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November 2016

Anticancer agents from a marine mollusc

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chemistry in Australia

November 2016


Stuart Woollett

cover story

From snails' eggs to anticancer agents: compound development and evaluation

18

Researchers at the University of Wollongong and the Illawarra Health and Medical Research Institute have discovered a new group of molecules showing promising results against multidrug-resistant cancers.

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Chemistry and cancer research

In our cover story this month, University of Wollongong and Illawarra Health and Medical Research Institute researchers Kara Perrow and colleagues report on their encouraging results with the eggs of a marine snail (*Dicathais orbita*) found on the coasts of Australia and New Zealand. The *N*-alkylisatin derivatives at the centre of the study are proving lethal to drug-resistant cancer cells in the laboratory (p. 18).

Also in this issue, an Australian native plant (*Scaevola spinescens*) with a bush medicine story has been the subject of several theses and was used by the Western Australian ChemCentre to produce an aqueous extract for some patients with life-limiting cancers, says Geoff Taylor, previously a chemist at the WA Government Chemical Laboratories (now the ChemCentre) (p. 22).

Multidrug resistance is a big challenge to current management practices for cancer. This problem exists for a variety of cancers, including those of the prostate, bowel and breast, some of the most prevalent cancers in Australia. The Australian Institute of Health and Welfare estimates that 130 466 cases of cancer will be diagnosed in Australia this year (www.aihw.gov.au/acim-books). As RACI approaches its centenary year, it seems a good time to think about some of the valuable cancer research of our members.

Natural products continue to be a source of novel compounds in cancer research. A group of Western Australian researchers, including Scott Stewart MRACI CChem from the School of Chemistry and Biochemistry at the University of WA, recently reported encouraging results for the novel cancer drug EBC-46, sourced from the berries of *Fontainea picrosperma*, which grows in the Atherton Tableland region in Queensland (http://dx.doi.org/10.1016/j.ejmech.2016.03.015). Australian life sciences company Qbiotics is conducting a safety evaluation of EBC-46 in a clinical phase I trial. Potential indications for EBC-46 include some of the multidrug-resistant cancers.

At the Faculty of Pharmacy, University of Sydney, Associate Professor Colin Duke MRACI CChem is investigating a high-flavonoid propolis (resin-like substance) found in residues of *Acacia paradoxa* on the legs of honeybees on Kangaroo Island.

In the School of Chemistry at the University of New South Wales, a focus of Associate Professor Shelli McAlpine FRACI CChem and her group is small molecules that target heat-shock protein 90 (Hsp90). The inspiration for this project was cyclic depsipeptide sansalvamide A, isolated from the marine fungus *Fusarium*, found near the Little Sansalvador islands in the Bahamas. McAlpine's group has designed molecules that selectively and effectively target Hsp90 in cells. 'Hsp90 is a chaperone, or protein "parent" that regulates over 200 other proteins within the cell; as such it controls multiple pathways involved in cancer. Our molecules bind to Hsp90 and stop them from facilitating these cancer pathways, which kills the cells,' she says.

Medicinal chemists at Monash Institute of Pharmaceutical Sciences (MIPS) are strongly engaged in anticancer drug discovery programs. The medicinal chemistry labs of the CRC for Cancer Therapeutics are located at MIPS, and group leaders and RACI Fellows Bernard Flynn, Peter Scammells, Jonathan Baell and Philip Thompson have active programs pursuing oncology targets with funding from NHMRC, National Breast Cancer Foundation and Cancer Council Victoria. Some of the other participants in the CRC collaboration are CSIRO Materials Science and Engineering, Walter and Eliza Hall Institute and Peter MacCallum Cancer Centre, as well as biotechs, clinical trials specialists and organisations for health education and advocacy.

Earlier this year, Melbourne biotech MecRx, CSIRO and Peter Mac began joint work on new ways to identify promising molecular starting points in drug discovery. RACI Fellows Jack Ryan and Paul Savage are part of this project. The group has already identified a potential inhibitor of a regulator gene associated with uncontrolled cell division in a number of cancers.

Renate Griffith FRACI CChem, chair of the organising committee for AIMECS2017, the 11th in the series of International Medicinal Chemistry Symposia organised by the Asian Federation for Medicinal Chemistry and one of the partner conferences of the RACI Centenary Congress, is busy planning topics for next year. She says that the themes of epigenetic targets (organised by the American Chemical Society Division of Medicinal Chemistry) and kinase inhibitors will be particularly pertinent to cancer researchers.

According to Cancer Research UK, the research behind last year's Nobel Prize in Chemistry (see February 2016 issue, p. 14, and April 2016, p. 20) – discovering a suite of molecules that repair mistakes in DNA – has revolutionised cancer research in a number of ways: by leading a new field of research, by inspiring different treatment methods, by offering knowledge that provides new ideas for targeting cancer cells, and by revealing how Epstein Barr Virus disrupts DNA, which can lead to cancer (bit.ly/2bPLidE). 2015 Nobel laureate in Chemistry Tomas Lindahl was the first director of Cancer Research UK-funded labs at Clare Hall in London, when it opened 30 years ago.

Finally, we mustn't forget the vital role of chemists in developing agents for cancer diagnosis, and in improving existing drugs used for cancer treatment and palliative care.

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Sally Woollett (editor@raci.org.au)
Thanks to the RACI members who helped me with content and contacts for this editorial.

Communication or not

In the August issue (p. 16), George Koutsantonis and John Wade posed the question of whether Communications are still needed as an article category in the *Australian Journal of Chemistry*.

As they point out, needs have changed. In addition, I want to mention the important fact that, whereas Communications really used to be Rapid Communications with very little experimental detail (and sometimes none at all), this has changed (I had the 'Rapid' in Rapid Communications removed a few years ago). It is now a requirement that all compound characterisation data, for example, be published as Supplementary Material. Therefore, the need for a full paper on the same work as a follow-up has vanished. This development has been detrimental for smaller journals like *Aust. J. Chem.*, because it used to be not uncommon (say, 30–40 years ago) to publish a Rapid (and short) Communication on important results, for example in *Chemical Communications*, and then a follow-up full paper in *Aust. J. Chem.*

Given these developments, we do not really need Communications any more. It seems that Communications in *Aust. J. Chem.* are nowadays sometimes used by authors to publish a small but not necessarily particularly important piece of work. There should be nothing wrong with publishing such papers as short, full papers instead. All papers are subject to the same refereeing procedure anyway.

Communications in high-impact journals such as *Angewandte Chemie*, *Chemical Communications*, *Journal of the American Chemical Society*, *Science* and *Nature* are seen as very prestigious because it is generally known to be rather difficult to get such papers accepted. If *Aust. J. Chem.* wants to keep Communications as a category, it should be not because they are more rapidly published (they are not), but because they are more prestigious, which would imply tougher refereeing and acceptance criteria.

Curt Wentrup FRACI CChem, former editor *Australian Journal of Chemistry*

Icebergs and oil platforms

Having read the article about the Hibernia platform off the coast of Newfoundland in the September issue (p. 34), I am minded to make the following point for the interest of readers.

In the article, possible collision with an iceberg is mentioned, and this can be expressed quantitatively. In risk analysis of the platform, the frequency of impact of the platform with an iceberg of mass one megatonne was calculated as 2×10^{-3} per year, signifying that such an event would occur once in 500 years (Jones J.C., Russell N.V. *Dictionary of energy and fuels*, Whittles Publishing, 2007). Such a figure is of course subject to review as circumstances change or as existing circumstances are reconsidered.

Clifford Jones FRACI CChem

More reflections on Sydney Technical College

I read with interest Dave Solomon's recollection (September issue, p. 6) of the old Tech days, in response to Bob Ryan's note of June (p. 5).

Dave's comment about his administrative officer 'keeping him out of jail' reminded me that Dave is the only person I know to have been booked for speeding on a push bike. He did not have an admin officer then but fortunately speeding was not a hanging offence. A couple of years later it might have earned him a medal at the Olympic games.

One favourite story is about a group who were required to make a pilot quantity of a particular chemical. In desperation they went to purchase from Selby's (Cricket House in George St). After waiting several months for Selby to get the stock in, they eventually found that Selby's supplier was the Tech College.

Mervyn Crawford FRACI CChem

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chemistry in Australia
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EDITOR
Sally Woollett
Ph (03) 5623 3971
editor@raci.org.au

PRODUCTION EDITOR
Catherine Greenwood
catherine.greenwood@bigpond.com

ADVERTISING SALES
Gypsy Media & Marketing Services
Marc Wilson, ph 0419 107 143
marc@gypsymedia.com.au

PRODUCTION
Control Publications Pty Ltd
science@control.com.au
www.control.com.au

BOOK REVIEWS
Damien Blackwell
damo34@internode.on.net

RESEARCH HIGHLIGHTS
David Huang
david.huang@adelaide.edu.au

GENERAL ENQUIRIES
Robyn Taylor
Ph/fax (03) 9328 2033/2670
chemaust@raci.org.au

PRESIDENT
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Curtin scientists probe to make invisible gold visible

Scientists are using the new Geoscience Atom Probe Facility at Curtin University to study mineral deposits containing locked resources of gold in refractory ores.

Curtin Western Australian School of Mines Research Associate in Applied Geology Dr Denis Fougerouse and fellow researchers have found metallic gold nanoparticles only a few nanometres in diameter within the mineral arsenopyrite – a common mineral found in Australian mines.

Fougerouse said the study was believed to be one of the first of its kind, and the discovery challenges the understanding of nanoparticle formation and allowed the team to establish the main controls on gold incorporation in sulfides.

Curtin University

The application of atom probe microscopy in geosciences is relatively new. The technique is based on field-evaporation of atoms from tiny, needle-shaped specimens to provide three-dimensional sub-nanometre scale.

Dr Denis Fougerouse, WA School of Mines Research Associate in Applied Geology

New material to revolutionise waterproofing

Scientists at the Australian National University (ANU) have developed a new spray-on material with a remarkable ability to repel water (doi: 10.1021/acsami.6b03414). The new protective coating could eventually be used to waterproof mobile phones, prevent ice from forming on aeroplanes or protect boat hulls from corroding.

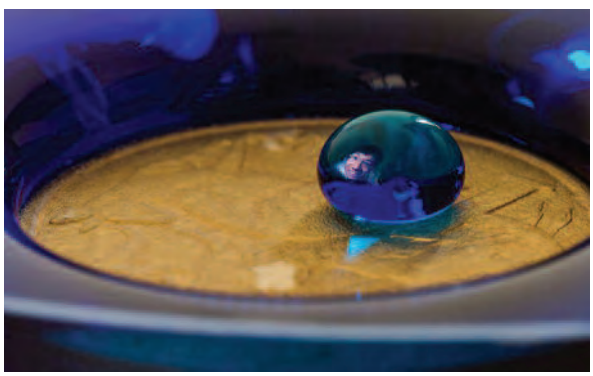
The scientists created a much more robust coating than previous materials by combining two plastics, one tough and one flexible. The water-repellent or superhydrophobic coating is also transparent and extremely resistant to ultraviolet radiation.

The team developed two ways of creating the material, both of which are cheaper and easier than current manufacturing processes. One method uses a flame to generate the nanoparticle constituents of the material. For lower temperature applications, the team dissolved the two components in a sprayable form.

In addition to waterproofing, the new ability to control the properties of materials could be applied to a wide range of other coatings, said PhD student William Wong, from the Nanotechnology Research Laboratory at the ANU Research School of Engineering.

'A lot of the functional coatings today are very weak, but we will be able to apply the same principles to make robust coatings that are, for example, anti-corrosive, self-cleaning or oil-repellent,' he said.

Australian National University



It will keep skyscraper windows clean and prevent the mirror in the bathroom from fogging up.

Associate Professor Tricoli, lead researcher and head of Nanotechnology Research Laboratory, ANU

Immune breakthrough: unscratching poison ivy's rash

We all know that a brush with poison ivy leaves us with an itchy painful rash. Now, Monash and Harvard researchers have discovered the molecular cause of this irritation. The finding brings us a step closer to designing agents to block this mechanism and sheds light on other serious skin conditions, such as psoriasis.

The international team of scientists have shown, for the first time, a connection between an immune molecule found in the skin and skin sensitisers – the research was published in *Nature Immunology* (doi: 10.1038/ni.3523).

Professor Jamie Rossjohn, co-lead author with Dr Florian Winau, Harvard Medical School, confirmed that the body's immune molecule, CD1a, plays a crucial role in mediating skin inflammation and irritation after contact with urushiol – the active ingredient in plants endemic to Northern America and parts of Europe and Australia.

Dr Tang Yongqing and Dr Jerome Le Nours said the research team needed a combination of scientific creativity and ingenuity to crack the CD1a–urushiol code.

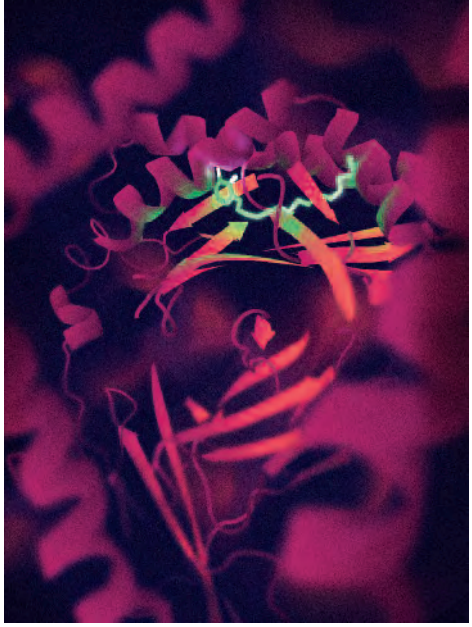
'For over 35 years we have known CD1a is abundant in the skin,' said Le Nours. 'Its role in inflammatory skin disorders has been difficult to investigate and until now has been really unclear. Our work represents clear evidence that CD1a is instrumental in skin-related diseases. We are the first scientists to image the CD1a–urushiol connection.'

'Our results were strengthened by in vivo and clinical studies at Harvard Medical School, in the United States,' Yongqing said.

The studies in Boston also showed that blocking the function of CD1a prevents the triggering of this skin-based allergic reaction, giving the researchers further evidence of just how important CD1a is.

'Future research could lead to the development of new treatments to combat minor skin irritations as well as chronic inflammatory skin diseases like psoriasis, eczema and rosacea,' said Yongqing.

Centre of Excellence in Advanced Molecular Imaging



Centre of Excellence in Advanced Molecular Imaging

Stylised image: Urushiol (in green), the active ingredient in poison ivy, entrapped by CD1a molecule (in pink), which mediates the inflammatory response.

Our basic discovery may make a big difference in the future treatment and prevention of inflammatory skin diseases.

Dr Jerome Le Nours, Australian Research Council Centre of Excellence in Advanced Molecular Imaging at the Monash Biomedicine Discovery Institute

Household pesticides pose risk for small children

Calls to a poisons hotline have revealed a disproportionate number of young children referred to hospital following suspected exposure to a household bug and spider spray. The University of Queensland analysed insecticide-related calls made to the Queensland Poisons Information Centre during 2014. About half of the almost 750 insecticide-related calls were for young children.

PhD candidate Karin English said the study found cockroach baits and ant liquid to be the most common sources of suspected insecticide exposure for children under five, accounting for 39% of calls. Bug sprays containing pyrethroids, pyrethrins, piperonyl butoxide – and the more harmful organophosphate diazinon – accounted for almost 26% of calls.

English said cockroach bait casings reduced poison exposure. She said ant liquids were often placed in open containers on the floor, where children could access them.

The study has been published in the *Australian and New Zealand Journal of Public Health* (doi: 10.1111/1753-6405.12551).

University of Queensland

This highlights the need for more comprehensive regulation of insecticides in Australia, and for improvements in childproof packaging of pest control products.

Karin English, University of Queensland PhD candidate

Lack of copper in ancient soil regulates nitrification

Australia is home to some of the most ancient soils in the world.

Researchers from the University of Western Australia and Newcastle University (UK) have discovered that copper levels in the soil affect the delicate balance of microbes responsible for soil nitrification, which affects how well crops grow.

Soil nitrification has critical implications for the environment. Lack of nitrogen in the soil can limit plant growth but too much nitrogen can cause algal blooms and greenhouse gas emissions.

The research differs from previous studies that suggested nitrogen fertilisers played a large role in affecting the microbes (archea and bacteria) that are responsible for soil nitrification.

Soil nitrification has been an important process in the global nitrogen cycle since the Earth was first oxygenated.

One of the biggest farming costs globally is the use of nitrogen fertilisers to aid crop productivity and this latest discovery has important implications in developing further understanding of soil nitrification for the agricultural industry.

Professor Tony O'Donnell, Dean of the University of WA's Faculty of Science, said the soils in Australia were some of the oldest in the world, compared to soils in the northern hemisphere where most global research has been done to date.

'In testing ancient Western Australian soils, we found a relationship between the soils' age and the levels of archea and bacteria microbes,' O'Donnell said.

'When we looked into this further, we found that in ancient Western Australian soils, the lack of copper limited the archea microbial population, which in turn limited their soils' nitrification; instead bacterial nitrification dominates.'

Professor Daniel Murphy, University of WA Chair of Soil Biology, said the only way to effectively manage nitrogen in farming systems was to understand the microorganisms responsible and what affected their growth.

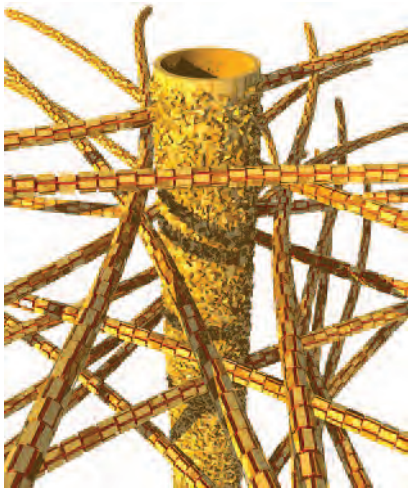
'These findings are an important step forward in developing targeted solutions to manage nitrification in soil,' he said.

'Use of nitrogen fertilisers is only 50–60% effective so understanding the nitrification process in soils is very important.'

The study has been published in *Scientific Reports* (doi: 10.1038/srep30733).

University of Western Australia

Dentin nanostructures: a 'super-natural' phenomenon



Dentin's biological structure: tubules and mineral nanoparticles are embedded in a network of collagen fibres. Jean-Baptiste Forien, © Charité – Universitätsmedizin Berlin

Dentin is one of the most durable biological materials in the human body. Researchers from Charité – Universitätsmedizin Berlin were able to show that the reason for this can be traced to its nanostructures and specifically to the interactions between the organic and inorganic components. They showed that it is the mechanical coupling between the collagen protein fibres and mineral nanoparticles that renders dentin capable of withstanding extreme forces. Results from this research have been recently published in *Chemistry of Materials* (doi: 10.1021/acs.chemmater.6b00811).

In humans, teeth come into contact almost 5000 times per day under normal use, but it is surprisingly rare for healthy teeth to break. It is widely accepted that the structure of teeth makes teeth tough, where the dentin inner core supports the outer hard enamel cap. The secret to the marked toughness lies in the structural details. Dentin is a bone-like substance, which is composed of mineral nanoparticles, collagen and water. While both enamel and dentine are composed of the mineral carbonated hydroxyapatite (cHAP), dentin represents a complex nanocomposite material. It consists of inorganic cHAP nanoparticles embedded in an organic matrix of collagen protein fibres. A group of researchers, led by Dr Jean-Baptiste Forien and Dr Paul Zaslansky from Charité's Julius Wolff Institute, had previously shown that residual stress in dentin contributes to the high load-bearing capacity of this biological structure.

Compression stress within the material can explain why damage or cracks in enamel do not extend catastrophically into the dentin bulk. As part of the new findings, Zaslansky's team measured how nanoparticles and collagen fibres interact under humidity-driven stress.

The researchers increased the compressive stress inside the dentin samples. The samples were also dried by heating them to 125°C. This resulted in the collagen fibres shrinking, leading to huge stress being exerted on the nanoparticles. The ability to withstand forces of up to 300 MPa is equivalent to the yield strength of construction grade steel, and is comparable to 15 times the pressure exerted during mastication of hard food, which usually remains well below 20 MPa. Heat treatment did not lead to the destruction of the protein fibres, suggesting that the mineral nanoparticles also have a protective effect on collagen.

Analysis of the data also showed a gradual reduction in the size of the cHAP crystal lattices as one moves deeper into the tooth.

Such a structure could be used as a model system for new materials development, for example when designing novel dental restoration materials. The findings of this study are also of interest to dentists. Zaslansky explained: 'Our findings highlight an important reason for doctors to keep teeth moist during dental procedures, such as when inserting dental fillings or installing crowns. Avoiding dehydration may very well prevent build-up of internal stresses, the long-term effects of which remain to be studied.'

Charité – Universitätsmedizin Berlin

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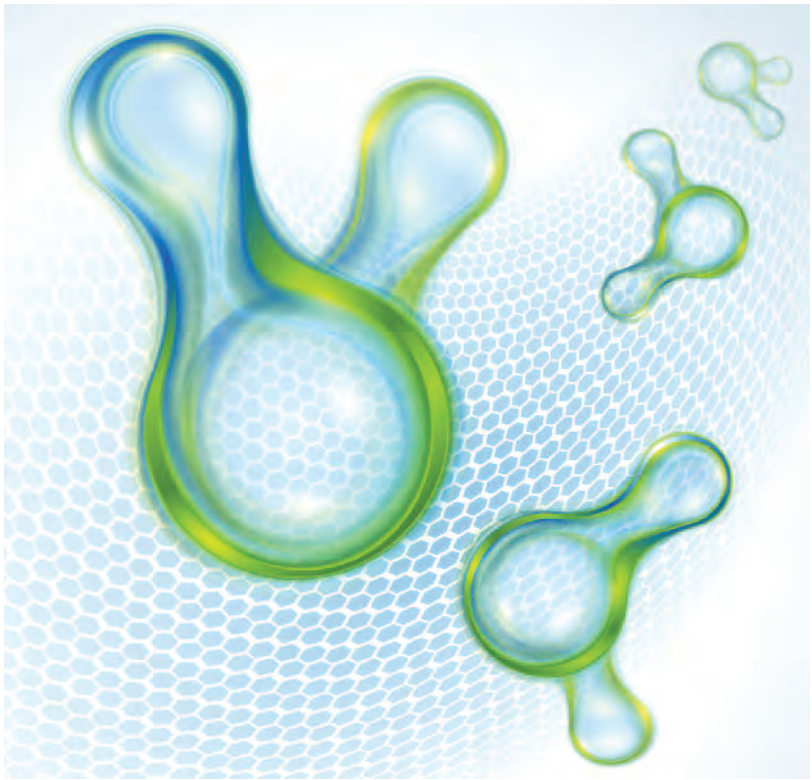
Scientists glimpse why life can't happen without water

A study published in *Proceedings of the National Academy of Sciences* (doi: 10.1073/pnas.1602916113) provides the strongest evidence yet that proteins can't fold themselves.



Anna Kuzilina/iStockphoto

Rather, the work of folding is done by much smaller water molecules, which surround proteins and push and pull at them to make them fold a certain way in fractions of a second, like scores of tiny origami artists folding a giant sheet of paper at blazingly fast speeds.

Dongping Zhong, leader of the research group at the Ohio State University that made the discovery, called the study a 'major step forward' in the understanding of water–protein interactions and said it answers a question that's been dogging research into protein dynamics for decades.

'For a long time, scientists have been trying to figure out how water interacts with proteins. This is a fundamental problem that relates to protein structure, stability, dynamics and – finally – function,' said Zhong, who is the Robert Smith Professor of physics at Ohio State.

'We believe we now have strong direct evidence that on ultrafast time scales (picoseconds, or trillionths of a second), water modulates protein fluctuations,' he concluded.

Zhong, who is also a professor of chemistry and biochemistry, and his team used ultrafast laser pulses to take snapshots of water molecules moving around a DNA polymerase, the kind of protein that helps DNA reproduce.

The key to getting a good view of the interaction was to precisely locate optical probes on the protein surface, he said. The researchers inserted molecules of the amino acid tryptophan into the protein as a probe, and measured how water moved around it.

Water molecules typically flow around each other at picosecond speeds, while proteins fold at nanosecond speeds – 1000 times slower. Previously, Zhong's group demonstrated that water molecules slow down when they encounter a protein. Water molecules are still moving 100 times faster than a protein when they connect with it, however.

In the new study, the researchers were able to determine that the water molecules directly touched the protein's side chains, the portions of the protein molecule that bind and unbind with each other to enable folding and function. The researchers were also able to note the timing of movement in the molecules.

Computer simulations at the Ohio Supercomputer Center helped the researchers visualise what was going on: where the water moved a certain way, the protein folded nanoseconds later, as if the water molecules were nudging the protein into shape.

Water can't arbitrarily shape a protein, Zhong explained. Proteins can only fold and unfold in a few different ways depending on the amino acids they're made of.

'Here, we've shown that the final shape of a protein depends on two things: water and the amino acids themselves. We can now say that, on ultrafast time scales, the protein surface fluctuations are controlled by water fluctuations. Water molecules work together like a big network to drive the movement of proteins.'

Pam Frost Gorder, Ohio State University

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Science ship becomes floating classroom

Dr Leanne Armand (left), coordinator of CAPSTAN. © MNF

Australia's future marine scientists are getting a boost from a new training program set to transform CSIRO's science research vessel the RV *Investigator* into a floating classroom.

The unique program will give students and trainers dedicated time on board the *Investigator* and expose them to a range of world-class scientific equipment and technology.

The postgraduate training initiative is called CAPSTAN – Collaborative Australian Postgraduate Sea Training Alliance Network.

The program is an Australian first and will provide a collaborative national approach to teaching future generations of marine scientists and mariners.

Director of CSIRO Marine National Facility, Mr Ron Plaschke, said the new CAPSTAN program provides a fantastic opportunity for Australian marine scientists.

The centrepiece of the program is *Investigator*, which can operate anywhere from the ice edge to the equator and study the deepest parts of our region's oceans, as well as the atmosphere above.

Research voyages in 2016 have already discovered undersea volcanoes, investigated climate change, mapped tectonic plate boundaries, found rare deep-sea creatures and provided important information to monitor changes in our ocean environment.

Macquarie University's Dr Leanne Armand, program coordinator for CAPSTAN, said this was one of the most exciting programs she has been involved with.

Using *Investigator*'s high-tech capabilities, teachers and trainers on board are even able to share their experiences with students across Australia through live ship-to-shore video broadcasts.

The first participants in the CAPSTAN program are expected to join a transit voyage on *Investigator* later next year.

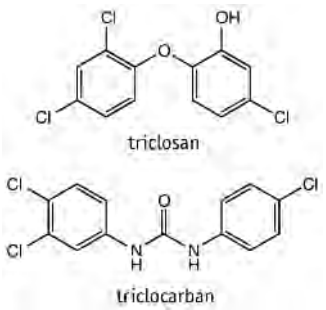
The CAPSTAN application process is expected to open in early 2017 and further details are available on the program website.

CSIRO

US FDA issues final rule on safety and effectiveness of antibacterial soaps

The US Food and Drug Administration has issued a final rule establishing that over-the-counter consumer antiseptic wash products containing certain active ingredients can no longer be marketed. Companies won't be able to market antibacterial washes with these ingredients because manufacturers did not demonstrate that the ingredients are both safe for long-term daily use and more effective than plain soap and water in preventing illness and the spread of certain infections. Some manufacturers have already started removing these ingredients from their products.

This final rule applies to consumer antiseptic wash products containing one or more of 19 specific active ingredients, including the most commonly used ingredients – triclosan and triclocarban. These products are intended for use with water, and are rinsed off after use. This rule does not affect consumer hand 'sanitisers' or wipes, or antibacterial products used in healthcare settings.



The agency issued a proposed rule in 2013 after some data suggested that long-term exposure to certain active ingredients used in antibacterial products – for example, triclosan (liquid soaps) and triclocarban (bar soaps) — could pose health risks, such as bacterial resistance or hormonal effects. Under the proposed rule, manufacturers were required to provide the agency with additional data on the safety and effectiveness of certain ingredients used in over-the-counter consumer antibacterial washes if they wanted to continue marketing antibacterial products containing those ingredients. This included data from clinical studies demonstrating that these products were superior to non-antibacterial washes in preventing human illness or reducing infection.

Antibacterial hand and body wash manufacturers did not provide the necessary data to establish safety and effectiveness for the 19 active ingredients addressed in this final rulemaking. For these ingredients, either no additional data were submitted or the data and information that were submitted were not sufficient for the agency to find that these ingredients are generally recognised as safe and effective. In response to comments submitted by industry, the FDA has deferred rulemaking for one year on three additional ingredients used in consumer wash products – benzalkonium chloride, benzethonium chloride and chloroxylenol – to allow for the development and submission of new safety and effectiveness data for these ingredients. Consumer antibacterial washes containing these specific ingredients may be marketed during this time while data are being collected.

Washing with plain soap and running water remains one of the most important steps consumers can take to avoid getting sick and to prevent spreading germs to others. If soap and water are not available and a hand sanitiser is used instead, the US Centers for Disease Control and Prevention recommends that it be an alcohol-based hand sanitiser that contains at least 60% alcohol.

Since the FDA's proposed rulemaking in 2013, manufacturers have started phasing out the use of certain active ingredients in antibacterial washes, including triclosan and triclocarban. Manufacturers will have one year to comply with the rulemaking by removing products from the market or reformulating (removing antibacterial active ingredients) these products.

US Food and Drug Administration

(Editor's note: At the time of printing, the Therapeutic Goods Administration was reviewing the FDA's ruling.)

filipfoto/iStockphoto

Uncovering the missing link in Darwin's theory of evolution

Research has found that selenium correlates to nearly every major extinction and growth event in Earth's 4.5-billion-year history.

In 1859, Charles Darwin declared that evolution on Earth was driven by adaptation to changes in the environment. But Darwin couldn't explain why there were periods of significant growth and periods where very little evolution took place at all.

Distinguished Professor Ross Large, University of Tasmania, has uncovered the missing link in Darwin's theory of evolution. That link is the trace element selenium.

'We have discovered that selenium is the critical element for life. When levels of selenium have been low, major extinction events have occurred. When levels have been high, life has flourished; like for example the evolution of giant fish,' he said.

It is movement of the Earth's continents that influences the amount of selenium in the oceans. As the continents move and collide, mountains are created. These mountains erode over time and disperse nutrients via rivers into the ocean.

Levels of selenium become low when there is little movement in the continents. Selenium is a rare trace element, so without an active supply it can become dormant in the sediment on the ocean floor. Without it, things begin to die and life cannot flourish again until the continental plates collide, releasing selenium back into the oceans.

Large and his team have developed a method for mapping the ocean's trace elements over their 3.5-billion-year history. The method is only possible using the unique facilities at the University of Tasmania, which is the only lab of it's kind in the world.

The lab houses three different laser types that allow for fine-scale imaging of trace element distribution and an X-ray fluorescence spectrometer for trace element analysis.

University of Tasmania

on the market

Whirl-Pak sampling bags

Invented in 1959 and manufactured in the US at a facility certified to ISO 9001, Whirl-Pak® bags were the first sterile laboratory sampling bag on the market and continue to be the world leader in sample collection. Whirl-Pak® bags can be used for the sampling of liquids, solids and semisolids across many different markets including food and beverage, dairy, water treatment, environmental, veterinary, microbiology and more!

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The bags also go through a separate sterilisation process after manufacturing using ethylene oxide gas at an independent ISO-certified facility. Sterility documents are available online 24/7 for each lot number. You simply will not find a better quality bag out there!

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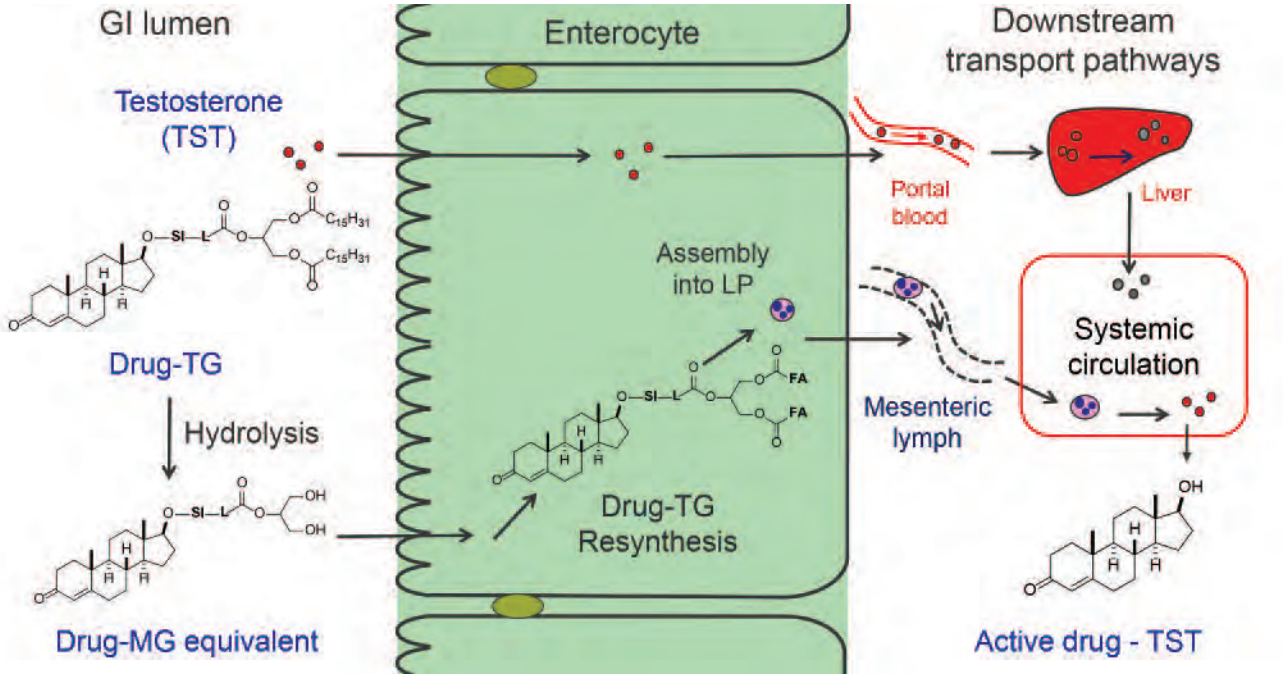
are easier to label, have an integrated closure system, are unbreakable, and are guaranteed sterile – negating the need to spend time and money washing and sterilising!

Contact your local Rowe Scientific Pty Ltd office or go to www.rowe.com.au and search for Whirl-Pak.

Lipid-mimetic prodrugs to promote bioavailability



The liver plays a vital role in protecting the body from toxins that may be absorbed from the intestine. For orally administered drugs, however, this can present a major challenge to utility, resulting in significant metabolism prior to entry into the systemic (general) circulation. To overcome this 'first pass' metabolism, Professor Chris Porter, Dr Jamie Simpson and co-workers at the Monash Institute of Pharmaceutical Sciences describe the synthesis of prodrugs that direct absorption away from the intestinal (portal) blood and instead promote integration into lipid transport pathways that deliver the drugs into the intestinal lymphatics (Hu L., Quach T., Han S., Lim S.F., Yadav P., Senyschyn D., Trevaskis N.L., Simpson J.S., Porter C.J.H. *Angew. Chem. Ind. Ed.* 2016, doi: 10.1002/anie.201604207). Unlike the portal blood, which flows directly to the liver, blood in the intestinal lymphatic capillaries bypasses the liver and instead flows directly into the systemic circulation, avoiding first-pass metabolism. The prodrugs mimic the structure of natural lipids to direct transport into the lymph and employ self-immolative linkers to promote drug release in the systemic circulation. For testosterone, a drug with a very high first metabolic liability, this approach resulted in remarkable increases (up to 90-fold) in plasma exposure when compared with the current commercial product (testosterone undecanoate).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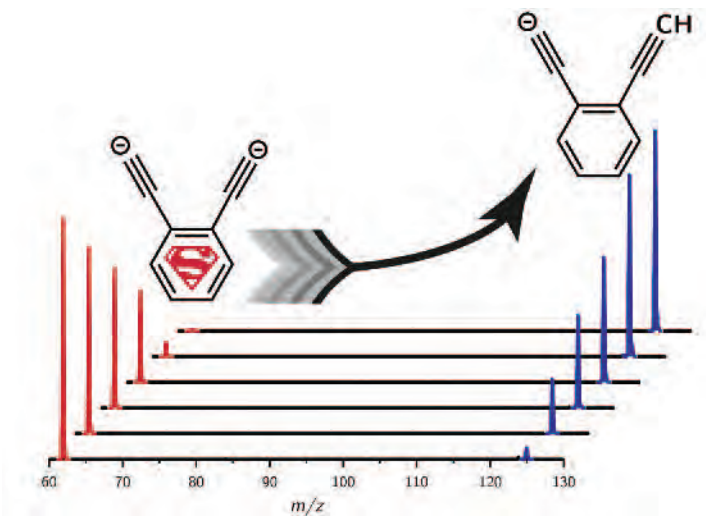
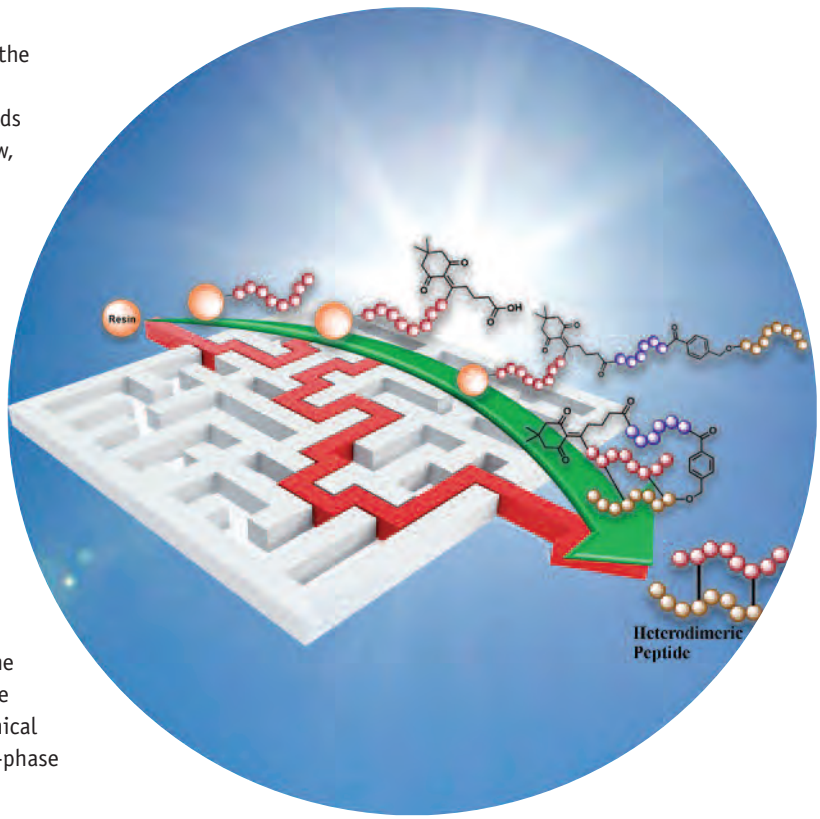
Most basic base

According to the Brønsted–Lowry definition, an acid is a compound that acts as a proton donor and a base is a compound that acts as a proton acceptor, with species at the extreme ends of the scale described as superacids and superbases. In the gas phase, how tightly a compound holds onto a proton is quantified by its proton affinity. Until now, the strongest reported superbase was the lithium oxide anion. But Dr Berwyck Poad at the Queensland University of Technology and a team from the University of Sydney, ANU and the University of Wollongong have recently shown that multiply charged anions can be even more basic (Poad B.L.J., Reed N.D., Hansen C.S., Trevitt A.J., Blanksby S.J., Mackay E.G., Sherburn M.S., Chan B., Radom L. *Chem Sci.* 2016, **7**, 6245–50). Multiply charged anions should be good proton acceptors, but loading negative charges onto molecules leads to Coulombic instability, particularly in the gas phase. Poad and his colleagues first used a theoretical model to search for superbasic multiply charged anions with inherent stability. Diethynylbenzene dianions were chosen as targets because of the weak acidity of the acetylene functionality. The dianion that they prepared, the *ortho*-diethynylbenzene dianion, was shown to deprotonate water and benzene. Furthermore, high-level quantum chemical calculations showed that this dianion has the highest gas-phase proton affinity of any molecule prepared to date.

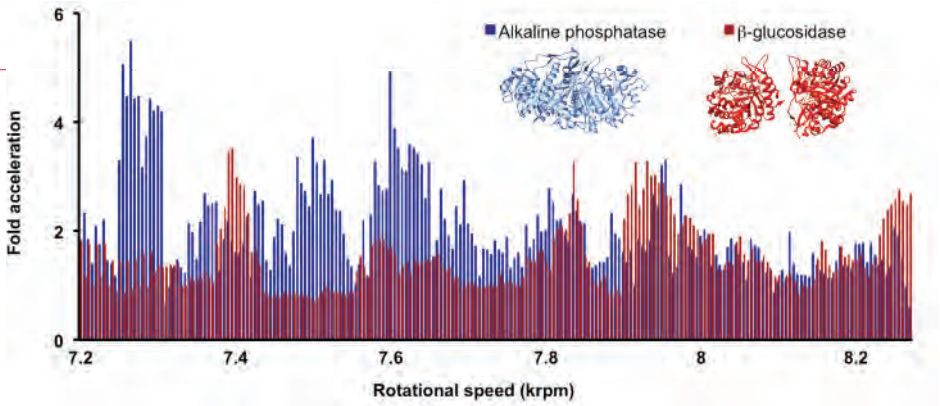


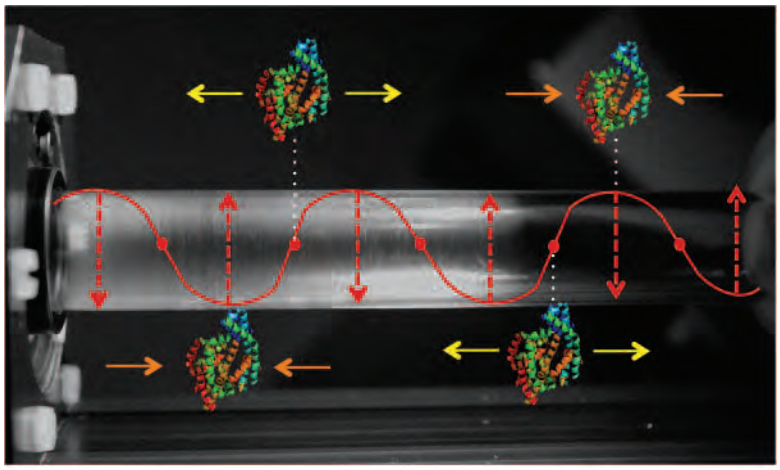
Simply linking peptide chains



Heterodimeric peptides or proteins linked by disulfide bonds, such as insulin and relaxin, are attractive drug targets. But their chemical assembly can be tedious, time-consuming and low yielding. Inspired by the cellular synthesis of pro-insulin, in which the two constituent peptide chains are expressed as a single-chain precursor separated by a connecting C-peptide, a team of medicinal chemists led by Dr Mohammed Akhter Hossain of the Insulin Peptides Laboratory at the Florey Institute of Neuroscience and Mental Health have developed a novel chemically cleavable bis-linker tether that allows two peptide chains to be conveniently assembled as a single 'pro'-peptide on the same solid support (Patil N.A., Tailhades J., Karas J.A., Separovic F., Wade J.D., Hossain M.A. *Angew. Chem. Int. Ed.* 2016, doi: 10.1002/anie.201604733). Following peptide cleavage and post-synthetic modifications, this bis-linker tether can be removed in one step by chemical means. The method was developed and used by a PhD student at Hossain's lab, Nitin Patil, to synthesise a drug delivery-cargo conjugate, TAT-PKCi peptide, and a two-disulfide-bridged heterodimeric thionin analogue. This technique is the first one-pot chemically cleavable bis-linker strategy for the facile synthesis of cross-bridged two-chain peptides to be reported.

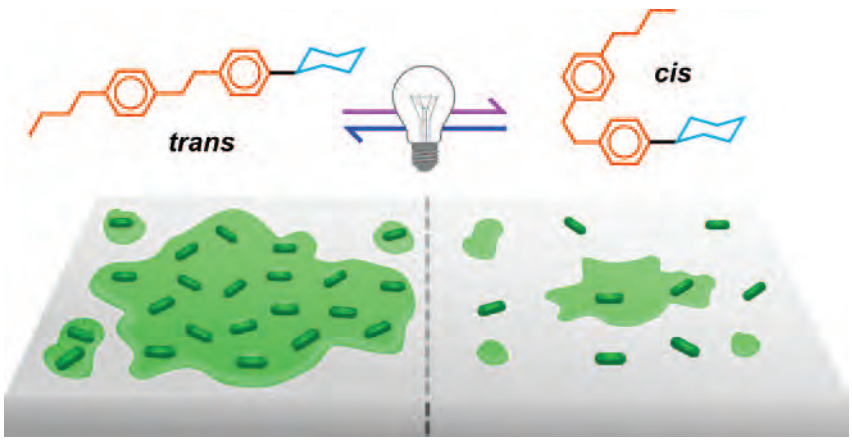
Accelerating enzymatic catalysis in dynamic thin films





Nature uses highly efficient proteins to perform diverse and challenging transformations to make life possible. Although these transformations are rapid in vivo, using enzyme proteins for organic synthesis is often difficult. Sluggish reaction rates, protein instability and inhibition often deter researchers. To improve biocatalysis viability, researchers from the University of California, Irvine, and Flinders University have used vibrational waves to drive enzymatic catalysis an average of 15 times faster than normal (Britton J., Meneghini L.M., Raston C.L., Weiss G.A, *Angew. Chem. Int. Ed.* 2016, **55**, 11 387–91). Using a vortex fluidic device to impart vibrations into a thin film containing an enzyme and substrate revealed a new way to control biocatalysis. Each protein has a distinct fingerprint that accelerates its activity under specific conditions. The pinnacle of this research was accelerating a highly valuable C–C bond-forming enzyme, an aldolase. Aldolases synthesise important fragments that are used to create active pharmaceutical ingredients such as Lipitor, a cholesterol-lowering medicine. Having demonstrated accelerated enzyme activity, the researchers have now shifted focus to using this method to develop complex-molecule syntheses for a greener approach to catalysis.

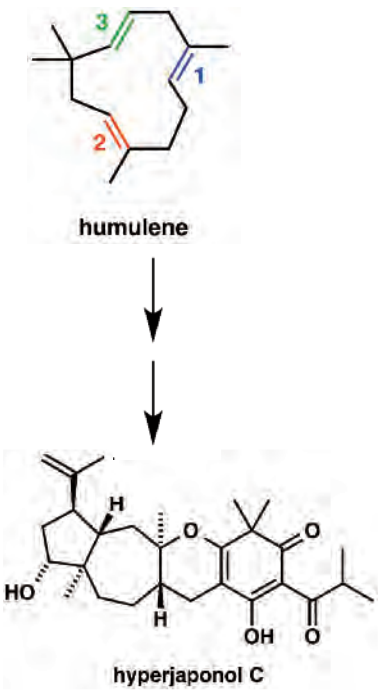
Shining light on mechanisms of bacterial biofilm formation



Antibiotic drug resistance represents a global health emergency, creating an urgent need for new clinical agents with novel and unconventional modes of action. Amphiphilic carbohydrates are an emerging class of antimicrobial agent that possess promising and intriguing bioactivity. But current understanding of the complex mechanisms of action are limited to a handful of well-characterised systems. To gain a clearer picture, researchers at the University of New England, Monash University and RMIT University have developed a family of photoswitchable carbohydrate-based surfactants as light-controllable inhibitors of bacterial growth and biofilm formation (Hu Y., Zou W., Julita V., Ramanathan R., Tabor R.F., Nixon-Luke R., Bryant G., Bansal V., Wilkinson B.L. *Chem. Sci.* 2016, doi: 10.1039/c6sc03020c). Irradiation of these surfactants with UV light triggers a reversible change in their self-assembly properties and interfacial activity, which was found to influence biofilm formation, bacterial motility and growth of multi-drug resistant strains of Gram-negative *P. aeruginosa* and methicillin-resistant Gram-positive *S. aureus* (popularly known as 'Golden Staph'). Several compounds were identified as possessing bacteria- and photoisomer-specific activity against these strains. This work paves the way for the development of new light-responsive materials as tools for probing the dynamic mechanisms of bacterial biofilm formation.

Humulene on me

Cascade reactions inspired by a biosynthetic hypothesis can often be applied to the rapid construction of complex natural products. This approach was recently used by organic chemists at the University of Adelaide in a four-step total synthesis of hyperjaponol C, a polycyclic meroterpenoid isolated from the flowering plant *Hypericum japonicum* (Lam H.C., Spence J.T.J., George J.H. *Angew. Chem. Int. Ed.* 2016, **55**, 10 368–71). The synthesis used three consecutive reactions of the alkenes of humulene, a cyclic sesquiterpene natural product that is responsible for the hoppy aroma of many beers. A hetero-Diels–Alder reaction at double bond 1 (blue) was followed by epoxidation at double bond 2 (red), and a final carbocation rearrangement was then initiated at double bond 3 (green). In this manner, the predisposed order of reactivity of the alkenes of humulene was fully exploited in the total synthesis of hyperjaponol C. In addition, the paper also describes the divergent synthesis of hyperjapones A–E, hyperjaponol A, and several 'undiscovered natural products' that are predicted to exist in nature on the basis of biosynthetic hypotheses.



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.

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What can you do to ensure that your submission has the best possible chance of publication?

The title – it sounds basic but this is the first thing we read and it should convey the message the paper is bringing to the world and excite the imagination. The title should accurately reflect the content of the paper; otherwise, it will elicit a response from the referees.

The introduction should put the work presented into context and position the work into that which has come before. The temptation here is to wax lyrical about the state of the art, the importance of the problem and the enormous benefits that will flow from the solution to the addressed problem. Resist doing this if your work is but a small piece of the puzzle and focus your introduction more on the aspect of the problem you are addressing. This helps make the expectations of the reviewers more reasonable.

Next, report your results and ensure that your conclusions are supported by the facts presented. Sounds simple! Often the desire to appear erudite obfuscates the clear connection to the obvious flow of conclusions. Don't leave obvious questions to be asked by the reviewers: 'Why didn't they use those analogues?' or 'Why didn't they measure the $^{31}P\{^{1}H\}$ spectrum of that complex?'. Confront these gaps head on and reviewers can be swayed to respond to these omissions by cogent argument. This is particularly relevant to missing characterisation data, such as microanalysis data (maybe this is just my pet hate, but I always ask for it). The journal suggests 'accurate mass measurement of a molecular ion is acceptable as evidence for chemical composition provided that *independent evidence* for sample purity is given.' We have instructions easily available on the web; please use them.

Lastly, make every effort to ensure that the English is acceptable. The late Allan White, on receiving a draft of a paper I was working on, went out and bought me a copy of the *The chemist's English* written by a previous editor of the journal, Robert Schoenfeld. I think it has helped, but you should be the judge of that.

George Koutsantonis FRACI CChem Co-editor in Chief, *Australian Journal of Chemistry*

From snails' eggs to anticancer agents

Compound development and evaluation

Researchers at the **University of Wollongong** and the **Illawarra Health and Medical Research Institute** have discovered a new group of molecules showing promising results against multidrug-resistant cancers.

Natural products or direct derivatives from them have provided nearly half of all clinically useful cancer chemotherapeutics, and the search for new potent and selective agents continues. Multidrug resistance, whereby cancers develop resistance to chemotherapy drugs and are no longer responsive to treatment, is a major limitation to the current management of the disease. It affects patients with a variety of blood cancers and solid tumours, including breast, ovarian, pancreatic and lower gastrointestinal tract cancers. Any new active compound that has an effect on multidrug-resistant cells has major implications for improving survival in these patients and ultimately reducing relapse.

At the University of Wollongong and the Illawarra Health and Medical Research Institute, we have found that a group of molecules called *N*-alkylisatin derivatives killed 100% of drug-resistant cancer cells in the lab in just 48 hours. In comparison, a chemotherapy drug commonly used to treat breast cancer killed only 10% of cells in the same time period.

N-Alkylisatin derivatives, which have proved particularly potent against colorectal, prostate and breast cancers, work by targeting the skeleton of the cell, which is critical for a cell to continue dividing. These targets are called microtubules and our compounds interfere with the assembly and disassembly of these structures – essentially disassociating them so that the cell cannot undergo

White rock shell (*Dicathais orbita*) and egg masses. K.L. Perrow

any further division, at which point, it dies.

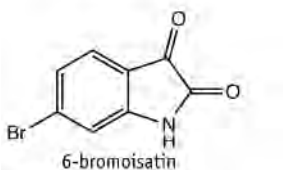
Our work in this area started from a somewhat unlikely source – the egg masses of the marine snail *Dicathais orbita*, also known as the white rock shell or cart-rut shell.

This snail is commonly found on rocky shores around Australia and New Zealand. Dr Kirsten Benkendorff had undertaken pioneering work at the University of Wollongong on chemical defences in these apparently very vulnerable egg masses, which help to protect them from, for example, predation and bacterial attack (Benkendorff K. et al. *J. Chem. Ed.* 2000, vol. 26, p. 1037).

One such compound identified in the egg masses was tyriverdin, which was shown to have potent antibacterial activity. With this in mind, and noting

... *N*-alkylisatin derivatives killed 100% of drug-resistant cancer cells in the lab in just 48 hours.

tyrindoleninone



6-bromoisatin

that some known antibiotics also display cell toxicity activity, Dr Kara Perrow (nee Vine) then looked at other biological activities of these compounds, particularly cytotoxicity against cancer cells growing in vitro, with Dr Benkendorff and Professor Marie Ranson in Wollongong. In addition to their moderate antibacterial activity, tyrindoleninone and 6-bromoisatin, two of the other natural egg mass compounds, were identified as having more promising activity against cancer cells. Tyrindoleninone was rather unstable, so 6-bromoisatin was used as a starting point for further synthetic studies to try and optimise activity. Thus, nature provided the critical lead.

Isatins are widely prevalent in nature and display a variety of biological activities. As such, these

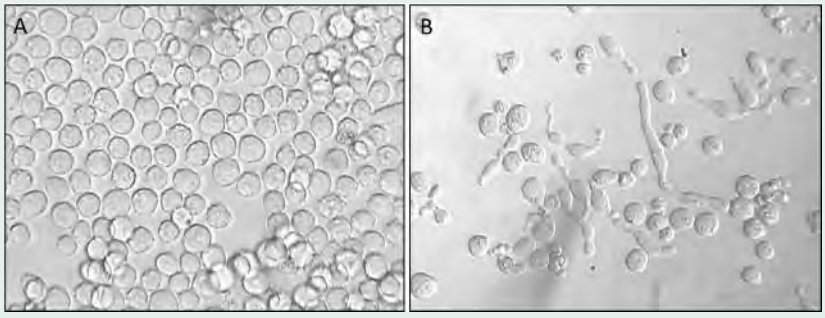
A classical medicinal chemistry approach

A classical medicinal chemistry approach was used in stepwise modifications of the starting 6-bromoisatin lead compound, focusing on substituents in the aromatic ring of the isatin core, and the variation of substituents on nitrogen in the five-membered ring, as well as limited modification of the ketonic group in this ring. Early on, it was found from studies by Dr Julie Locke that 5,7-dibromo substitution in the aromatic ring, rather than just 6-bromo substitution as in the natural product, increased cytotoxic potency. In addition, this disubstitution pattern was more readily accessible synthetically than mono 6-substitution (Vine K.L. et al. *Bioorg. Med. Chem.* 2007, vol. 15, pp. 931, 3951).

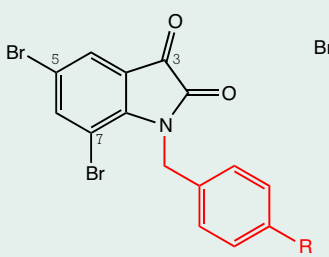
Further studies by Dr Lidia Matesic and co-workers involved the introduction of a variety of *N*-substituent groups, mainly arylalkyl groups, from which the potent compounds (1)–(4) emerged. In contrast, structural modifications to the carbonyl group in position 3 or the addition of an extra ring system between the nitrogen atom and position 7 were detrimental to the biological activity.

Compounds (1)–(4) boosted the cancer cell killing properties many-fold over the starting natural product lead, 6-bromoisatin. In vitro cytotoxicities (IC_{50} values – concentration required to inhibit the growth of 50% of the cell population) against breast, colorectal and prostate cancer cells ranged from about 1 to 8 µM. Much greater potency was observed against lymphoma and leukemic cells; compounds (1), (2) and (4) displayed sub-micromolar IC_{50} values against U937 lymphoma cells following a 24-hour exposure to the compound.

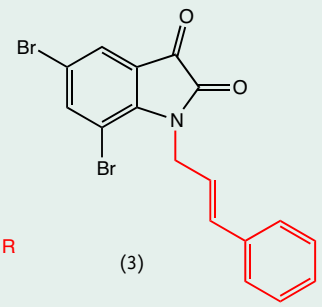
Encouragingly, another closely related *N*-arylalkyl dibrominated isatin that we made was also shown to be considerably more toxic to lymphoma and leukemic cancer cells than to normal human cells (freshly isolated human peripheral blood lymphocytes). We have shown that these compounds mediate their cytotoxicity through arresting cell division by interfering with microtubule assembly and disassembly and then inducing cell death. Essentially, the cells are disassociated with an elongated morphology and cannot undergo further division (Vine K.L. et al. *J. Med. Chem.* 2007, vol. 50, p. 5109; Matesic L. et al. *Bioorg. Med. Chem.* 2008, vol. 16, p. 3118).



Effects on the morphology of human lymphoma cancer cells (U937) on treatment with either a DMSO vehicle control (A; no adverse effect) or with *N*-substituted isatin (4) (B; cell elongation) for 24 hours (brightfield microscopy images; magnification 40×). K.L. Perrow



(1) R = CH_2OH
(2) R = Ph



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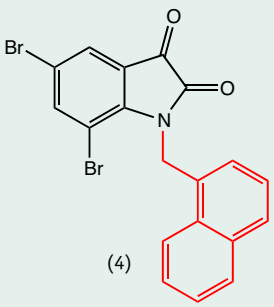


(4)

compounds and derivatives are often observed as 'hits' in drug screening operations. Thus, for their development, it is important to focus on enhancing target selectivity and increasing potency by making more selective synthetic derivatives.

By tweaking the chemical composition of the original egg formula, we eventually boosted its cancer-killing properties by about 400 times. We then took lab-grown cancer cells that were either sensitive or resistant to commercial chemotherapies and exposed them to different concentrations of *N*-arylalkylisatins for up to 48 hours. We screened these compounds against a panel of different cancer cells that we grow in the lab and found that they had activity against all of them (see box).

Even though many drugs used for the treatment of cancer and infectious diseases are derived from natural products – of either terrestrial or marine origin – we were still surprised at the results. Because our molecules have similar properties to some of the chemo-therapeutics that are currently used, we weren't expecting them to have such an effect on cancer cells that are normally resistant to these types of molecules.

One important multidrug resistance mechanism is mediated by P-glycoprotein efflux pumps in the cells. These cell-membrane-bound pumps can very effectively remove or pump out anticancer agents from within the cell, thus reducing their concentration to sublethal levels, resulting in the persistence of the cancer cells. We have now found that the isatins (1)–(4) retain their potency against multidrug-resistant human lymphoma cancer cells and uterine sarcoma cells as efficiently as against their corresponding (non-resistant) parent cancer cells (Vine K.L. et al. *Heliyon* 2016, vol. 2, e00060). This is an exciting result and the compounds could potentially be used as the basis for single or combination therapy for

Lead researcher Kara Perrow. Paul Jones, University of Wollongong Media

... the isatins (1)–(4) retain their potency against multidrug-resistant human lymphoma cancer cells and uterine sarcoma cells as efficiently as their corresponding (non-resistant) parent cancer cells.

treating multidrug-resistant cancers, or as alternatives to other known isatin-β-thiosemicarbazones that have selective killing ability against multidrug-resistant cancer cells (Hall M.D. et al. *J. Med. Chem.* 2011, vol. 54, p. 5878)

Dr Perrow is now working to optimise the drugs so that they are safe for use in humans. This involves packaging the *N*-alkylisatin derivatives into small lipid-based nanoparticles so they become non-toxic and safe for injection. In addition she is surface-functionalising these nanoparticles so that they can be transported safely and selectively to cancer cells. After injection, the isatin-derivative-loaded nanoparticles release their drug payload only once they are taken up into the cancer cells, thus minimising unwanted off-target effects.

In the future, these drugs could be used as therapy after the first round of chemotherapy fails, as a completely new therapy to replace the current standard of care, or in combination with a number of anticancer drugs to reduce the chance of multidrug resistance. This would be an exciting prospect for future cancer chemotherapy using homegrown compounds, initially sourced from snails' eggs.

We are sure nature has many more unexpected leads to discover and follow up – but we need to keep looking, particularly in unusual places, while keeping in mind Aristotle's observation from long ago: 'In all things of nature there is something of the marvellous'.

Kara Perrow (nee Vine) is a senior research fellow and group leader of the Targeted Cancer Therapeutics Laboratory, School of Biological Sciences, and the Illawarra Health and Medical Research Institute (IHMRI), University of Wollongong. **Lidia Matesic** MRACI CChem is a radiochemist at ANSTO Radioisotopes & Radiotracers, Sydney. **John Bremner** FRACI CChem is an emeritus professor at the School of Chemistry and IHMRI, University of Wollongong. **Danielle Skropeta** MRACI CChem is an associate professor at the School of Chemistry and IHMRI, University of Wollongong. Article prepared with Elise Pitt, University of Wollongong Media.

Scaevola spinescens

A short history of medicinal use and potential

The Australian native plant *Scaevola spinescens* has an interesting back story of bush medicine and chemical research.

BY **GEOFF TAYLOR**

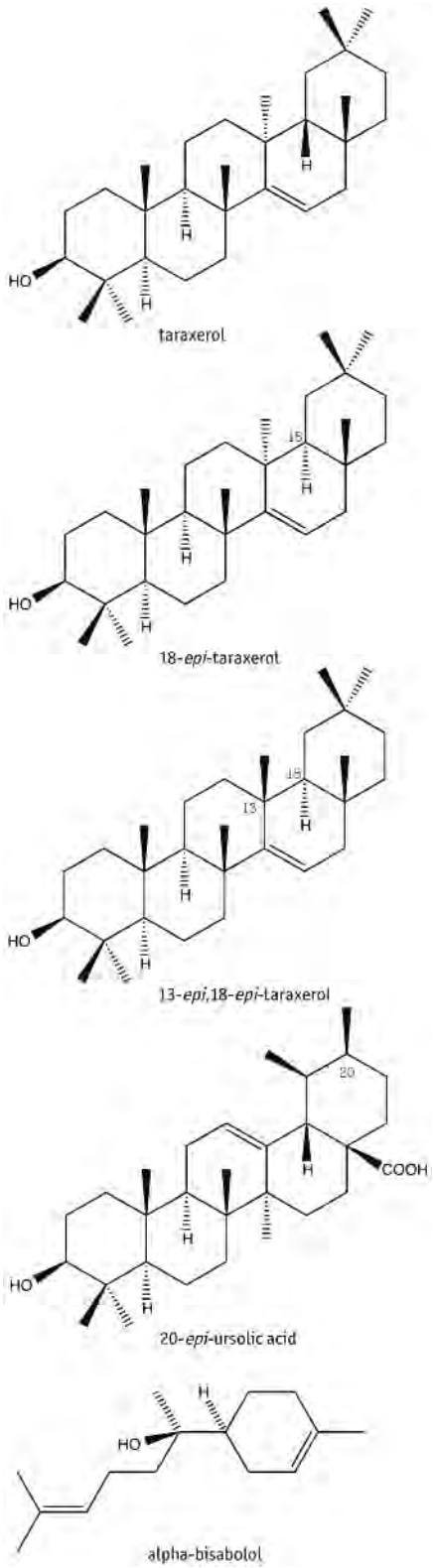
The native bush *Scaevola spinescens* excites a number of people who think it has medicinal potential and some who take an aqueous extract of the chipped stems and twigs regularly. *S. spinescens* has been used therapeutically by Aboriginal Australians, including the Yamatji people in Western Australia and Adnyamathanha people of South Australia. The plant has also been the subject of detailed scientific research in recent years.

The cause of *S. spinescens* was pushed hard by a senior policeman, Athol Monck, who in 1946 had heard of its successful use in 1937 on the diseased tongue of Albert Nibberong from the northern goldfields of Western Australia. Nibberong had apparently discharged himself from the local country hospital after misunderstanding the effect a tongue biopsy would have, and instead treated himself with the plant. There were local witnesses of Albert's healed tongue. Intrigued, Monck tried successively stronger extracts to establish a tolerable dose.

Last year, Dr Robert Pearce, a plastic surgeon involved in melanoma research, piqued my interest in this native bush after a consultation. That interest arose partly because I had worked as a chemist at the WA

Scaevola spinescens **(above and opposite), native to Australia and an Aboriginal bush medicine, is also known as *poontoo*, *murrin murrin, yudli* and spiky fanflower.**

Department of Agriculture and Food, Western Australia



Taraxerol epimers (taraxerol, 13-*epi*-taraxerol and 13-*epi*,18-*epi*-taraxerol), 20-*epi*-ursolic acid and alpha-bisabolol.

Government Chemical Laboratories (now the ChemCentre) until the 1980s and was aware of the extract being made. For 50 years until 2008, the ChemCentre produced an aqueous extract of the milled plant and supplied it to patients with a wide variety of cancers on production of a doctor's letter. There were about 870 patients, of whom about 100 outside WA were accepted for supply of the extract in 1990 (the extract had been discussed by TV personality Derryn Hinch). For some, it was a last chance after conventional treatments available at the time had not been effective. The extract seemed to reduce pain and improve mood. A number of patients had noted the calming and appetite stimulating effect of the extract.

There was a break in the supply of the extract from 1961 to 1969 after a WA Department of Health review. The review, involving seeking follow-up from treating doctors, was conducted to ascertain what, if any, positive results had emerged. The review took a negative view on the basis of the results for 60% of the patients. However, requests from cancer patients' relatives and then WA Opposition Leader John Tonkin, as well as a *Sunday Times* newspaper article, brought about the resumption of supply in 1969. The last patients were accepted in 1991.

Tests for the Department of Health in the 1950s prior to supply of the extract had shown no evidence of toxic components such as alkaloids and cyanogenetic glycosides, but nor had they shown any beneficial bioactivity. More recently, tests by Ian Cock and Lisa Kukkonen (2011) at Griffith University also showed a lack of toxicity. Commercial supply exists in Australia today, but *S. spinescens* is classified as a Schedule 4 drug in WA only and a doctor's prescription is required.

The production by the WA Government had a degree of altruism at a time when fewer cancer treatments were available than there are today. A number of testimonials were penned by cancer patients, some of whom made their own formulations from privately sourced *S. spinescens*. From these, the extract (or in some cases a concentrated paste) mainly seemed to be effective when in direct contact with an affected area. A few patients managed to obtain it for oral treatment of ulcerative colitis and were impressed. Three cancer patients taking the extract in 1991 were still taking it 17 years later.

So what excited some people about this plant that grows over much of our mainland? I found two relevant PhD theses, one by Philip Kerr (now of Charles Sturt University) at Curtin University in 1999, another by Sally Nobbs at the University of Adelaide in 2001, and an MSc thesis by Michele Mejin at the same university in 2009. The researchers used techniques such as liquid chromatography, IR spectroscopy, UV–vis spectroscopy, melting point, optical rotation, NMR spectroscopy and GC–MS, and inferences from biosynthetic pathways.

Between them, the researchers reported the discovery and characterisation of more than 50 compounds in *S. spinescens*. A number of these compounds were of possible pharmacological interest.

Kerr reported finding 38 compounds (four queried), not counting myricadiol esters, by using extraction techniques suggested by US National Cancer Institute work. The Institute had reported on cancer cell line tests of *S. spinescens* in 1990, initiated by Bob Longmore at Curtin University. The Institute found cytotoxicity across 60 cell lines, by using its extraction protocol, but its brief was to be more specific as to disease type, Kerr noted. Kerr and colleagues found that two compounds in *S. spinescens*, scaevolal and xanthyletin, gave good results in an antitumour test. Myricadiol and lupeol showed significant but lesser antitumour activity. Kerr also noted that the anti-5HT (serotonin) activity of *S. spinescens* might be due to nodakenetin and scaevolal, which could explain the calming effect.

Nobbs found 15 new compounds in *S. spinescens*, of which four – emmarin (different from ammarin found by Kerr), alidyjosioside, katecateroside and 13-*epi*,18-*epi*-taraxerol – were novel. Mejin found one novel compound, 18-*epi*-taraxerol, among the compounds she identified.

Nobbs and Mejin also ran tests for pharmacological activity, as did Cock and Kukkonen, A.R. Goss and colleagues at the University of Western Australia (1971) and Susan Semple and colleagues at the University of Adelaide (1998), reporting in published papers. This was contrary to disappointing results from earlier such bioactivity work in labs in Australia, the UK and the US.

The most recent work on bioactivity of *S. spinescens* has been done by Quan Vuong and colleagues at the University of Newcastle (2014), using cancer cell lines, and testing solvent fractions. The research overall has covered a range of extraction solvents, not just water.

Some individual compounds in *S. spinescens* are of known biochemical interest because they occur in a range of generally well-

Compound	Properties	Also occurs in
alpha-Bisabolol	Antitumour, antileishmaniasis, anti human glioma, anti primary leukaemia, used in skin creams	German camomile, Candeia tree, *Myoporum crassifolium* (may contain epimer)
beta-Sitosterol (glycoside is daucosterol)	Anti benign prostate hyperplasia, anti blood cholesterol, anti urinary frequency	Avocados, cashew fruit, saw palmetto, wheatgerm, soybeans, carrots, dark chocolate, pistachios, sesame seed, canola oil, cauliflower, bananas, apples, peaches
Betulinic acid	Antitumour, melanoma apoptosis (cell death) in vitro and in vivo	*Melaleuca cajuput*, London plane tree, Chinese jujube (red date)
Decursinol	Analgesic	*Angelica gigas* Nakai roots (donggui tea)
2-Deoxy-D-chiro-inositol	Insulin and polycystic ovary syndrome effects	Common buckwheat, as galactose derivatives
20-*epi*-Ursolic acid (*cis*-20-methyl)	Ursolic acid (*trans*-20-methyl) is anti-inflammatory, affects CXCL4/CXCR12 axis, *epi* (*cis*-20) has higher antibacterial activity, both isomers attack *Staphylococcus aureus*	Ursolic acid (*trans*-20-methyl) in, for example, prunes, apples, loquat leaves
Lupeol	Anti-pancreatic and prostate tumours, anti-angiogenic, anti-inflammatory	Lupins, strawberry, mango, figs, olive oil, grapes, saw palmetto, *Pimenta racemosa* var. ozua (bay)
Myricadiol	Anti-inflammatory	Southern bayberry (US) (*Myrica cerifera*) bark
Nodakenetin (marmesin)	Vitiligo therapy	*Peucedanum decurvum*, *Angelica glauca*
Scaevolal (7,10-epoxy-11-hydroxybis-abolol-3-en-15-al)	Crown gall tumour assay – positive	
Taraxerol	Anticancer	*Taraxacum mongolicum* (dandelion), *T. officinale*
Taraxerol acetate	COX 1 and COX 2 inhibitor	Southern bayberry (*Myrica cerifera*) bark, *Artemisia roxburghiana*
Xanthyletin (isomer seselin)	Antiplatelet action	Citrus

... the researchers reported the discovery and characterisation of more than 50 compounds in *S. spinescens*. A number of these compounds were of possible pharmacological interest.

studied medicinal and nutritional plants. These compounds include iridoids, coumarins, terpenoids, including phytosterols, and flavonoids (see table). Kerr noted the huge variety of bioactivity attributed to beta-sitosterol.

One compound in *S. spinescens* that dominates in terms of quantity is myricadiol; this is followed by lupeol. However, myricadiol seems to offer little potential in relation to cancer. Another compound, taraxerol, has recently been studied in relation to its molecular docking because it appears to affect the COX-2 inflammation pathway. What is interesting about *S. spinescens* is that it contains up to three taraxerol epimers – taraxerol, 18-*epi*-taraxerol and 13-*epi*,18-*epi*-taraxerol, each of which might have different docking characteristics. As you can see (p. 23), 18-*epi* has the 18-H below the plane of ring D (ring A is on the left); 13-*epi*,18-*epi*-taraxerol also has the 13-methyl above the plane of ring D.

Another compound is ursolic acid, which research suggests may reduce obesity, glucose intolerance and fatty liver disease by increasing skeletal muscle and brown fat, and is favoured by bodybuilders for changing fat–muscle balance. Ursolic acid can suppress cancer cell proliferation, and is also reported to reduce rheumatic pain. It suppresses the CXCR4/CXCL12 signalling axis, this pathway being a major contributor to the ability of cancer cells to metastasise. Mejin found that *S. spinescens* contains the 20-epimer of this acid, which might exhibit enhanced or reduced biochemical behaviour.

A third compound, alpha-bisabolol, has been shown to have apoptotic (cell death) activity against a leukaemia strain, and a patent exists for its use in treatment of mammary gland adenocarcinoma.

Of course, a synergistic effect of several of the *S. spinescens* compounds is possible, and 'carrier' compounds can overcome problems of biological uptake and bioavailability due to limited solubility, or unfavourable functional groups. But there is also a range of emerging pharmacological solutions to such problems. These include proniosomes (water-soluble carrier particles coated with surfactant), carbon nanotubes, and beta-cyclodextrin-encapsulated microspheres.

If the plant does have benefits, there is work to be done on which plant parts contain the chemical compounds of particular interest, on the extraction techniques, and on the seasonal, geographical and soil variations affecting the levels of those chemical compounds. I am encouraged by the work of Dr Youyou Tu, who received the 2015 Nobel Prize in Physiology or Medicine for her work on *Artemisia annua* as a malaria therapy.

In 2015–16, I tracked down the 23 archived files on the *S. spinescens* extract, and then compiled essential data in confidence working with Robert Pearce and Martin de Haas, a lawyer with an interest in the topic. This was to support a possible epidemiological study on recipients of *S. spinescens*. That research is currently being considered.

Patent law doesn't favour work on naturally occurring compounds, and this affects funding sources, but chemical derivatives and new approaches to pharmacological delivery can be patented. *S. spinescens* may still produce a winner for an Australian chemist working in the right multidisciplinary environment.

Acknowledgments

I acknowledge the provision of access to the *Scaevola* files by the CEO of the ChemCentre, Peter Millington, and the WA State Records Office; the assistance of Dr Russell-Weisz CEO and Neil Keen Chief Pharmacist of the Department of Health; the longstanding interest in *S. spinescens* of Dr Robert Pearce; and Jeanie Crago who has among other things compiled a book on *S. spinescens – Nature's helping hand*: Scaevola spinescens, *history and use in Western Australia: the maroon bush story*. Also, I acknowledge information from Dr Quan Vuong, Dr Chris Scarlett, Dr Philip Kerr, Dr Sally Nobbs, Dr Ian Cock, Michele Mejin, Dr David Harris (formerly of the ChemCentre), Dr Tim Threlfall (Department of Health) and Pene Whipple. I further acknowledge the Yamatji and Adnyamathanha people and other Indigenous groups, who have long known of this bush, and the support of Martin de Haas.

Geoff Taylor is an adjunct professor in the Department of Civil Engineering, Curtin University, and was a member of the former Chemicals Standing Committee of Worksafe Australia. Full reference details of studies are available from the author (wsha@iinet.net.au).

Science in the Third Age

KatarzynaBialasiewicz/iStockphoto

Martin Gellender discusses his approach to teaching science to mature-age students.

Most of us are aware of the challenges of motivating and inspiring students to study science in high school and in university. However, we rarely (if ever) hear about efforts to inspire and engage mature adults to become interested and involved in the sciences. But this is exactly what I set out to do after retiring in late 2012, when I accepted a redundancy from the Queensland Government.

Pondering the question of what to do with the rest of my life, I thought about how much I enjoyed the period of my life as an undergraduate and then a postgraduate student. I considered pursuing a Masters degree for my own interest and enjoyment; however, the fees to pursue another degree 'just for fun' seemed quite excessive. That's when I discovered the University of the Third Age (U3A), which allows those who wish to share their knowledge, expertise and interest (usually developed over decades of work experience and training) with others who are retired, semiretired or approaching retirement. U3A provides courses and other intellectually stimulating activities for older people who have a common goal of learning for pleasure. U3A has branches in many cities and regional areas of Australia, and I joined the Brisbane branch.

Having been trained as a physical chemist, which provided an excellent background to specialise in energy technology, I initially offered to teach a course in 'Energy technology' for the fourth term of 2012. The end of year is not the best time to offer a new course, but even so, I was struck by the response – not a single enrolment or enquiry! My proposed course had obviously not resonated with the cohort of U3A students. The problem, I concluded, was that my proposed course did not relate to the issues relevant to their lives.

U3A students, mostly baby boomers

like myself, have many years of life experience and lived through an extraordinary period of history. They are keen to understand developments that have steered the course of their lives, and that will impact on the future for themselves, their children and their grandchildren. An understanding of scientific principles provides an invaluable perspective to consider the major issues facing humanity, and this is what I decided to focus on in my course.

Accordingly, at the start of 2013, I offered to teach a course called 'Science and the big issues of our time'. The response was an immediate flood of enrolments and enquiries – enough to completely fill the small classroom initially allocated for the class. Since then, the class has grown to fill the larger classrooms that were progressively made available as U3A Brisbane expanded into new premises. Currently, about 45 students are enrolled, with about 30 attending each weekly class.

Teaching a course at U3A requires a completely different mindset and is a different experience from teaching a typical high school or undergraduate university class. There is no set curriculum for the course, so teachers can cover whatever topics appeal to their own interests and those of the class. Class discussion is guided to a significant degree by questions and comments posed by the students. Discussion can digress in entirely unforeseen directions. There is no pressure to cover prescribed material, or to prepare for exams or assessment. There are no exams and no grades. U3A gives no degrees, diplomas or certificates. There is no generational difference between students and teachers, and no stigma attached to not knowing 'the answer'. Students are not seeking career advancement, because they are all retired, semiretired or approaching retirement. The result, I find, is a liberating sense of intellectual freedom and fun – as close as I have seen to the ideal of what education should be all about.

Students in my course vary widely in background and education. Many have little background in science but, as a group, they bring to class more than 2500 years of life experience. They are interested in how our present world came to be, and where society is likely to go in the future. I apply chemistry and physics concepts to try to shed some light on these questions.

Teaching the course provides a great source of intellectual stimulation and enquiry on my part. I reflect on the huge scientific and technological developments and challenges during my lifetime and before. I explain these to the class in term of scientific concepts that I learned 45 years ago and what I have learned or figured out since. It challenges me to reconsider, and view in a new light, concepts that I simply accepted as a student.

Teaching a science course at U3A presents special challenges that generally don't arise in traditional chemistry/science classes.

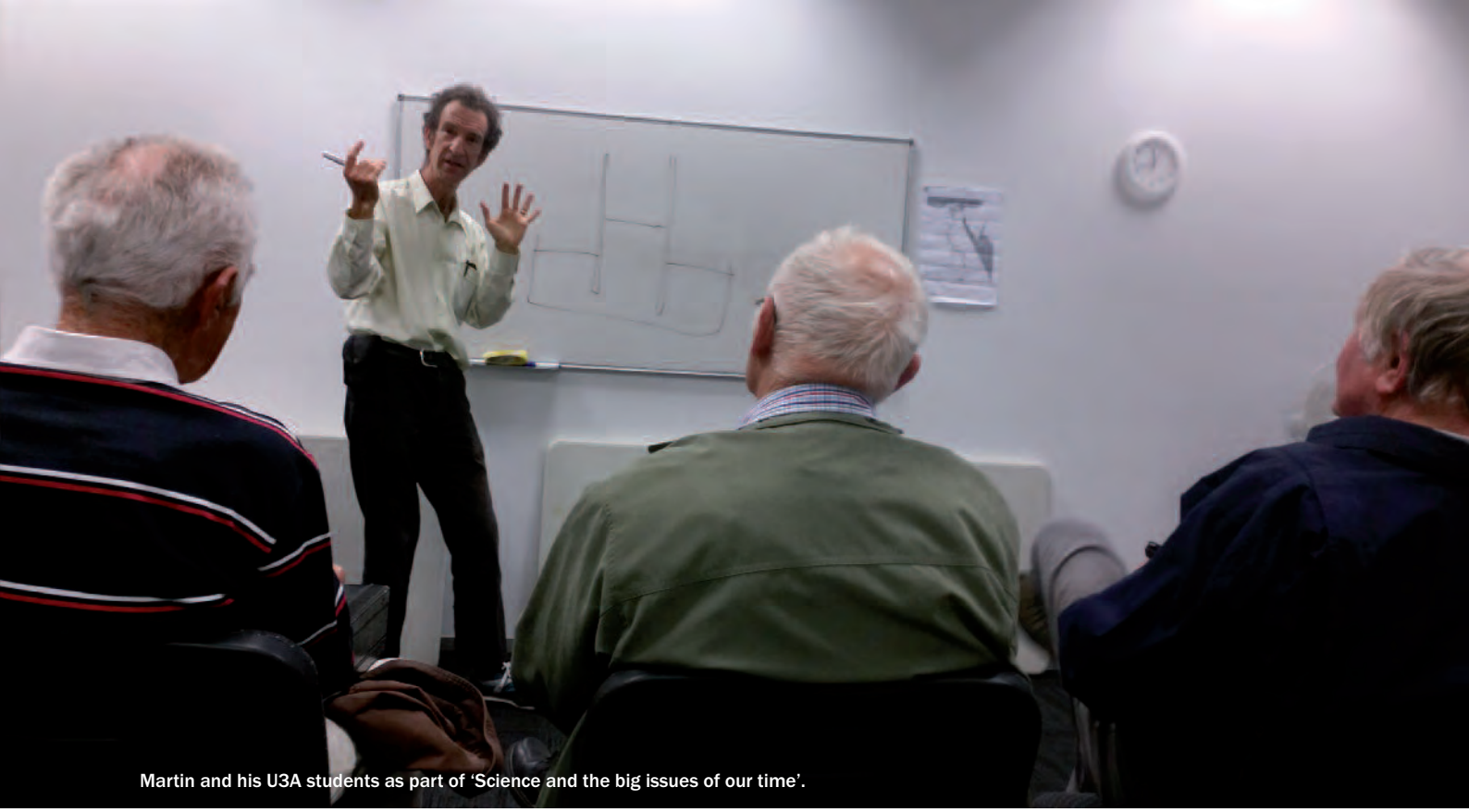
- The course has a strong focus on issues and applications, which largely determines which content and concepts are discussed and explained. This applications-based approach is the opposite of traditional chemistry curricula, in which each class builds step-by-step upon earlier foundations in a systematic way. Taking an issues-based approach requires each topic to be approached essentially on a stand-alone basis, starting 'from scratch'.
- Each topic is discussed without drawing heavily on material covered in previous terms. A few new students join the class each term, and a few leave, so prior knowledge cannot be assumed.
- Throughout a given year, many students undertake overseas travel, are engaged in family commitments or undergo medical procedures, and may miss class for several consecutive weeks.

The result ... is a liberating sense of intellectual freedom, and fun – as close as I have seen to the ideal of what education should be all about.

To allow for continuity and to reinforce the material discussed in class, I write detailed and well-illustrated notes for each class and circulate these to the students by email. After two years of the course, the notes comprised an extensive, quality resource which, I reasoned, would be valuable for students in the course and perhaps a much broader audience.

I edited the notes and self-published a book with the same title as the course, *Science and the big issues of our time*. The book is sold at cost to U3A members and (for those who are comfortable reading on a screen) I provide pdf files of the entire content to anyone who requests it. Printed copies of the book can be purchased (for $20) through Amazon (www.amazon.com/exec/obidos/ASIN/0646936808/wwwcampusboocom587-20) and some other online distributors. Like the course, the book's content is not limited to chemistry. It covers some astronomy (orbital motion, escape velocity, rocket fuels and rocket engines, and space satellites), metals, electrochemistry and batteries, fuel cells, electric vehicles, petroleum refining, plastics and thermodynamics (engines, refrigeration, weather and even agriculture).

I teach the course in a traditional style of 'chalk and talk' (using a whiteboard), with which my baby boomer generation is familiar and comfortable. Digital technology does have a role, but I use it selectively – only where it offers something that I



Martin and his U3A students as part of 'Science and the big issues of our time'.

cannot do in class. Classrooms are well equipped with internet-connected computers and projectors, and I sometimes show short videos that show a chemical reaction or other phenomena being discussed. For example, a two-minute video of a spherical blob of water drifting through the International Space Station (www.youtube.com/watch?v=s63JXdsL5LU) shows the effect of surface tension far more effectively than I could on Earth. I keep in mind that students can watch videos any time at home, but this doesn't provide the personal interaction that is a major motivator for people to come to U3A.

Small, simple props are very effective in promoting discussion and providing a tangible look or feel to abstract concepts. A golf ball dropped from above head height shows a kinetic energy of one joule. A 10-millilitre plastic syringe allows students to feel the increase in pressure when air is compressed. A digital kitchen scale shows the weight that can be applied to a strip of fettucine before it buckles and snaps, or the weight that a truss made from fettucine can support before it fractures. In such cases, a webcam is ideal to project a greatly expanded image onto a screen that can be viewed by the entire class. A fist-sized plastic globe of the Earth (borrowed from my grandchildren) provided a simple reference scale to visualise relative distances within our solar system and beyond. (On this scale, Neptune is 35 kilometres away!)

My course is not the only chemistry/science course offered by various branches of U3A. Another tutor at U3A has taught a one-semester chemistry course, and I attend a U3A geology course (which runs one year, and is then repeated). Each tutor is entirely free to teach their course as they see fit, and has their own individual style. The U3A branch in Geelong, Victoria, seems to be quite active in science, running courses in geology, astronomy, the environment and anthropology, and the Dubbo branch convenes a 'Science for seniors' and an 'Exploring science' course.

U3A operates as a voluntary organisation, staffed entirely by people who volunteer their time teaching, undertaking administrative office roles, providing IT support, or serving on a management committee. The Brisbane branch is very active, with over 3700 members and offering 260 courses. Other branches operate in other cities and regional areas of Australia, and overseas. Each branch operates autonomously, although national and regional U3A conferences are held. In the Brisbane branch (and I imagine other branches operate similarly), operating expenses, primarily for leasing of classroom and office space, is obtained by collecting a $40 annual membership and a charge of $5 per class attended.

My science course has run continuously for three and a half years, constantly extending into new topics and subject areas (and sometimes, pushing the boundaries of the subject areas in which I feel confident). I am compiling my notes from the second two-year period of the course to be printed as a second book (with the tentative title of *The science of stuff: why the air, oceans, materials, structures, the Earth and living things behave the way they do*).

Search U3A online for your state or capital city (useful links: www.worldu3a.org, www.u3aonline.org.au).

Dr Martin Gellender is a U3A lecturer and part-time consultant.

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RACI researcher runner-up in Falling Walls Lab

Dr Justin Chalker (centre) with judges Dr Alan Finkel (left) and Professor Brian Schmidt (right). Bradley Cummings

RACI member Dr Justin Chalker from Flinders University has achieved second place in the Falling Walls Lab, held in Australia for the first time in August and hosted by the Australian Academy of Science. First place was awarded to Dr Kim Van Netten from the University of Newcastle. In third place was Dr Stephanie-Anne Croft from the Auckland University of Technology.

The Falling Walls competition focuses on global challenges and how rising leaders and innovators will solve these problems. Twenty young Australian and five New Zealand contestants gathered at the Shine Dome in Canberra to give a three-minute presentation on their innovative research, a business model or an initiative based on the concept 'Which walls will fall next?'.

Dr Chalker's presentation described new polymers invented in his Flinders laboratory that capture mercury pollution. These polymers are made entirely from industrial waste. He described the problem of mercury pollution and how it is encountered in a variety of sectors, including the oil, gas and coal industries. He also explained how mercury is used intentionally in artisanal gold mining in developing nations. This practice exposes more than 15 million people to neurotoxic mercury. Dr Chalker's lab is committed to ending this environmental and public health crisis.

'Mercury pollution, especially in developing nations, threatens the health of many millions of people. We are working to provide inexpensive materials and solutions that capture this toxic metal and protect the environment and human health,' Dr Chalker said.

Competition winner Dr Van Netten presented on breaking the wall of tailing dam disasters. Tailing dams hold toxic waste and have the potential to cause serious environmental disasters; treating the water can be difficult, slow and expensive given their scale. Her team has been using a novel binder to cling to harmful elements, so that it creates particles large enough to filter from the water. Dr Van Netten will travel to Berlin in early November, where she will represent Australia and compete against academics from around the world.

Winners were chosen by a distinguished judging panel including Australia's Chief Scientist, Dr Alan Finkel; Nobel Laureate and ANU Vice Chancellor, Professor Brian Schmidt; and New Zealand's Deputy Chief Scientist, Professor Stephen Goldson.

The Falling Walls Lab Australia is organised by the Australian Academy of Science, in association with the Embassy of the Federal Republic of Germany in Australia and the Australian National University.

With Justin Chalker MRACI and Australian Academy of Science

Virtual Special Issue deadline extended

The Virtual Special Issue (VSI) *Highlights of Analytical Chemistry Research in Australia* is devoted to research presented at two conferences of the RACI: the 23rd RACI R&D Topics Conference (December 2015) and the Analytical and Environmental Chemistry Division National Symposium (July 2016). The deadline for the VSI has been extended to 1 December 2016.

Papers accepted in the Elsevier journals *Analytica Chimica Acta*, *Talanta* and *Journal of Chromatography A* containing research presented at the national symposium, can be included in the VSI.

To submit your article, log in to the Elsevier Author centre for the relevant journal and begin your manuscript submission. When asked to select the article type, choose **VSI: RACI National Symposium 2016**. This will align your article with the VSI. Complete the remainder of the submission as usual. The manuscript will then be subjected to the normal peer review process.

Papers accepted to the VSI will first be published in a normal issue of the respective journal (without delay), and then at a later date there will be VSI website that gives details of the conference and links to all the associated papers in the three journals.

For further information, please contact Professor Paul Francis, Chair RACI Analytical and Environmental Chemistry Division (paul.francis@deakin.edu.au).

Lectureship and student bursary recipients

Athel Beckwith Lectureship

Generously supported by the John Morris Group

The Athel Beckwith Lectureship recognises outstanding, recently appointed, organic chemists. The award provides the recipient the opportunity to travel around Australia to present the results of their research work. The recipient receives a travel grant of up to $3500, which is generously provided by the John Morris Group.

The recipient of the Athel Beckwith Lectureship for 2016 is Dr Thanh Vinh Nguyen (tvnguyengroup.wordpress.com/about). Dr Nguyen is recognised with this award for his development of new organocatalytic reaction methodology using aromatic cations and N-heterocyclic olefins.

Dr Nguyen did his PhD in organic chemistry with Professor Michael Sherburn at the Australian National University, Canberra, where he developed new synthetic methodologies for application in natural product synthesis and worked on the design and synthesis of synthetic host molecules for drug-delivery modelling. He then pursued postdoctoral studies with Professor Dieter Enders at the Institute of Organic Chemistry, RWTH Aachen, Germany, under the auspices of an Alexander von Humboldt Postdoctoral Fellowship, in the field of organocatalysis.

In June 2013, Dr Nguyen began his independent research career at Curtin University, and in June 2015, he moved to the School of Chemistry at the University of New South Wales as Lecturer and DECRA Fellow. His current research interests are focused on organocatalysis, aromatic cation activation, the synthesis of naturally occurring and bioactive compounds, and medicinal chemistry.

We congratulate Dr Nguyen on his award and wish him well in the future.

Dr John Tsanaktsidis FRACI CChem, Chair Organic Chemistry Division

Student bursaries for conference travel

Generously supported by CSIRO Manufacturing

The RACI Organic Chemistry Division supports current RACI student members, who have been a member for at least one year, with bursaries to assist with attendance at organic chemistry-related conferences within Australia.

The successful students for the current round are:

Wenyi Li

Thomas Peter Nicholls

Dylan Innes

Dr John Tsanaktsidis FRACI CChem, Chair Organic Chemistry Division

New Fellow

Research group leader for Solar Energy Systems in CSIRO Energy and principal research scientist for Next Generation Photovoltaics, **Gregory J. Wilson** is a solar energy specialist with over 15 years' research experience and a recognised authority for materials research into mesoscopic photovoltaic devices, most notably the dye-sensitised solar cell and perovskite thin-film photovoltaics.

In 2015, he was awarded the Office of Chief Executive Julius Career Award for CSIRO Energy and recognised for his leadership as the 2010 Queensland University of Technology (QUT) Faculty of Science and Technology, Outstanding Young Alumni of the Year.

In the 15 years since graduating in applied chemistry and forensic chemistry from QUT and further first class honours and PhD in physical chemistry, Wilson has been an RACI corporate member across three states (Queensland, Victoria and New South Wales).

His contributions to the chemistry field, in addition to his primary research areas, include the identification of ambiguous use of nomenclature for a (now common) room temperature ionic liquid (or RTIL). He petitioned the Standing Committee Chair of the IUPAC Interdivisional Committee on Nomenclature, Terminology and Symbols, requesting resolution of the ambiguous use of imide/amide in this class of compounds. His recommendations were referred to IUPAC journal editors and eventually published in *Chemistry International*.

In partnership with another CSIRO solar researcher, Wilson initiated a new communications medium for CSIRO through the establishment of the Solar@CSIRO blog (csirosolarblog.com), opening a more social, public interface for CSIRO Solar R&D. He has also been an invited delegate member at ATSE International Workshops and an RACI and a CSIRO delegate at Science Meets Parliament. He works as an ambassador for CSIRO Scientists in Schools and is a regular at National Science Week.

Wilson primarily engages as a connector and integrator in his role and as research group leader for Solar Energy Systems, where he leads the largest solar research effort within CSIRO, a research portfolio with an annual budget in excess of $11.9 million. The more than 39 R&D projects consist of over 60 group members and 34 full-time engineers and scientists, bringing together a multidisciplinary research group of mechanical and software engineers, optical and device physicists, material and physical chemists, chemical process and electrical engineers.

Gender equity in the RACI and beyond

Gender equity in science research has been making headlines over the past year, with high-profile cases of harassment at US universities as well as extensive reporting on the difficulties faced by women in being hired, publishing, obtaining grants and being promoted. The evidence indicates that these difficulties often result from the cumulative effects of unconscious bias, which is inherently difficult to identify and combat.

The RACI is not immune to accusations of gender inequality, which came to a head in 2014 when the incoming RACI Board (with eight members and the CEO) did not include a single female member. For the RACI, the gender statistics from 2014 are provided in the table and no major changes have occurred since then. While 23% of members are female, they are overrepresented in the junior categories of membership, as students, associate members and postgraduate members. This reflects the gender imbalance in academic chemistry departments in Australia where despite a near 50:50 mix of males and females in the student population, only 24% of all continuing academic staff are female, and the percentage drops to under 17% at professorial level.

In addition to having an all-male Board for a short period (two female members were elected to the Board in September 2015), other examples of gender inequality observed within the functions of the RACI are: the annual list of RACI prize winners typically includes only one or two women, while many of the prizes have never been awarded to a woman; and many conferences and symposia supported by the RACI have a very poor gender balance, particularly in the prestigious roles of plenary and keynote speakers.

Clearly, there is room for improvement.

Some Board members have made the argument that because the RACI is a volunteer organisation, it is up to women to volunteer more (for example, for Board membership). However, this is a simplistic view that ignores the sociological aspects of working in an unwelcoming atmosphere. In addition, for many roles a level of seniority is expected or required in order to volunteer, and the impediments to career advancement faced by women prevent many from achieving that seniority. In 2016, there are only 16 female professors of chemistry in Australia, and for some roles a professorship is expected. Thus, the wicked problem of female career progression in science research is reflected in the lack of women volunteering for significant roles within the RACI. Compounding this, most senior women are invited and expected to perform multiple volunteer roles and have limited time available.

The RACI was an industry partner on an ARC linkage grant from 2011 to 2014 on the topic of 'Women in the Science Research Workforce' led by Sharon Bell and Lyn Yates. That project investigated the complex causes of the differential participation of men and women in the science research workforce and led to the development of many resources available on the website www.womeninscienceresearch.org.au. However, these resources have not been widely promoted or used within the RACI.

At the December 2014 RACI Assembly Meeting, there was extensive discussion of gender equity within the RACI in response to the all-male Board membership at that time. This resulted in drafting of a diversity policy for the RACI that was endorsed by the Board in 2015. The brief policy is available at www.raci.org.au/document/item/2172. In mid-2016 the Board agreed to the formation of a new Gender Equity Subcommittee

Equity, equality, balance and bias

Gender equality is equal enjoyment by women and men of socially valued goods, opportunities, resources and rewards. Equity leads to equality. (www.unfpa.org/resources/frequently-asked-questions-about-gender-equality)

Gender equity is the process of being fair to women and men. To ensure fairness, strategies and measures must often be available to compensate for women's historical and social disadvantages that prevent women and men from otherwise operating on a level playing field.

Gender balance can be defined as an observed gender ratio for a particular function that matches the population gender ratio (for example, keynote speakers compared with attendees at a conference).

Unconscious bias is a mental attitude held at a subconscious level. It leads to stereotypes about certain groups of people that individuals form without conscious awareness.

Ten rules for conference speaker gender balance

1. Collect the data
2. Develop a speaker policy
3. Make the policy visible
4. Establish a balanced and informed program committee
5. Report the data
6. Build and use databases
7. Respond to resistance
8. Support women at meetings
9. Be family-friendly
10. Take the pledge

Source: journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1003903

Percentage of women by RACI membership category, 2014

	Student	Assoc	Postgraduate	MRACI	CChem	FRACI	HonS	Totals
Total current no.	194	140	252	465	2452	445	401	4349
% of total	4.5	3.2	5.8	10.7	56.4	10.2	9.2	100.0
% of female members	39.2	40.7	38.9	36.8	22.1	9.4	3.7	23.0

to be first chaired by Amanda Ellis. The new subcommittee is still being formed and its terms of reference were not finalised at the time of writing.

Outgoing RACI president Paul Bernhardt is supportive of efforts to improve the gender balance within the RACI. For example, he has expressed the goal of having a 50:50 mix of male and female plenary speakers at the 2017 Centenary Congress. The poor representation of women among prizewinners is also something he is concerned about, saying: 'There has to be a better way to encourage females to be nominated for these awards (both National awards and Divisional awards). The gender imbalance in these awards is truly appalling. Again it does require peer support to encourage females (and to a lesser extent males) to be nominated for awards and clearly there have not been nearly enough females nominated relative to their current representation in RACI.'

The movement within the RACI to act to improve the gender balance parallels the implementation in Australia of the Science in Australia Gender Equity (SAGE) pilot program (see February issue, p. 22). This program is based on the Athena Swan program, which has been in place in the UK since 2005. The programs assist organisations to improve their gender equity through an iterative, consultative process. Currently 40 Australian institutions have signed up to the SAGE pilot and initial committees have been formed.

Jenny Martin, head of Griffith University's Eskitis Institute, has published *Ten simple rules to achieve conference speaker gender balance* (see box). We suggest that this process should be adopted for all RACI-endorsed meetings and that any meeting that does not follow these rules should not be supported by the RACI. As a large professional organisation with significant influence, the RACI has the opportunity to be a role model and show leadership on this issue.

Further excellent information and resources have been published by VicHealth in a toolkit available at www.vichealth.vic.gov.au/media-and-resources/publications/equal-footing-toolkit. This toolkit is designed to help workplaces understand gender discrimination and inequality and what can be done to tackle the issue in a practical and sustainable way in order to achieve better diversity and fairness.

Madeleine Schultz MRACI CChem, **Kate Jolliffe** FRACI CChem and **Emily Hilder** FRACI CChem. Madeleine Schultz maintains an email list for Australian women in chemistry to share information about jobs, grants and relevant articles. If you would like to be added to the list, email madeleine.schultz@qut.edu.au.

... for many roles a level of seniority is expected or required in order to volunteer, and the impediments to career advancement faced by women prevent many from achieving that seniority.

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HOBART 03 6272 0661 rowetas@rowe.com.au
MELBOURNE 03 9701 7077 rowevic@rowe.com.au
PERTH 08 9302 1911 rowewa@rowe.com.au
SYDNEY 02 9603 1205 rowensw@rowe.com.au

RACI Mentoring Program Applications Open

The advantages and benefits of mentoring are abundantly clear, both for the mentee and the mentor. RACI (www.raci.org.au) runs a small mentoring program concept, with extremely successful results. Both the mentor and the mentees report an extremely positive experience, particularly in job-readiness and tangible outcomes (professional network and job interviews versus other graduates).

The RACI NSW Branch has up to ten spaces available in the 2017 Mentoring Program for young scientists keen to develop industrial/commercial careers. The program involves:

- regular guidance and support (every few weeks), typically via calls and occasional casual meetings
- support in developing professional networks, for example through facilitated networking (the mentor generally introducing the mentees to RACI contacts and helping include the young scientists in conversations at RACI events)
- career support and advice
- advice and support throughout the process of finding a first job.

Mentoring is a two-way process. To be of full value, the mentee has to be an active participant. As guidance, the ideal mentee will:

- be energetic and enthusiastic
- be an undergraduate student, preferably in your final year of the chemical sciences
- be more oriented to an industrial/commercial career rather than academia
- actively participate in the mentoring process
- participate in occasional networking events
- be eligible for membership of the RACI.

You don't need to be the top student in your class. You just need to want a good start into your career, and be willing to put in the effort to achieve that.

As this mentorship is intended to assist you through to your first career role, you must be an Australian citizen or permanent resident to apply. You also need to become a student member of the RACI.

To apply for the mentorship opportunity, please send your resumé and a covering letter introducing yourself and your goals to Pam Chantrell at the NSW Branch office, raci-nsw@raci.org.au.

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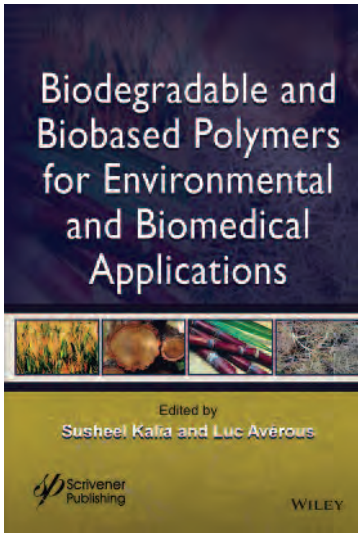


Biodegradable and biobased polymers for environmental and biomedical applications

Kalia K., Luc Avérous L., Wiley and Scrivener Publishing, hardcover, 2016, ISBN 9781119117339, 515 pp., $321.95

Biodegradable and biobased polymers for environmental and biomedical applications is a very ambitious title indeed. To some it may send shivers down the spine. Chesterton's characters in *The flying inn* sang a little ditty, 'I don't care where the water gets, if it doesn't get into the wine!' Analogously, biodegradability is just fine, if it doesn't get into the recycling paths, where it can potentially wreak havoc on materials we don't want to degrade. Equally, biobased is fine too, as long as making biobased polymers doesn't start chomping up too much of the material that could otherwise be food for people or animals.

Currently, most synthetic polymers are produced from oil. Essentially, the naphtha fraction from a refinery is cracked to, almost quantitatively, produce, ethylene, propylene and butadiene. From these simple molecules most polymers are synthesised. So, in essence, we tear up the big molecules in oil into tiny little bits and then put them all back together again to make big (polymer) molecules. Sounds a bit silly when you put it like that! And it all takes a lot of energy to do it, and creates pollution and waste along the way.

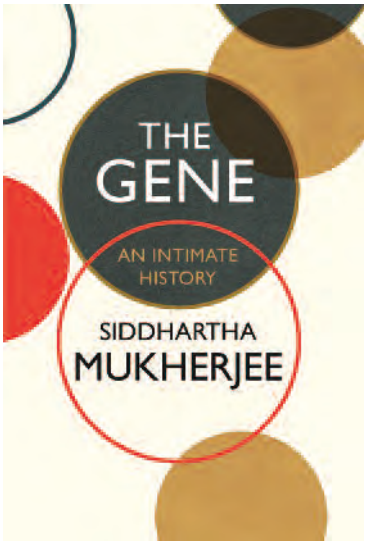
So, why stick to oil? Why not find some other way to make polymers? After all, isn't oil a shrinking resource? What will we do when the oil runs out? Well, we could do several things. We could make hydrocarbons from coal via a Fischer–Tropsch process, or we could raid agricultural sources for feedstock (possibly creating famine in some places) and carry on as before. Alternatively, we could look for clever new ways of making polymers, like, for example, enzymatic processes that may be energetically less demanding and environmentally less deleterious, as well as offering novel opportunities for uses, particularly in biomedical and environmental fields. This book provides a good review of these newer areas of polymer science. Each chapter is, in essence, a literature review and is extensively referenced.

Editors Susheel Kalia and Luc Avérous have assembled a capable team to provide a reasonably comprehensive tour of biodegradable and biobased polymers, particularly for environmental and biomedical applications. The chapter on polyhydroxyalkanoates is particularly interesting, ranging across agricultural applications, biodegradable packaging, drug delivery systems, implants and scaffolds for tissue engineering and regrowth. Another highlight is the discussion of modified drug delivery systems and the concept of a drug delivery matrix as a way of controlling drug release as well as a way of getting antitumour drugs to their target site. Cellulose is also widely discussed, both as microfibrils to reinforce commodity plastics in automotive and engineering applications, and as the potential to use nanocellulose as a sustainable absorbent for water pollutants, principally 'heavy' metals, organics, dyestuffs, oil and carbon dioxide. And, there is much more besides.

Overall, this is a well-balanced and very useful book. It should appeal to polymer scientists and researchers, particularly those interested in novel ways to make polymers, as well as 'green' chemists, those involved with medical and pharmaceutical sciences, and those with an interest in sustainability. The book is well worth perusing and a useful guide to future trends and applications of polymer science.

R.J. Casey FRACI CChem

The gene. An intimate history



Mukherjee S., Penguin Random House, paperback, 2016, ISBN 9781847922649, 595 pp., $35

Are you ready for a journey? A quest? An adventure? It's all here, and more.

I thought I was reasonably well informed about the gene. I have read, many times, about Mendel and his peas, Darwin and the increasingly appreciated Wallace, Crick and Watson and the ever-underappreciated Rosalind Franklin. I had what I thought was an adequate understanding of what genes are and how they work, how they go wrong and can sometimes be fixed. I am well acquainted with some of the controversy over genetically modified (GM) organisms from a stint in public relations and from work with several development agencies on GM crops.

And then I read Siddhartha Mukherjee's book *The gene*.

This is a beautifully crafted book and Mukherjee writes with eloquence and wit. By opening with a brief recount of his own family history, he reminds us how easily we all are and can be affected by the subtle and often unpredictable twists and turns of the chemistry within us. From the first page, I feel this book is about me.

Mukherjee then starts off on what at first appears to be a familiar path from pre-enlightenment ideas to Mendel to Darwin to Watson and Crick and beyond to the present day. What he does differently though, and what even highly knowledgeable

readers will appreciate, is fill in the detail. This is not 'tax accounting' detail but pointillist detail, 'in which small, distinct dots of colour are applied in patterns to form an image.'

That image is the rather breathtaking arc of a journey that began in a pea patch around about 1857 and in the space of 150 years has brought us to the edge of taking control of our own genome, our own destiny as a species. What once was science fiction has become researchable objectives.

The 'small, distinct dots of colour' are those many people who, like Sherpas, prepared the path for the headline breakthroughs and Nobel Prize nominations; people such as William Bateson, also known as Mendel's bulldog and who coined the term 'genetics'; Thomas Hunt Morgan, who showed that genes reside on specific chromosomes; Frederick Griffith, who showed that genes could be transferred; Alfred Sturtevant, who made the first genetic map of a chromosome; Barbara McClintock and Harriet Creighton, Jean Brachet, Salvador Luria, Erwin Chargaff, Raymond Gosling and so many more.

Aside from the sheer excitement of following the trail (What will happen next!) *The gene* illustrates how science is not great leaps from one discovery to the next, but a plodding, often stumbling path with false trails and dead ends and which depends as much on chance discoveries and the invention of new methods and techniques as it does on brilliant insights, not to mention legions of graduate students.

There are technical patches where the reader will need to put in some effort, but Mukherjee's style is a great help. One of the hallmarks of a good science writer is he or she respects the reader, doesn't dumb it down and doesn't spoonfeed the reader with simplistic Sunday supplement metaphors, but keeps zooming out to the big picture so we don't lose our way.

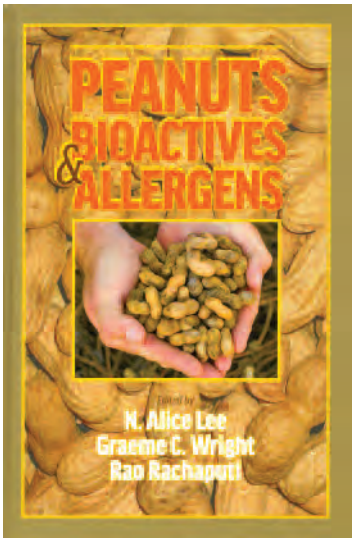
The gene reminds us that science has a dark side as well. We all know the horrors of the Holocaust, but do we know it was part of a bigger picture that was eugenics? I was vaguely aware of Francis Galton and the clumsy elitist Victorian attempts to 'improve society'. I confess, however, to being largely ignorant of the extent of the American eugenics movement, how it preceded the polices of National Socialism, resulted in the forced sterilisation of 64 000 individuals, and continued quietly and unchallenged up until the 1970s. In the final sections of *The gene*, Mukherjee grapples with our continued attempts to 'improve society'. The post-humanist utopia seems within our reach more so than ever, and our tools are so much more powerful.

In the end, Mukherjee brings us not to a conclusion, but to the edge of a new and yet to be explored continent. We have learned so much about the gene in such a short time, enough to know there is so much more to learn, least not about our own dreams and desires, but about our own humanity.

Terry Erle Clayton

Peanuts, bioactives and allergens

Lee N.A., Wright G.C., Rachaputi R. (Eds), DEStech Publications, hardcover, 2016, ISBN 9781605950365, 382 pp. $123.50



Peanuts are an important source of food, animal feed and oil world-wide, their value marred only by an allergic reaction to certain of their proteins, a reaction that is increasing in frequency for no clear reason. Some 1–3% of people are affected globally. In Australia, the estimate is around 0.2% of children. The allergy is not one that is outgrown. The condition is very distressing and potentially life-threatening.

Peanuts, bioactives and allergens is a splendid compilation of essays put together to present current understanding and research on aspects of the composition and allergenic proteins of peanuts. It covers a broad range of subjects in commendable detail, beginning with the fatty acids of peanut oil glycerides and finishing with possibilities for oral immunotherapy for allergy sufferers. The authors come from various organisations and departments, Australia being well represented.

There are 13 chapters, each written by at least two authors. Some authors appear more than once, a number are also the editors. Each chapter stands alone but follows a logical progression. The chapters are well-referenced; Chapter 2, for example, has 222 references. Good use is made of summary tables. Some of the aspects discussed are subject to very active research, so the reader may have to top up the knowledge presented, but for any scientist or student wishing to gain an appreciation of the state of play in the subject fields, this will be an invaluable point of reference. A minor criticism might be made: with more rigorous editing, particularly of syntax in Chapters 1 and 2, the book would have been easier to read.

The fatty acids, phytoalexins (substances produced in response to stress) and antioxidants present in peanuts are explored in detail along with their current and potential health effects. Analytical issues with these groups make interesting reading; for example, the 'result' for antioxidant concentration depends on the selected method(s) for extraction and hydrolysis as well as on all the details of the test parameters. A timely comment reminds us that correlation is not causation: 'Studies correlated total dietary fat with breast cancer, but more extensive studies showed that the association was in fact with *trans* monounsaturated fats'.

Chapter 6 considers general approaches to breeding for enhanced functional food traits, with special reference to peanuts. Breeding has already produced cultivars that have high oleic content in the fatty acids, but there are many other compounds of potential interest present, including hypo-

allergenic proteins. Possibilities of breeding versus bioengineering to achieve hypoallergenicity are examined in Chapter 12.

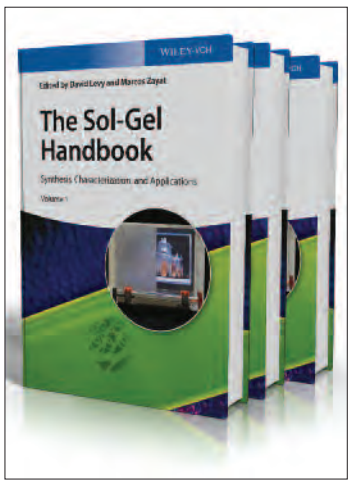
Chapter 7 assesses the allergenic proteins in great detail; 17 have been identified to date, of which four seem chiefly responsible. They display unique characteristics such as thermal stability and resistance to proteolytic hydrolysis. It is likely the Maillard reactions that add to flavour add also to allergenicity!

The next chapter discusses very clearly the regulatory approaches to disclosure of allergens and to ascribing limits, as well as the potential for risk analysis to inject some science into arbitrary decisions. Even the compulsory declaration of the presence of known allergens has the problem of over-stating the risk and hence dismissal by the consumer. The complexities of assessing and combining the probabilities of consumer uptake from eating habits with the no-effect level (which can vary up to five orders of magnitude among individuals) are severe.

Later chapters cover industry approaches to containing cross-contamination of foods by allergens and the rather daunting challenges of immunological assays. Next are the possibilities of utilising linked mass spectrometry for highly specific characterisation and measurement of individual proteins. To date, the rewards here have been more in the area of defining reference substances than providing a tool for routine assays.

Finally, work to desensitise allergy sufferers is explored. At the time of last citation (2011), oral treatment had been demonstrated to succeed, though not without treatment difficulties, and many aspects such as tolerance and longer-term side-effects remain to be investigated.

Bruce Graham FRACI CChem



The sol-gel handbook. Synthesis, characterization and applications

Levy D., Zayat M. (Eds), Wiley-VCH, hardcover, 2015, ISBN 9783527334865, 1616 pp., $872.95

The sol-gel handbook consists of three sizable volumes: the first is dedicated to sol-gel chemistry and materials; the second focuses on characterisation of sol-gel materials and their properties; while the final volume explores applications of sol-gel materials.

This is a very detailed and specific reference source. It certainly deserves the label of handbook, since all areas of sol-gels are covered in enough detail to truly satisfy the reader, and if more information is required, then there are ample references cited to investigate further.

Editors David Levy and Marco Zayat (who have experience in sol-gel optical applications) have drawn together an impressive author list of 116 contributors, with many leading experts on sol-gels; though with the high number of authors contributing, the quality across chapters is not consistent throughout. Apart from the difference in language style, it is obvious some authors have put a lot of effort into their chapter, while others have to a lesser extent. This makes for a difficult review, because there were outstanding sections on sol-gel chemistry and biomimetic sol-gel materials in Volume 1, optical properties in Volume 2 as well as environmentally green products and energy storage in Volume 3. Yet on the flip side, a number of chapters missed their mark, or covered content already present in prior chapters.

Volume 3 on sol-gel applications was the highlight for me because the authors clearly set out a range of systems where sol-gel materials are currently being used or have potential application. This information was detailed and specific, not the generalisation so commonly given in many chemical discussions. I was surprised at the importance of sol-gels in energy storage systems, most importantly solid oxide fuel cells, and the challenges in formulation and processing required to maximise their functionality. Equally, the presence of sol-gel materials in optical and luminescent devices was very … illuminating!

In contrast, the discussion about characterisation techniques in the second volume was not as strong. This comes about because many of the techniques mentioned are already used in other material systems. Consequently, providing information on them, I believe, is not warranted as the book's most likely reader will most certainly have a strong grasp of chemistry. This practice seems common to many reference books – the need to discuss and elaborate many techniques in common use in other aspects of chemistry and science in general. I believe it would be more productive to focus such chapters on how fundamental chemistry techniques can be tailored for the sol-gel materials under discussion and highlight where the differences lie.

It is clear from much of the material presented in *The sol-gel handbook* that sol-gel research will be an active area for many years to come and new applications will arise as more novel sol-gel materials are developed. Hence, this three-volume handbook is a worthy reference source for any chemist working in this field.

Colin Scholes FRACI CChem

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Montreal and Kyoto – a personal view of two protocols

The Montreal and Kyoto Protocols concern limiting and phasing out certain gases that affect the global climate. To be effective, the protocols require all countries to be involved.

Both the Montreal and the Kyoto Protocols have had and continue to have a profound impact on the chemical industry. The Montreal Protocol (agreed in 1987) places limits on ozone-depleting gases (particularly chlorofluoro compounds (CFCs)) and is seen largely as successful and to be emulated in the control of other gases of concern. The Kyoto Protocol (agreed in 1997) seeks to limit the emission of greenhouse gases (particularly carbon dioxide) and has struggled to achieve its objectives. The poor outcome of the Kyoto Protocol is often compared with the relative success of the Montreal Protocol. But the two are quite different.

The origins of the Montreal Protocol lie in the discovery of holes in the protective ozone layer in the upper atmosphere above the polar regions. The invention of the electron capture detector for gas chromatographs, which could detect chlorine in extremely low concentrations, suggested that ozone was being destroyed by chlorine atoms released from CFCs in the upper atmosphere.

By the 1970s, CFCs had largely displaced other refrigerant gases (such as propane and ammonia), especially for smaller devices such as domestic fridges and air conditioners, including vehicle air conditioners. Other uses included fire extinguishers, such as BCF. With some health and firefighting exceptions, the Montreal Protocol set out to stop the production and use of CFCs and control the collection and disposal of the remaining stock.

During the 1980s, there was rising concern that emissions of carbon dioxide, a known greenhouse gas (GHG), were having an adverse effect on global temperature by increasing the greenhouse effect. The Kyoto Protocol was an attempt to mitigate this effect by limiting emissions of GHGs to the atmosphere.

Both protocols seek to control the emission of gases seen as pollutants on a worldwide basis. The key differences are set out in the table. The first major difference is who the protocols affect. The Montreal Protocol probably affected only about ten producers, who were all very large industrial conglomerates. Closure of CFC production did not have a major impact on company revenues and each company was in a position to research and develop substitutes. The producers agreed and the Montreal Protocol was easy to implement and did not lead to leakage by technology transfer.

By contrast, GHG emissions affect virtually every manufacturing company and household. In recognition of this, the main curbs were aimed at developed economies with developing countries not required to limit GHG emission. This led to the mass transfer of GHG-intensive industries from developed economies (including Australia) to developing countries. This is widely known for China and India, but in 1997 both Qatar and Singapore were in the developing country camp and consequently benefitted. Now both have significantly higher GHG emissions per capita than Australia and significantly higher incomes per capita.

As well as transfer to other countries, the Kyoto Protocol encouraged green-washing by individual companies by which greenhouse-intensive operations were sold or transferred to others, hence improving the GHG credentials of an individual market brand relative to its peers. The Montreal Protocol demanded and obtained CFC plant closure.

Another issue is verification. Although many different chemicals are covered by the Montreal Protocol, verification is relatively straightforward because there are still comparatively few producers with product being used in small specialist industries. For the Kyoto Protocol, although there are relatively fewer chemicals, the widespread emission of GHGs makes verification difficult. This is exacerbated by the opposition of some major country emitters to independent verification.

CFC substitutes or lesser ozone-depleting materials were quickly developed and used without having to resort to dangerous materials such as propane or ammonia for domestic appliances. By contrast, because of widespread opposition to nuclear power, it is debatable if any of the GHG-reducing substitutes actually result in lower GHG emissions. For instance,

Comparison of Montreal and Kyoto Protocols

	Montreal Protocol 1987	Kyoto Protocol 1997
Problem	Ozone depletion	Global warming
Limits to	CFCs	GHGs
Affecting	Major conglomerates	All industry and households
Number being affected	Probably <10	Millions
Countries affected	Major industrials (G8)	Primarily OECD countries
Outcomes	CFC production stopped	GHG emissions transferred to developing countries
Leakage	None	Widespread
Verification	Straightforward	Difficult if not impossible
Overall	Effective reduction of CFCs	Ineffective
Overall outcome	Some closure of ozone holes; scheduled closure 2050–70	No observable effect
Sceptics and alternative theories	Largely ignored and relegated to areas of historical interest	Denounced as heretical

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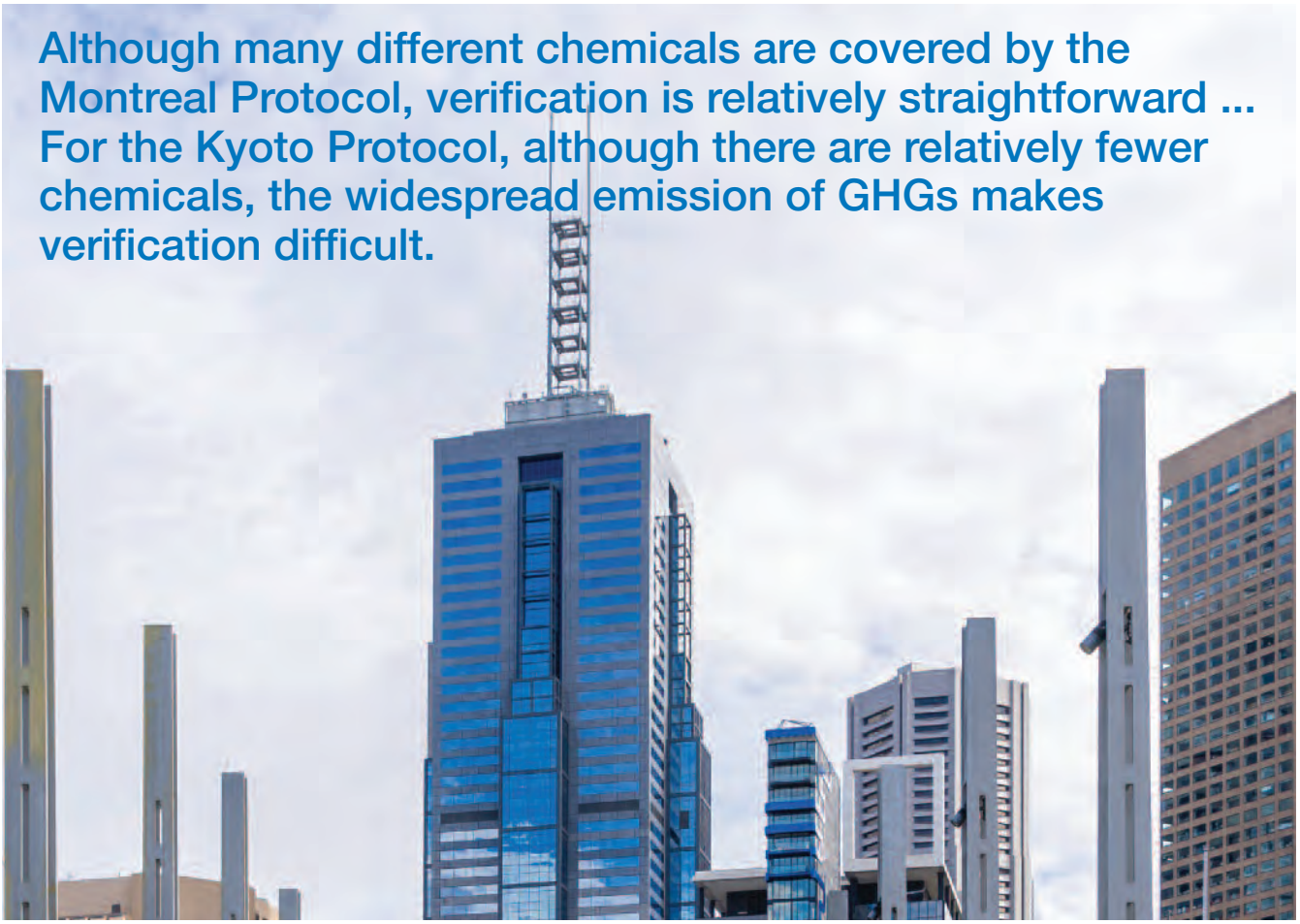


Although many different chemicals are covered by the Montreal Protocol, verification is relatively straightforward ... For the Kyoto Protocol, although there are relatively fewer chemicals, the widespread emission of GHGs makes verification difficult.

photovoltaic (PV) cells are produced by using cheap coal-fired power, particularly in China, and consequently many PV generators (such as domestic roof-top solar) result in more GHG emissions than they save. Furthermore, many of the GHG emission savings (such as the US power sector) have occurred from forces other than the Kyoto Protocol (in the US power case, the availability of cheap gas displacing coal generators).

We should note that despite meeting its technical objectives, the Montreal Protocol has been slower than expected in closing the ozone holes. This is being tackled by further elimination of ozone-depleting chemicals, including some of the earlier CFC substitutes.

At this time, although there is little questioning of the background theory that ozone depletion was the consequence of CFCs, this was not always the case. There were several issues, one of which was the fact that the largest ozone hole is over the Antarctic whereas most CFC emission was in the northern hemisphere. One theory to explain this was that the hole has always been there and was due to sodium chloride catalysing ozone depletion, the salt having been transported to the higher latitudes by the great southern vortex. Proponents of this theory were largely ignored and the CFC theory adapted to explain the phenomenon. Should the hole not close by 2070 (say), this possibility may be revisited.

Contrast this with the Kyoto Protocol. No alternative theory to global warming by GHGs is tolerated. Alternative theories and their proponents are denounced and it is even suggested they receive psychological treatment. This also affects the scientific elite. I have heard one luminary on a UK radio program state that all scientific theories are subject to question and inquiry and a week later on another radio program in Australia state that global warming by GHG was an indisputable fact.

The conclusion is that the Montreal Protocol was relatively easy to agree with and implement and its continued success is assured at this time. By contrast, Kyoto is extremely complex and difficult to enforce. Its failure has led to a reappraisal (the Paris Accords), which is much weaker in its demand for action. Verifying emissions appears impossible, with several countries opposing independent inspection. We have to look forward to continued major conferences (in exotic locations) aimed at trying to improve the situation, but from this observer's point of view these seem to be rather self-serving by GHG regulators rather than trying to find tangible solutions.

Duncan Seddon FRACI CChem is a consultant to coal, oil, gas and chemicals industries specialising in adding value to natural resources.

Synthetic wine, perhaps?

Esperanza33/iStockphoto

Recently Sally, our editor, alerted me to an article in *New Scientist* entitled 'Synthetic wine made without grapes claims to mimic fine vintages' (bit.ly/1rSahQY). This immediately stimulated my interest because of the contradiction in the title. The words 'wine' and 'without grapes' are not acceptable in Australia because our wine regulations define wine as 'the product of the complete or partial fermentation of fresh grapes, or a mixture of that product and products derived solely from grapes' (bit.ly/2bN5fBO). This grape/wine regulation also applies in the EU, but not in the US.

The proponents of the concept of synthetic wine, Mardonn Chua and Alec Lee, promote the idea of 'designer wines' and have even established a web address for the 'winery' (www.avawinery.com). Wines are 'engineered' in a laboratory after extensive chemical profiling by GC-MS.

Chua and Lee are now promoting the release of their simulated 'Dom Pérignon'. Presumably the chemical mix will be dosed with carbon dioxide to give the required bubbles for the sparkling character. Carbonation, as it is called in Australia, is a fairly common practice at the lower price end of the market. No special labelling is required here although the EU requires 'aerated sparkling wine' to be used. Bubble behaviour is critical to the appearance and aroma profiling of a sparkling wine and carbonated wines tend to have larger bubbles with fast rise compared to those produced by secondary fermentation.

Gérard Liger-Belair and colleagues have examined the chemical composition of Champagne aerosols and found that a large number of surface-active compounds are preferentially partitioned in the aerosols (*PNAS*, 2009, vol. 106, pp. 16 545–9). Whether this chemical distribution can be achieved by carbonation remains to be seen.

While it is true, as Chua and Lee suggest, that all wines share the same basic set of compounds, it is difficult to see how a mixture of chemicals can replicate the delicate nuances that result from the fermentation of grapes. For example, my experience with alcoholic spirit used in making fortified wines has shown me that there is a distinct varietal character associated with the spirit. Accessing commercially available spirit that is sufficiently neutral would be a challenge.

As one might expect, there are critics of the synthetic wine concept. In the *New Scientist* article, Professor Alain Deloire, Director of the National Wine and Grape Industry Centre in Wagga Wagga, expressed his reservations about the concept. Alain's comment would appear to be based on what can be called the terroir effect on grape composition and the reflection of this terroir in the finished wine that generates characters that many consumers seek.

I am convinced of the existence of molecular aggregates in both red and white wine. These aggregates or assemblies influence the colour and taste response of wine. Mixing of chemicals may well simulate aspects of aroma, but I am yet to be convinced that the chemical mix will replicate the aggregates.

The *New Scientist* article reports one comparative tasting of a synthetic Moscato d'Asti and a Ruffino 2014 (presumably the Ruffino Prosecco). The comments on the synthetic wine were not particularly positive with expressions such as 'smells like cleaning alcohol or plastic' and 'a smell like inflatable sharks used in swimming pools'. Comments regarding taste were more positive with 'fruity pear/peach' characters. I do not, however, understand why the comparison was made with a wine other than an actual Moscato d'Asti. First, the grape varieties used for Prosecco and Moscato d'Asti are different. Second, there is no secondary fermentation in the production of Moscato d'Asti; rather, the fermenting grape juice is transferred to a pressure tank towards the end of fermentation, whereby the bubbles are trapped, before pressure filtering and bottling. Clearly, the impact of the secondary fermentation on aroma and palate structure are not present in Moscato d'Asti.

If synthetic wine is not your thing, then you might consider 'chemical-free wine' (www.chemicalfreewine.com.au). I am not exactly sure what is meant by 'chemical free' in this instance, but I expect it relates to the absence of additions in the wine production process. An image on the home page of the website supposedly compares the 'natural' and 'non-natural' additive content of various production styles. Purists in the natural wine movement will not add tartaric acid for acidity/pH adjustment, even, it seems, if the acid is extracted from grape residues. Fermentation is carried out by the microflora on the skin of the grape; that is, there is no inoculation with *Saccharomyces* yeast. Sulfur dioxide is not used nor are other anti-oxidant/antimicrobial reagents.

I have tried several natural wines. Some were acceptable to my palate. But not all. Some showed unfortunate aromas resulting from bacterial activity, and one red wine, with its brown colour and plenty of solid material, reminded me of Melbourne's Yarra River after heavy rain.

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.

Whose nose knows?

When I was an undergraduate at the University of Melbourne in the late 1950s, and for some years afterwards, there was a strong 'chemical' smell in the foyer of the Chemistry building. Nobody seemed to worry about it – chemistry departments just smelled like that. Years later, when I was at Monash, the staff working in the chemistry store complained about the smell, on the grounds of amenity, of course, but also on health grounds. Were they being slowly poisoned as they went about our business?

Roger Brown and I were instructed to find out what the problem was and then do something about it. We toured the shelves where chemicals were stored, first identifying some smelly spots and then examining the individual bottles to find the sources. What we found was that the contents of a number of bottles had caused the corks (yes, the bottle were that old) to rot away and so release the vapours that were leaking into the airspace. Even plastic stoppers and screw tops in some cases had been degraded and cracked. Amines of various kinds seemed to be the most aggressive substances and most of them had strong and not altogether pleasant odours. Rebottling and resealing the containers fixed the problem and gave the staff some respite. It took a while for the air to clear, but the smell never went away entirely, so Roger and I had to go back for another nose-patrol. A second round of rebottling brought the problem to an end.

Chemists, at least organikers like me and Roger, are supposed to have good senses of smell, and I have heard of chemists being employed to sniff the fractions as they come out of the gas chromatograph with a view to identifying them or at least judging if they could be useful perfumery constituents. Animals are better at it, and I have from time to time encountered dogs at airports that had been trained to sniff out illegal substances. Military and police organisations use dogs for the detection of explosives and are employed by disaster relief personnel to help find people buried by landslides, avalanches and building collapses, especially those caused by earthquakes as we saw recently in the news from Italy. Sniffing out buried bodies is another task that authorities assign to dogs.

Last year I was at a reception where the man sitting next to me had a dog garbed in a coat with a logo I did not recognise but clearly one that suggested it was a working dog. The man seemed to have excellent eyesight, so I concluded this was not a seeing-eye dog, but it was clear the dog was not just a pet. In response to my inquiry, I was told it was a diabetes dog that was trained to detect, from the man's breath, when his blood glucose level was dangerously low. 'He sleeps with me', the diabetic owner said, 'and he will wake me if he detects a dangerous change in my condition'. Some dog! Once awakened, the owner can check his blood sugar level and take appropriate action to get back into the safe zone. A can of soft drink

Georgia Summers

The substance that diabetes dogs are detecting is most likely acetone ...

usually suffices to bring the glucose concentration up to a satisfactory 4 mmol/L (about 70 mg/dL). Clinical chemists seem to like the decilitre, perhaps because the numbers are convenient to work with. When I looked in my personal pathology file I found that although most of the volume units were litres, there some exceptions: haemoglobin (normal range 11.5–16.5 g/dL) and cholesterol (200 mg/dL seems to be a dividing line).

The substance that diabetes dogs are detecting is most likely acetone that is formed from acetoacetic acid and β-hydroxybutyrate, in turn formed by degradation of fatty acids and deamination of amino acids. These processes come into play when there is insufficient glucose available for energy generation in the body, and characterise a condition known as ketoacidosis.

In the comics and teenage literature that I read as a boy, school classes in chemistry were always described as 'stinks'. The implication is that chemistry is associated with bad smells, and that could relate to the production of hydrogen sulfide in simple school experiments. The Royal Society of Chemistry encourages schools to use odours in a module – its title is a play on words, 'Chemistry stinks' – that includes natural products like carvone, vanillin and limonene. So good stinks are OK, especially in the food industry. At the Nestlé headquarters in Vevey, Switzerland, there are 'smelling sticks' to give us the aroma of chocolate, coffee, cinnamon and other inducements to consume.

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

Women in Chemistry AGM
16 November 2016
www.raci.org.au/events/event/women-in-chemistry-agm

36th Australian Polymer Symposium
20–23 November 2016, Lorne, Vic.
www.36aps.org.au

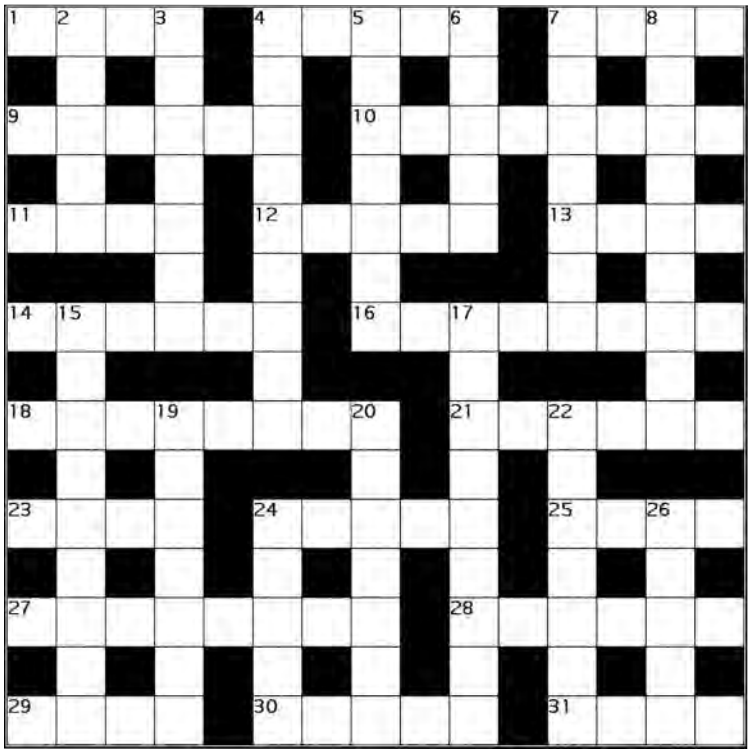
Hazards Australasia
23–24 November 2016
Melbourne Cricket Ground, Melbourne, Vic.
www.icheme.org/hazardsaus2016

Chemical Engineering for Non-Chemical Engineers
30 November – 2 December 2016, Brisbane, Qld
www.icheme.org/shop/events/courses/2016/aus%20and%20nz%202016/chemical%20engineering%20for%20non-chemical%20engineers.aspx

R&D Topics 2016, NSW
5–7 December 2016, Parramatta, Sydney
www.raci.org.au/events/event/r-d-topics-2016

RACI events are shown in blue.

cryptic chemistry



Across

1 Perhaps crow regarding first boost in research dividend. (4)
4 Shakes ore. (5)
7 Groups of firms. (4)
9 Negative! They are 2 Down. (6)
10 Parallel chemical compound of different composition but similar in structure. (8)
11 RCO– in carefully calibrated regression. (4)
12 Xenon is central to Inner Mongolian urban ecology citizenship. (5)
13 Swipe over instrument. (4)
14 Occur with time to take phosphorus and a small molecule eliciting an immune response. (6)
16 Mentioned free new radical Shiraz, perhaps. (8)
18 Rose keen over fuel. (8)
21 Stunner! Uranium mislaid – destroying Nobel Prize winner. (6)
23 Bring back informer's celebrity. (4)
24 Cover protactinium/tin alloy. (5)
25 Peak monkey unknown. (4)
27 Emotional susceptibility makes for a weak position. (4,4)
28 No file gets to be unsaturated. (6)
29 Take care of lean. (4)
30 Trips badgers. (5)
31 7 Across with time over to take sulfur exam. (4)

Down

2 Four elements with a charge. (5)
3 Fall grant is such a small amount. (7)
4 Six elements which display mesomerism. (9)
5 Room for methylidyne gemstone. (7)
6 Room for orbital expert. (5)
7 Curtailed, quiet, bringing up retro. (7)
8 Outrates my first experiment as they readily interconvert with each other. (9)
15 Open at zero, then shift, dropping nitrogen which cannot be separated by simple distillation. (9)
17 Count fins determining behaviours. (9)
19 Rostered off, losing radical who made the first connection between electricity and magnetism. (7)
20 Time's up. Put out to dry. Put out! (7)
22 & 24 Down Page parent re failed quick test. (7,5)
24 See 22 Down.
26 20 Down current discharges. (5)

Graham Mulroney FRACI CChem is Emeritus Professor of Industry Education at RMIT University.
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