chemistry in Australia
June 2018

Chain of thought: a chemical version of CRISPR

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- Biocides and the battle with biofouling
- The chemical truth about teeth
- On Lewis structures and banning the octet rule

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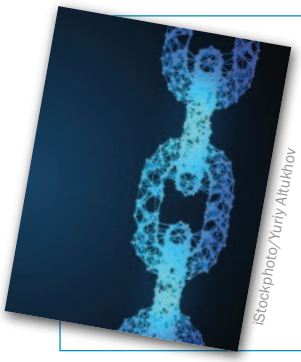
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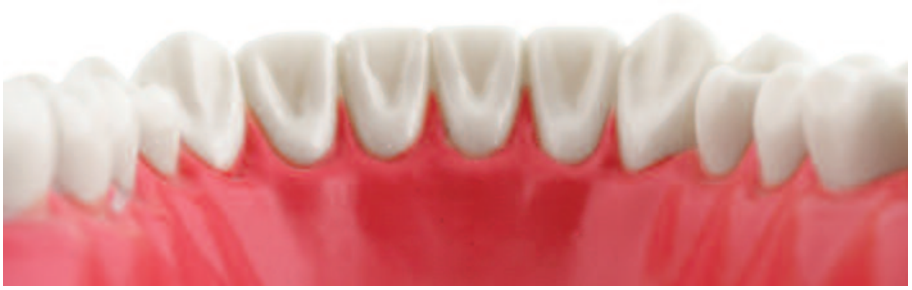
cover story



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The centenary that was

This month marks the conclusion of RACI's centenary year. A century ago, RACI was celebrating its first birthday. World War I had entered its final six months and John Monash had recently taken command of the Australian Corps.

Australian chemist and industrialist David Zeidler was born in 1918. He joined the RACI in 1937 and became a fellow in 1954. He joined CSIR, then ICI, becoming chair in 1973.

As head of CSIR's chemical engineering section during World War II, Zeidler oversaw the planning, construction and operation of eight pilot plants, including producing ethylene from alcohol, ethylene chlorhydrin for ethylene (required for novocaine synthesis), and using the Freney–Lipson process for shrink-proofing woollen army socks. Historian Peter Yule's biography of Zeidler (davidzeidler.com.au) includes a description of Zeidler by then-colleague Ian Wark as having:

… a talent for chemical engineering research, the recognition of which has earned for him the profound respect of the other members of the division. He is among the most co-operative and self-sacrificing men I have known and every officer has had help from him.

Zeidler held committee roles with the Walter and Eliza Hall Institute, Australian Academy of Technological Sciences and Engineering and the Defence Science Committee. He received a Commander of the Order of the British Empire 'for services to industry, science and education', and he was made a Knight Bachelor and a Companion of the Order of Australia.

The RACI centenary kicked off with a successful five-day congress at the Melbourne Convention Centre last July, featuring the RACI Centenary National Conference and 17th Asian Chemical Congress umbrella event, and six specialist partner conferences, plus seminars, specialty partner meetings, one-day symposia, panel sessions, workshops, development and outreach days, official functions and competitions. The congress brought together more than 3300 delegates from Australia, New Zealand, China, Japan, South Korea, Europe and the US. The congress organiser, RACI staff and volunteers (including 24 different organising committees) and 16 sponsors made this event possible. An exhibition program included 126 exhibitors, and 1400 posters were presented. Many smaller meetings and events have been held across the country, organised by RACI branches and divisions.

The RACI centenary book *RACI 1917–2017: a century of bonds*, edited by long-time member Helmut Hügel, was given to congress delegates (copies are available for purchase from the National Office).

Sixteen research students were awarded RACI bursaries to assist them to travel to the Congress. You can read about their experiences at raci.org.au/raci-news/raci100-student-experience.

100 Reactions for RACI100: A Centenary Project, led by the University of Tasmania's Nathan Kilah, invited video submissions highlighting chemistry research or outreach capabilities. Dave Sammut recounted his foray into the spotlight at the National Measurement Institute and Fledge Innovation Labs, with seasoned science communicators Rob Morrison and Deane Hutton, in his article in the August 2017 issue (p. 22).

Late last year, the National Office produced an advent calendar of 25 living Australian chemists as part of the centenary year: raci.org.au/events-awards/advent-calendar.

The RACI Board, branches and divisions are wrapping up the celebrations by suggesting names for consideration for fellowship status. Congratulations to those centenary fellows announced so far (in our April and May issues).

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Porous liquid discovery leads to new spin-out company

Scientists at Queen's University Belfast, UK, who invented a liquid that can dissolve remarkably large amounts of gas have launched a new spin-out company Porous Liquid Technologies Ltd.

The experts took the product from technology demonstration to commercialisation in less than three years.

Originally, the researchers had targeted applications in large-scale industrial separations for their new liquid materials, but the product is already attracting interest in a number of other applications, such as medical diagnostics and household products.

The project team, which includes experts from the School of Chemistry and Chemical Engineering at Queen's, along with colleagues at the University of Liverpool, published their initial findings in 2015 but have since been carrying out further research to increase the yield and effectiveness of the porous liquids.

Professor Stuart James from the School of Chemistry and Chemical Engineering at Queen's University is a co-founder of the new company. He said, 'Porous liquids are a new class of liquid materials that contain microscopic cavities or pores, each the size of a single molecule. They contain up to 10 000 times the number of cavities that are found in conventional liquids, and up to around 20% of the liquid is actually empty space – creating new substances with a far greater absorption capacity than the base solvents.

'Thanks to these cavities, porous liquids can absorb large amounts of gas and they can be tuned to selectively absorb one gas over another. The major benefit of porous liquids is that, unlike solids, they can be circulated, meaning that they can be applied in a host of processes. They can be used in continuous flow separations, such as the removal of impurities from natural gas, which currently relies on inefficient and energy-intensive methods.

'Porous liquids could be used as replacements for liquid absorption systems based on conventional liquids, such as amine solutions. Currently, 40% of natural gas reserves are contaminated with impurities that need to be removed, but the existing technology for removing the impurities requires large amounts of heat energy. The new material would be much more energy efficient.'

A patent examination process is underway for the core material. QUBIS, the commercialisation arm of Queen's University, has invested in the new spin-out company Porous Liquid Technologies Ltd, which will explore a broad range of technological applications.

Queen's University Belfast

Reef ‘sun shield’ trials show promise to prevent coral bleaching

A ‘sun shield’ made from an ultra-thin surface film is showing promise as a potential weapon in the fight to protect the Great Barrier Reef from the impacts of coral bleaching.

Great Barrier Reef Foundation Managing Director Ms Anna Marsden said the results from a small-scale research trial led by the scientist who also developed Australia’s polymer bank notes were very encouraging.

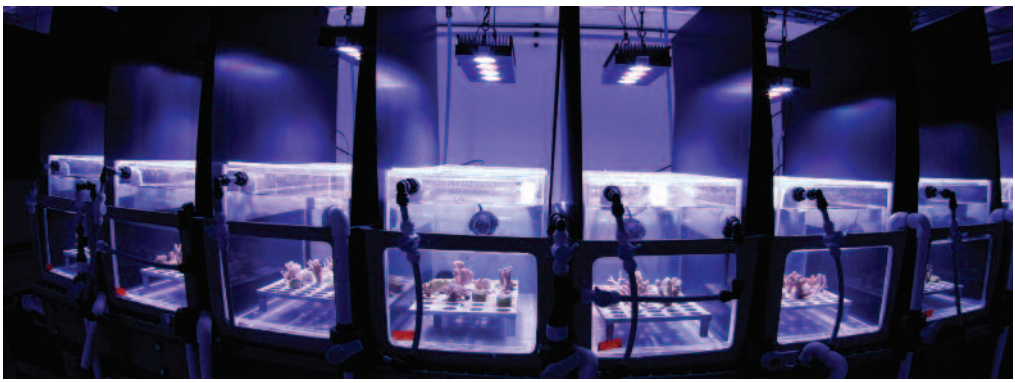
‘We’ve partnered with scientists from the University of Melbourne and the Australian Institute of Marine Science to develop sun protection for the Reef’, Marsden said.

‘The “sun shield” is 50 000 times thinner than a human hair and completely biodegradable, containing the same ingredient corals use to make their hard skeletons – calcium carbonate. It’s designed to sit on the surface of the water above the corals, rather than directly on the corals, to provide an effective barrier against the sun.’

‘While it’s still early days, and the trials have been on a small scale, the testing shows the film reduced light by up to 30%.

‘Scientists tested the effectiveness of the one-molecule-thick film on seven different coral species in simulated coral bleaching event conditions at the Australian Institute of Marine Science’s National Sea Simulator (SeaSim).

‘The surface film provided protection and reduced the level of bleaching in most species.’



Surface testing at the National Sea Simulator, Australian Institute of Marine Science.
Phil Mercurio, Australian Institute of Marine Science

With the surface film containing the same ingredient that corals use to make their skeletons, the research also showed the film had no harmful effects on the corals during the trials.

‘This is a great example of developing and testing out-of-the-box solutions that harness expertise from different areas. In this case, we had chemical engineers and experts in polymer science working with marine ecologists and coral experts to bring this innovation to life’, Marsden said.

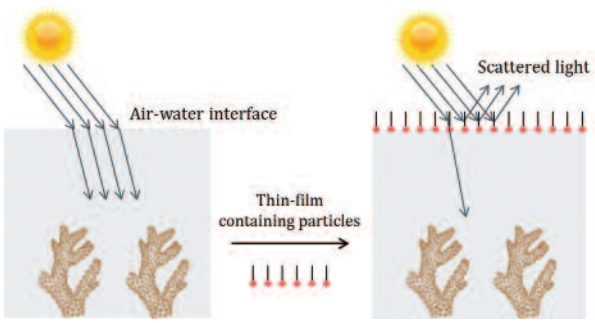
‘The project set out to explore new ways to help reduce the impact of coral bleaching affecting the Great Barrier Reef and coral reefs globally and it created an opportunity to test the idea that by reducing the amount of sunlight from reaching the corals in the first place, we can prevent them from becoming stressed, which leads to bleaching.

‘It’s important to note that this is not intended to be a solution that can be applied over the whole 348 000 square kilometres of Great Barrier Reef – that would never be practical. But it could be deployed on a smaller, local level to protect high-value or high-risk areas of reef.

‘The concept needs more work and testing before it gets to that stage, but it’s an exciting development at a time when we need to explore all possible options to ensure we have a Great Barrier Reef for future generations.’

The research team comprised Professors Greg Qiao FRACI CChem and David Solomon AC, FRACI CChem, and Dr Joel Scofield from the University of Melbourne, Dr Emma Prime (formerly University of Melbourne, now Deakin University), and Dr Andrew Negri and Florita Flores from the Australian Institute of Marine Science. Solomon was the winner of the Prime Minister’s Prize for Science in 2011 for his exceptional contributions to polymer science.

Great Barrier Reef Foundation



How the surface film works.
University of Melbourne

Software can help spot new forms of fentanyl and other drugs

Fentanyl, the synthetic drug that is driving a US overdose epidemic, is not only a killer; it's also a shape shifter. Illicit chemists are constantly cooking up new forms of fentanyl, each with a slightly different chemical structure, stymieing law enforcement and putting users at greater risk.

To control fentanyl, which mimics heroin but is far more potent, forensic chemists need to identify it. But when they encounter a new type of fentanyl – a fentanyl analogue – it will not yet be in the chemical databases they use to identify illegal drugs. Now, the US National Institute of Standards and Technology (NIST) has released a free software tool to help.

The NIST tool contains an algorithm for searching chemical databases that can recognise new fentanyl analogues even if there are no matches in the database. This method, called hybrid similarity search, was recently described in *Analytical Chemistry* (doi: 10.1021/acs.analchem.7b03320).

'If you search for one compound, you will find all the compounds that have a similar chemical structure', said Arun Moorthy, a NIST postdoc fellow and mathematical statistician who worked on the algorithm. 'That should help law enforcement and public health authorities react more quickly when a new and deadly drug hits the streets.'

The method also works with synthetic cathinones – more commonly known as 'bath salts' – synthetic marijuana and other drugs.

Molecules have fingerprints

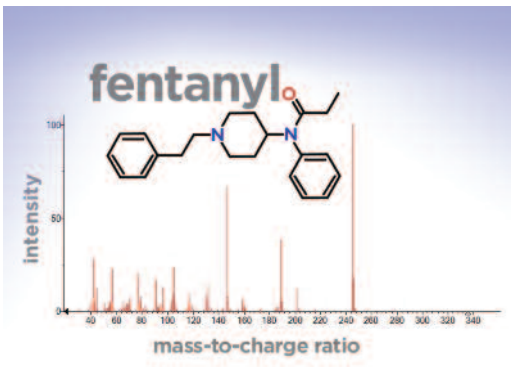
When crime lab chemists receive a bag of powder that might contain illegal drugs, their first step is to use mass spectrometry to get 'molecular fingerprints' of whatever is in the powder, then run those fingerprints against a database of known suspects to look for a likely match.

One of the most commonly used databases of molecular fingerprints is maintained by the Scientific Working Group for the Analysis of Seized Drugs (SWGDRUG). If forensic chemists search that database, which currently contains 88 fentanyl analogues, and get a hit, they will do further tests to confirm the identification. But if they don't get a hit, the substance will remain unknown.

A whack-a-mole game

Why do illicit chemists invent new fentanyl analogues? One reason is that tweaking the structure of the compound can enhance its narcotic effect, producing what users might consider a better high. Another reason is to dodge law enforcement. Before presenting evidence about a new analogue in court, forensic chemists need to discover it and work out its chemical structure.

'Putting a new molecule in the books takes time, and before you know it, there's another one out there', said Sandra



The mass spectrum of the synthetic opioid fentanyl. NIST

Rodriguez-Cruz, a senior research chemist with the Drug Enforcement Administration's Southwest Laboratory in Vista, California. 'It's a whack-a-mole game.'

To create a new analogue, illicit chemists change some of the atoms in the molecule while leaving the core structure intact. They might add a chlorine atom to one branch or remove a hydrogen from another. This almost always changes the compound's fingerprint by changing the mass spectrum.

'Our algorithm corrects for those shifts, so you can find related compounds', said Stephen Stein, the NIST research chemist who oversaw the development of the algorithm.

How it works

An experienced chemist can also correct for those changes manually. But the manual method takes time and has to be done separately for each known compound that the unknown might be related to.

'The concept is intuitive to chemists, but it has never been captured in an algorithm before', Moorthy said. Now that it has, a computer can churn through an entire database looking for related compounds.

If you're a chemist, you can try it out yourself. Hybrid similarity search is already built into the NIST 17 MS Search software, which you may already own. If not, download it from this NIST webpage. Copy a database such as SWGDRUG into the same folder, then run the program and submit the mass spectrum for an unknown compound.

The program will return a list of the most closely related compounds. If that list contains fentanyl or any of its analogues, the unknown might be a fentanyl analogue as well. That list can also give you a head-start on elucidating the new compound's chemical structure.

'Hybrid search is not the silver bullet that will solve the opioid epidemic, but it is a very useful tool', Rodriguez-Cruz said. 'If you have a difficult molecule, it can speed up your workflow significantly.'

US National Institute of Standards and Technology

World's first waste microfactory

The world's first microfactory that can transform the components from electronic waste (e-waste) items such as discarded smartphones and laptops into valuable materials for re-use has been launched at the University of New South Wales, Sydney.

Using technology developed following extensive scientific research at UNSW's Centre for Sustainable Materials Research and Technology (SMaRT Centre), the e-waste microfactory has the potential to reduce the rapidly growing problem of vast amounts of e-waste causing environmental harm and going into landfill.

In launching the microfactory at the SMaRT Centre laboratories, NSW Minister for the Environment Gabrielle Upton said it was exciting to see new technological innovations that could transform waste management and recycling.

SMaRT Centre Director, Professor Veena Sahajwalla, said the e-waste microfactory was the first of a series of microfactories under development and in testing at UNSW that can also turn many types of consumer waste streams such as glass, plastic and timber into commercial materials and products.

For instance, from e-waste, computer circuit boards can be transformed into valuable metal alloys such as copper and tin, while glass and plastic from e-devices can be converted into micromaterials used in industrial grade ceramics and plastic filaments for 3D printing.

'Using our green manufacturing technologies, these microfactories can transform waste where it is stockpiled and created, enabling local businesses and communities to not only tackle local waste problems but to develop a commercial opportunity from the valuable materials that are created', Sahajwalla said.

Sahajwalla said microfactories presented a solution to burning and burying waste items that contain materials that can be transformed into value-added substances and products to meet existing and new industry and consumer demands. This was a truly sustainable solution to our growing waste problem, she said, while offering economic benefits available to local communities.

NSW Minister for the Environment, Gabrielle Upton (left), and Professor Veena Sahajwalla at the new microfactory.

'We have proven you can transform just about anything at the micro-level and transform waste streams into value-added products. For example, instead of looking at plastics as just a nuisance, we've shown scientifically that you can generate materials from that waste stream to create smart filaments for 3D printing', she said.

'These microfactories can transform the manufacturing landscape, especially in remote locations where typically the logistics of having waste transported or processed are prohibitively expensive. This is especially beneficial for the island markets and the remote and regional regions of the country.'

The modular microfactories can operate on a site as small as 50 square metres and can be located wherever waste may be stockpiled. A microfactory is one or a series of small machines and devices that uses patented technology to perform one or more functions in the reforming of waste products into new and usable resources.

The e-waste microfactory that reforms discarded computers, mobile phones and printers, has a number of small modules for this process and fits into a small site. The discarded devices are first placed into a module to break them down. The next module may involve a special robot for the identification of useful parts. Another module then involves using a small furnace, which transforms these parts into valuable materials by using a precisely controlled temperature process developed through extensive research.

These transformed materials include metal alloys and a range of micromaterials. The micromaterials can be used in industrial-grade ceramics, while the specific quality plastics from computers, printers and other discarded sources can be put through another module that produces filaments suitable for 3D-printing applications, while the metal alloys can be used as metal components for new or existing manufacturing processes.

While the SMaRT Centre is expanding its partnerships with industry, investors and local councils, the challenge is to commercialise and create incentives for industry to take up this technology – and to change behaviour – as societies and communities around the world seek to be more sustainable.

University of New South Wales

Call for science to solve global mercury pollution

Mercury poisoning through artisanal and small-scale gold mining is increasing – with critical health dangers affecting more than 15 million people a year. However, Dr Justin Chalker, senior lecturer in synthetic chemistry at Flinders University, believes that chemists can provide cheap and effective solutions to curb the damage. He is calling for a united international effort by chemists to effect a swift and efficient end to the mercury problem in gold mining.

A review of these concerns is calling for action as new research has been published in *Chemistry, A European Journal* (http://onlinelibrary.wiley.com/doi/10.1002/chem.201704840/full).

Chalker's team at Flinders University is taking a decisive lead, having created a polymer made from waste canola oil and sulfur (a low-cost by-product from petroleum production) that can extract mercury from polluted soil, water and air.

After successful field trials in December 2017, Chalker is excited by the prospect of its large-scale production and widespread application – particularly for artisanal and small-scale gold mining, which is the world's largest source of mercury pollution.

More than 15 million people use mercury to mine for gold in about 70 countries – representing up to 25% of the world's gold production, he said.

The process involves using liquid mercury to form an amalgam as it extracts fine traces of gold from ore.

The resulting mercury–gold amalgam is then heated to boil off the mercury from the gold, but the subsequent release of mercury from vapours and tailings exceeds 1000 tonnes each year – accounting for 37% of global mercury emissions.

Health effects on mining communities are dire, with inhaled mercury leading to neurological damage, kidney damage and other critical health issues – while mercury contamination of water and soil affects foods. It is also responsible for children suffering physical and mental disabilities.

Liquid mercury is used in artisanal and small-scale gold mining. (a) Trommels are used to crush rock and mix mercury with ore. (b) As much as 1 kilogram of liquid mercury is added to each trommel along with water and 20 kilograms of ore. (c) Excess mercury is recovered, but mercury-rich mine tailings are often released directly into the environment. (d) Additional mercury is used on the mercury–gold concentrate to form a solid amalgam, which may be isolated by hand. (e) The mercury–gold amalgam is heated with a torch to distill the mercury and allow isolation of gold. (f) A sample of gold isolated in an artisanal mine.

All images are used with permission from Yayasan Tam-buhak Sinta (YTS) and Pure Earth.

Still, gold mining by these dangerous methods is on the rise, particularly in poor and remote areas of Asia, Africa and South America. It forms the backbone of an informal economy that operates without licenses or legal authorisation, making it especially difficult to enforce regulations about preventing mercury use.

Chalker said the answer is not banning mercury use in gold mining – which can't be effectively policed – but to instead develop and promote new mercury-free strategies for mining, tailings processing, and remediating damaged environments.

He believes chemistry is the key to this solution, and that novel, inexpensive innovations are necessary, as resources are scarce in poor communities that favour mercury-dependent gold mining.

'Now is the time to take immediate action', said Chalker, noting the 2017 Minamata Convention on Mercury – ratified by more than 50 parties, but not Australia – represents a comprehensive effort to control the trade, use and emissions of mercury.

Parties to the convention have three years to develop and implement a national plan of action, which means that advances in environmental chemistry and innovative extractive technologies must be initiated now to meet the deadline for action.

'Chemists can play a central role in solving these mercury problems', he said.

'Introducing portable and low-cost mercury sensors, inexpensive and scalable remediation technologies, novel methods to prevent mercury uptake in fish and food crops, and efficient and easy-to-use mercury-free mining techniques are all ways in which the chemistry community can help.'

To meet these challenges, Chalker emphasised that it is critical that new technologies and techniques are low cost and adaptable to the remote and under-resourced areas in which mercury-dependent gold mining is most common.

Flinders University

Metrohm welcomes BioSystems food and wine solutions

BioSystems' analytical reagents and instruments for agro and wine laboratories are now available and fully supported by Metrohm in Australia and New Zealand.

Since 1981 BioSystems SA (Spain) has developed and manufactured effective and reliable analytical systems for laboratories around the world. These systems are composed of photometric analysers (automatic or semi-automatic), colorimetric (enzymatic and chemical) reagent kits, ELISA kits and rapid tests.

BioSystems' Enology line was specifically developed for wine laboratories, offering instruments and reagents designed and validated for the wine industry.

The FoodQuality line provides excellent analytical and control solutions for various sectors within the agri-food diagnostic industry, such as juices and other beverages, meat and processed foods, fish and seafood, milk and dairy products, cereals/nuts and derivatives.

Since it was first launched, the line has been introduced into new geographical regions and by 2017 had reached a total of 15 countries, eight of them the largest wine producers in the world. These 15 markets account for 88% of worldwide wine production: Spain, Italy, France, USA, Argentina, Chile, Australia, China, Portugal, Russia, Romania, Brazil, New Zealand, Japan and Turkey.

For further information, please phone Metrohm Australia on (02) 8899 5200, email info@metrohm.com.au, or visit www.metrohm.com.au or mep.metrohm.com.au.

Protein 'mat' can soak up pollution

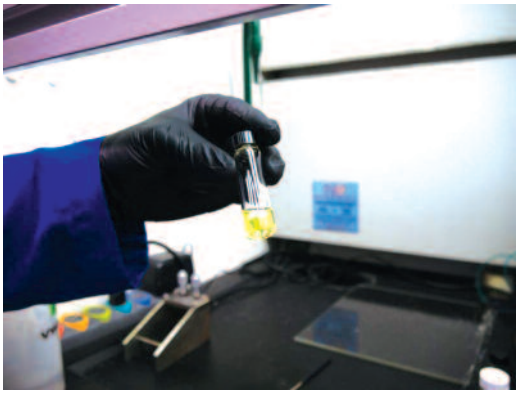
In a breakthrough that could lead to a new class of materials with functions found only in living systems, scientists at the University of California, Berkeley, USA, have worked out a way to keep certain proteins active outside of the cell. The researchers used this technology to create mats that can soak up and trap chemical pollution. The study was published in *Science* (doi: 10.1126/science.aao0335).

Despite years of effort to stabilise proteins outside their native environments, scientists have made limited progress in combining proteins with synthetic components without compromising protein activity. The new study shows a path towards exploiting the power of proteins outside the cell by demonstrating a unique way to keep proteins active in synthetic environments. The materials presented in the study could enable on-demand biochemical reactions where they were once not feasible.

'We think we've cracked the code for interfacing natural and synthetic systems', said Professor Ting Xu, whose research group led the work.

When proteins are removed from their native environments, they tend to fall apart. To function properly, proteins must fold into a specific structure, often with the help of other proteins. To overcome this challenge, Xu's group analysed trends in protein sequences and surfaces to see if they could develop a synthetic polymer that provides all the things a protein would need for its structure and function.

Xu's lab then created random heteropolymers (RHPs). RHPs are composed of four types of monomer subunits, each with chemical properties designed to interact with chemical patches on the surface of proteins of interest. The monomers are connected to mimic a natural protein to maximise the flexibility of their interactions with protein surfaces. The RHPs act as unstructured proteins, commonly seen inside cells. They increased membrane protein folding in water during protein translation and preserved water-soluble protein activity in organic solvents.



The fibre mats contain random heteropolymers that stabilise organophosphorus hydrolase, an enzyme that breaks down a well-known insecticide. Christopher DelRe and Charley Huang

Researchers at Northwestern University ran extensive molecular simulations to show that the RHP would interact favourably with protein surfaces, wrap around protein surfaces in organic solvents and weakly in water, leading to correct protein folding and stability in a non-native environment.

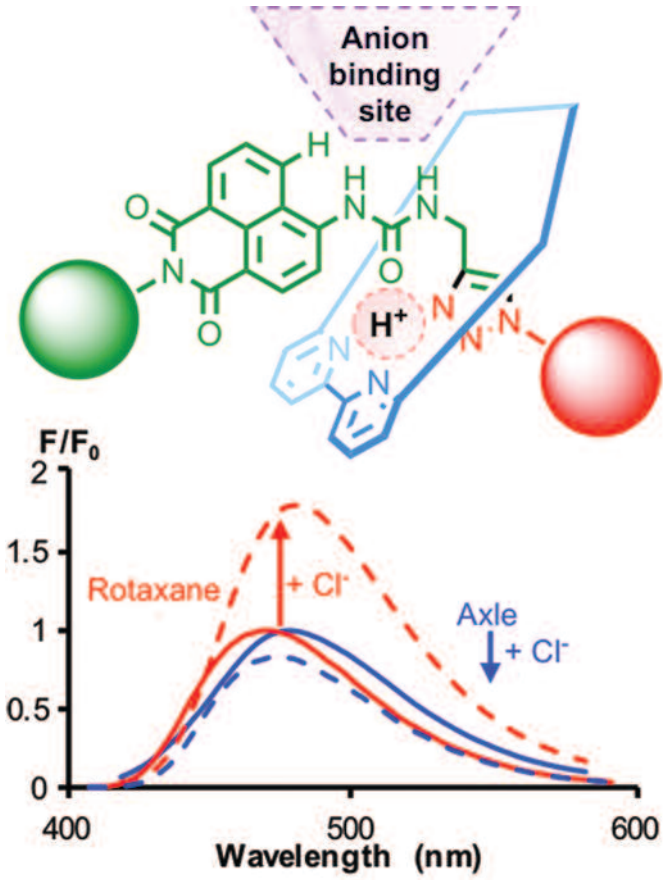
The researchers then tested whether they can use an RHP to create protein-based materials for bioremediation of toxic chemicals. They mixed RHP with a protein called organophosphorus hydrolase (OPH), which degrades toxic organophosphates in insecticides and chemical warfare agents.

The researchers used the RHP/OPH combination to make fibre mats, submersed the mats in a well-known insecticide and found that the mats degraded an amount of insecticide weighing about one-tenth of the total fibre mat in just a few minutes. This opens the door to the creation of larger mats that could soak up toxic chemicals in places like war zones.

'Our study indicated that the approach should be applicable to other enzymes', Xu said. 'This may make it possible to have a portable chemistry lab in different materials.'

University of California, Berkeley

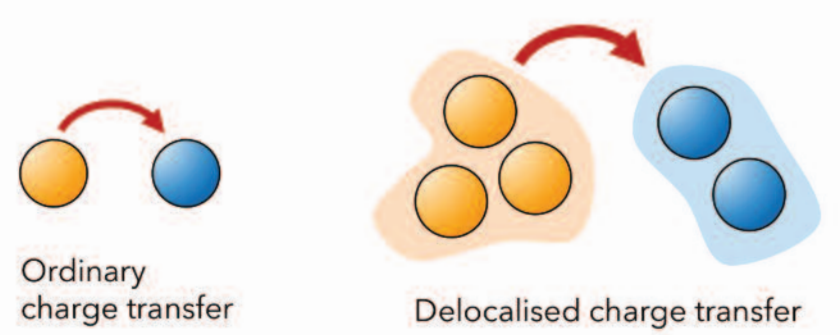
Rotaxane fluorescent sensor for ion pairs



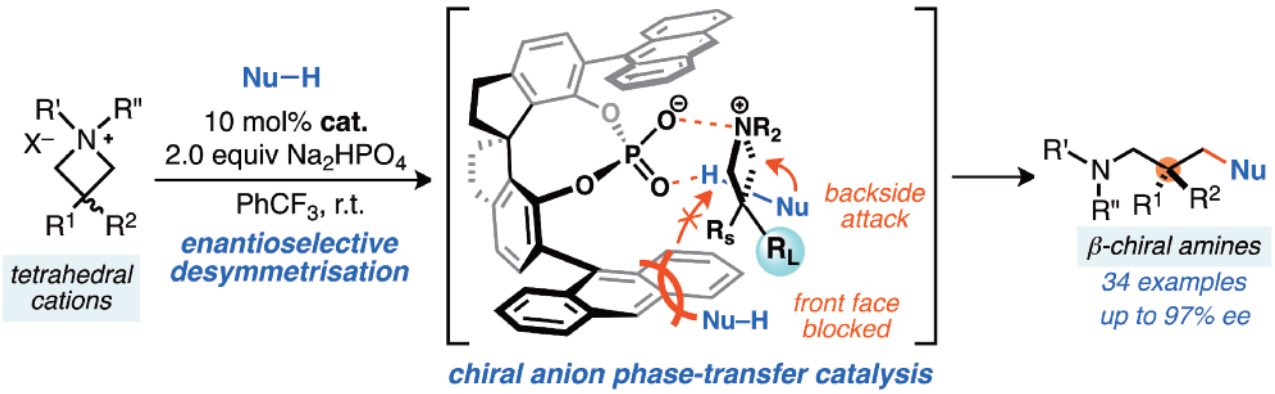
The mechanical bond in interlocked molecules can provide these systems with properties that differ from their non-interlocked components. Although interlocked molecules are famously components of molecular machines, their use as sensors is less well explored. A team led by Kate Jolliffe at the University of Sydney and Stephen Goldup at the University of Southampton, UK, have constructed an interlocked molecule containing an anion-recognition site, together with a fluorescent reporter, in which the mechanical bond alters the recognition properties compared with the anion-binding axle alone (Denis M., Qin L., Turner P., Jolliffe K.A., Goldup S.M. *Angew. Chem. Int. Ed.* 2018, https://doi.org/10.1002/anie.201713105). Combining a simple fluorescent axle with a bipyridine-containing macrocycle yields a rotaxane that acts as a ditopic host, with a turn-on fluorescent response to a separated HX ion pair but not to the anion alone. The selectivity of the rotaxane for anions differs from that of the axle alone, which can bind to anions without protonation, as a result of both the ditopic nature of the binding event and the size selectivity imparted by the crowded environment of the mechanical bond.

Charge transfer when the charge is smeared out

Charge transfer is the simplest chemical reaction, underpinning solar cells, batteries, photosynthesis, combustion, corrosion and molecular electronics. Marcus theory is widely used to describe charge transfer, but is limited to transfer from one donor molecule to one acceptor. However, within many molecular systems – from photosynthetic complexes to organic photovoltaics – charges are coherently delocalised across multiple molecules, making ordinary Marcus theory inapplicable. The only alternatives are simulations that treat the donor and acceptor aggregates as supermolecules, but these are expensive and make it difficult to understand how components of the aggregate contribute to the overall transfer. Researchers at the University of Sydney and the University of Queensland (Taylor N.B., Kassal I. *Chem. Sci.* 2018, **9**, 2942–51) have shown that it is possible to describe charge transfer between delocalised aggregates in terms of the properties of the constituent molecules and couplings between them. The new theory provides qualitative insight into the impact of delocalisation on charge dynamics, predicting effects such as charge supertransfer, a cooperative enhancement of the charge transfer rate above what would be possible with single molecules. This work is expected to clarify charge motion in various molecular systems, including photosynthetic reaction centres, organic photovoltaics and conducting metal–organic frameworks.



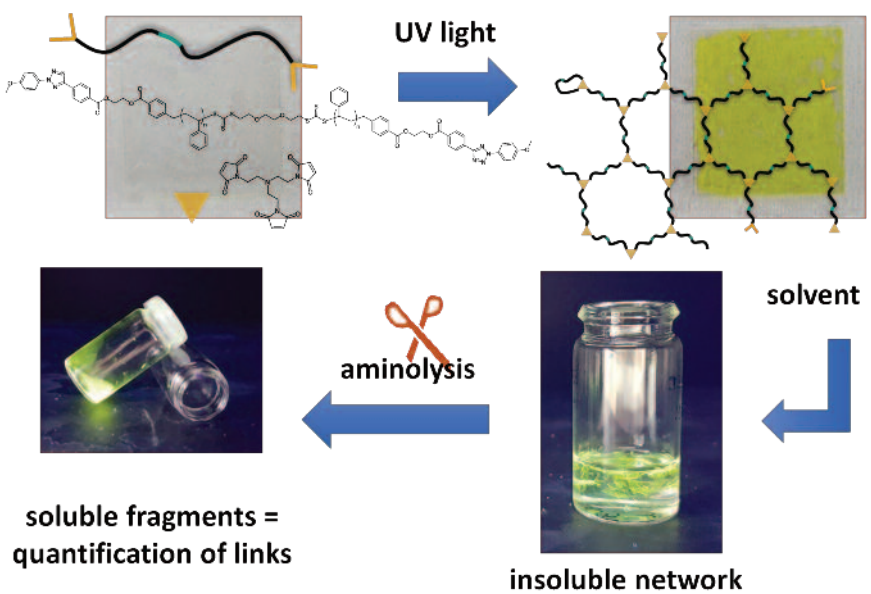
Chiral amines made easy



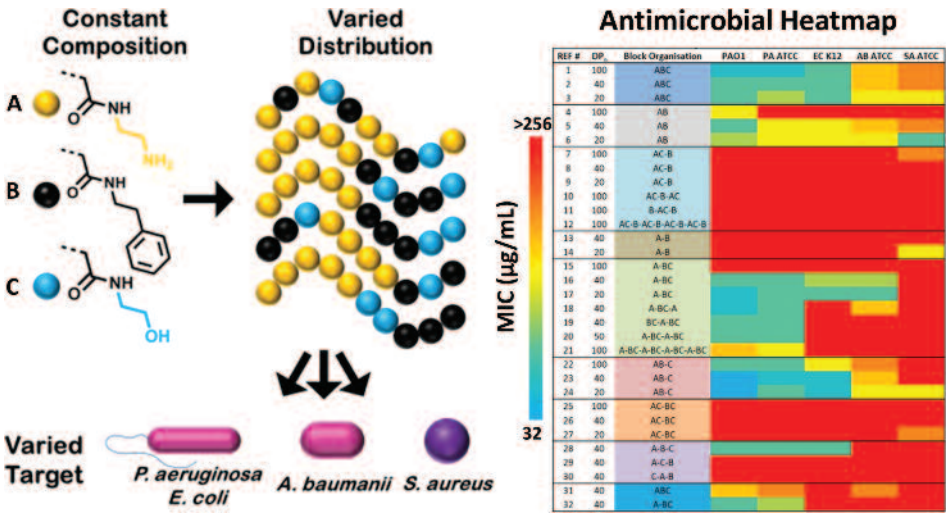
Most reports of counteranion-directed catalytic asymmetric processes have used prochiral electrophiles featuring planar reactive centres in which facial differentiation is relatively well defined. In comparison, the stereoselective functionalisation of non-planar tetrahedral cations by such strategies presents a greater challenge. Recently, researchers from the Hong Kong University of Science and Technology and the University of Tasmania have exploited chiral anion phase-transfer catalysis to develop a novel method for enantioselective desymmetrisation of azetidinium salts to provide β-chiral amines under mild conditions (Qian D., Chen M., Bissember A.C., Sun J. *Angew. Chem. Int. Ed.* 2018, **57**, 3763–6). By design, the use of a non-polar solvent ensures that the azetidinium is sparingly soluble, disfavouring the uncatalysed background reaction. But under these conditions the soluble chiral SPINOL-derived organocatalyst can pair with this cation. The increased solubility of the ensuing chiral ion pair then allows the nucleophile to efficiently attack this species with high asymmetric control. Notably, this approach also allows diastereoisomeric mixtures of azetidinum salts to be converted into chiral amines with excellent stereocontrol.

Every click counts

Polymer-based networks and gels are an important class of materials for biomedicine, controlled drug release, separations and catalysis. But their quantification on the molecular level – for example, the evaluation of the number of cross-linking points in a network – remains challenging. Now a team led Leonie Barner at the Queensland University of Technology and the Karlsruhe Institute of Technology, Germany, has developed an elegant method to quantify the number of linkages within a network by a fluorescence-based methodology (Estupiñán D., Barner-Kowollik C., Barner L. *Angew. Chem. Int. Ed.* 2018, https://doi.org/10.1002/anie.201713388). Polystyrene-based networks were first prepared via nitrile imine-mediated tetrazole-ene cycloaddition under UV irradiation using a trimaleimide as the linker and polystyrene strands capped with tetrazoles as network meshes. Consequently, a fluorescent pyrazoline ring was formed for each linkage point. As the polystyrene strands were synthesised via reversible addition–fragmentation chain-transfer polymerisation, the network could be dissembled via aminolysis of the trithiocarbonate functionalities embedded in the meshes. Importantly, degradation of the network did not affect the number of pyrazoline groups, affording a fluorescence read-out of every network pyrazoline group in solution and enabling quantification of network linkages.

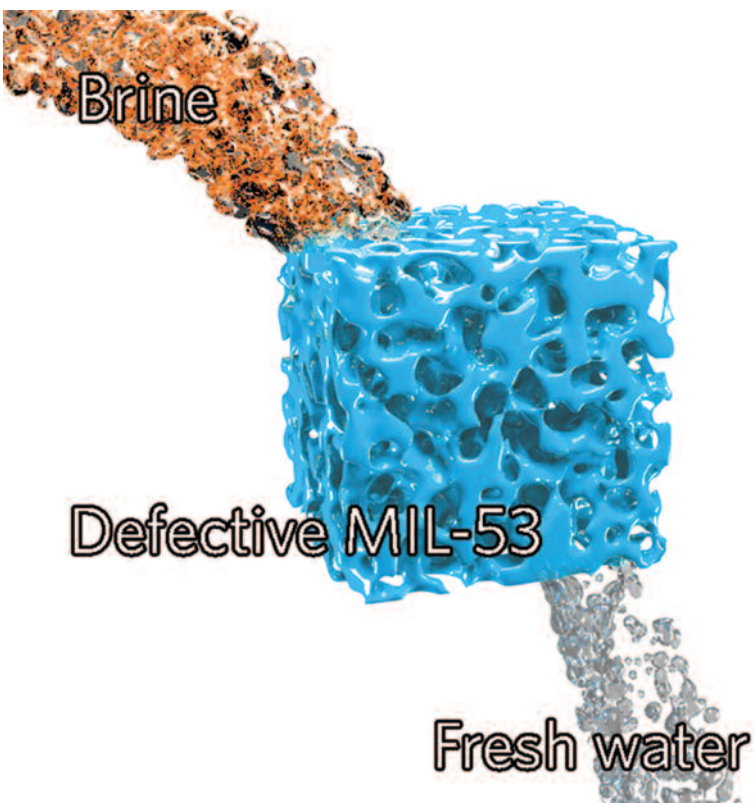


Polymer block order matters



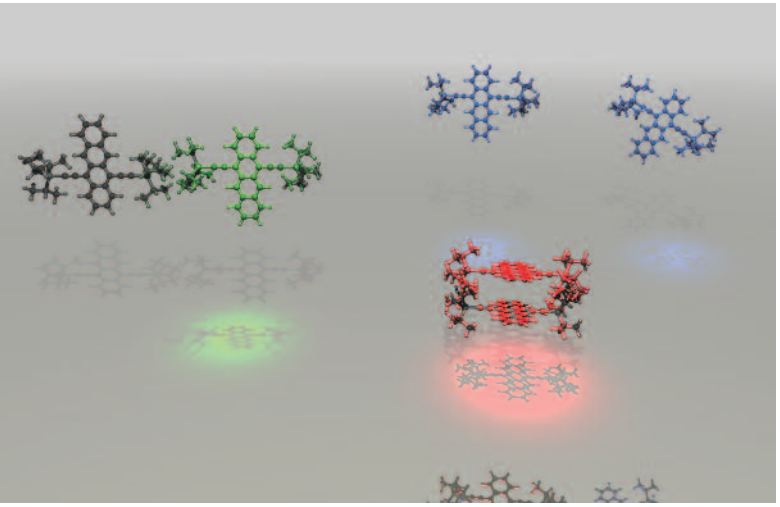
Naturally occurring antimicrobial peptides (AMPs), which are biopolymers that consist of three key types of amino acid functionalities (cationic, hydrophobic and neutral hydrophilic), represent a promising class of antibacterial agents in combating multidrug-resistant bacteria. The bacterial genus specificity of AMPs is highly dependent on the sequence of functional groups on the polymer chain. Mimicking the sequence-defined nature of AMPs, Cyrille Boyer, Edgar Wong and co-workers at the University of New South Wales recently demonstrated the ability to tune bacterial genus specificity by tailoring the order of functional group placement in synthetic multiblock copolymers (Judzewitsch P.R., Nguyen T.-K., Shanmugam S., Wong E.H.H., Boyer C. *Angew. Chem. Int. Ed.* 2018, **57**, 4559–64). These multiblock copolymers can be efficiently prepared via photoinduced electron/energy transfer reversible addition–fragmentation chain-transfer (PET-RAFT) polymerisation. The research showed that manipulation of individual block structures within a synthetic polymer chain, rather than global composition, could yield specific biological outcomes akin to those endowed by the precise monomer sequence and secondary structures in AMPs. This study reveals key insights into the design of synthetic antimicrobial polymers.

Defective MOFs boost water desalination



Desalination using conventional pressure-driven membranes for filtration has a number of drawbacks, including the need to overcome high osmotic pressures, which is technically challenging and energy demanding. Membrane pervaporation is a promising technique but, to date, membranes for this purpose have suffered from low desalination productivity and poor operational stability with concentrated brine feeds. Now, researchers in the Schools of Chemistry and Chemical Engineering at the University of Sydney, University of New South Wales and University of Cambridge, UK, have shown that the incorporation of defective aluminium fumarate metal–organic frameworks (MOFs), known as MIL-53s, into polyvinyl alcohol pervaporation membranes effectively promotes freshwater production from concentrated brines, with salt rejection of >99.999% (Liang W., Li L., Hou J., Shepherd N.D., Bennett T.D., D'Alessandro D.M., Chen V. *Chem. Sci.* 2018, **9**, 3508–16). The engineering control of defects in MOF structures was achieved by facile microwave synthesis techniques to produce materials with hierarchical porosity. This work provides evidence that topological engineering of MOF surfaces is related to their physical and chemical behaviour in a polymeric matrix, opening up the possibility of MOF defect engineering to realise selective separations, drug delivery, catalysis and sensing within a polymeric matrix.

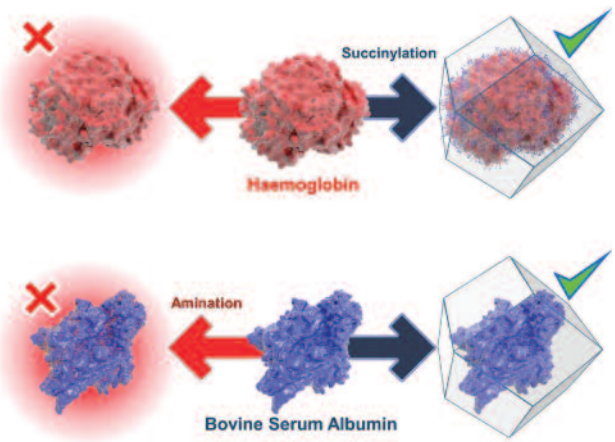
Current doubling – it's a trap!



Conventional solar cells use only a fixed amount of the energy that they capture from the sun, even if the colour of light carries more energy. Light that carries twice the usable energy can be processed through a fission material. The material splits the light into two usable energy packets, leading to more than 100% quantum efficiency. Recently, researchers at the ARC Centre of Excellence for Exciton Science have shown that close alignment of molecules in the fission material should be prevented. On the basis of optical measurements of fission in progress, it was previously believed that fission was a two-step process, with spectra attributed to initial, intermediate, and final states. However, the intermediate that results from close molecular alignment does not have enough energy to produce the final state. A team from the University of New South Wales, University of Adelaide, University of Kentucky, USA, and University of Sydney ran the process backwards (Dover C.B., Gallaher J.K., Frazer L., Tapping P.C., Petty II A.J., Crossley M.J., Anthony J.E., Kee T.W., Schmidt T.W. *Nat. Chem.* 2018, **10**, 305–10). In the reversed experiment, the intermediate spectrum never appeared, proving that the intermediate is not a step towards fission. Instead, it is a step towards energy loss. (It's a trap!)

Surface tuning traps proteins in a protective coat

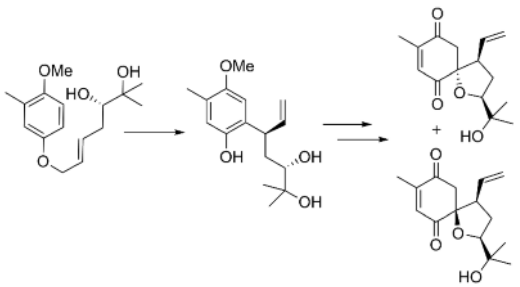
University of Adelaide researchers, in collaboration with colleagues from the Technical University of Graz, Austria, have recently demonstrated that simple chemical modifications to the surface of a protein can be used to reliably induce crystallisation of a protective metal–organic framework (MOF) shell around the biomolecule (Maddigan N.K., Tarzia A., Huang D.M., Sumby C.J., Bell S.G., Falcaro P., Doonan C.J. *Chem. Sci.*, 2018, https://doi.org/10.1039/C8SC00825F). While many biomolecules have potential applications (e.g. enzymes for biocatalysis of chemicals or proteins as therapeutic agents), their fragile structures can be denatured under the inhospitable conditions to which they are exposed. This deficiency can be overcome by a protective process, termed 'biomimetic mineralisation', whereby a MOF shell is formed around the protein to stabilise it under thermal, pH and chemical stress. Zeolitic imidazolate framework-8 (ZIF-8) has been the most widely studied material, with previous work proposing that zinc ions, which form part of the ZIF-8 coating, are attracted to the protein surface and induce crystallisation. In this latest work, the researchers showed that this phenomenon can be manipulated, enabling proteins normally resistant to biomimetic mineralisation to be encapsulated through surface modification of the protein.



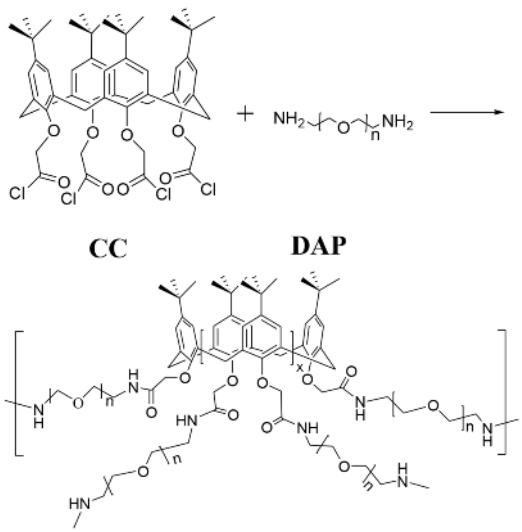
Compiled by **David Huang** MRACI CChem (david.huang@adelaide.edu.au). This section showcases the very best research carried out primarily in Australia. RACI members whose recent work has been published in high impact journals (e.g. *Nature*, *J. Am. Chem. Soc.*, *Angew. Chem. Int. Ed.*) are encouraged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

Highlights from the May issue

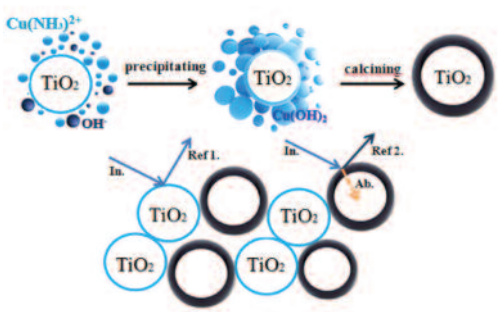
The May 2018 issue of *Australian Journal of Chemistry* consists of 11 research reports from diverse laboratories including from Australia, South Africa and China. Norcott and McErlean from the School of Chemistry, University of Sydney, report the improved synthesis of the sunflower-derived herbicidal natural products (–)-heliespirone A and (+)-heliespirone C, which are potential agricultural chemicals. Computational methods were employed to design the improved route, which is not only shorter than a previous approach (eight steps for the longest linear synthesis) but features a diastereoselective aromatic Claisen rearrangement in which the stereocontrolling unit is distal to the rearranging bonds. Both natural products were obtained with excellent enantiopurity. The stereochemical fidelity of the synthetic strategy and comparison of the optical properties support the hypothesis that the heliespirones are scalemic natural products.



Liu and his colleagues from the Tianjin Key Laboratory of Advanced Fibers and Energy Storage, Tianjin Polytechnic University, China, report the development of an interfacial polymerisation (IP) method for the effective introduction of calixarenes into a thin-layer construction. A series of monolayer thin films was prepared at the interface of hexane and water to investigate the film formation ability of monomers through IP. It was shown that a tetra-calix[4]arene chloride derivative (CC) and a diamino-terminated PEG-1000 (DAP) produced a high-strength membrane. IP was consequently used to prepare a composite membrane with CC and DAP on a polysulfone (PSF) bulk membrane used for ultrafiltration. Attenuated total reflectance-FTIR and X-ray photoelectron spectroscopy data confirmed that a polyamide was formed on the surface of the PSF substrate. The skin layer was a three-micrometre-thick smooth thin film as determined by field-emission scanning electron microscopy. Pure water flux also confirmed that the surface layer was dense. The calixarene-containing network also had an affinity for metal cations, making it easy for metal cations to transfer through. This composite membrane may have application in other separation areas as a result of the special structure imparted by using the calixarenes as cross-linking knots.

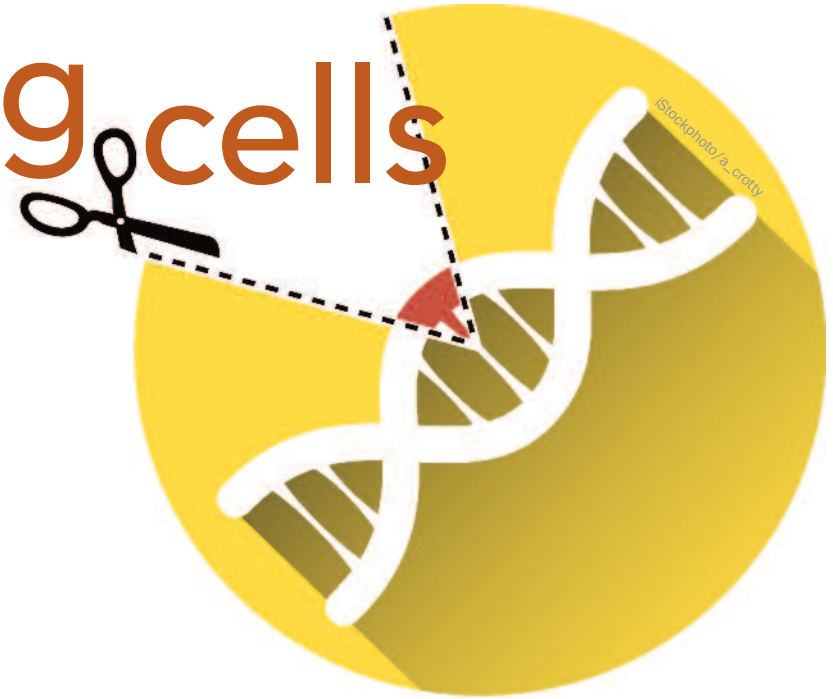


Energy saving is a major goal for scientists and government agencies due to depletion of natural resources, increasing energy prices, and global warming. In highly urbanised populations, the development of thermal insulation materials for roof insulation is an important means to effectively reduce building energy consumption. Although white solar reflective coatings are the coolest building surface materials, they have disadvantages, including an inability to meet aesthetic needs, a high glare, and tendency to contamination that reduces their solar reflectance. There is thus a clear need for reflective dark materials. Yao and colleagues at the School of Chemistry and Chemical Engineering, Jiangnan University, China, report the efficient preparation of dark grey composite pigments having high solar energy reflectance propensity. They used a compositing–precipitation method to prepare pigments with a TiO_2/CuO core–shell structure through calcination of precursors obtained from the precipitation of $Cu(OH)_2$ on TiO_2 particles. The resulting materials show good heat and chemical resistance. The unique core–shell structure imparts not only darker colours to the pigments but also a higher solar reflectivity. Compared with blended pigments, such composite inorganic colour pigments have a higher high near-infrared reflectivity and a deeper colour. In addition, the core–shell structure helps to reduce the use of transition or rare metals. Therefore, the TiO_2/CuO composite pigment may be a promising candidate for inexpensive environmentally friendly cool pigments.



George Koutsantonis FRACI CChem and **John D. Wade** FRACI CChem Co-Editors-in-Chief, *Australian Journal of Chemistry*

Hijacking cells



The hunt for a chemical equivalent of CRISPR

Ian Linney shares his perspective on finding protein targets for drug discovery programs.

Fundamental understanding of specific disease biology can pinpoint proteins that may be involved in a disease of interest. For example, elevated levels of protein X are associated with an increased risk of cancer. The next step in the target validation process would traditionally involve the generation of genetically modified animals in which the gene coding for protein X has been removed in utero, thus generating a 'knock-out' animal model. The knock-out animal no longer produces protein X and subsequently lacks that protein's biological processes. We then compare the knock-out animal with its wild-type cousin in models of our disease of interest to assess the impact of removing protein X.

If the knock-out animal shows an improvement in the progression, severity or in some cases immunity of disease, then X becomes a protein of interest (POI). We also class the response of this animal in the disease models as the knock-out phenotype.

The use of RNAi and CRISPR techniques has expanded our ability to generate these knock-out phenotypes both in mature animals and in individual cells. The advantage of these techniques is that removal of our POI occurs in a mature animal, thus removing any adaptions that may occur in the maturation of a traditional knock-out animal.

As a medicinal chemist, I have spent over half my professional life trying to recapitulate the phenotype observed in these genetically modified knock-out animals by using small molecules that block the function of the POI in the wild type system. Using well-established medicinal chemistry techniques, I can design a small molecule that will be able to interact with our POI with sufficient potency and efficacy, and have the appropriate properties to enable inhibition of the function of the protein in vivo.

Unfortunately, this small molecule approach does not always fully imitate what happens in the POI knock-out animal. One reason for this difference is that while the RNAi and CRISPR gene editing techniques remove the POI in its entirety, my small molecule can only block its function, which could be both partial and transient in nature.

To borrow from Donald Rumsfeld, there are 'the unknown unknowns – the

The degradation of a protein via the ubiquitin proteasome pathway involves a discrete two-step process ...

ones we don't know we don't know'. In our case, there may be unexpected impacts of removing the POI, which may not be related to its function. For example, is our POI involved with other processes unrelated to its perceived function and is it through this route that the required phenotype is generated? This is especially true of protein kinases for which there is an increasing body of literature describing a variety of their non-catalytic roles, such as scaffolding, allosteric regulation of other proteins and even protein–DNA interactions.

So, to come back to my first point – in some cases will the functional inhibition of the targeted POI ever replicate the phenotype observed in the traditional knock-out animal? We have already discussed the advantages of the CRISPR and RNAi biological techniques, so is it therefore possible to have a chemical equivalent to CRISPR? Can we use small molecule medicinal chemistry to remove the POI from a mature test animal and ultimately in the clinic?

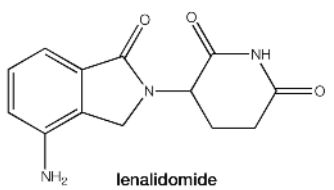
Pioneering work from the laboratory of Craig Crews, Yale University, US, may now provide a means of removing the POI by small molecule techniques by hijacking the cell's own garbage disposal system, the ubiquitin proteasome pathway. The 2004 Chemistry Nobel Prize-winning work of Ciechanover, Hershko, Rose and others has delineated the molecular mechanisms involved in the ubiquitin pathway of protein degradation and it is upon this work the Crews group has developed the concept of PROTACs.

The degradation of a protein via the ubiquitin proteasome pathway involves a discrete two-step process – the first step requires the tagging of the protein with ubiquitin molecules and the second step recognises the specifically tagged protein and subsequently destroys the protein in the proteasome. The key step in the ubiquitination of the protein involves an enzyme called an E3 ligase. It is this E3 ligase that catalyses the transfer of the ubiquitin molecule from the ubiquitin-containing enzyme to an available lysine on the protein that is to be degraded.

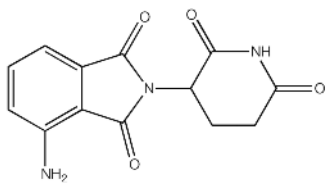
The revolutionary approach from Crews and others was to design heterobifunctional molecules (molecules that are capable of binding contemporaneously to two different targets) that could bind both to the E3 ligase and to our POI. The heterobifunctional molecules are termed PROTACS (PROteolysis TArgeting Chimera).

It is the formation of this ternary complex, PROTAC/E3 ligase/POI, that is key for the degradation of our POI. The E3 ligase component of this tertiary complex then transfers the ubiquitin to our POI, which thus starts the process that eventually ends with the destruction of our POI in the proteasome (see scheme below). After the tagging of the POI with ubiquitin, the PROTAC is free to dissociate from the tertiary complex and is then able to interact with further molecules of our POI and E3 ligase. In this setting, the PROTAC is acting in catalytic mode since one molecule of PROTAC has the potential to degrade multiple copies of the protein.

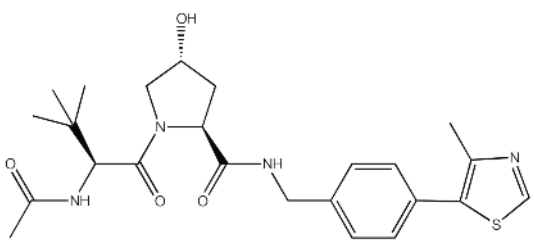
From traditional medicinal chemistry work, we already have discovered a plethora of small molecules that inhibit multiple POIs, so the key requirement in the development of this approach was to now identify suitable small molecules that could bind to the E3 ligase. The discovery that the immunomodulatory drugs lenalidomide and pomalodomide exert their therapeutic effect through binding to the E3 ligase cereblon provided the second part of the jigsaw. An alternative area of E3 ligase exploration has focused on the von Hippel-Lindau complex and its primary ligand hypoxia-inducible factor 1a (HIF-1α). Elegant structure activity work with HIF-1α has provided compound VHL ligand 1 as an additional ligand for the E3 ligase to lenalidomide and pomalodomide.



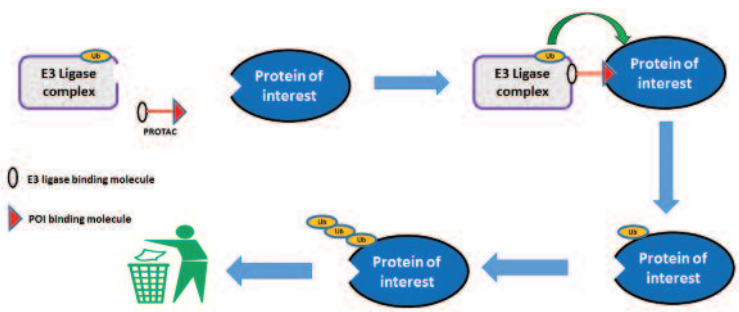
lenalidomide



pomalidomide

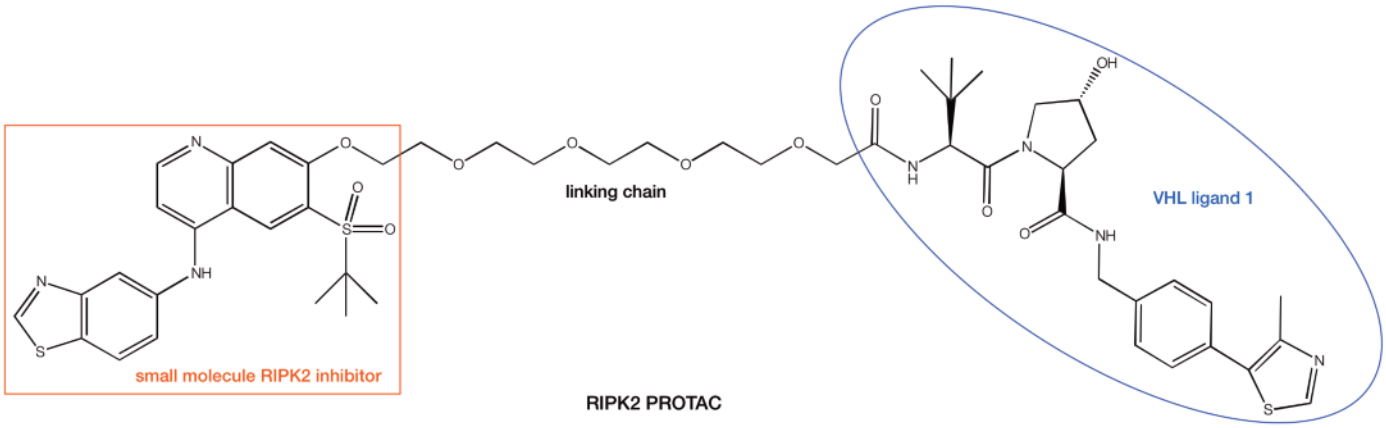


VHL ligand 1



With two pieces of the PROTAC jigsaw now available, it just remains to find suitable methodology to connect them to each other. A significant number of small molecule drug discovery programs are driven by the use of X-ray crystallography studies to rationalise how small molecule ligands bind to their POIs. Analysis of this structural information helps to direct where to append a linking chain to our small molecule to avoid disruption of binding to the POI. The presence of the free nitrogen atom in lenalidomide and pomalodomide provides a suitable anchor point for the other end of the linking chain. In the case of the VHL ligand 1, unmasking the terminal amide provides another amine nitrogen atom suitable for using as a linkage point. Utilisation of this strategy arrives at a compound such as the RIPK2 PROTAC shown below. Work from the the laboratory of Alessio Ciulli, University of Dundee, UK, another of the other pioneers of the PROTAC approach, has recently solved the first ternary complex crystal structures, which aid in the design of the linking chain.

A recent edition of the *Journal of Medicinal Chemistry* (https://pubs.acs.org/toc/jmcmar/61/2) highlights the number of protein targets that are amenable to this approach, including kinases (such as



RIPK2 PROTAC

What is CRISPR gene editing, and how does it work?

You've probably read stories about new research using the gene editing technique CRISPR, also called CRISPR/Cas9. The scientific world is captivated by this revolutionary technology, since it is easier, cheaper and more efficient than previous strategies for modifying DNA.

The term CRISPR/Cas9 stands for Clustered Regularly Interspaced Short Palindromic Repeats/CRISPR associated protein 9. The names reflect important features identified during its discovery, but don't tell us much about how it works, as they were coined before anyone understood what it was.

What does CRISPR/Cas9 do?

CRISPR/Cas9 is a system found in bacteria and involved in immune defence. Bacteria use CRISPR/Cas9 to cut up the DNA of invading bacterial viruses that might otherwise kill them.

Today we've adapted this molecular machinery for an entirely different purpose – to change any chosen letter(s) in an organism's DNA code.

We might want to correct a disease-causing error that was inherited or crept into our DNA when it replicated. Or, in some cases, we may want to enhance the genetic code of crops, livestock or perhaps even people.

So do we just snip the unwanted gene out and replace it with a good one?

We first have to remember that animals and plants are composed of millions of cells, and each cell contains the same DNA. There is no point editing just one cell: we would have to edit the same gene in every single cell. We'd have to snip out millions of genes and paste in millions of new ones.

And not all cells are easy to get to – how could we reach cells buried in our bones or deep within a brain?

A better approach is to start at the beginning and edit the genome while there is only one cell – a very early embryo.

So, all we need is a giant microscope and a tiny pair of scissors. And that is basically what we use.

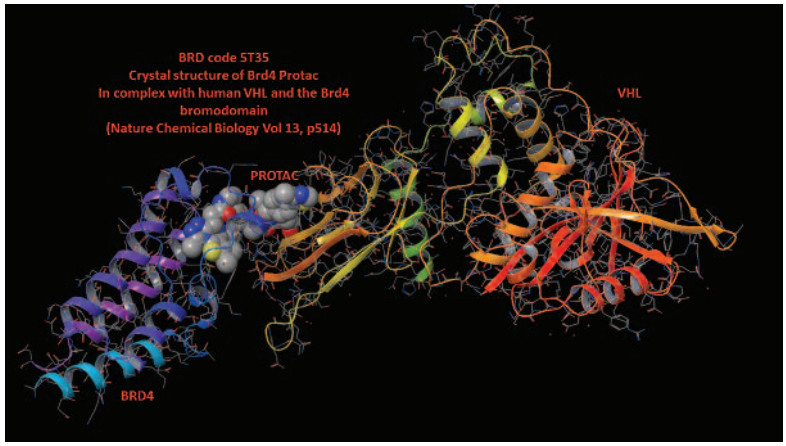
Cas9 is the technical name for the virus-destroying 'scissors' that evolved in bacteria. The CRISPR part of the name comes from repeat DNA sequences that were part of a complex system telling the scissors which part of the DNA to cut.

Find, cut and then paste

In order to target our Cas9 scissors, we link them to an artificial guide that directs them to the matching segment of DNA.

Remember, DNA comes in two strands, with one strand fitting alongside the other. We make a guide with a code that will line up with only one part of our three billion base pair long genome – it's like a Google search. It's truly possible for our guide to comb through vast amounts of genetic material to

With the PROTAC approach, we only have to design molecules that bind to our POI because the pharmacology is now driven by removal of the POI.



X-ray structure from a PROTAC bound to both a POI and the VHL.

the RIPK2 example), epigenetic modifiers (bromodomains and sirtuins) and nuclear hormone receptors (oestrogen and androgen receptors).

Two further features of the PROTAC that offer exciting possibilities in the drug discovery world are the catalytic nature of the PROTAC process and the fact that the small molecule that I design now only needs to bind with our POI; no longer would my small molecule need to inhibit the POI.

The catalytic nature of the PROTAC has led to what Crews has termed 'event-driven pharmacology' rather than the classical exposure-driven pharmacology. In the traditional drug design, the efficacy of the drug is determined by a combination of pharmacokinetics (exposure), pharmacodynamics and target engagement. With the PROTAC's ability to eliminate the POI, the desired efficacy need not match the exposure but is actually driven by the re-synthesis rate of our POI.

With the PROTAC approach, we only have to design molecules that bind to our POI because the

find the one section it matches exactly. Then our 'scissors' can make the cut in exactly the right place.

Once the Cas9 scissors cut the DNA just where we intend, the cell will try to repair the break using any available DNA it can find. So, we also inject the new gene we want to insert.

You can use a microscope and a tiny needle to inject the CRISPR/Cas9 together with the guide and the donor DNA, the new gene. Or, you can punch holes in cells with electric currents and let these things just float in, use guns to shoot them in stuck-on tiny bullets, or introduce them encapsulated in bubbles of fat that fuse with the cell membrane and release their contents inside.

But how does the new gene find the right place to embed itself? Imagine you wanted to put in the last piece of a jigsaw puzzle with three billion pieces, and it's inside a cell, filled with goop like a passionfruit.

What you'd do is fabricate a jigsaw piece of precisely the right shape and inject it into the passionfruit. Then it's just a case of jiggling around until eventually the piece finds its way to the correct part of the puzzle and slots into the only place it fits.

You don't need to be able to see the DNA in our genome through the microscope – it's too small. And you don't really have to jiggle either – random diffusion (called Brownian motion) will always deliver the jigsaw piece to the place where it fits in the end.

First, the guide will jiggle along and find the right place for the scissors to cut, and then the new donor DNA will similarly line up where it fits and will be permanently stitched into the DNA strand via natural DNA repair mechanisms.

Recently, though, new CRISPR editing systems have been created that don't even require a cut through the DNA. In this case, the CRIPSR/Cas and guide system can deliver an enzyme to a particular gene and alter it, changing perhaps an A to a G or a C to a T, rather than cutting anything out or putting anything in.

What are we doing with CRISPR/Cas9?

Most experiments use mouse embryos or cells grown in petri dishes in artificial liquid designed to be like blood. Other researchers are modifying stem cells that may then be re-injected into patients to repopulate damaged organs.

Only a few labs around the world are actually working with early human embryos. This research is highly regulated and carefully watched. Others work on plant cells, as whole plants can be grown from a few cells.

As we learn more, the scope of what we can do with CRISPR/Cas9 will improve. We can do a lot, but every organism and every cell is different. What's more, everything in the body is connected, so we must think about unexpected side effects and consider the ethics of changing genes. Most of all we, as a society, should discuss and agree what we wish to achieve.

Merlin Crossley is Deputy Vice-Chancellor Academic and Professor of Molecular Biology, University of NSW. First published at theconversation.com.

pharmacology is now driven by removal of the POI. This will increase the number of protein targets we as medicinal chemists can target since it is suggested that current therapies only target 13% (400 out of 3000 genes) of the therapeutic proteome (the proteome being the entire set of proteins expressed by an organism at a certain time).

On the basis of our current drug discovery paradigms, a molecule with the physical characteristics of a PROTAC owing to the conjugation of two effective protein binders (high molecular weight, high polar surface area and high logD) would be unlikely to demonstrate activity after oral dosing. However, studies from the Crews group and others have shown in vivo efficacy in animal models after their PROTACs were dosed orally.

These findings have been the basis of two fledgling biotech companies, Arvinas (a 2015 Fierce 15 company) and C4 Therapeutics (a 2016 Fierce 15 company), forming to take this technology into the clinic. In late 2017, Arvinas announced the progression of the first PROTACs into clinical trials – ARV-110 as an orally bioavailable degrader for the androgen receptor for the treatment of metastatic castration-resistant prostate cancer and ARV-378 as a PROTAC targeted against the oestrogen receptor for the treatment of metastatic breast cancer.

We are currently awaiting the read-outs from the current clinical trial using the CRISPR technology and from Arvinas to see if this chemistry-based technology will complement CRISPR.

PROTACs may also find a home in phenotypic screening. Exploiting cell-based phenotypic screening is an increasingly frequent strategy deployed in drug discovery. This approach can identify new protein targets with novel modes of action; however, these proteins are often poorly characterised, and lack readily identifiable enzymatic activity, tool ligands and biomarkers of target engagement. A recent report has used a PROTAC to probe against the poorly understood and non-catalytic target pirin. Pirin has no known enzymatic function in mammalian cells, no reported endogenous ligands and no described validated proximal biomarkers. Previously the team at the Institute of Cancer Research had used classical pull-down techniques to identify that the target of their small molecule was pirin. Switching to the PROTAC containing the small molecule, they were able to show degradation of their POI, pirin, and begin to understand the pharmacology associated with this target. Again, PROTACs are acting as the chemical equivalent of classical knock-out/down techniques in the understanding of the role of specific proteins in the cell.

The pioneering work from Crews and Ciulli can now provide PROTACs as an alternative to the biology-based CRISPR and RNAi techniques. It will be interesting to see how the PROTACs will stack-up against the CRISPR techniques. In the near future, the first read-outs will be available from the relative clinical trials. If the PROTACs are successful in the clinic, then the drug development route would follow the standard small molecule CMC pathway. I look forward to seeing if the PROTAC approach will complement or surpass the potential of CRISPR.

Ian Linney is Group Leader, Medicinal Chemistry, Discovery at Charles River Laboratories International, Cambridge, UK.

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The hard truth

BY DAVE SAMMUT AND CHANTELLE CRAIG

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These fascinating facts about the chemistry of teeth make for perfect conversation next time you're in the dentist's chair – if you can get a word in.

Few sounds inspire such universal loathing as the high-pitched whine. The mosquito in a dark room, the midnight toddler, the dentist's drill – all are generally met with dread and revulsion. So we hope that our teeth and gums will let us avoid the dentist's chair. Our teeth are much more chemically complex than most of us realise. Most chemists would think of bone and teeth as hydroxyapatite, $Ca_{10}(PO_4)_6(OH)_2$. In fact, this mineralisation is of a more complex form, carbonated, with substantial fluoride and cation substitution (mostly Na, but also Mg, K): $Ca_{10-x}Na_x(PO_4)_{6-y}(CO_3)_z(OH)_{2-u}F_u$. The carbonate substitutes phosphate, but not on a 1:1 stoichiometric basis, and the resulting lattice structure is appreciably disrupted.

During tooth decay, the mineral is subject to two primary forms of attack: direct acid dissolution, and decalcification via chelation with dissociated organic acids such as citrate or lactate. Mineral acids such as hydrochloric would, of course, be even more effective in their attack, but are relatively uncommon in the mouth.

Acids can come from your food and drink, but bacteria make matters even worse. These bacteria, particularly *Streptococcus mutans*, feed on sugars in your mouth, creating organic acids (such as lactic acid). *Lactobacilli* are then involved in the progression of decay.

The two main mineralised components of teeth – dentine and enamel – have quite different structures, notwithstanding their similar components:

carbonated hydroxyapatite, water and organic molecules (mostly protein and lipids). Featherstone and Lussi (*Dental Erosion*, doi: 10.1159/000093351) show that while enamel contains 96% by weight mineral, this is only 85% by volume, the presence of 12% water and 3% protein/lipid by volume allows molecules to diffuse through the enamel. As Mrs Marsh said in a well-known toothpaste advertisement back in the 1970s, the liquid *really does* get in.

By contrast, dentine – the substructure of the tooth, underlying the enamel – has a much lower mineral content: 47% by volume, with 20% water and a much higher organic content (33% by volume). The higher water and organic content allows greater and more rapid diffusion of dissolved attacking species, and therefore makes the dentine more vulnerable to attack.

The chemistry of dental decay is yet more complex. Both dentine and enamel are composed of very fine-grained individual crystals. In enamel, about half of the organic material is present as a very thin covering over these individual crystals, with the other half being lipid. As such, any liquid-based chemical attack must first diffuse past any surface plaque, the pellicle (a continually regenerated surface layer of salivary proteins and phospholipids), the enamel crystal lattice, and then the protein sheathing on the crystals themselves.

The chemistry of the attack is strongly pH dependent. This directly influences the available H^+, but it also affects the dissociation of organic acids. At pH 2, the hydrogen ions in citric acid directly attack the mineral surface. At pH 7, citrate draws calcium out of the mineral, and at intermediate pH both mechanisms occur.

Conversely, if the calcium level is saturated (a strongly pH-dependent relationship), then as saliva neutralises the acid in the presence of fluoride, fluorapatite ($Ca_{10}(PO_4)_6F_2$) forms near the surface. This is much stronger than carbonated hydroxyapatite, and the added protection it provides is the basis for the fluoridation of toothpaste.

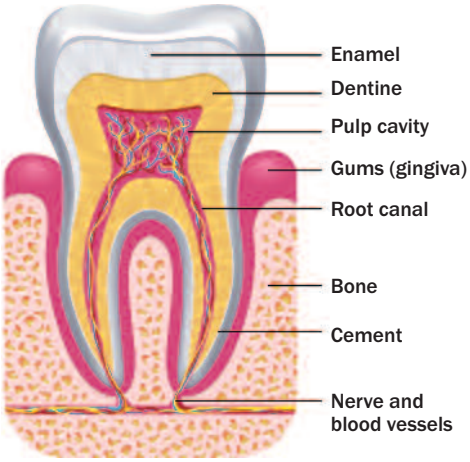
In the event of the cavity comes the drill. Even prehistoric humans were apparently willing to give that a go (as evidenced by teeth found at a site in Pakistan, dating to about 7000 BCE), but I'd imagine that the whining came from the patient, not the flint.

For the past 150 years, dentists have been filling cavities with mercury amalgam. The technique comes in various forms, but the dominant variety uses liquid mercury mixed at the point of use with a 1:1 ratio of fine-powdered dental amalgam alloy (typically 67–74% Ag, 25–28% Sn, and up to 6% Cu, 2% Zn and 3% Hg). The resulting mixture is more than 50% mercury. It sets into position rapidly, and then cures within hours to form a relatively resilient moulded shape that prevents ingress of bacteria and liquid.

The setting amalgam is placed into the prepared tooth cavity and compressed firmly. Excess mercury rises to the surface, where it is removed by the dentist. The two phases react to form a body-centred cubic γ1 Hg–Ag phase and γ2 Hg–Sn phase, with a significant proportion of unreacted Ag_3Sn and Hg from the two starting materials, which continue to react very slowly.

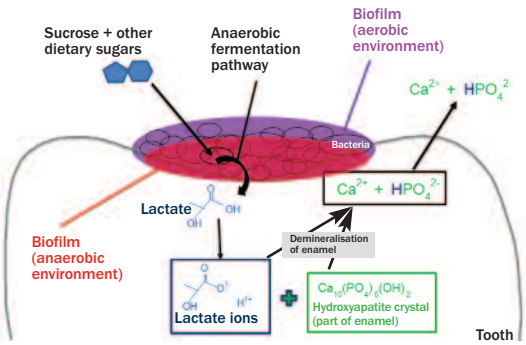
Understandably, this technique has yielded significant concern about the potential toxicity of (particularly) the mercury to both the patient and dental staff, both during emplacement and removal, and with long-term exposure. Over time, the amalgam tarnishes (especially through sulfidisation) and undergoes galvanic corrosion between the more electronegative γ2 phase and the γ1 phase. Moreover, there is additional concern about the toxicology of dental amalgam in crematoria and safe disposal from dental offices.

A 2006 study by the European Commission concluded that 'there is no scientific evidence [that] risks of adverse systemic effects exist and the current use of dental amalgam does



Anatomy of a tooth. iStockphoto/MicrovOne

During tooth decay, the mineral is subject to two primary forms of attack: direct acid dissolution, and decalcification via chelation with dissociated organic acids such as citrate or lactate.



Microbe communities attach to the tooth surface and create a biofilm. As the biofilm grows, an anaerobic environment forms from the oxygen being used up. Microbes use sucrose and other dietary sugars as a food source. The dietary sugars go through anaerobic fermentation pathways, producing lactate. The lactate is excreted from the cell onto the tooth enamel, and then ionises. The lactate ions demineralise the hydroxyapatite crystals, causing the tooth to be degraded.
Wikicommons/Alsheik4/CC BY-SA 4.0

not pose a risk of systemic disease.' (bit.ly/2GbePxT)

Nonetheless, the emplacement of mercury amalgam requires the drilling of larger cavities (greater tooth tissue removal) than newer technologies, it doesn't bond well with the tooth surface, and the resulting fillings are not tooth-coloured. They are therefore typically not used except for posterior teeth. The technique is being taught at fewer dental schools, and it is banned altogether in Norway and Sweden.

There are many alternatives to dental amalgam: composites, glass ionomer cement, compomers, giomers and sealants, as well as gold and indirect materials such as dental porcelain, which are prepared externally. Gold and indirect materials are not favoured because they are costly and require time-consuming procedures.

The substantial number of variations makes quick description difficult. In simple terms, composites consist of some combination of a polymerisable resin base (for in situ placement) and a ceramic filler (for strength) varying from nano to macro size (0.005–100 μm), usually with other components such as etching and surface bonding agents. Curing is usually initiated using a laser, plasma-arc or other high-intensity light source, often within narrow wavelength bands in the visible spectrum (470 ± 20 nm).

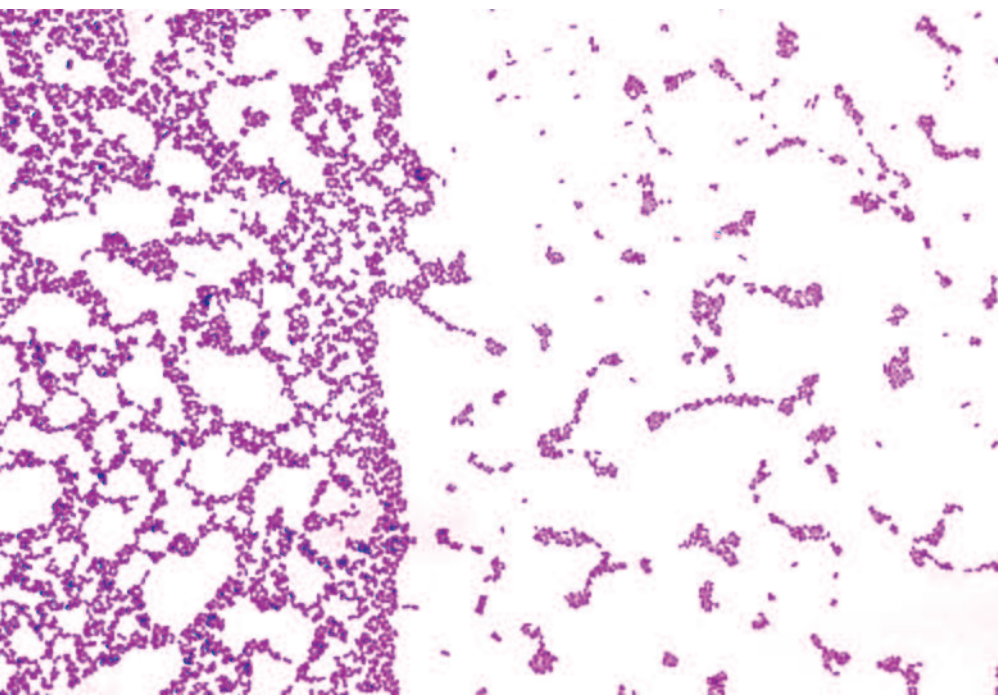
The resin could include a wide range of aromatic and diacrylate monomers, such as bisphenol A-glycidyl methacrylate (Bis-GMA), ethoxylated bisphenol A-methacrylate (Bis-EMA), triethylene glycol dimethacrylate (TEGDMA) and urethane dimethacrylate (UDMA). These monomers then require a non-toxic solvent, which must evaporate quickly during curing.

The filler particles are typically inorganic – silica/alumina glass and/or sodium fluoride – often coated with silane coupling agents (such as trialkoxysilate) to foster covalent coupling between the filler and resin matrix.

Early versions of composite materials were not favoured by dentists because the etching, bonding, emplacement and curing steps were separate, consuming clinical time. More recent materials combine these steps, seeing greater clinical take-up, with the ultimate goal being to achieve a single-step composite.

Glass ionomers, compomers and giomers are different polymerisable combinations of monomers and hard-wearing materials. Ultimately, the goal in every case is to create a filling that is malleable to the cavity in the first instance, then durable and physically stable so that it protects the tooth without excessive shrinkage, cracking or wear on either the tooth itself or its touching opposite (which is a problem with some of the harder ceramic materials). Even one-millimetre cracking or shrinkage can be a major problem, given that *Streptococcus mutans* is only 0.1 millimetres in size.

The bacterial effect of the material is also an issue. It is believed that



Photomicrograph of *Streptococcus mutans* bacteria using the Gram stain technique. The *S. mutans* organism can cause subacute bacterial endocarditis and dental cavities.

Centers for Disease Control/Dr Richard Facklam

... the goal ... is to create a filling that is malleable to the cavity in the first instance, then durable and physically stable so that it protects the tooth without excessive shrinkage, cracking or wear on either the tooth itself or its touching opposite.

Fillings that heal your teeth

Researchers from the University of Nottingham, UK, and the Wyss Institute at Harvard University, USA, have developed therapeutic synthetic, light-curable, biomaterials for dental treatments that support native dental stem cells inside teeth to repair and regenerate dentine.

The approach could significantly affect millions of dental patients each year by dental fillings that help heal teeth when they are injured from dental disease or dental surgery.

The research received second prize in the materials category of the Royal Society of Chemistry's Emerging Technologies Competition 2016.

Dr Adam Celiz, formerly Marie Curie Research Fellow at the University of Nottingham, said 'Existing dental fillings are toxic to cells and are therefore incompatible with pulp tissue inside the tooth. In cases of dental pulp disease and injury, a root canal is typically performed to remove the infected tissues.

'We have designed synthetic biomaterials that can be used similarly to dental fillings but can be placed in direct contact with pulp tissue to stimulate the native stem cell population for repair and regeneration of pulp tissue and the surrounding dentin. Our approach has great promise to impact the dental field and this prize provides a great platform to develop this technology further with industrial partners.'

In 2014, Celiz was awarded a Marie Curie International Outgoing Fellowship to build his own research program at the Wyss Institute for Biologically Inspired Engineering at Harvard University.

Last year, Celiz received yet more recognition for his innovative development of biomaterials for dental treatments. He was awarded the Larry Hench Young Investigators Prize by the UK Society for Biomaterials (UKSB) for developing dental alternatives to root canal treatment. The £500 prize is awarded to a promising young research scientist in recognition of outstanding and innovative contributions in a selected field of biomaterials research.

In May last year Celiz won first prize in the 'Innovation and Entrepreneurship' category of the 2017 Marie Curie Awards. He is now part of the Department of Bioengineering at Imperial College London.

University of Nottingham

mercury amalgam is mildly bactericidal. However, TEGDMA stimulates the growth of *Streptococcus mutans* and *Streptococcus salivarius* in a pH-dependent manner. If the bacteria can continue to grow under the filling, then the possibility of secondary cavities can continue to cause problems.

The European Commission study also assessed the potential risks with these newer, alternative dental treatments, and concluded that 'dental health can be adequately ensured by both types of material [amalgam and composite]. All the materials are considered safe to use and they are all associated with very low rates of local adverse effects with no evidence of systemic disease.'

Ultimately, 9 out of 10 dentists (shown only from the rear) would recommend the proven preventative strategies for oral health: regular brushing and flossing, avoiding sugary foods and snacking between meals, fluoridation of the water supply, and regular check-ups with your dentist. It seems that the dental chair can't really be avoided after all.

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.

Battling biofouling with, and without, biocides

Barnacles scattered across the antifouling coating on the vertical sides of a dredger after only eight months of operation in south-east Asian waters.

From Phoenician times to the present day, biofouling has been a challenge to the operation of marine vessels.

BY **JOHN A. LEWIS**

Any surface immersed in the sea becomes the potential home for myriad organisms, from bacteria and microalgae to corals and giant kelps. Ship and boat hulls are no exception – within minutes of immersion, the biofouling process begins. First is a conditioning phase in which organic and inorganic matter is adsorbed onto the surface. Then, within hours, small bacteria begin primary biological colonisation, followed by secondary colonisation by stalked or filamentous bacteria, diatoms and other microalgae, and protozoans. Multicellular algae and invertebrates begin to settle within days and, in the absence of any antifouling agent, the growth will cover the surface. It then builds in complexity, with slow-growing, long-lived organisms displacing the initial fast-growing, short-lived opportunists, organisms growing on organisms, and mobile organisms occupying the interstices within the growth mass.

Although essentially the same process takes place on natural substrates, the term *biofouling* largely refers to where the growth is unwanted, such as on immersed maritime structures and vessel hulls. On ships and boats, biofouling growth is not only unsightly but, more significantly, it impacts on vessel performance by increasing surface drag with a consequent increase in fuel consumption. Biofouling increases financial costs associated with this fuel use, and environmental costs also rise as a result of increases in gaseous emissions, including nitrous and sulfur oxides, carbon dioxide and other greenhouse gases, and particulate matter. Carbon dioxide emissions from shipping have been calculated to amount to more than 2.5% of global CO_2 release. Biofouling can also accelerate corrosion of metallic substrates and translocate invasive marine species.

Attempts to prevent biofouling on vessel hulls date back to at least the Phoenicians who, at around 400 BCE, applied a mixture of arsenic, sulfur and oil to the sides of the vessels. The Greeks applied tar and wax to ships' bottoms in the third century and, by the 13th–15th centuries, pitch, oil, resin and tallow were in use. However, despite these efforts, vessels still

needed to be beached every few months to enable manual removal of fouling growth.

The first authenticated protective coating applied to a vessel was copper sheet attached to the wooden hull of the naval frigate HMS *Alarm* in 1758. The success of this led to the general use of copper sheathing until, with the introduction of iron ships in the early 19th century, a new solution was needed because of the corrosive effect of copper on iron.

The solution was antifouling paints, and the first practical compositions of hot soap containing copper came into widespread use in the latter 19th century. Over the next century, copper-based coatings became the mainstay of antifouling protection, but effective life rarely exceeded 12 months. The search for longer lasting and more effective coatings therefore continued. Among the advantages of antifouling coatings were ease of manufacture, ease and low cost of application, durability and applicability to many structural forms and substrates. Disadvantages were the limited life, the necessity to regularly dry-dock vessels for cleaning and repainting, the need to remove old coatings prior to new coating applications, and the tolerance of some biofouling organisms to copper.

The effect of antifouling coatings is through the continuous release of active biocide through the paint surface to kill or deter settling organisms, and this release rate must be maintained above the critical level to inhibit the most tolerant of potential fouling organisms. For cuprous oxide formulations, a continuous release rate exceeding 10 μg Cu/cm^2/day is necessary for effectiveness. The challenge for antifouling paint chemists was therefore to have both a durable paint matrix that could slowly release biocide, and to have biocides that were:

- toxic to fouling organisms, but not toxic to applicators or non-target species when released
- stable to enable persistence in the paint, but not so stable that they would not break down in the environment
- broad spectrum across biofouling types, but not so broad as to have a harmful effects in the environment
- leachable, but not too fast, or too slow.

Biofouling on damaged and depleted antifouling paint on a platform supply vessel after three years of service in Bass Strait.

Conventional antifouling coatings are free-association paints in which the biocide particles are physically dispersed through the paint binder. When immersed, seawater penetrates the surface of these coatings and contacts the biocide, which dissolves and migrates to the coating surface by simple diffusion. The two types of conventional coating are 'soluble matrix' and 'contact leaching' coatings. In soluble matrix coatings the binder, commonly natural wood rosin, is soluble in seawater and fresh biocide is continually released as the binder dissolves. The binder in contact leaching coatings is largely insoluble and biocide release depends on a high enough concentration of biocide particles in the paint film to ensure continuous contact through the film. As particles dissolve at the surface, seawater can penetrate through the micro-channels created to contact biocide deeper in the film. Contact leaching coatings were based on chlorinated rubber of vinylic resin polymers.

The search for more effective biocides transitioned through mercury and arsenic in the early 1950s, subsequently banned on occupational health and safety and environmental grounds, to organotin compounds in the 1960s. The organotins – tributyltin (TBT) oxide, TBT fluoride and triphenyltin fluoride – were found to have broad spectrum biocidal properties and were soon commercialised in antifouling paint products. A further significant technological advance came with the development of organotin copolymer paints in the mid-1970s, in which the copolymer provided both the biocide and acrylic binder for the paint. When immersed, a hydrolytic reaction between seawater and the copolymer caused a cleaving of the TBT from the copolymer, which was released as an active biocide. The residual polymer then changed from insoluble to soluble, with release generating a 'self-polishing' effect and constant biocide release rates.

The advantages of TBT self-polishing copolymer (SPC) coatings

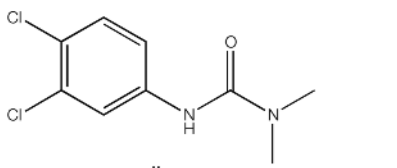
were an effective life of five or more years (proportional to coating thickness), controllable biocide release rates, ability to overcoat without loss of activity, no depleted coating to be removed before repainting, efficient use of biocide, continuous replacement of active surface, and a self-polishing action that resulted in erosion of peaks of roughness that provided increasing hull smoothness and fuel efficiency with time in use. The fouling problem on ships appeared to have been solved.

However, although TBT compounds were thought to be environmentally safe because of relatively rapid microbial degradation of TBT in seawater to the less toxic dibutyl and monobutyl tins, then to non-toxic inorganic tin, adverse impacts began to show, particularly among shellfish, including commercially farmed oysters. The degradation rate in areas of high input and low water exchange, such as marinas and boat harbours, was insufficient to prevent environmental TBT concentrations impacting on non-target species, particularly highly sensitive molluscan species. When TBT concentrations were detected in whales and dolphins, the die was cast, and the ongoing use of TBT antifouling paints was doomed.

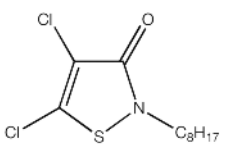
Many countries, including Australia, initially introduced restrictions on the use of TBT paints on small craft, but a global ban on use on all international vessels was subsequently implemented by the IMO International Convention on the Control of Harmful Anti-Fouling Systems on Ships, 2001. The resulting challenge was to find antifouling products that would match the performance achieved with the TBT copolymer antifouling coatings.

Several approaches have been developed. First, for small vessels and ships not needing long antifouling service intervals, the performance of conventional coatings with cuprous oxide or cuprous thiocyanate as the primary active was boosted by incorporating secondary, or booster, biocides and refining the binder properties. Second, TBT-free self-polishing coatings were formulated by incorporating cuprous oxide and booster biocides into silyl, zinc or copper acrylate copolymer or other hydrolysable binders. Third, non-biocidal 'foul release' coatings, based on silicone elastomers, were developed. They deter or minimise the adhesive strength of biofouling organisms that results in the sloughing of attached growth when the vessel is underway. Although providing effective solutions, the costs of these new products exceeds that of the almost universally applicable TBT SPC coatings, with an almost magnitude of difference in price between conventional and TBT-free SPC coatings, and TBT-free SPC coatings and foul release coatings.

Another consequence of the TBT saga was the development of a national approval and registration system for biocidal antifouling products. This responsibility lies with the Australian Pesticides and Veterinary Medicines Authority (APVMA), whose primary responsibilities are the approval of veterinary medicines and agricultural chemicals containing active substances. For antifouling paints, any active must be approved to assure quality in manufacture and to ensure human and environmental safety. Then, any product containing an approved active must also be individually approved to ensure quality, safety and efficacy. Approval requires the submission of extensive data packages, and the assessment of even



diuron



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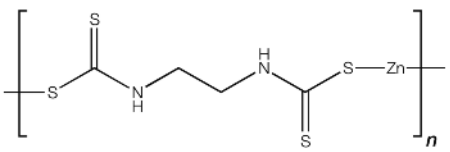
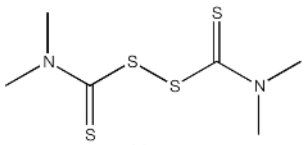
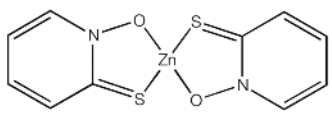


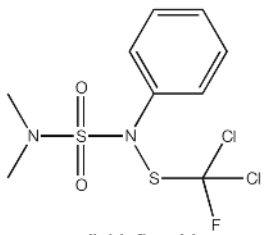
zineb



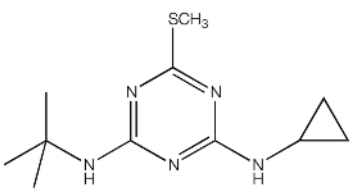
thiram



zinc pyrithione



dichlofluanid



cybutryne

... only seven booster biocides are approved: diuron, zineb, thiram, dichloro-octyl-isothiazolin (DCOIT), dichlofluanid, zinc pyrithione and copper pyrithione.

a seemingly straightforward product application can take up to 24 months.

Currently, only 50 biocidal antifouling paints are approved by the APVMA. In these, to supplement copper, only seven booster biocides are approved: diuron, zineb, thiram, dichloro-octyl-isothiazolin (DCOIT), dichlofluanid, zinc pyrithione and copper pyrithione. Copper pyrithione is the only new antifouling active approved during the past 10 years. An application for the approval of cybutryne was submitted in the 1990s, but was rejected when adverse effects began to appear. This biocide has been used in many other parts of the world, but there is now a proposal before the IMO to also ban this under the AFS Convention. In New Zealand, the use of diuron in antifouling paints has been phased out, and thiram will similarly be phased out over coming years.

Effective biofouling management is essential for not only the economic operation of vessels, but also to reduce harmful gas emissions and the spread of invasive marine species by shipping. Some concerns have been raised about the environmental impact of copper released by antifouling paints, but copper remains the mainstay of effective biofouling management. Non-toxic foul release coatings are effective for some types of vessel, but these are not a universal solution owing to cost and operational limitations. The need for antifouling coatings is reflected by the market: the global antifouling paints and coatings market is projected to grow from more than US$5.5 billion in 2015 to more than US$9 billion by 2021. In Australia, where the majority of the market is to small vessels, sales of antifouling paints in the 2016–17 financial year amounted to $17.4 million, up on $16.6 million in 2015–16.

Barnacles and filamentous hydroids growing on ineffective antifouling coating on a seawater intake grate.

Balancing operational requirements and environmental protection is far from simple when it comes to antifouling.

John A. Lewis is Principal Marine Consultant at ES Link Services Pty Ltd, Castlemaine, Victoria.

Nanosurfaces inspired by carnivorous plants delay degradation

A team of chemistry researchers from the University of Sydney Nano Institute has developed nanostructured surface coatings that have antifouling properties without using any toxic components.

Since the banning of the toxic antifouling agent tributyltin, the need for new non-toxic methods to stop marine biofouling has been pressing.

Leader of the research team, Associate Professor Chiara Neto, said, 'We are keen to understand how these surfaces work and also push the boundaries of their application, especially for energy efficiency. Slippery coatings are expected to be drag-reducing, which means that objects, such as ships, could move through water with much less energy required.'

The new materials were tested tied to shark netting in Watsons Bay, Sydney, showing that the nanomaterials were efficient at resisting biofouling in a marine environment.

The research has been published in *ACS Applied Materials & Interfaces* (doi: 10.1021/acsami.7b14736).

The new coating uses 'nanowrinkles' inspired by the carnivorous *Nepenthes* pitcher plant. The plant traps a layer of water on the tiny structures around the rim of its opening. This creates a slippery layer. causing insects to aquaplane on the surface, before they slip into the pitcher where they are digested.

Biofouling can occur on any surface that is wet for a long period of time, for example aquaculture nets, marine sensors and cameras, and ship hulls. The slippery surface developed by the Neto group stops the initial adhesion of bacteria, inhibiting the formation of a biofilm from which larger marine fouling organisms can grow.

In the lab, the slippery surfaces resisted almost all fouling from a common species of marine bacteria, while control Teflon samples without the lubricating layer were completely fouled. Not satisfied with testing the surfaces under highly controlled lab conditions with only one type of bacteria the team also tested the surfaces in the ocean.

Test surfaces were attached to swimming nets at Watsons Bay baths in Sydney Harbour for a period of seven weeks. In the much harsher marine environment, the slippery surfaces were still very efficient at resisting fouling.

The antifouling coatings are mouldable and transparent, making their application ideal for underwater cameras and sensors.

University of Sydney

The *Nepenthes* pitcher plant traps a lubricating layer in the structure of its peristome. The nanowrinkles developed by the team function in the same way, trapping a lubricating layer that stops the adhesion of bacteria and other marine organisms, and could have drag-reducing properties.

New Fellows

Oliver Jones is an analytical chemist based at RMIT University in Melbourne where he holds the title of Associate Professor. Originally from Manchester in the UK, Jones was awarded a BSc(Hons) from Queen Mary University of London and obtained his MSc and PhD from Imperial College London, working with Professor John Lester and Dr Nick Voulvoulis. He then held a postdoctoral fellowship in biochemistry with Professor Jules Griffin at the University of Cambridge (where he was also head of the postdoctoral society). Jones left Cambridge to take up a one-year lectureship at the University of Durham, before moving to RMIT in 2012.

Jones's group conducts research in analytical methods and technologies, predominantly in multidimensional chromatography and NMR, for a range of applications, particularly metabolomics and the trace analysis of environmental pollutants. Recently, he has extended his work to include forensic and food chemistry. At RMIT, he is Deputy Director of both the Water: Effective Technologies & Tools (WETT) Research Centre and the Centre for Environmental Sustainability & Remediation (ENSURE). Jones also has a passion for teaching. He was the 2014 RACI VIC Hartung Youth Lecturer and, with his wife, Associate Professor Michelle Spencer, he recently developed a mobile game app called Chirality-2 to help teach organic chemistry.

Jones is very active within the Australian chemistry community. He is currently (since 2015) a member of the Australian Academy of Science National Committee for Chemistry and was a member of the executive board of the Academy's Early to Mid-Career Researcher forum from 2012 to 2015. He is President of the Australian and New Zealand Metabolomics Network (ANZMN); secretary and board member of the Australian and New Zealand Society for Magnetic Resonance (ANZMAG), a board member of the International Metabolomics Society and, until recently, a member of the RACI Victorian Branch Food, Nutrition and Analytical Chemistry Group. He has written numerous articles and book reviews for *Chemistry in Australia* and also writes regular, popular newsletters for the ANZMN and ANZMAG. Jones also tweets about science (as @dr_oli_jones), is an associate editor of *RSC Advances* and has been on the organising committee of several conferences and given many invited talks and lectures.

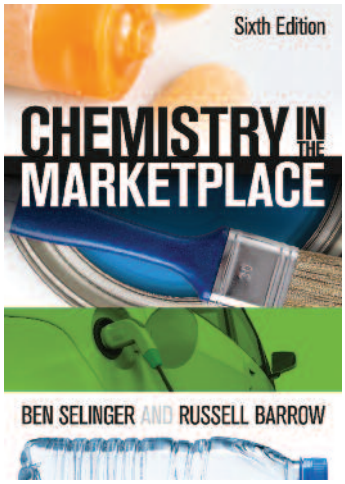
Jones has won several awards for his work, including the 2015 ANZMAG Sir Paul Callaghan Medal and the RMIT College of Science Engineering and Health Media Star Award. He has more than 80 peer-reviewed publications, including papers in the *Lancet* and *TRENDS in Biotechnology*, with more than 3690 total citations and an *h*-index of 25.

Born and raised in Iceland, **Pall Thordarson** (Palli) obtained his BSc from the University of Iceland in 1996 and a PhD in organic chemistry from the University of Sydney in 2001. Following a Marie Curie Fellowship in the Netherlands, he returned to the University Sydney in 2003 and in 2007 was appointed to the School of Chemistry, University of New South Wales (UNSW), as a senior lecturer. In 2012, he obtained an ARC Future Fellowship, becoming an associate professor in 2013. He was promoted to the position of professor in 2017. He is currently the Deputy Head of School of Chemistry at UNSW.

Thordarson's main research activities are self-assembled materials for nanomedicine, focusing on novel tissue culture materials based on self-assembled gels. His other key research interest area is protein chemistry and systems chemistry, including pre-biotic chemistry and the origin of life. Thordarson has developed a popular open access website – supramolecular.org – allowing people to use his binding models which has received more than 20 000 visits from around the world. Thordarson has published more than 100 papers in refereed journals, including recently in *Nature Communications*, *Journal of the American Chemical Society* and *Angewandte Chemie*. Fifteen PhD and 30 Honours students have completed their degrees under his supervision. Thordarson is active within the chemistry community on Twitter and has published several YouTube videos on experimental techniques in chemistry with thousands of viewers.

Thordarson has received a number of awards for his work, including the Young Tall Poppy Science Award – NSW 2008, the International JPP/SPP Young Investigator Award in 2010 and the 2012 Le Fèvre Memorial Prize from the Australian Academy of Science for outstanding basic research in chemistry. He is a member of the ARC College of Experts and serves as NSW state representative on the board of the RACI Organic Chemistry Division. He is a Fellow of the Royal Society of Chemistry (UK).

Thordarson is married with two children aged 8 and 6 and lives in the Southern Highlands of NSW.



Chemistry in the marketplace

Selinger B., Barrow R., CSIRO Publishing, 2017, 6th edn, paperback, ISBN 9781486303328, 552 pp., $69.95

In praise of *Chemistry in the marketplace*, this book is suitable for the science enthusiast with or without a science degree. My introduction to this book of the same title was in 1989, the time of the fourth edition. Since then I have acquired the fifth and sixth editions, as I am always keen to read about consumer chemistry.

This book improves the image of chemistry by portraying the variety of ways in which chemical understandings influence us everyday, and it increases chemical knowledge and skills for those who require a more technical explanation. The book describes real chemistry, is relevant and is useful.

Both authors have impressive bios and commitment to chemical education. Ben Selinger, a physical chemist and original author of the book, is an Honours/Masters graduate of the University of Sydney. His PhD studies took him to Stuttgart's Technical University in Germany. He is an emeritus professor of chemistry at the Australian National University (ANU). The study of chemistry is his passion and as an advocate for promoting a better understanding of our use of chemicals, *Chemistry in the marketplace* has been in print since 1975.

This book improves the image of chemistry by portraying the variety of ways in which chemical understandings influence us everyday …

Six editions of *Chemistry in the marketplace* is no mean feat! This is echoed by the experience of Associate Professor Russell Barrow (ANU), co-author of this edition. Barrow is a PhD graduate from the University of Melbourne, specialising in organic chemistry, and currently works in the Chemistry Department at ANU, which is where he and Selinger met.

The latest edition comprises 19 chapters and 535 pages. It introduces more chapters than the fifth edition, including surface chemistry, the chemistry of health and risk, swimming pool and beach chemistry. Two chapters focus more on biochemical/biological aspects as opposed to a physical chemistry approach. Topics describing chemistry in the laundry, kitchen, garden, dining room, cosmetics, hardware (plastics, glass, fibres, fabrics, yarns, paints), energy and ionising radiation remain consistent with previous editions.

Chemistry in the marketplace has influenced my teachings of high school students, where my mantra is: 'Chemistry is the fundamental science most directly related to everyday life'. Most useful is the relevance of sourcing Australian data, and the many experiments throughout have value either as demonstrations or as references for major student investigations. In Chapter 13, a deeper insight is given to the common demonstration of burning magnesium in air by considering the volume change during the reaction rather than tagging the mass change. When the volume change is analysed, students can gain a deeper understanding of the relative strength of ionic and metallic bonds for MgO and Mg–Mg respectively.

The breadth of topics covered in this book means there is always an interesting snippet to convey as a 'starter' to a lesson, such as 'Tooth is stranger than fiction' in Chapter 8.

It is also pleasing to read evidence about whether or not organic food is 'better'. For instance, in Chapter 12 the authors state 'the published literature lacks strong evidence that organic foods are significantly more nutritious than conventional foods. Consumption of organic foods may reduce exposure to pesticide residues and antibiotic-resistant bacteria'. There is an abundance of such useful information in this book, such as 'popular budget supermarket brands of shampoos and conditioners … contain all the important ingredients to give a good wash with minimum irritation and build-up of residues'.

Chemistry in the marketplace is a useful reference book that incorporates further readings by providing relevant web references at the end of each chapter.

In conclusion, *Chemistry in the marketplace* is a must-read book to understand why you use what you do and why chemistry matters!

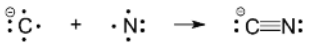
Alison McKenzie

Lewis structures: ban the octet rule

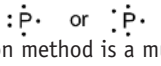
Lewis structures are a key concept in chemistry education because they can be used to predict molecular geometries, relative bond lengths and bond dissociation energies, aromaticity and other properties. They can also be used to confirm if the molecular and ionic composition of a chemical formula is reasonable.

Lewis structures are representations that explicitly show all atoms, all valence electrons and formal charges. The valence electrons are usually arranged in pairs, which are either localised on particular atoms or localised between a pair of adjoining atoms. Bonding pairs of electrons are usually denoted by line segments, representing covalent bonds. A double bond is represented by a pair of parallel line segments, while a triple bond is represented by three parallel line segments. Formal charges of atoms indicate the difference between the positive nuclear charge and the total number of (core and valence) electrons, on the formal basis that bonding electrons are shared equally between atoms they join.

One common method is to assemble Lewis structures from the Lewis symbols for individual atoms:

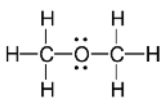


This method is confusing for students when hypervalent atoms are involved:

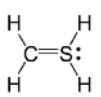


A second common method is a multistep algorithmic approach that counts valence electrons, arranges atoms and distributes electrons to form bonds and lone pairs, in order to either fulfil the 'octet rule' or minimise formal charge.

Lewis structures such as HSO_4^-, $C_2H_3O_2^-$ and CO, with multiple bonds or charges, are problematic for students who are new to Lewis structures. Problems associated with drawing structures with more than one central atom (e.g. $N_2F_5^+$, P_2S_3, HSO_4^- and $C_2H_3O_2^-$) or with an atom from beyond the second row of the periodic table (e.g. S, P, Br and I) often persist into second-year undergraduate studies. In one research study with a group of second-year organic-chemistry students, around 80% of students were able to draw correct Lewis structures with one carbon atom (e.g. CH_2O, HCN, CH_3OH, CH_6N^+ and CH_5O^+), but only around 30% were able to draw correct structures with two or more carbon atoms (e.g. CH_3COOH, $C_2H_5O^-$ and $C_2H_3O_2^-$). The ability to draw a correct Lewis structure can depend on how information is presented: more than 90% of the group were able to draw the structure for methanol when given the condensed formula (CH_3OH), but only around 60% could when given the molecular formula (CH_4O). When asked to draw structures for C_2H_6O and CH_5S, students often prefer symmetrical or 'balanced' structures:

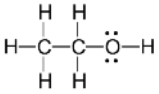


methoxymethane
(dimethyl ether)

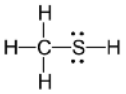


(incorrect)

and felt uncomfortable with unsymmetrical structures:

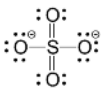


ethanol

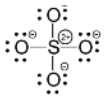


methanethiol

Educators also have problems with Lewis structures, but for different reasons. An 'octet-rule' Lewis structure for sulfate anion would have four S–O single bonds, while a 'minimal-formal-charge' structure would have an 'expanded octet', which is usually explained by invoking the involvement of d-orbitals in the bonding:



sulfate



sulfate

Note that only five elements (C, N, O, F and Ne) *always* obey the octet rule of having eight valence bonding and lone-pair electrons: *all* the other elements can have 'depleted octets' or 'expanded octets'. Argon compounds have been synthesised and have expanded octets.

Some researchers argue that the expanded-octet structures of the oxides, oxoacids and oxoanions of the 3p–5p non-metals (e.g. P, As, S, Se, Te, Cl, Br, I and Xe) are more consistent with experimental bond lengths than structures that obey the octet rule. Other researchers point out that expanded octets are unrealistic because the energies of the d-orbitals are too high to be involved in bonding.

Some quantum chemistry studies show that the electron densities of a series of P–O, S–O and Cl–O bonds are more consistent with expanded octets, while other studies show that the calculated molecular orbitals are more consistent with the octet rule.

Most recently, quantum chemistry studies have shown the valence s- and p-electrons can form 'recoupled pair bonds' instead of lone pairs (see Takeshita et al. *J. Phys. Chem. A,* 2015, vol. 119, pp. 7683–94). It is therefore possible to form up to four bonds for carbon and six bonds for sulfur. It would seem that the approach of minimising formal charges where possible is correct, but without involvement of the d-orbitals.

Both the single-bonded octet-rule and the hexavalent minimal-formal-charge structures for sulfate would lead students to predict a tetrahedral geometry using VSEPR theory. Ultimately, we should remember that Lewis structures are pictorial representations or models; they are not reality. Like all tools, Lewis structures are useful constructs: we should teach Lewis structures for their predictive utility, and not as an end in itself. And we should place greater emphasis on the drawing of structures with more than one central atom and structures with at least one atom with an expanded octet. We should also ban the term 'octet rule'.

Kieran F. Lim (林百君) FRACI CChem
(kieran.lim@research.deakin.edu.au) is an associate professor in the School of Life and Environmental Sciences at Deakin University.

Protecting chemical inventions – practicalities and pitfalls

Dr Toby Thompson, UK and European-Qualified Patent Attorney, FB Rice

Developing an effective IP strategy is important for all companies, including those working in chemical research. While the patenting process can be complex, having an awareness of issues relevant to your technology helps in navigating the field.

Know what your invention is

It sounds obvious, but it is critical to get the science right; otherwise your patent can end up covering the wrong invention. This situation is rare, but in one example from a few years back the structure of a clinical anticancer compound ONC201 was found to be wrong, by which time a patent (US8,673,923) had granted covering the inactive structural isomer. This was further complicated by the researchers who identified the correct structure also filing their own patent. At the very least, situations like these lead to uncertainty, and in extreme situations can result in a worthless patent.

Experimental data matters

For almost all chemical inventions, it is necessary to include experimental details in the original patent application, demonstrating (a) how substances are made and (b) what they do. Otherwise, problems can arise associated with whether the patent properly discloses how to carry out the invention, or whether there is an inventive step.

The question also arises as to how broadly the invention can be claimed in view of the examples provided. Ideally, a patent should cover all ways in which an inventive advance can be put into use. However, where very broad claims are underpinned only by a small number of examples, this can lead to difficulties. This occurred in the well-known T0939/92 AgrEvo case in Europe, where it was not considered credible that triazole compounds across the scope of the claims had inventive herbicidal activity, based on the limited data. Some Asian patent offices are rather strict in this area, often requiring claims for chemical inventions to conform closely to the examples, and support requirements in Australia have also increased in recent years.

Despite this, in many cases early stage experimental data (e.g. in vitro assay results) will still often be enough to meet the requirements, and some patent offices will also consider additional data filed later on. However, the recommendation is to include as much experimental data as possible in the initial patent application.

Coordinate patenting and publication

Many chemical inventions originate from universities, or companies where publishing is important. Patenting should not prevent publication, but it is important to be aware of possible issues. Fundamentally, if your invention is published in a journal or press release before you file a patent, it can be fatal since the patented invention is no longer new. Some countries provide grace periods allowing your earlier publication to be disregarded, but not all. For example, Europe has no effective grace period. A sensible practice is to ensure that there is oversight of what your organisation is publishing, and that new patent filings are made before details of valuable new technologies are made public.

Process vs product patents

There is often a perception that process patents are of limited worth compared to product patents. That may be true for some cases where it is not possible to determine whether a competitor's process carried on behind closed doors actually infringes, or if there is an easy workaround. However, some process patents are highly valuable; for example, where there is an associated cost advantage, or where regulatory requirements limit the allowable impurity profile of a product so that it can only be produced by the patented process.

For more information, email tthompson@fbrice.com.au.

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IP The IP Navigators

What are antioxidants? And are they truly good for us?

Antioxidants seem to be everywhere: in superfoods and skincare, even chocolate and red wine. Products that contain antioxidants are marketed as essential for good health, with promises to fight disease and reverse ageing.

But are they really as good for us as we're led to believe?

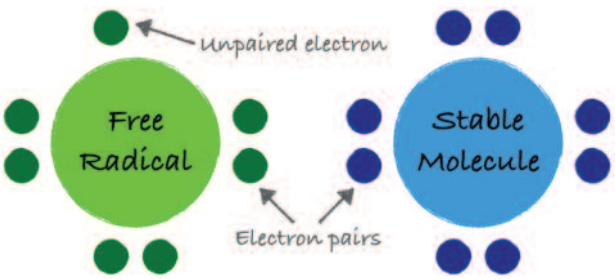
What are antioxidants?

The term 'antioxidant' covers a wide range of molecules (atoms bound together by chemical bonds) that protect other molecules from a chemical process called oxidation. Oxidation can damage vital molecules in our cells, including DNA and proteins, which are responsible for many body processes.

Molecules such as DNA are needed for cells to function properly, so if too many are damaged, the cell can malfunction or die. This is why antioxidants are important. They can prevent or reduce this damage. In the body, uncontrolled oxidation is typically caused by highly reactive molecules known as free radicals.

What is oxidation?

Oxidation is a common chemical reaction where electrons are transferred from one molecule to another. Electrons are one of the subatomic (smaller than an atom) particles that make up pretty much everything. As electrons move during an oxidation reaction, bonds can be broken and the structure of the molecules changed.



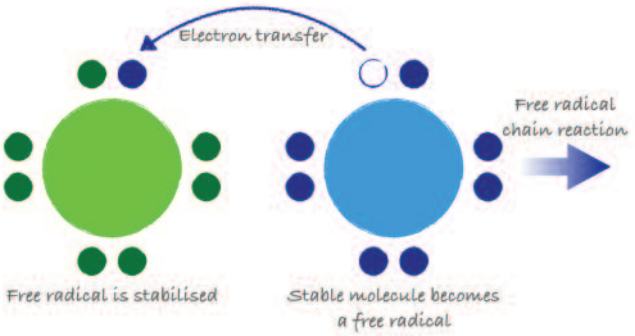
Unpaired electrons make free radicals unstable and highly reactive. Author provided

Not all oxidation reactions are bad. They are essential for life and involved in many important processes. In cellular respiration, glucose (a sugar from the food we eat) is oxidised by oxygen (from the air we breathe), producing carbon dioxide, water and energy to fuel our bodies. Household bleaches oxidise coloured stains into colourless molecules.

What are free radicals?

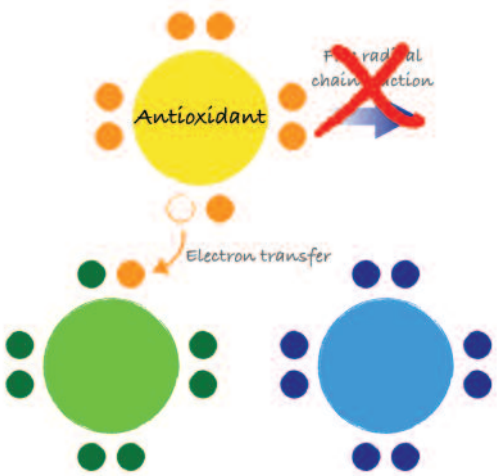
Free radicals are simply molecules with one or more unpaired electrons. Electrons like to be in pairs, so unpaired electrons can result in unstable and highly reactive molecules. To become stable, the free radical must steal an electron from another molecule (or give one away). When a molecule loses an electron, that molecule has been oxidised and itself becomes a free radical.

This new free radical can steal an electron from another molecule, starting a chain reaction. This process permanently changes the structure of the molecules, causing irreversible damage.



A free radical can steal an electron from another molecule, which then becomes a free radical. Author provided

But if an antioxidant is present, it can donate an electron to the free radical, stabilising it and stopping the chain reaction. The antioxidant sacrifices itself and is oxidised instead of the other molecule, becoming a free radical. But unlike most molecules, the antioxidant is able to stabilise the unpaired electron and does not become highly reactive. This process deactivates the antioxidant.



An antioxidant donates an electron to a free radical and stops the chain reaction. Author provided

Free radicals aren't always bad for you. Their highly reactive and destructive nature is used by the body's immune system. Certain white blood cells, called phagocytes, can engulf foreign particles, such as bacteria, then seal them off and release free radicals to destroy them.

Free radicals are generated naturally by our bodies, but can be increased by lifestyle factors such as stress, poor diet,

pollution, smoking and alcohol. Our bodies can handle some free radicals, but if too many are formed, it can overwhelm the body's normal defences.

Free radical damage is thought to be one of the causes of ageing and contribute to various diseases. For example, free radical damage to DNA can cause genetic mutations and promote cancer.

All antioxidants aren't equal

So, if free radicals are dangerous and cause ageing and disease, and antioxidants can neutralise them, then getting more antioxidants should be good for you, shouldn't it? Unfortunately, it's not as simple as that. Yes, high antioxidant levels and low oxidative stress are associated with good health, but not all antioxidants are equal.

Antioxidants come from many sources. Some are naturally produced in the body and some naturally occur in foods we eat. Antioxidants (natural or synthetic) can also be added to foods that don't normally contain them, either for their (supposed) health value or to preserve the food (antioxidants also prevent oxidation in foods).

A healthy diet is the most effective way to get the antioxidants your body needs. Fruits, vegetables, grains, eggs and nuts are all useful sources of antioxidants. Despite the marketing hype, antioxidants found in so-called superfoods are no more effective than those in regular fruit and veg, so you're better off saving your money.

But it's a different story when it comes to antioxidant supplements. Research has found antioxidant supplements may cause more harm than good. A 2012 meta analysis of over 70 trials found antioxidant supplements are ineffective or even detrimental to health. The reasons are unclear, but the added nutritional benefits from consuming antioxidants in a healthy diet is likely to contribute to this. Also, the high concentrations of antioxidants associated with supplement use can lead to problems.

Too much of a good thing

There are a number of reasons why high concentrations of antioxidants may be harmful. At high concentrations, antioxidants may:

- act as pro-oxidants, increasing oxidation
- protect dangerous cells (such as cancer cells) as well as healthy cells
- reduce the health benefits of exercise
- have unwanted side effects, such as nausea and headaches, or even reach toxic levels.

There is no magic pill, but a healthy diet can provide you with all the antioxidants you need to fight free radical damage.

Jacqui Adcock is a Research Fellow in Analytical Chemistry, Deakin University.
This article was first published at theconversation.com.

Touchy feely

Thermal conductivity

What do you notice when you open your dishwasher after it has just finished and is still hot? The plastic containers are cool to touch but still have water droplets sitting in them. Meanwhile, the ceramics and glass plates are moderately hot and dry while the stainless steel pots and pans and cutlery are very hot.

Before you blame the dishwasher, consider this. The differences are mainly due to the thermal conductivity of the materials – the ability to transfer heat to water or to your fingers. The low thermal conductivity of plastics means they do not supply enough heat to evaporate the water on them effectively. As well, water sits up as droplets on plastic, so they have less surface area, but it spreads out on clean glass and metal.

Hot pots

Glass and ceramics are intermediate heat conductors and metals are generally good heat conductors. To test the theory, pour some boiling water (adults only) into a standard (non-induction) stainless steel pot or stovetop espresso bottom unit. The sides aren't too hot because stainless steel is a relatively poor conductor of heat. However, the base is very hot!

The bases of these pots have a veneer of stainless steel coating on both sides of a thicker layer of either copper or aluminium, both of which are excellent heat conductors. Pots for induction stoves have an extra base that allows an induction current to heat it directly, and this material is also attracted to a magnet.

Cool jewels

A first pass for testing minerals and gemstones is to touch them to assess their thermal conductivity. You could ask to touch the many-carat stone in the special cabinet at the jeweller's (purely for the purposes of science), to check whether it is cool. The staff reaction is probably going to be likewise.

Surprisingly, diamond holds the record for thermal conductivity, with aluminium oxide (ruby and sapphire) quite high in the rankings.

Thermal and electrical conductivity generally go hand in hand for metals, but not for non-metals. Thus diamonds, rubies and sapphires are very good electrical insulators. Heat is transferred in solids by vibrating atoms, namely via resonant sound waves called phonons. In contrast, it is weakly bonded electrons that carry electricity.

This is all very sound science and is terribly important when designing ever-smaller electronic components, to ensure that they don't overheat.

Magnetic personalities

There is a huge variety of stainless steels. The common or kitchen variety is 18:8 Cr:Ni, and for our purposes we'll assume its thermal behaviour is roughly similar to that of standard iron carbon steel.

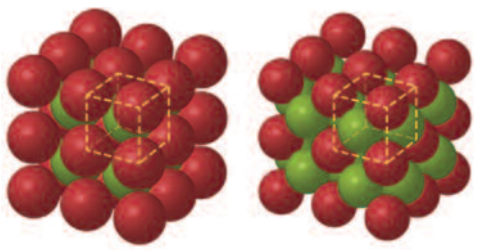
Test some cutlery with a (fridge) magnet. For cheap cutlery, the knife and handle are both attracted to the magnet. For standard cutlery, the blade is attracted but not the handle. If neither the blade nor the handle is attracted, you probably have a butter knife. Sometimes some residual permanent magnetism is induced. Other stainless steel objects that need to be sharp, such as scissors, will also be magnetically attractive.

The composition is generally the same for the steel parts but the heat treatment has been different, although in some cases you might see a thin line where two pieces may have been joined.

Oranges and grapes

Atoms, like oranges, pack closely together in a number of different ways. Iron with additives provides several examples, depending on heat treatment and composition.

Ferrite and austenite adopt two of these equally efficient atomic packing arrangements (see February issue, p. 38). Below 910°C, iron has a body-centred cubic (bcc) ferritic packing structure, whereas above that temperature (but below 1400°C) it has a face-centred cubic (fcc) austenite structure.



Body-centred cubic structure **Face-centred cubic structure**

In the holes between the large iron atoms, you can fit small atoms of carbon, like placing grapes between packed oranges. This carbon can also combine with iron to form iron carbide, cementite (Fe_3C). More carbon can dissolve in the high-temperature austenite form than in the low-temperature ferrite.

If austenite is cooled slowly, it forms a banded structure of pure iron (ferrite) and cementite that is tough and strong but not particularly hard. Examples are knife handles, non-inductive pots and pans, kettles and the kitchen sink. However, if it is cooled quickly, the carbon atoms do not have sufficient time to move to form cementite and become trapped. This quenching is called martensite hardening and is used for knife blades, scissors and fridge cladding.

Why the first form is non-magnetic and the second is magnetic is a wee bit more complicated. Have fun roaming with a magnet.

Ben Selinger FRACI CChem is Emeritus Professor of Chemistry at ANU and, along with ANU colleague Associate Professor Russell Barrow, released the sixth edition of *Chemistry in the marketplace* (CSIRO Publishing) in June 2017. For more information, visit www.publish.csiro.au/book/7366.

p-value abuse distorts scientific publication

In the first article, I outlined the origin and the theoretical foundation of the *p*-value in scientific analysis. In this second and last part, we take a closer look at the consequences of the use and misuse of *p*-values in modern science.

It is a well-known fact that insignificant test results are under-reported – either because scientists keep them quiet, or because the scientific journals prefer significant results and are hesitant to publish negative outcomes – so-called publication bias.

Using the *p*-value for significance testing also causes scientists to overestimate the size of the observed effects, because only the effects that are particularly powerful (due to random fluctuations) pass the significance limit.

As an analogy, picture a sailor who defines rough seas as when the waves come crashing over the deck of ship – the nautical equivalent to passing the statistical significance limit. Generally speaking, the sailor will overestimate the bad conditions by omitting the times when the sea was choppier than usual, but not rough enough to crash over the deck of the ship.

This inflation effect is called the winner's curse – a term from the auction house, where the highest bidder risks paying too much for an item compared to its actual market value.

The problem becomes worse when the power of the experiment is low, and when other scientists repeat the experiments they often find a disappointingly small effect or even none at all.

This inability to replicate previously published test results has been called a reproducibility crisis, and has attracted much attention particularly in behavioural psychology and the medical sciences.

Significance test showdown

There are many reasons for this crisis, but a central problem is the way we use the *p*-value – with the five per cent probability (or any other percentage) as a be-all and end-all in terms of establishing whether there is a significant effect or not.

Several solutions have been presented to combat the problem. One of the more extreme is to ban researchers from reporting any *p*-values, as done at the journal *Basic and Applied Social Psychology*.

Another approach is to lower the conventional significance limit from five per cent to, for example, 0.005 per cent. Such low boundaries are already the norm in some sciences, such as astrophysics.

This solution makes *p*-hacking harder, but it is not without problems. Both in bioscience and drug trials, such a low *p*-value limit would require the use of more test subjects, which is an ethical and a financial challenge.

A fundamental objection to significance tests based on *p*-values is that they do not tell the scientists what they really want to know. Ronald Fisher asked: 'If a certain hypothesis is true, what is the probability that the observation is real?'

But scientifically speaking, the opposite is much more interesting: what is the probability that a given hypothesis is true, based on a given observation? Estimating this so-called 'a posteriori' probability is the goal of what is known as Bayesian statistics.

A fundamental objection to significance tests based on *p*-values is that they do not tell the scientists what they really want to know. Ronald Fisher asked: 'If a certain hypothesis is true, what is the probability that the observation is real?'

The problem with the Bayesian approach is that in order to calculate the a posteriori probability of the hypothesis, according to the laws of probability theory, you also have to know the probability of the hypothesis before you make your observation.

This 'a priori' probability is only precisely known in certain cases, for example screenings for an illness whose frequency in the population is already known.

There is still hope for the *p*-value

By now, you may have the impression that quantitative science is fumbling around in the dark. But it is not that bad.

After all, we are learning about the world and developing new and improved medicine every day. But in recent years, scientists have been paying more and more attention to the problems outlined here – in part because *p*-value significance tests are used more frequently than ever before.

Besides focusing attention on the importance of the size of observed effects, statisticians and scientific journals have also highlighted the need to increase the power of experiments.

Bayesian methods will probably play a bigger role in time. They can be computationally heavy, but that problem will be reduced as computing power continues to increase.

It has also been suggested that original experiments should be replicated more systematically, and that 'boring' repetition tests are given a higher scientific status than they have currently.

Finally, reasonable arguments have been made that the *p*-value should be exempt from significance tests and instead assessed independently for what it is: a graduated measurement of evidence against the null hypothesis.

As long as the *p*-value is not abused, we do not need to abandon it just yet.

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First published at sciencenordic.com. Part 1 was published in the May issue.

Is all soil more acidic than we thought?

Our research suggests that it is and that we've been measuring soil acidity wrong for years. This could have big implications for our understanding of many fundamental biological processes.

Soil acidity, or pH, is essential for the existence of plants, animals, and bacteria in soil, how organisms work together, and the presence of toxic chemicals.

So, apart from being one of the most important environmental factor for ecosystems, pH is also a significant factor in the traditional risk assessment of poisonous chemicals where their availability to plants and animals depends on pH.

New, robust field-electrodes allow us to measure the soil pH directly in the soil rather than in the laboratory, which is the traditional method.

As part of a new study, we measured pH in forest and heath soils, and the results showed that most measurements were extremely acidic, measuring less than pH 2.6 and 3.2, when we would have expected them to be around pH 4.

One pH unit means that there are ten times as many hydrogen ions in a sample. In these extreme low pH conditions, plants and burrowing animals are in theory exposed to a geochemical environment that is dominated by a high concentration of soluble iron compounds and other poisonous heavy metals. In other words, we wouldn't expect plants or animals to thrive in such an environment.

The richness of fauna in coniferous forests and heathlands suggest that low pH is not inhospitable to all life. Wikicommons/Paul Evans/CC BY-SA 2.0

Textbooks have taught us that organisms cannot live in soils of less than pH 3. But our results suggest that they do, and they are apparently alive and kicking. Our results are published in the scientific journal *Soil Biology and Biochemistry* (https://doi.org/10.1016/j.soilbio.2017.08.003).

But what can explain this deviation from what we would expect?

Lower pH when samples are measured in the field

We measured pH in the upper layers of soil in a heath and a forest throughout the growth season, from March to October.

We first measured the pH on site using a portable pH meter.

Then we took the same soil samples back to the laboratory and measured them again using traditional laboratory methods. This involves drying the sample, crushing it, and then adding deionised water to measure the pH of the soil–water solution.

The results were surprising, as the samples measured in the field were consistently 0.5–1 pH units less than those made in the laboratory. How the exact same soil samples could give such different answers was a mystery.

Abundant life despite what the textbooks say

Such low pH has never before been measured in natural soils.

According to common ecological theory, these low pH values should be inhospitable to biological organisms.

For example, at such low pH, the largely insoluble iron oxides and manganese-rich minerals should dissolve, making the soil water even more acidic, while most nutrients will be unavailable to animals, and most soil processes, such as the breakdown of organic matter, will occur more slowly.

This suggests that a large part of the nutrient-poor soils found in heaths, peat bogs and coniferous forests, should be largely without biological life, which is clearly not the case.

We also found a rich content of fauna in the extremely acid heath soils. One reason for the difference in measurements could be related to these tiny creatures.

In the laboratory, the first stage of analysing pH is to dry the soil samples. During this process all of these tiny animals shrink to a size where they are no longer visible. The second stage is to crush the samples, which now includes these tiny animal remains.

We know that animal pH is typically neutral, between pH 6 and 7. So the question is, whether these animals, plants and fungi contribute to the soil pH measured in the laboratory, and whether this can explain the difference between the field and laboratory measurements.

This is what we will now investigate.

We need a new method for soil pH

Our results have implications for many fields of research, from measurements of soil pH over time, to the study of the relationship between soil pH and biological and geochemical processes, such as the breakdown of organic matter, the availability of nutrients or toxins, the occurrence of species, and weathering processes.

They also mean that we should review how we measure pH around the world, and consider direct measurements instead of laboratory measurements.

And finally, they beg the question of what processes actually occur in soil to produce these low pH values and how the buffering capacity of soil (the ability of a soil to resist a change in pH) changes at such low pH.

The results pose some fundamental questions about what the actual pH of the Earth is and suggest that crushed animal remains may have skewed all previous laboratory measurements to higher values.

We don't know enough about low-pH environments

There is a wealth of relationships between biological processes and soil acidity in the scientific literature.

The best example is that of acid rain and forest death in the 1980s. But most of these are only described for soils with a pH greater than 4.

We need more information on what happens in soils of a lower pH.

Climate research in the northern boreal forests or the Arctic similarly rely on laboratory measurements of pH to study the release of soil CO_2 into the atmosphere via respiration.

Incorrect pH measurements matter

So what's the problem with incorrect pH measurements?

As scientists, we establish relationships between biological processes based on pH. This means that much of our understanding of these relationships is in the best case scenario incomplete, and perhaps entirely wrong.

All in all, we need much more research into the many processes that rely on accurate measurements of soil pH.

Knud Erik Nielsen is at the Department of Bioscience, Aarhus University, Denmark. **Morten Tune Strandberg** is at the Department of Bioscience, Aarhus University, Denmark. First published at sciencenordic.com.

RACI National Awards 2018
Call for nominations

Nominations are called for the following awards. You can apply for some of these awards yourself; others require nomination. **All national awards except the Post Graduate Student Travel Bursary (closing date 15 May) close on 15 June.**

- Applied Research Award
- C.S. Piper Award
- Citations
- Cornforth Medal
- Distinguished Contribution to Economic Advancement – Weickhardt Medal
- Distinguished Fellowship
- Fensham Medal for Outstanding Contribution to Chemical Education
- H.G. Smith Memorial Award
- Leighton Memorial Medal
- Margaret Sheil Lectureship Award
- Masson Memorial Medal
- MRACI Post Graduate Student Travel Bursary
- RACI Chemistry Educator of the Year Award
- Rennie Memorial Medal
- Rita Cornforth Lectureship

See www.raci.org.au/events-awards/awards or email awards@raci.org.au for more information about the requirements for nominations for each award.

Wine and oral health

The consumption of red wine, especially wines high in polyphenols, can lead to discolouration of the teeth. There are plenty of almost frightening images on the web of teeth with red wine stains. In addition to staining, wine consumption can lead to tooth decay because the acidity (pH 3.0–3.5) is capable of breaking down the enamel. This in turn can cause tooth sensitivity and gum recession. Geoff Cowey from the Australian Wine Research Institute writing in the Institute's *Technical Review* (bit.ly/2JgkvUV) summarises the issues from a winemaker's perspective. Geoff points out that winemakers and wine judges are possibly most at risk, noting that tasting more than 50 wines a week is considered 'high risk'. Recommendations about dental care for winemakers are included in Geoff's article.

So, it was rather intriguing to receive via Sally, our editor, from a reader and occasional columnist of this magazine, a link to an article in ScienceDaily that outlined the potential benefits to dental health from wine polyphenols (bit.ly/2sLkKmS). The 2018 paper (*J. Agric. Food Chem*. vol. 66, pp. 2071–82) was based on research performed at the Instituto de Investigación en Ciencias de la Alimentación, Madrid, Spain. The group, led by Dr Victoria Moreno-Arribas, is well-known for its work on wine polyphenols and health and this particular project looked at the anti-adhesive capacity of red wine components with respect to bacteria sticking to the gums.

Using an in vitro model of human gingival fibroblasts, a model for gum tissue, the various interactions between three bacteria known to be involved in dental problems, *Porphyromonas gingivalis, Fusobacterium nucleatum* and *Streptococcus mutans*, and the phenolic compounds vitaflavan (a grape seed extract), provinols (a red wine extract) as well as the phenolic acids caffeic acid and *p*-coumaric acid. Some experiments were performed with added *Streptococcus dentisani*, an oral probiotic. A lot of time was clearly spent culturing and counting colonies!

The results are quite intriguing. While the two phenolic extracts showed considerable influence on *P. gingivalis* inhibition, there was little effect on the other two bacteria. The two phenolic acids were more effective than the phenolic extracts in 'cutting back the bacteria's ability to stick to the cells', to use the words of the ScienceDaily article (bit.ly/2sLkKmS). Intriguingly, the combination of one or other phenolic acid with *S. dentisani* increased the inhibition potential against *S. mutans*. To cap off these new insights in the role of wine compounds in assisting dental health, the authors also observed, using ultra-high performance liquid chromatography coupled with tandem mass spectrometry, some metabolism of the wine phenolic compounds in the oral cavity that could lead to either increase or loss of benefit depending on the extent of metabolism.

The authors do point out that their results are at an early stage in terms of designing a dental health strategy. Critics of the potential benefits of wine consumption may well be sceptical of the in vitro model used. I say this as I have had work rejected for publication when attempting to publish a toxicology study on grain fumigants. On the positive side, the results of the Madrid group's study form the basis for a more intensive study of the mechanisms of the phenolic compound interactions with the bacteria and what combinations will give the most effective protection.

Not content with examining the relationship between wine phenolic compounds and tooth health, the group from Madrid has extended its work to investigate how wine composition can influence aroma release in the oral cavity (*Food Chem*. 2018, vol. 243, pp. 125–33). One of the critical roles of the oral cavity is the sensory analysis of material before swallowing. There is now increasing evidence for the creation of an 'aroma depot' in the oral cavity due to adsorption of aroma compounds on mucosa, leading to release over time, thereby giving rise to aroma persistence.

There is now increasing evidence for the creation of an 'aroma depot' in the oral cavity due to adsorption of aroma compounds on mucosa, leading to release over time, thereby giving rise to aroma persistence.

The major challenge in this Madrid work was the development of a sampling protocol that allowed the reliable intra-oral assessment of aroma. Three steps were involved. First, 15 millilitres of wine was taken and held in the mouth for 30 seconds to ensure equilibration and after spitting, a two-centimetre SPME fibre was inserted and held in the mouth for two minutes. Finally, the fibre was removed for GC-MS analysis. I cannot imagine how one could bear having the fibre in one's mouth. The process was repeated three times for each of the 12 wines studied: 36 experiments in one's mouth. Perhaps it is not surprising that only three volunteers were involved. Phenolic compounds were important in aroma release with, for example, caffeic acid enhancing the release of linalool while anthocyanins decreased the release of ester compounds such as ethyl hexanoate.

Wine phenolic compounds, so long associated with taste sensations, obviously have a major role to play in protection gums for bacterial decay as well as impacting on aroma release. Maybe we might get to the stage of matching our salivary mucosa with a wine's phenolic profile for the best health and sensory outcomes.

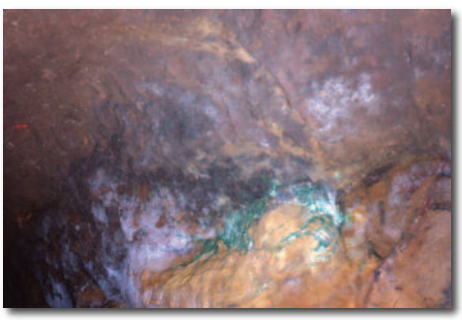
Geoffrey R. Scollary FRACI CChem (scollary@unimelb.edu.au) was the foundation professor of oenology at Charles Sturt University and foundation director of the National Wine and Grape Industry Centre. He continues his wine research at the University of Melbourne and Charles Sturt University.

Was it Roscoe?

A couple of years ago, I was contacted by English chemists who are preparing a biography of the English chemist Henry Enfield Roscoe. In gathering information about their subject, they had come across information that Roscoe's death was noted in Australian journals and newspapers ... some 27 years before he actually died. The biographers sought my help to access a local account of Roscoe's premature end.

The notice appeared here first in the Brisbane *Courier* on Thursday 19 April, in a collection of news items received by cable from London. It was picked up a few days later by Queensland's *Warwick Argus* and other regional newspapers but not reported in Melbourne and Sydney papers. However, in May there was an extensive obituary in the *Australasian Journal of Pharmacy* that gave as its source a cablegram, dated London, 18 April.

Roscoe was born in 1833 and studied at University College London and then with Bunsen at the University of Heidelberg, where he contributed to the development of spectrum analysis. Returning to England in 1857, he was appointed as Professor of Chemistry at Owen's College, which in 1886 became the Victoria University of Manchester. Roscoe researched mainly in the field of inorganic chemistry and his best-known work concerned the element vanadium. In 1865, his attention was drawn to the unusual properties of a minor component of the ores recovered from a copper mine at Alderley Edge, a few kilometres south of Manchester, and from it he isolated the oxide of vanadium. Berzelius had examined vanadium oxide some 30 years earlier and assigned to the metal an atomic weight that Roscoe found to be in error. Writing in his autobiography in 1906, Roscoe described it as the best piece of scientific work he ever did because 'vanadium, which had hitherto been wandering among the elements like a stray goddess (Vanadis being the Scandinavian name for Venus) was brought home to her relations and placed in an assured position among the elements'.



In addition to the fame and awards that his chemistry brought him, Roscoe took a prominent part in public life, being elected to parliament as MP for Manchester South (1885–95), following which he became a Privy Councillor. He was knighted in 1884.

Roscoe died in 1915 at the age of 82, so ... how did his death come to be reported in 1888? The answer is to be found, I think, in the obituary notice that appeared in the Brisbane *Courier* 'The death is announced of Sir Henry Roscoe, M.P., F.R.S., Professor of Chemistry at Owen's College; and Mr Roscoe Conkling, formerly a prominent member of the United States Senate'. The first bit was fake news, but the second bit was true.

Henry Enfield Roscoe (1833–1915), photograph by Walery c. 1880.
Wikicommons/Wellcome Collection/CC BY 4.0

Conkling (1829–88) was a lawyer who practised in upstate New York before his election to the House of Representatives, where he served 1859–63 and again 1865–7. Moving to the Senate, he was in office 1867–81, a Republican noted for his abstemious habits (no alcohol or tobacco) and his support for the rights of African Americans.

It was, and still is, common for newspapers to hold files of draft obituaries (called 'advancers') that, come the death of a prominent person, could be quickly updated and published. Maintaining these files was often the job of staff who worked on them when they were not assigned to news stories. Sometime the 'pre-dead' subject is consulted about the content of what is described to him or her as a personal file. Mistakes in releasing the 'advancers' can occur, but I would expect a senior staff member to handle the final version and ensure that there was good reason to publish the obituary. Staff can get up to mischief, too, but I can't think of a reason that anyone would want to prematurely decease Sir Henry.

I am not sure if it's the one that Roscoe made famous, but I have been in one of the old mines under Alderley Edge. I was walking on the Edge one day when a trapdoor lifted up and out came a man in caving gear. I asked what was going on and, learning that it was an old mine that went back to Roman times, I was able organise a place on the next outing. My hosts were members of the Derbyshire Caving Club who look after the mine workings as well as some of the limestone caves further to the east. There's still a bit of copper in the Alderley Edge mine, as you can see from the photograph I took.

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 provides advice on chemical hazards and pollution.

events

22nd Annual Green Chemistry & Engineering Conference
18–20 June 2018, Portland, Oregon, USA
gcande.org

Macro 18 – World Polymer Congress
1–5 July 2018, Cairns, Qld
macro18.org

ICCE2018 – International Conference on Chemical Education
10 July 2018, University of Sydney, NSW
ivvy.com.au/event/CED681

ICCCE 2018 – 9th International Conference on Chemistry and Chemical Engineering
11–18 July 2018, University of Liverpool, Liverpool, UK
iccce.org

ICABC 2018 – 5th International Conference on Advances in Biology and Chemistry
6–8 August 2018, National Taipei University of Technology, Chemical Engineering & Biotechnology, Taipei, Taiwan
icabc.org

8th IUPAC International Conference on Green Chemistry
9–14 September 2018, Bangkok, Thailand
greeniupac2018.com

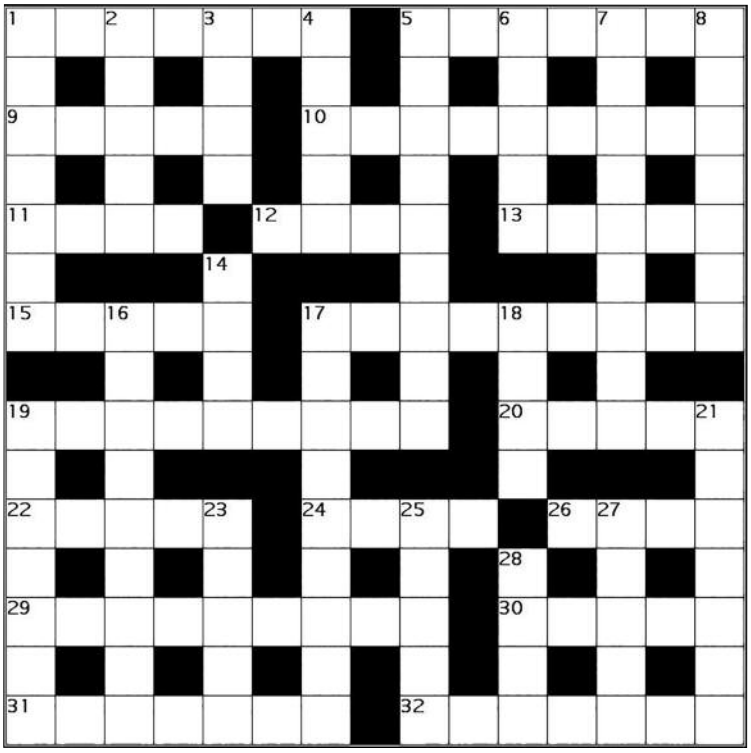
8th International Conference on Environmental Chemistry and Engineering
20–22 September 2018, Berlin, Germany
environmentalchemistry.conferenceseries.com

CBEE 2018 – 10th International Conference on Chemical, Biological and Environmental Engineering
27–29 September 2018, Hotel Berlin, Berlin, Germany
icbee.org

Organic 18 – 24th RACI Organic Chemistry Conference
2–6 December 2018, University of Western Australia, WA
ivvy.com.au/event/OGD780

RACI events are shown in blue.

cryptic chemistry



Across

1 Less work re malls. (7)
5 I express doubt in pursuit of nerve element. (7)
9 Top Adelaide player wears number 7. (5)
10 Nitrocellulose gram count about a hundred. (9)
11 Accomplished with competence. (4)
12 A celebrity with a heavenly body? (4)
13 14g makes 40% single covalent bond. (5)
15 Point of supply, we hear, for booze. (5)
17 Remodelling biokinetics bilateral centres lay out. (9)
19 Study my richest state. (9)
20 Lacks being born with beginnings of distinctive status. (5)
22 33216 remains. (5)
24 A lens defect characterised by formation of a pear-shaped image of the luminous cloud at the head of a comet. (4)
26 Used to be tungsten before. (4)
29 Aromatic ion-bed reaction over first zinc enhanced neptunium. (9)
30 Beginnings of International Mycological Institute notification of HN=. (5)
31 Products of rock lustres. (7)
32 Found spilt cold tea. (7)

Down

1 Mixers stir oil sacs. (7)
2 A payment for the islands. (5)
3 Some of 17 Across ancestry. (4)
4 Proper privilege. (5)
5 Code recovery in most cases. (9)
6 Spirals over reel. (5)
7 Giant tree axed and put together. (9)
8 Friend of Daniel Spooner's order. (7)
14 Half a truck. (4)
16 Hear tunes singing compounds. (9)
17 Test coder for sensors. (9)
18 Fluorine, nickel and neon. (4)
19 Carbon, hydrogen and gold-coloured room. (7)
21 Editors cut compound. (7)
23 Metal brace. (5)
25 Display form. (5)
27 Be flame first. (5)
28 30 last in 6. (4)

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

A challenging Chemistry quiz for school students!

Invitation to ANCQ 2018

The RACI invites all students to participate in the ANCQ 2018, being held in Australia on Thursday 2 August 2018.

The quiz has been in operation since 1982, growing from humble beginnings into an international event spread over 21 countries, seven languages, 1400 schools and more than 100 000 students.

The ANCQ is a unique chemical education activity.

It provides a major focus for secondary school students on the relevance of chemistry in an exciting and stimulating way. It is not a nationwide assessment of chemistry knowledge, but rather a promotion of chemistry that allows teachers and students to gauge their level of teaching and learning.

The quiz comprises 30 multiple-choice questions and takes one hour to complete. It is available both in hard copy and online.

Registrations close: Friday 8 June 2018

Entry cost: $6 per student

Website: www.ancq.com

For further information, including quiz dates for other countries, visit the website, email ancq@raci.org.au or phone (+61) 03 9328 2033.

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