basis for this claim seems highly speculative. There have been a small number of limited studies that have tried to show that there is no difference in wine sensory perception between a bottle left uncovered and one with a spoon in the neck. Most lack replication and are often performed in a domestic setting.

It is essential to note some of the critical features of sparkling wine bubbles. In his book *Uncorked*, Gérard Liger-Belair from the Université de Reims Champagne-Ardenne demonstrated that the amount of carbon dioxide lost depends on the way the wine is poured into the glass: pouring into a tilted glass retains more carbon dioxide than pouring into a vertical glass. Using laser tomography (see April 2013 issue, p. 39), Liger-Belair was able to track the flow of the bubbles in a glass and separately showed that the bubbles are in fact aerosols containing aroma compounds that impact on the taster's impression. To add to the complexity, the release of bubbles depends on the inside surface of the glass.

Bubble behaviour is therefore complex so that any study needs to be replicated to ensure that one is measuring a real effect and not an artefact of a one-off trial. One such study was carried out on champagne by Michel Valade and colleagues from the Comité Interprofessionnel du vin de Champagne (CIVC) in Epernay, France, and published in *Le Vigneron Champenois* in 1994 (copy in French available on request). The work entitled *Le mythe de la petite cuillère* (The myth of the teaspoon) was designed to address the claim that a teaspoon, preferably a silver one, could 'defy all the laws of physics and possess some legendary efficiency to protect the bubbles escaping from an open bottle' (my translation).

Three strategies were used by the CIVC researchers to assess the impact of 'bubble conservation' on the wine: the change in pressure, the loss of weight and sensory analysis. After opening, wine was decanted, leaving 500 millitres in one set and 250 millitres in a second set. The wines were then stored at 12°C with several methods to conserve the bubbles: open bottle, silver teaspoon, stainless steel teaspoon, cork stopper (hermetic seal) and crown seal. Each approach was performed in triplicate.

In the CIVC experiments, the initial bottle pressure was 6 atmospheres, dropping after decanting to 4 atmospheres (500 mL remaining) and 2 atmospheres (250 mL remaining), After 48 hours of storage, the pressure in open bottles and those with a teaspoon inserted in the neck had dropped by a further 50%, indicating a significant loss of bubbles. Clearly there was no teaspoon effect. Those sealed with a cork stopper or crown seal had a pressure drop of only 10%, demonstrating the significant advantage of using a proper closure.

To add to the evidence for the need to use a proper closure, the CIVC researchers also measured the change in the weight of the bottle after storing open, with an inserted teaspoon and with a proper closure. No decrease in weight was observed for the tightly sealed bottles, whereas for the fully open bottles and those with a teaspoon in the neck, the loss in weight was significant and the same for both methods.

To finalise the evidence to dispel the myth of the teaspoon, the wines were subjected to sensory analysis using tasters with experience in tasting champagne. All wines showed some characteristics of oxidation, due to oxygen ingress during opening. However, those sealed with a hermetic seal were clearly more effervescent and livelier than those unsealed or with an inserted teaspoon.

The authors of the CIVC study concluded that the laws of physics 'are not broken' and that the teaspoon effect is clearly a myth. So, if you need to store a partly used bottle, go and buy a proper sparkling wine stopper.

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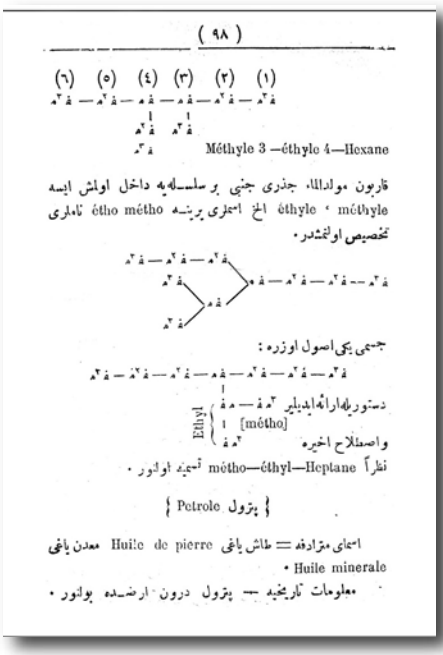
This column was first published in *The Conversation* on 31 December 2021 ('No, putting a spoon in an open bottle of champagne doesn't keep it bubbly – but there is a better way' (bit.ly/33K3TUU). The author holds an adjunct professor position at Charles Sturt University. It is republished here with some modifications by Geoff based on comments on his original piece.

Discovering Charles Bonkowski

I mentioned in my previous Letter that I recognised the names of most of those organic chemists who contributed to the development of systematic nomenclature in the early 1890s. There are a few that I had never heard of, however, and so I spent the summer hunting for information about them. Here I can tell you about Bonkowski Bey, the delegate from Turkey. The Turkish honorific 'bey' is the equivalent of 'gentleman', or perhaps 'esquire', so eliminating that honorific from my search was a simplification. However, 'Bonkowski' sounds more Polish than Turkish and that was a puzzle to be solved, so I reached out to the Turkish Chemical Society. They referred me to Professor Emre Dölen, a retired professor of analytical chemistry at Marmara University, who knows a lot about the history of chemistry in his country and was pleased to help.

Charles Bonkowski (1841–1905) was born in Constantinople (from 1930, Istanbul) to a refugee Polish family. In the first part of the 19th century, Poland was under Russian rule but extremely turbulent. After an uprising was suppressed in 1831, many people fled the country, mostly to settle in Western Europe, but Turkey in the case of Bonkowski's family, although they may have sojourned in some other country on the way. Charles was a successful student of chemistry in the 1860s, and he was sent by the Ottoman government to study in Paris, where he worked with Michel Eugène Chevreul (1786–1889) and Edmond Frémy (1814–1894) and where he also studied pharmacy. Back home in Istanbul in 1865, his career flourished, and he became a chemistry teacher at the Imperial Medical School and in 1894 Chief Chemist of the Sultan. He attended the Paris Chemistry Congress in 1892 and was appointed to the working group that prepared the scheme of systematic nomenclature. According to Professor Dölen, he was not at the Geneva meeting in 1892 and this is confirmed by Bonkowski's absence from the official photograph of the conferees, of which a copy appears in Maurice Crosland's *Historical studies in the language of chemistry* (1962).

I did find a publication of Bonkowski's, an 1876 study of the waters of the hot springs of Bursa – Brousse in French – in northwestern Turkey. Perhaps reflecting Bonkowski's time in Paris, or maybe just because the use of French was widespread in 19th-century scientific writing, the report was written in French. By the turn of the century, things were changing, and Turkey's first organic chemistry textbook, written by Ali Riza Bey and published in 1901, was in Arabic but included some transliteration into Latin characters. Riza had graduated from the medical school in 1888 and like Bonkowski before him he was sent by his government to study in Paris. He returned to Turkey in 1892 to take up teaching appointments at the Imperial Medical School and other institutions.


(٩٨)

(٦) (٥) (٤) (٣) (٢) (١)

Méthyle 3 —éthyle 4—Hexane

Petrole پترول

Huile de pierre معدن یاغی

Huile minerale

A page from Ali Riza's *Kimya-yi Uzvi* (*Organic chemistry*) (1901), Turkey's first organic chemistry textbook.

Charles Bonkowski (photo courtesy Professor Emre Dölen).

Professor Dölen pointed out that systematic nomenclature was followed in Riza's book. In the structure of methyl-3-ethyl-4-hexane shown here, the CH_2 and CH_3 groups are easily identified by their numbered positions, from 1 to 6, running from right to left above the carbon atoms. The Arabic numbers were easy but there is no good match between the Arabic and Latin letters so I couldn't be sure of element symbols. If the RACI membership is as culturally diverse as I hope it is, someone who knows Arabic might be able to help.

In addition to his academic positions, Bonkowski held military appointments, as colonel (1884), then brigadier general (1893) and lieutenant general (1904). In the scientific field, he represented the Ottoman government at a number of international meetings, in addition to the one on chemical nomenclature. He was delegate to the Congrés International des Mines et de la Métallurgie, held in Paris in 1889, where he delivered a report on the minerals of Asia Minor. In 1894, he was one of the Ottoman delegates to the International Sanitary Conference. This was one of a series of meetings, held in Paris starting 1851 and in 1892 adopting the International Sanitary Convention that aimed to stop the spread of plague typhus and other infectious diseases. I'm not sure if Bonkowski was there for that one, but his broad knowledge of things scientific and his European connections made him an ideal delegate for his government.

Ian D. Rae FRACI CChem (idrae@unimelb.edu.au) is a veteran columnist, having begun his Letters in 1984. When he is not compiling columns, he writes on the history of chemistry and is an editor of *Historical Records of Australian Science*.

events

For further details, visit raci.org.au/events

Vic Branch retirees' lunch
1 March, Carlton, Vic

Career Hack
4 March, webinar

Careers in Drug Development, Past and Future
9 March, Sydney, NSW

Chemraderie
17 March, online networking

Preservatives and Preservative Efficacy: Pharmaceuticals and Cosmetics
22 March, West Ryde, NSW

Vic Branch Welcome and Awards Night
7 April, Carlton, Vic

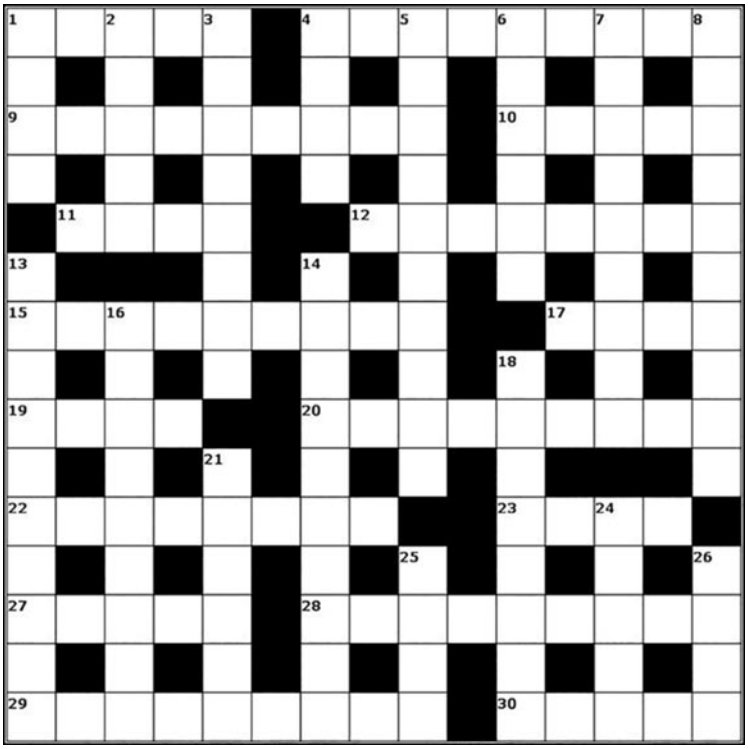
RACI 2022 National Congress
3–8 July, Brisbane, Qld

13th Australasian Organometallics Meeting
11–14 July, Cairns, Qld

Hazards Australasia
25–27 September, Melbourne Convention Centre, Vic.

International Conference on Micro Reaction Technology
27–30 November, Melbourne, Vic

cryptic chemistry



Across

1 Administer with delicacy. (5)
4 Bull! An idiot goes about adding eight. (9)
9 Participates together in scatter pattern. (9)
10 Subject to 15536. (5)
11 Loyal and on-target. (4)
12 Attendance to five elements. (8)
15 Ban cerium reaction to make $RR'R''C^+$. (9)
17 Defeat 10. (4)
19 The one or two elements. (4)
20 Bonded against decent reaction. (9)
22 Five elements found countrywide. (8)
23 Class enter data. (4)
27 Contributor to Spooner's hole in the wall. (5)
28 Anion ear bud. (9)
29 Hung up on ice. (9)
30 Appears to detect with instrument. (5)

Down

1 Peregrination error. (4)
2 Get into record. (5)
3 Compounds from Spooner via young people. (8)
4 A combination of three elements is the beginning of fairy tales. (4)
5 Device breaks down nutriments. (10)
6 Ernst was way after 1822. (6)
7 Hitting on pigment in mixture. (9)
8 Dilute 4 Down making adenosine monophosphate, for example. (10)
13 Cites anode changing compounds. (10)
14 Sacked and sent home. (10)
16 Scan 1 Across mixture to start with. (9)
18 Glucose biopolymers strand broken over flame. (8)
21 Channel classes. (6)
24 Coat dish. (5)
25 Conducting framework unconnected when off. (4)
26 Adds water over casserole. (4)

Graham Mulroney FRACI CChem is Emeritus Professor of Industry Education at RMIT University.
Solution available online at Other resources.

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