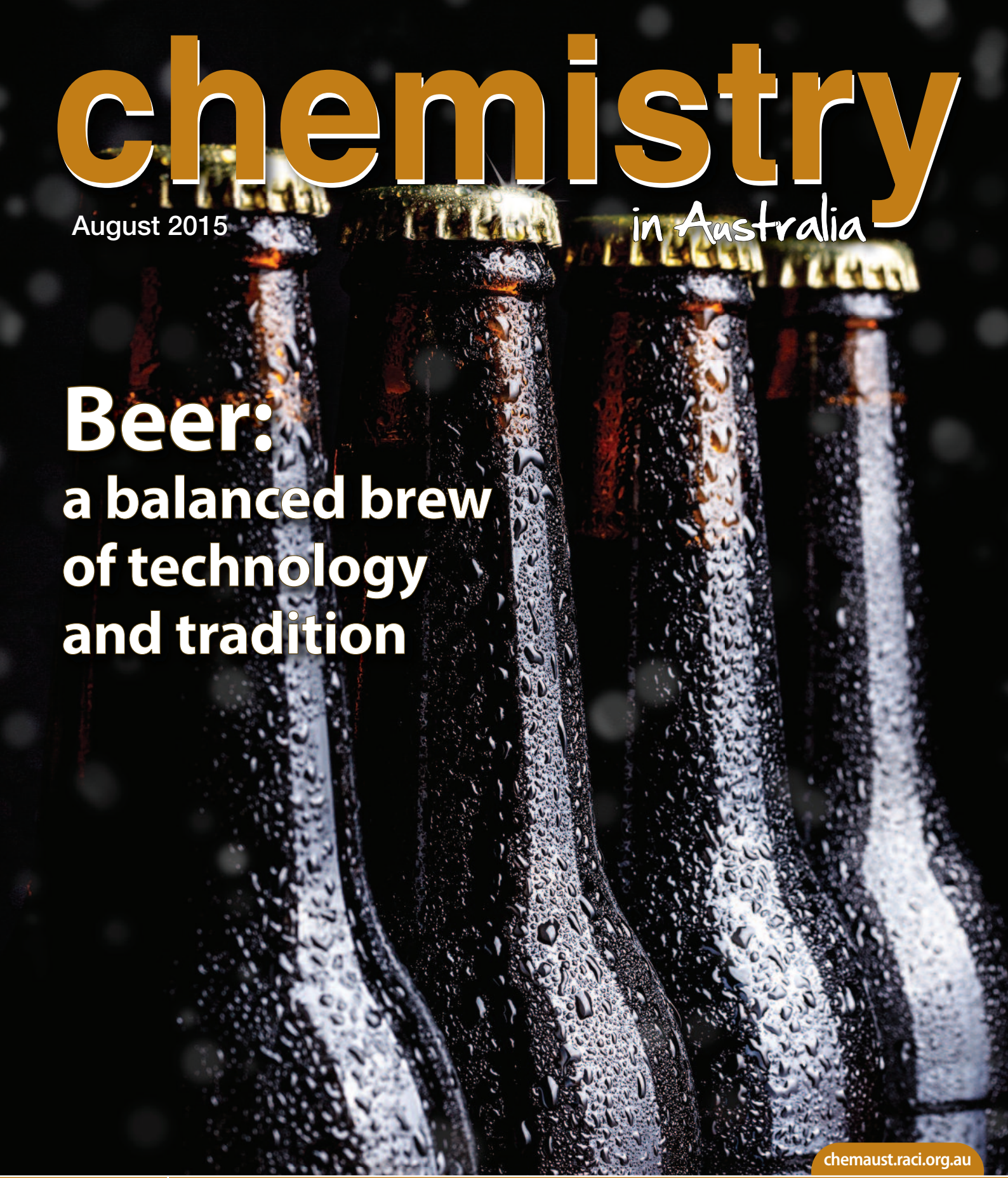
chemistry in Australia

August 2015



Beer:
a balanced brew of technology and tradition

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Royal Australian Chemical Institute

ALSO IN THIS ISSUE:
- Citizen science: the public as research recruits
- Hatching a strategy for your research career
- Economics of a biodiesel by-product

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cover story

Chemistry of beer

Whether you're mashing in a tun, boiling the kettle to make wort, pitching yeast or hopping a brew, the brewing of beer is both art and science.

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Limits and limitations of detection

A friend mentioned to me recently that his specialist has a preferred pathology group because their detection limits for a particular biomarker are 'lower'. I have read since that some assay manufacturers use limits of detection as a marketing tool.

The ability to detect smaller amounts of substance is a mixed blessing in medicine. There's the prospect of intervention to fix a problem that may or may not exist, sometimes with significant associated morbidity along the way, plus the social and economic implications for population screening to detect disease. Detection limits in environmental methods have similar dilemmas.

What about analytical methods and instrumentation in chemistry? I'm curious to know if the latest equipment hangs its hat on lower detection limits, and what the pitfalls of this might be.

How important are detection limits in the wider context of errors? The dangers of automation of analytical methods, particularly for the inexperienced, comes to mind. Some problems can be embedded in software code. You can see a long, fascinating and sometimes humorous error-related glossary at www.mistakeproofing.com/glossary.html.

Consider the measurement of analytes in human blood. Blood is such a complex matrix that it is a significant source of background 'noise'. Then there's calibration of equipment, accuracy of measurement of small sample volumes – the list is long. I remember that, in my previous life as a coal chemist, good sample prep ruled supreme. There are, of course, standard methods, but they too have their limits.

Lack of time, care or common sense can render well-intentioned methods ridiculous. At my daughter's local athletics track, events are regularly delayed because there are not enough volunteers to time all placegetters – which apparently must be done in triplicate. The thing is, they hadn't realised (until my partner pointed it out), that some race distances were being marked incorrectly and the kids were running several metres short.

I don't pretend to know the fine detail of the various limits, but just wading through the definitions, such as instrument detection limit, method detection limit, practical quantification limit and limit of quantification, is a feat in itself. Michael Thompson, Emeritus Professor of Analytical Chemistry at Birkbeck College, University of London, who has written about this subject over many years, describes detection limits as a 'preoccupation', saying 'there is a danger that this accumulation of theory and terminology will overwhelm understanding'. He argues that detection limits are not the best way to describe the 'bottom end of the useful range of analytical methods' (*Analyst* doi: 10.1039/A705702D).

What if we didn't rely so much on detection limits as we know them? In a more recent paper, Thompson and colleagues suggest that 'for many purposes detection limit and related limits are made redundant simply by reporting the measurement result and its uncertainty' (*Analytical Methods* doi: 10.1039/C3AY41209A). An oft-repeated quote of Einstein describes the folly of trying to solve a problem using the same level of thinking that created it. How do we think differently about limits of detection to come up with a better way?

I guess I'm not telling you anything new here. I've posed more questions than answers because I'm hoping you might have something to tell me. I would love to hear about your experiences and opinions, including about how the concept of detection limits is explained to students.

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ISSN 0314-4240 e-ISSN 1839-2539

raci

Chemists and vintners

The letter by John Harvey, 'Chemists, *laborateurs* and pharmacists' in the June 2015 issue (p. 5), reminded me of a similar situation I learned about when I visited Penfolds Wines at Nuriootpa, South Australia, in the early 1960s.

At that time I was working at the CSIRO Division of Chemical Physics, exploring the application of Alan Walsh's atomic absorption spectrometer to the measurement of the concentrations of metals in various materials, and helping other laboratories apply the new technique to their own analytical problems. Penfolds Wines had recently ordered an instrument from Techtron Pty Ltd, which manufactured them in Melbourne.

The Chief Chemist at Penfolds, Ray Beckwith, told me that when he joined the company in 1935, whoever was responsible for his appointment wanted to employ a chemist, but the directors of Penfolds would not consider having anyone with that title – winemaking was a traditional craft, and chemistry was not talked about in connection with it. So Ray was appointed initially as an 'assistant cellar hand'.

My visit to Nuriootpa had to be postponed for some time for a most unlikely reason. The spectrometer had been dispatched by road from Melbourne, but the truck had broken down and the driver had gone on foot to seek assistance (no mobile phones in those days). During his absence thieves broke into the truck and stole most of the contents, including the atomic absorption spectrometer. I have often wondered how a thief would go about disposing of this strange piece of equipment, of which he could only say 'I don't know what it is, but it fell off the back of a truck'!

Sadly, I lost contact with Ray Beckwith many years ago, but have now learned, via Google, that his distinguished career as a chemist in the wine industry was recognised very late in life by the award of an honorary doctorate from the University of Adelaide, and by a Medal of the Order of Australia. He died in 2012, still alert and active, at the age of 100.

John B. Willis FRACI CChem

Manners maketh the scientist

I would like to thank you and my colleagues at the RACI for allowing me to write for *Chemistry in Australia*. Although I am expert in almost nothing I write, I thoroughly enjoy the process of researching and new learning for each article I submit. And I welcome Sally's editorial oversight – every change she recommends makes me appear smarter than I truly am.

With the strength of our magazine and our society in mind, I would like to proffer a suggestion for the consideration of my colleagues. In some recent issues, I found an exchange of letters troubling. I have felt that the dialogue extended beyond the ideas to more personal disagreement, and I interpreted the tone as becoming aggressive, even bickering.

I truly believe in science as more than a profession. For me, it is a vocation. And I believe that we as scientists have a fundamental responsibility *to be wrong* … at least some of the time.

Clearly, I don't believe that we should intend to err, but rather that we must commit each day to the scrutiny of our work, and to the certain knowledge that our mistakes will improve our understanding.

We are each of us part of a grand, global endeavour spanning centuries of effort. In the interests of truth, our ideas must be tested and challenged. And it is our responsibility to participate in the resulting intellectual discourse openly, thoroughly, and above all *with respect*.

I therefore urge all of my colleagues at the RACI, when composing your letters to the editor, to please remember that we are all part of the same great endeavour. While you may disagree on certain points and concepts within the pages of this journal, I urge you to please keep the joy of science in your heart, and let every reader of your letter hear that joy.

Dave Sammut FRACI CChem

Got something to say?

As your RACI member magazine, *Chemistry in Australia* is the perfect place to voice your ideas and opinions, and to discuss chemistry issues and recently published articles.

Send your contributions (approx. 400 words) to the Editor at editor@raci.org.au.

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'Your say' guidelines

We will consider letters of up to 400 words in response to material published in *Chemistry in Australia* or about novel or topical issues relevant to chemistry. Letters accepted for publication will be edited for clarity, space or legal reasons and published in print and online. Full name and RACI membership status will be published. Please supply a daytime contact telephone number (not for publication).

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Vortex device makes for better cancer treatments

An Australian invention, responsible for unboiling an egg, has been used to produce a fourfold increase in efficacy of carboplatin, a commonly used drug for ovarian, lung and other cancers.

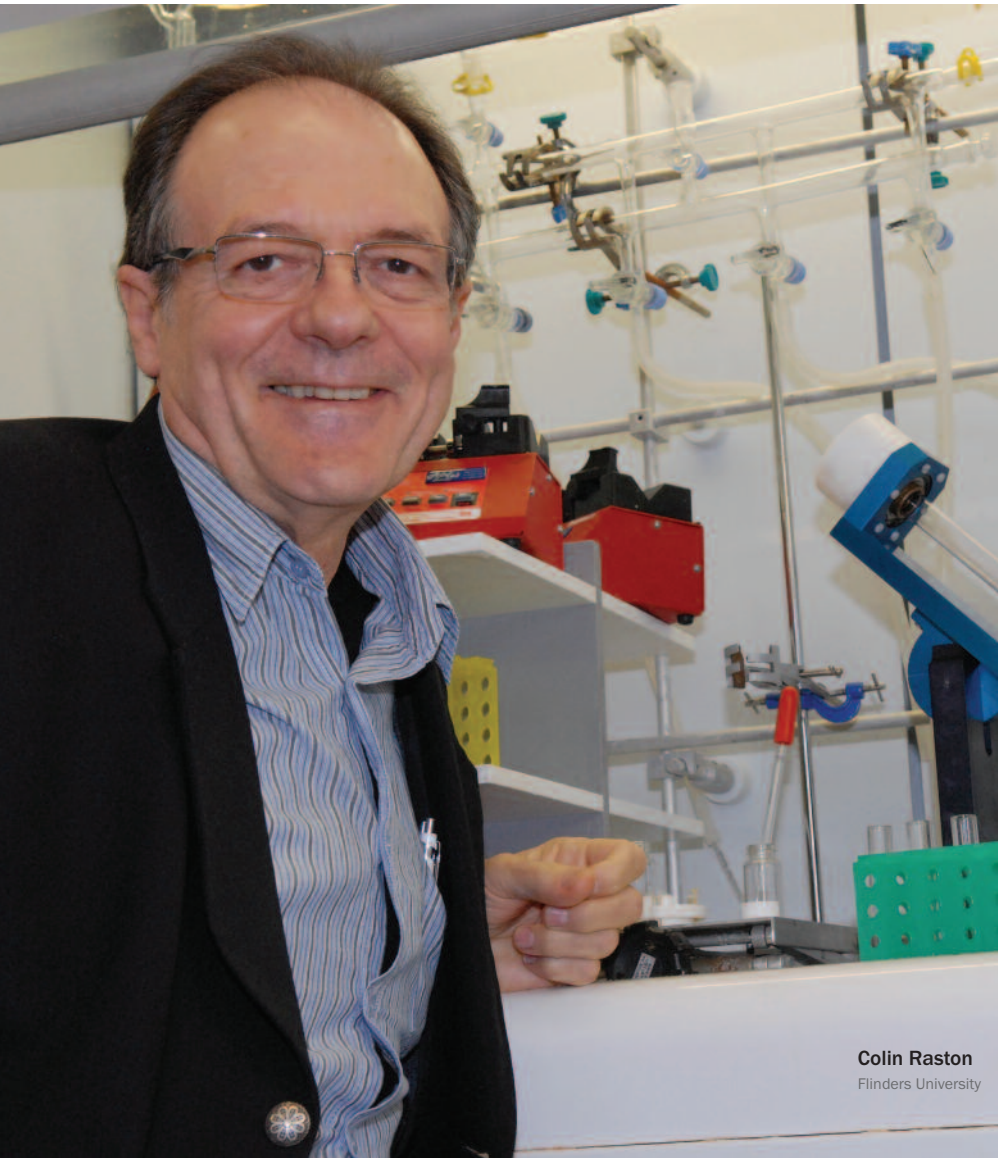
The latest research, published in *Scientific Reports* (doi: 10.1038/srep10414), is just one in a growing number of important applications for the vortex fluidic device (VFD) invented by the South Australian Premier's Professorial Research Fellow in Clean Technology, Flinders University Professor Colin Raston FRACI CChem.

The groundbreaking device is being manufactured at Flinders University and will soon be available to research organisations around the world.

Raston said the high-tech, yet simple device can be used in medical and pharmaceutical research along with a range of industries – all with a focus on cleaner, greener and cheaper production.

'This device creates a unique way to develop more sustainable and cost-effective products, services and technologies, which can accelerate innovation in a range of industries, from drug manufacturing to food and biodiesel production,' he said.

The device's unique ability to control chemical processes already has enabled scientists to 'unfold' proteins to their natural state, in a process likened to 'unboiling an egg', which could be used in protein-based drug research.



Colin Raston
Flinders University

The machine has the potential to revolutionise the delivery and manufacture of a wide range of pharmaceutical processes and products by 'streamlining the loading of drugs into nano-packages' for better results and less waste, Raston said.

'With ovarian cancer, we found that this technology can increase the loading of second generation anticancer carboplatin drugs into delivery vehicles from 17% to 75%,' he said.

'This not only would have a direct benefit of reducing the negative side-effects which affect patient health, but of being able to use less of the drug.'

Using more effective drugs would also reduce manufacturing waste, with up to half a tonne of waste generated from the production of just one kilogram of anticancer and other drugs.

'Much of the drugs end up in sewerage systems and possibly create superbugs in our environment,' Raston added.

Cancer kills about eight million people a year worldwide.

The start of VFD sales will escalate the application of this new scientific research work, Raston said.

'Our VFD will enable the pharmaceutical and many other industries to innovate – including further improvements in the chemical delivery of a range of existing approved drugs, as well as development of new improved drugs.'

Contributing authors on the latest proof-of-concept report, entitled 'Shear induced carboplatin binding within the cavity of a phospholipid mimic for increased anticancer efficacy', are Dr Jingxin Mo, Professor Lee Yong Lim and Muhammad Rizwan Hussain Ahamed (University of Western Australia), Dr Thomas Becker (Curtin University) and Dr Paul Eggers MRACI CChem, Dr Xianjue Chen and Professor Raston (Flinders University).

FLINDERS UNIVERSITY

Metal composite will (literally) float your boat

Researchers have demonstrated a new metal matrix composite that is so light it can float on water. A boat made of such lightweight composites will not sink despite damage to its structure. The new material also promises to improve automotive fuel economy because it combines light weight with heat resistance.

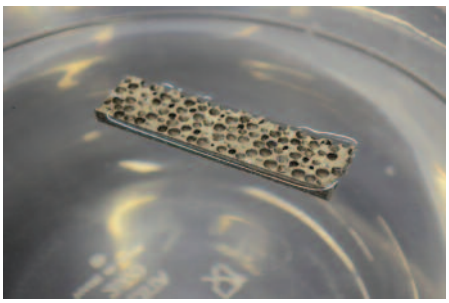
Although syntactic foams have been around for many years, this is the first development of a lightweight metal matrix syntactic foam. It is the work of a team of researchers from Deep Springs Technology (DST) and the New York University Polytechnic School of Engineering.

Their magnesium alloy matrix composite is reinforced with silicon carbide hollow particles and has a density of only 0.92 g/cm^3 compared to 1.0 g/cm^3 of water. Not only is its density lower than that of water, the metal matrix is strong enough to withstand the rigorous conditions faced in the marine environment.

Significant efforts in recent years have focused on developing lightweight polymer matrix composites to replace heavier metal-based components in automobiles and marine vessels. The technology for the new composite is very close to maturation and could be put into prototypes for testing within three years. Amphibious vehicles such as the ultra heavy-lift amphibious connector being developed by the US Marine Corps can especially benefit from the light weight and high buoyancy offered by the new syntactic foams, the researchers explained.

'This new development of very light metal matrix composites can swing the pendulum back in favour of metallic materials,' forecasted co-author Professor Nikhil Gupta, of the NYU School of Engineering. 'The ability of metals to withstand higher temperatures can be a huge advantage for these composites in engine and exhaust components, quite apart from structural parts.'

The syntactic foam captures the lightness of foams, but adds substantial strength. The secret of this syntactic foam starts with a matrix made of a magnesium alloy, which is then turned into foam by adding strong, lightweight silicon carbide hollow spheres. A single sphere's shell can withstand pressure of over 25 000 (psi) (170 MPa) before it ruptures – 100 times the maximum pressure in a fire hose.



The hollow particles also offer impact protection to the syntactic foam because each shell acts like an energy absorber during its fracture. The composite can be customised for density and other properties by adding more or fewer shells into the metal matrix to fit the requirements of the application. This concept can also be used with other magnesium alloys that are non-flammable.

The new composite has potential applications in boat flooring, automobile parts, and buoyancy modules as well as vehicle armour.

The findings are published in the *International Journal of Impact Engineering* (doi: 10.1016/j.ijimpeng.2015.04.008).

NYU POLYTECHNIC SCHOOL OF ENGINEERING

Chemical pathologist wins science measurement award

Two Australian scientists working in health and nanoelectronics have been recognised for excellence in metrology, the science of measurement.

The annual Barry Inglis Medal and the NMI Prize, awarded by Australia's National Measurement Institute (NMI), acknowledge and celebrate outstanding achievement in measurement research and excellence in practical measurements in Australia.

Sydney's St Vincent's Hospital chemical pathologist, Dr Graham Jones, was awarded the Barry Inglis Medal. Jones was recognised for his work to improve the accuracy and reliability of chemical pathology testing, via better measurement standards, techniques and clinical reference ranges.

The NMI Prize, awarded to an individual under 35 years of age, went to University of New South Wales research fellow Dr Alessandro Rossi. Rossi's work in nanoelectronics is helping to realise an improved definition of the ampere.

DEPARTMENT OF INDUSTRY AND SCIENCE

New era of astronomy as gravitational wave hunt begins

Australian scientists are in the hunt for the last missing piece of Einstein's general theory of relativity, gravitational waves, as the Advanced LIGO Project in the US comes on line.

LIGO (the Laser Interferometer Gravitational-wave Observatories) aims to find gravitational waves, ripples in the fabric of space and time caused by the most violent events in the universe such as supernovae or collisions between black holes.

'We'll find things we can't imagine – gravitational waves are a completely different messenger from light,' said Professor David McClelland from the Australian National University (ANU), who leads the Australian LIGO team.

Australia is a partner in Advanced LIGO with research groups from ANU and the University of Adelaide directly contributing to its construction and commissioning.

LIGO will ultimately be joined by detectors in Europe, Japan and India seeking evidence for gravitational waves, in the form of movements a fraction of the radius of a proton.

'Advanced LIGO is easily the most sensitive detector ever created, at the limits of the Heisenberg uncertainty principle,' said Professor Jesper Munch, leader of the University of Adelaide research group.

In his 1915 general theory of relativity, Einstein proposed that large masses such as stars cause curvature in space and time, which leads to gravity and also bends light.

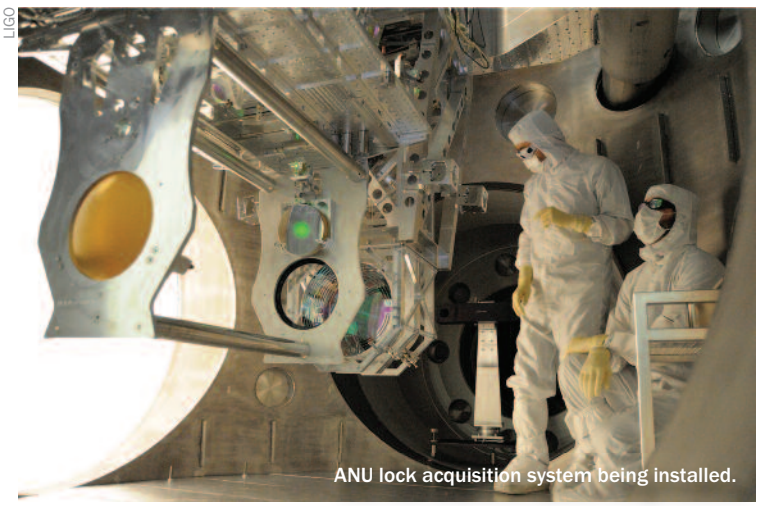
A number of observations in the past 100 years have confirmed other consequences of Einstein's theory, but only in regions of weak gravity, said LIGO team member Professor Daniel Shaddock, from the ANU Research School of Physics and Engineering (RSPE).

'Gravitational waves are produced when massive objects accelerate or collide,' he said.

'Finding gravitational waves would test our theories in a completely different scenario, where huge gravitational forces are at play. It is the ultimate test for general relativity.'

Gravitational waves have been proven to exist indirectly

LIGO



ANU lock acquisition system being installed.

LIGO

LIGO vacuum chambers.

through the decay of the orbit of two neutron stars rotating around each other. However, McClelland says direct detection of them is within our grasp.

'By the end of the year there's a chance that the 100-year search will be over,' he said.

'Or, if we don't see something in the next 12–24 months, then we may have found either a problem with Einstein's general relativity or some new insight about the universe,' he said.

LIGO is an identical pair of laboratories in opposite corners of the US. Each laboratory consists of two four-kilometre-long vacuum pipes at right angles to each other, with mirrors suspended at either end. A laser beam is sent back and forth between the mirrors to form an interferometer.

They were built by Caltech and MIT in the 1990s. However, they only now have the sensitivity levels required to detect gravitational waves with a tenfold improvement following a complete redesign and replacement of the detectors.

A gravitational wave passing through the interferometer should momentarily move the mirrors at a frequency of about a kilohertz somewhere in the region of 10^{-19} of a metre (one ten-thousandth of the radius of a proton), which will be picked up by the laser system.

The team at ANU have developed a system that locks the laser beam to the 40-kilogram mirrors to ensure that infinitesimal movements caused by a passing gravitational wave are identified, while other small movements are nullified.

The University of Adelaide group has developed a system to correct for any deformation of the mirrors due to heat, a crucial factor with the stored laser power of the system approaching half a megawatt.

'The technology required pushes the limit of all the components, including low noise detectors, high power lasers, quantum effects and technology such as optical polishing, coatings and vacuum systems,' said Munch.

'It is a crowning achievement in optical sensing as the world celebrates the International Year of Light in 2015.'

AUSTRALIAN NATIONAL UNIVERSITY AND UNIVERSITY OF ADELAIDE

Making antimatter: research provides foundation for future experiments

One of science's unresolved questions – where all of the antimatter at the origin of the universe went – may now be explored with the help of Curtin University research.

Professor Igor Bray, Head of Curtin's Department of Physics and Astronomy, said the university's theoretical physics research group utilised supercomputers at the National Computational Infrastructure (NCI) and the Pawsey Supercomputing Centre to look at ways to create neutral antimatter in a laboratory to help resolve the long-standing problem of matter–antimatter asymmetry in the universe (*Physical Review Letters* doi: 10.1103/PhysRevLett.114.183201).

'Laws of physics predict equal amounts of matter and antimatter at the origin of the universe, but it appears that presently this is not the case. In order to explore this, scientists require an adequate amount of antimatter in the laboratory, something that is currently not available,' Bray explained.

Scientists hope to measure how antimatter behaves under gravity, and its various energy levels to the same precision as is possible with ordinary matter. Antimatter must be in a neutrally charged state in order to be used in such experiments.

'The simplest neutral antimatter is the antihydrogen atom, which is a bound state of an antielectron, also called a positron, and an antiproton. The challenge for scientists to date has been to find a way to create the antihydrogen in a laboratory in enough quantity to be a viable material source for experiments,' Bray said.

'In our research, we looked at ways to create a suitable amount of antihydrogen atoms. One mechanism is to collide slow antiprotons with positronium, a bound state of an electron and a positron. Our calculations discovered that when positronium is in a laser-prepared excited state, the number of antihydrogen atoms created can be enhanced by a factor of 1000.

'The competitive mechanism for creating antihydrogen that this research has uncovered will be used at CERN, the European Organisation for Nuclear Research, where three different groups are in a race to make antihydrogen in sufficient quantities.'

The calculations for this research required over one million CPU hours following a decade of computer code development.

'This discovery would not have been possible without the modern supercomputers now available in Australia,' Bray said.

CURTIN UNIVERSITY

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Avoiding chocolate 'bloom'

Chocolate is one of the world's most popular foods, but when a whitish coating called a bloom appears on the confection's surface, it can make consumers think twice about eating it. The coating is made up of fats and is edible, but it changes the chocolate's appearance and texture – and not for the better. Now scientists report in *ACS Applied Materials & Interfaces* (doi: 10.1021/acsami.5b02092) new information that could help chocolatiers prevent blooms from forming.

Svenja K. Reinke and colleagues explain that baked goods and confectionery products, including chocolate, contain a mix of components that don't always stay in place. Fat blooms, for instance, occur when lipids from within a chocolate product wander to the surface. They've long been a scourge of chocolatiers, but no one fully understood what caused them. Reinke's team wanted to find out what factors were contributing to their formation.

The researchers investigated the microscopic structural changes that occur when chocolate blooms. They found that the lipids that are responsible move through pores and cracks in the chocolate. Along the way, they soften and dissolve solid cocoa butter into a liquid form. The researchers say reducing the number of pores and the liquid cocoa butter content of chocolate could help minimise blooms.

AMERICAN CHEMICAL SOCIETY

Holes in gold enhance molecular sensing

Non-metallic mesoporous structures have already demonstrated potential for applications in gas storage, separation, catalysis, ion-exchange, sensing, polymerisation and drug delivery. Metal mesoporous films could have fascinating and useful optical properties as they are effectively the inverse of nanoparticle arrays. Now for the first time a collaboration of researchers in Japan, Turkey, Korea and Sweden demonstrate a simple approach for producing metal films with regular tuneable mesopores, and show their potential for high-sensitivity optical detection (*Nature Communications* doi: 10.1038/ncomms7608).

When light is incident on nanostructures of noble metals such as gold, the electrons oscillate collectively – a so-called plasmon – and this greatly enhances the electromagnetic field close by. According to Babinet's principle in optics, the inverse structure – a mesoporous film – should lead to similar local electromagnetic field enhancements, but as Yusuke Yamauchi and his colleagues point out in their report, controlling gold crystal growth well enough to produce mesoporous films has so far been difficult.

The success of their approach relies on electrochemistry and micelle self-assembly. They dissolve hydrogen gold chloride (or chloroauric acid, $HAuCl_4$) and polystyrene-*block*-poly(oxyethylene) in a solution of tetrahydrofuran, which leads to the formation of micelles with a polystyrene core and polyoxyethylene shell. The micelles reduce the $AuCl_4^-$ ions so that gold deposits on the micelles. The result is highly regular gold mesopores with a size that can be tuned by varying the concentrations of the $HAuCl_4$ and polystyrene-*block*-poly(oxyethylene).

Calculations showed that hotspots of high electric field enhancement indeed exist in the pores of the structure, and the plasmon resonances can be tuned by changing the pore size. Further experiments confirmed the surface enhancement of protein spectral signatures, known as surface enhanced Raman scattering. The researchers conclude, 'The electrochemical approach is widely applicable to embed uniform mesopores in other metal and alloy systems, which are generally difficult to be synthesised.'

INTERNATIONAL CENTER FOR MATERIALS NANOARCHITECTONICS (WPI-MANA)

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For further details, contact ATA Scientific Pty Ltd, ph. (02) 9541 3500, email enquiries@atascientific.com.au or visit www.atascientific.com.au.

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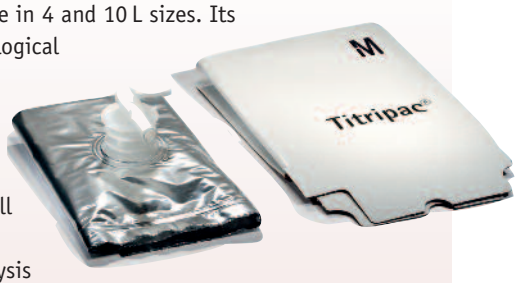

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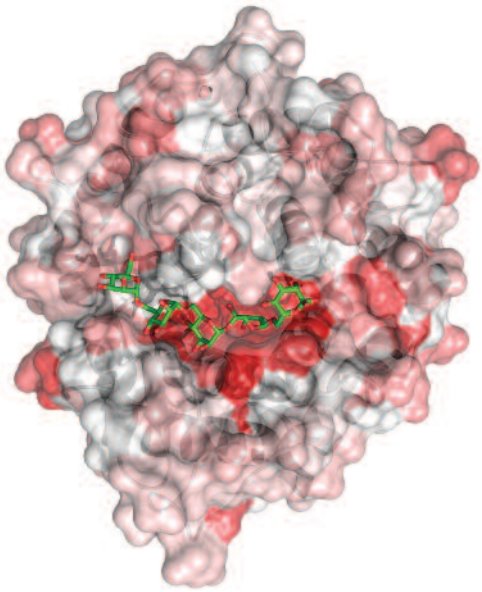
For more information, contact Merck Millipore, ph. 1800 335 571 or visit www.merckmillipore.com/titration.

Mushroom munchers: how bacteria metabolise the fungal cell wall

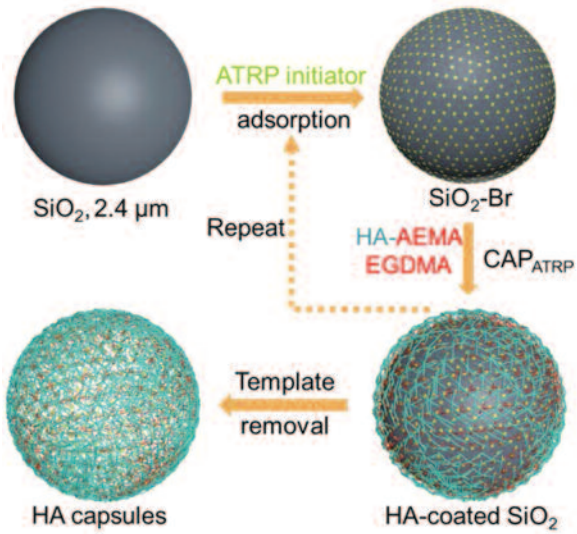
Earlier this year, researchers at the University of Melbourne showed that the cell walls of mushrooms and yeast consumed in our diet can be broken down by our gut microbiota (*Nature* 2015, **517**, 165–9; see *Chem. Aust.* June 2015, p. 13). The gut microbes use enzymes called GH76 endomannanases to metabolise fungal cell wall glycans to short-chain fatty acids that modulate our immune systems and nourish the endothelial cells of our distal gut. Now, in collaboration with groups from the UK and Spain, the group of Associate Professor Spencer Williams has clarified at a molecular level the catalytic mechanism by which the same highly specialised GH76 endomannanases in a soil bacterium, *Bacillus circulans*, metabolise fungal cell walls (Thompson A.J., Speciale G., Iglesias-Fernández J., Hakki Z., Belz T., Cartmell A., Spears R.J., Chandler E., Temple M.J., Stepper J., Gilbert H.J., Rovira C., Williams S.J., Davies G.J., *Angew. Chem. Int. Ed.* 2015, **54**, 5378–82). Using chemically synthesised enzyme inhibitors and substrate analogues, they were able to determine X-ray structures of enzyme–substrate complexes that mimicked the ground-state and transition-state bound forms of the enzyme. Supported by computational studies, the authors were able to identify the amino acid residues that are essential for catalysis and the conformational changes of the substrate that occur during the endomannosidase-catalysed reaction.

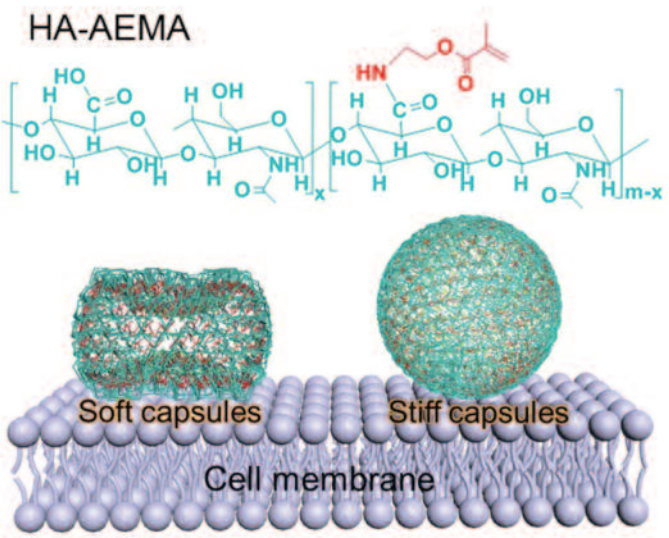


X-ray structure of mannopentaose bound to GH76 enzyme from *Bacillus circulans*. The protein is coloured according to amino acid sequence conservation. Red = highly conserved.

Cells have a soft spot for soft particles

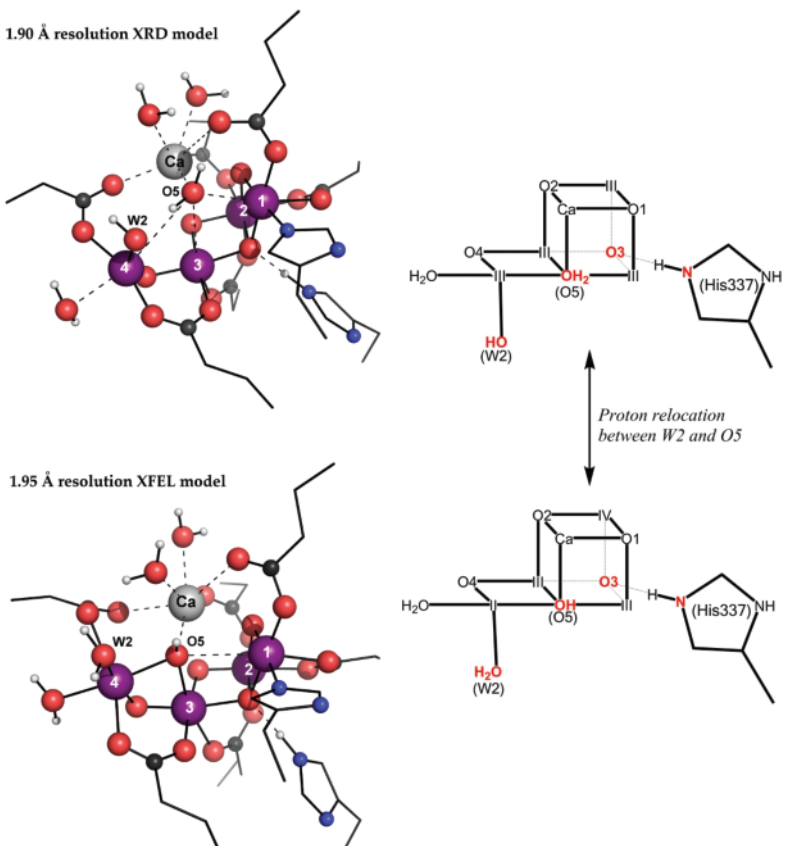
Many recent studies have been performed to understand how the physicochemical properties of particles (such as size, shape and surface chemistry) are correlated with their biological interactions. In particular, particle stiffness has been shown to influence in vivo circulation and in vitro cellular interactions. However, most reported studies have used particles with several differing properties, making it difficult to determine the influence of particle stiffness alone. By using the technique of atom transfer radical polymerisation mediated continuous assembly of polymers (CAP_{ATRP}) to control the wall thickness of hollow polymer particles called polymer capsules, a research team led by Professor Greg Qiao and Professor Frank Caruso at the University of Melbourne has prepared hyaluronic acid (HA) capsules with tunable stiffness while keeping other parameters constant (Sun H., Wong E.H.H., Yan Y., Cui J., Dai Q., Guo J., Qiao G.G., Caruso F. *Chem. Sci.* 2015, **6**, 3505–14). The effect of capsule stiffness on cellular interactions (surface binding, association and internalisation) and intracellular distribution was then systematically and quantitatively investigated. The researchers found that the softest HA capsules interacted more strongly and rapidly with cells than stiffer capsules and that cellular uptake was stiffness dependent. But regardless of capsule stiffness, all internalised capsules were deformed and accumulated in lysosomes. These findings highlight the importance of capsule stiffness on cellular processing and provide useful information for the rational design of polymer capsules for biomedical applications.



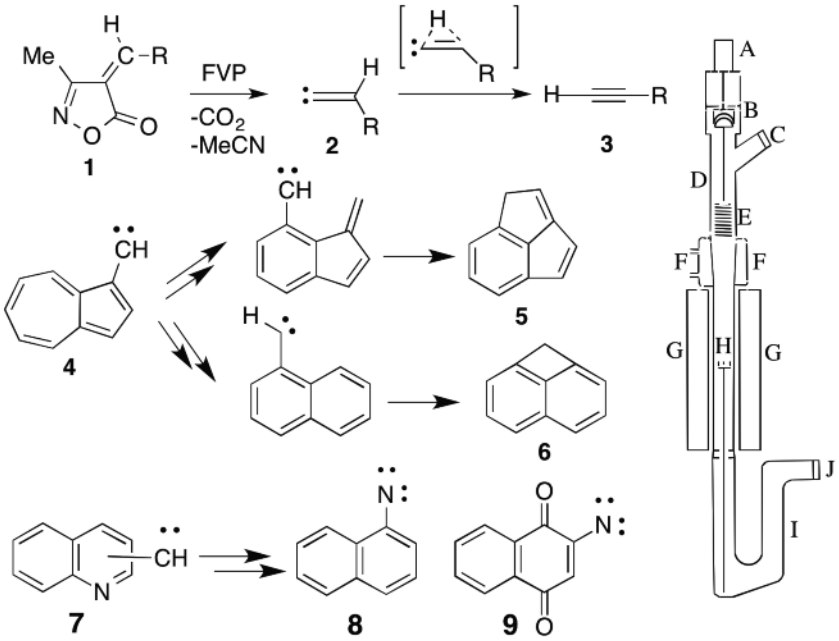


Resolving differences between photosystem II crystal structures

The structure and mechanism of the catalytic Mn_4Ca cluster in photosystem II, which oxidises two water molecules into molecular oxygen and protons, remain among the most challenging problems in bio-energetics. The reaction in nature exhibits unrivalled chemical efficacy and is the 'benchmark' for efficient electrolytic hydrogen production from water. Recently, great progress has occurred in characterising this water-oxidising complex (WOC), with a 1.9 Å resolution X-ray diffraction structure and now a 1.95 Å X-ray free-electron laser (XFEL) structure. However, apparent conflicts with other data have challenged these achievements. The earlier 1.9 Å structure disagreed with extended X-ray absorption fine structure (EXAFS) data, suggesting that the Mn centres in the WOC had suffered from X-ray photoreduction. For the latest 1.95 Å structure, Mn photoreduction was not an issue, but poor agreement with computational models, which commonly assumed a 'high' Mn oxidation state, again suggested that the structure was contaminated with 'reduced' WOC forms. However, new density functional theory modelling at the Australian National University shows that the distinct 1.9 and 1.95 Å WOC geometries can be straightforwardly explained if the Mn oxidation states are actually lower than commonly supposed (Petrie S., Pace R.J., Stranger R. *Angew. Chem. Int. Ed.* 2015, **54**, 7120–4). Remarkably, the two structures are simple tautomers, related by a single proton relocation from the O5 water group to the His337 amino acid residue.



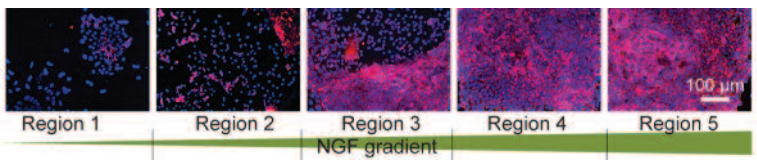
Arylacetylenes in a flash



The research group of Professor Curt Wentrup at the University of Queensland, together with co-workers in Germany, has developed an automated falling-solid flash vacuum pyrolysis technique (FS-FVP) that allows the rapid, efficient and high-yielding synthesis on a multigram scale of arylacetylenes **3** from aldehydes via 4-arylmethylidene-5(4*H*)-isoxazolones **1** with vinylidenes **2** as key intermediates (Wentrup C., Becker J., Winter H.-W., *Angew. Chem. Int. Ed.* 2015, **54**, 5702–4). The innovative centrepiece of the apparatus is a spinning brush (E) that acts as a vertical conveyor for the finely powdered solid starting material. Aryl- and heteroaryl-acetylenes, naphthylacetylenes and *p*-diethynylbenzene are readily obtained. The new method is advantageous in other applications. For example, 5-substituted tetrazoles are convenient starting materials for arylcarbenes but are often too involatile to be practical for FVP. Nevertheless, 1-azulenylcarbene **4** was generated from tetrazole and aldehyde tosylhydrazone precursors by FS-FVP and rearranges to cyclobuta[*de*]naphthalene **5** and cyclopenta[*cd*]indene **6**. Furthermore, 2-azulenylcarbene rearranges to 1-azulenylcarbene. FS-FVP has also been used to generate 4-, 3- and 2-quinolylcarbenes **7**, which all rearrange to 1-naphthylnitrene **8**, which was observed directly by ESR spectroscopy prior to ring contraction to 1-cyanoindene. In related work, 1,4-naphthoquinone-2-ylnitrene **9** has also been characterised by ESR spectroscopy as the first directly observed vinylnitrene (Sarkar S.K., Sawai A., Kanahara K., Wentrup C., Abe M., Gudmundsdottir A.D. *J. Am. Chem. Soc.* 2015, **137**, 4207–14).

Brain-on-a-slide: gradient surfaces to optimise neural differentiation

The cost of growth factor required to supplement cultures of human cells is currently a prohibitively large expense in translating promising laboratory-scale science to the clinical scale. In solution, growth factors are rapidly internalised into the cell and degraded. Binding these proteins to a solid substrate inhibits this process, but surface binding can potentially affect growth factor activity. Researchers at the University of South Australia have come up with a novel way to determine the minimum surface density of nerve growth factor (NGF) needed to induce differentiating mouse embryonic stem cells to form neurons, by constructing a gradient of immobilised NGF on a cell culture surface (Delalat B., Mierczynska A., Rasi Ghaemi S., Cavallaro A., Harding F.J., Vasilev K., Voelcker N.H., *Adv. Funct. Mater.* 2015, **25**, 2737–44). Underlying the NGF gradient is a polymer film prepared by plasma polymerisation containing a varying density of aldehyde functional groups, onto which NGF is covalently coupled by amination. Plasma polymer coatings can easily be scaled up and transferred onto porous scaffolds or tissue cultureware; thus this work aids the design of advanced nerve tissue engineering scaffolds and tissue culture surfaces for neural cell expansion. The immobilised biomolecule gradient can be generalised to other cell culture scenarios as a tool to develop affordable bioactive materials.



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.

Aust J Chem

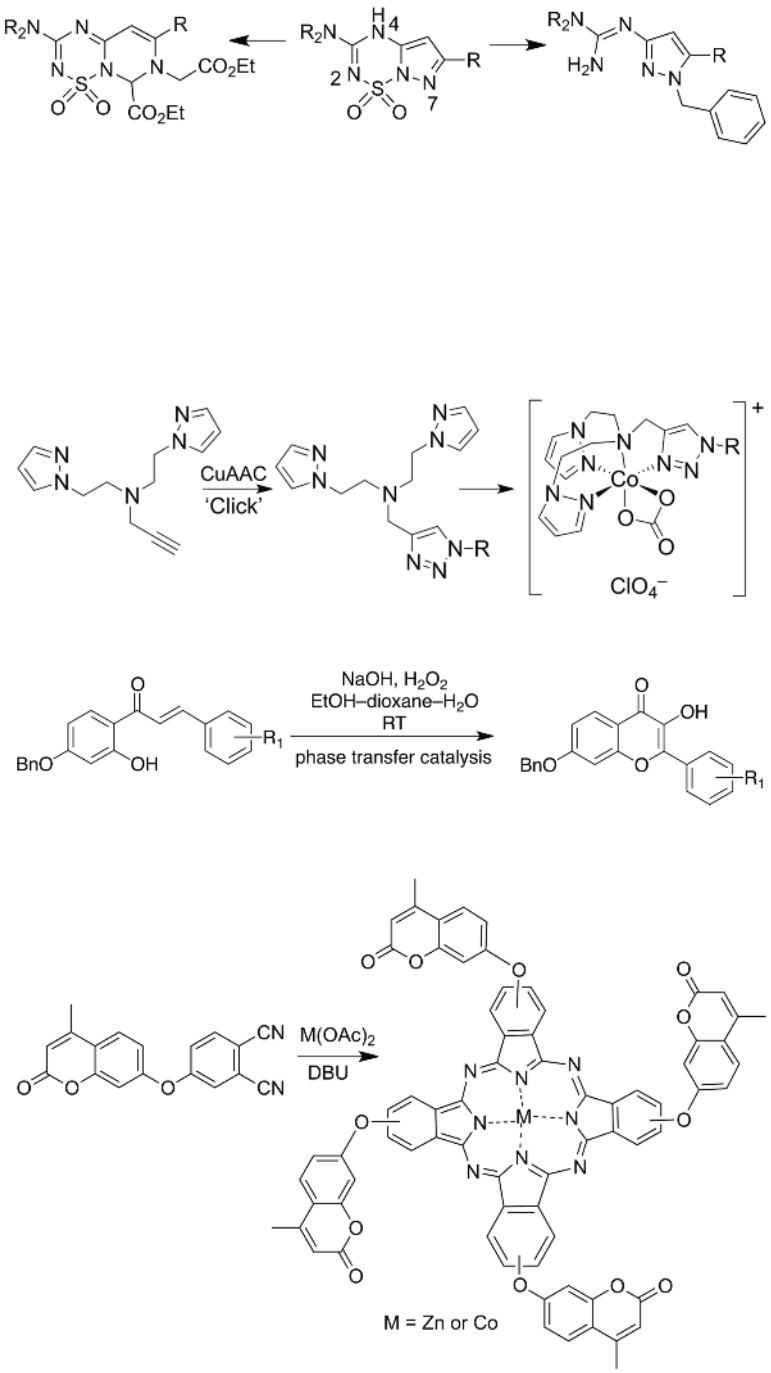
In the July issue of *Aust. J. Chem.*, Craig Francis (CSIRO, Clayton), Michael Perkins (Flinders University) and co-workers report several transformations of the pyrazolo[1,5-*b*][1,2,4,6]thiatriazine ring system. These molecules possess four nucleophilic sites (N2, N4, C5 and N7) and undergo alkylation predominantly at N4 and N7. Novel reactions include ring expansion of the pyrazole ring to yield a new ring system, pyrimido[1,6-*b*][1,2,4,6]thiatriazines. Catalytic amounts of acid caused extrusion of SO_2 to produce pyrazolyl-guanidines.

James Crowley and co-workers (Dunedin) have used the copper(I)-catalysed azide-alkyne 'click' reaction (CuAAC) to synthesise a family of tripodal tetramine ligands incorporating two pyrazolyl and one 1,2,3-triazolyl donor arm. Mono-, bis- and tris-tripodal ligand scaffolds were readily generated by this method. The coordination chemistry, spectroscopy and crystallography are described.

Flavanoids are widely consumed in food and for medicinal purposes as they possess important biological properties, including anticancer, anti-inflammatory, antimicrobial and antiviral. Nhu, Hawkins and Burns (Walter and Eliza Hall Institute) now report an efficient oxidative synthesis of flavones under phase transfer conditions.

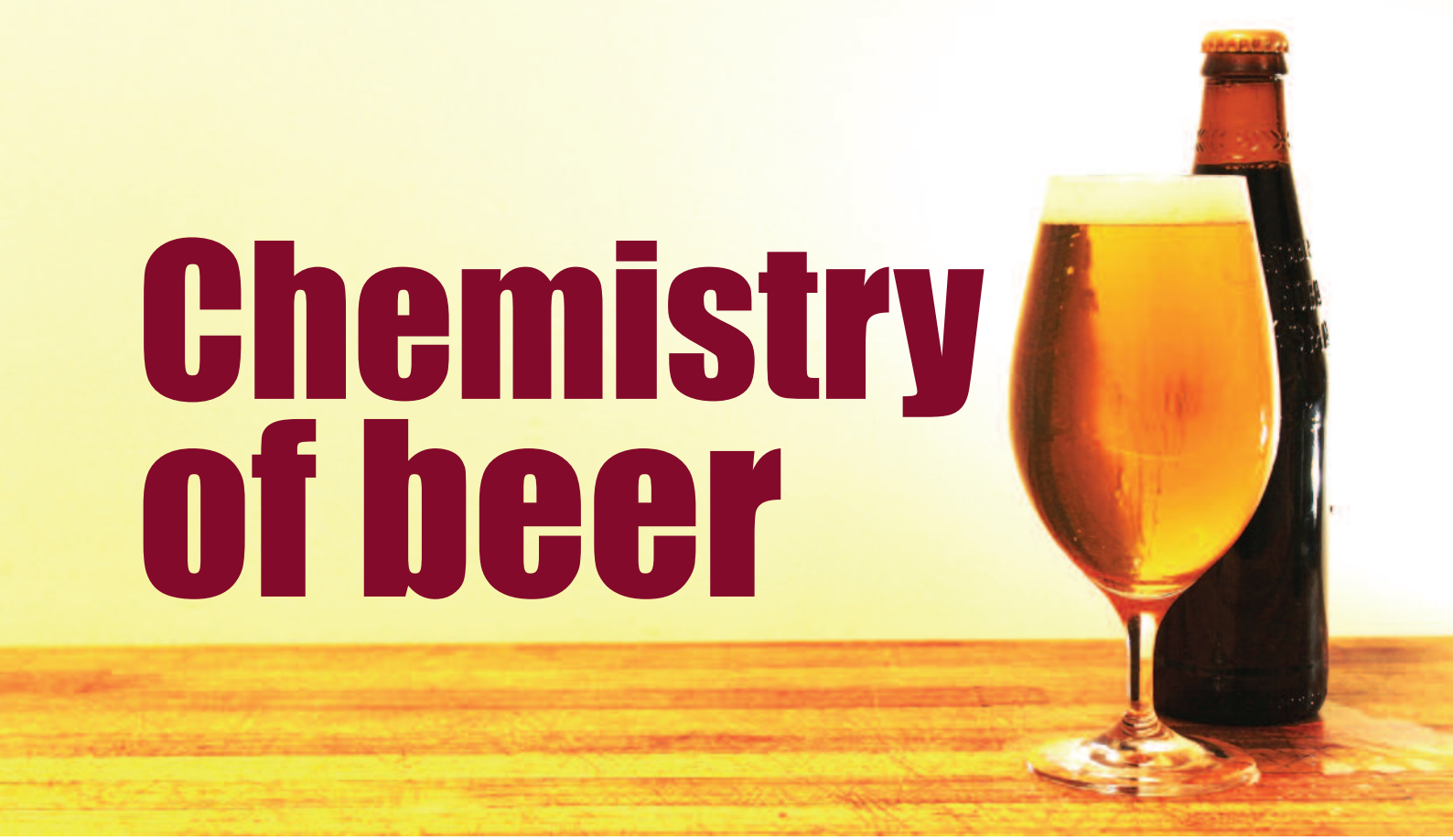
A photovoltaic application of coumarin derivatives is reported by Guo, Wang et al. (Tianjin, China), who synthesised 7-coumarinoxy-substituted zinc and cobalt phthalocyanine dyes and demonstrated a through-space electron transfer from the dye to TiO_2 films. The zinc complex achieves a higher conversion efficiency than reported for other, similar complexes because of its slower charge recombination rate and faster electron injection from the dye to the conduction band of the conducting glass.

Darryl Nguyen (University of Western Sydney) has developed a synthetic antibacterial 3D soft tissue with applications in wound healing. The artificial tissue is prepared from a mixture of collagen type I, the most abundant type of collagen in the dermal layers of skin, and simulated wound fluid (50% foetal calf serum and 50% physiological NaCl in 0.1% peptone), which is polymerised at 35°C. The tissue allows in-vitro assays of the potency of potential antimicrobial drugs under conditions that mimic the in-vivo environment of biofilm infections.



Curt Wentrup FAA, FRACI CChem (wentrup@uq.edu.au),
http://uq.edu.au/uqresearchers/researcher/wentrupc.html?uv_category=pub

Chemistry of beer



Whether you're mashing in a tun, boiling the kettle to make wort, pitching yeast or hopping a brew, the brewing of beer is both art and science.

BY **MELINDA CHRISTOPHERSEN**

Beer consists of just four basic ingredients – water, malt, hops (flowers of the *Humulus lupulus* plant) and brewing yeast (*Saccharomyces cerevisiae, Saccharomyces pastorianus*). Sound simple? Definitely not! Brewing is a very complex and delicate series of chemical reactions that are measured and controlled within specific conditions to ensure a high-quality final product. To the initiated, brewing is a microcosm of unique terminologies, tradition and some pretty serious chemistry. Brewers worldwide produce beer at an advanced technological level, yet always keep in mind the importance of tradition.

Before brewing begins, there is work to be done at the malthouse to prepare malted barley, which is the source of carbohydrates for conversion to alcohol. Unmalted starch sources such as wheat, barley, rice, corn and sorghum as an adjunct (additional carbohydrate source) are sometimes used regionally, except in Germany where the *Reinheitgebot* purity law allows only malted barley. Most beers produced globally contain a high proportion of malted barley.

Brewing barley contains mainly starch, protein, cell wall polysaccharides, and a smaller amount of fats and minerals. The modification of barley begins with steeping the grains in water to initiate germination in which enzymes break down the cell walls and some of the protein in the starchy endosperm. Enzymes (amlyases) are produced that are utilised later in the mashing process. The partially germinated grains are then kilned at high temperatures to halt germination and develop the desired biscuity and malty flavour and aromas. The level of kilning produces specialty malts that deliver a range of colour and flavour characteristics from amber malty lager to rich dark caramel-like stouts.

Off to the brewhouse where malt is milled to 'grist' and mashed in a tun with other prepared materials (adjuncts, salts or supplementary enzymes). A carefully controlled

amount of liquor (water) is added at a set temperature. During the mashing process, polysaccharides are enzymatically broken down by the amylases to simpler sugars. The mash is filtered through the bed of grain husks and the liquid known as 'wort' (pronounced *wert*) is collected into a kettle for wort boiling. This is where some of the most important chemistry takes place.

Heating the wort sterilises the liquor, resulting in colour development by 'non-enzymatic browning', via a Maillard reaction between amines, or amino acids, and carbonyl compounds, in particular reducing sugars. The pigments are melanoidins and the final product is caramel. Melanoidins have also been shown to exhibit antimicrobial and antioxidative effects, complexing with hydroxyl radicals, which in turn improves shelf-life stability. Wort boiling contributes to the final physical stability of the beer by coagulation of proteins, which are removed, clarifying the wort and promoting colloidal stability.

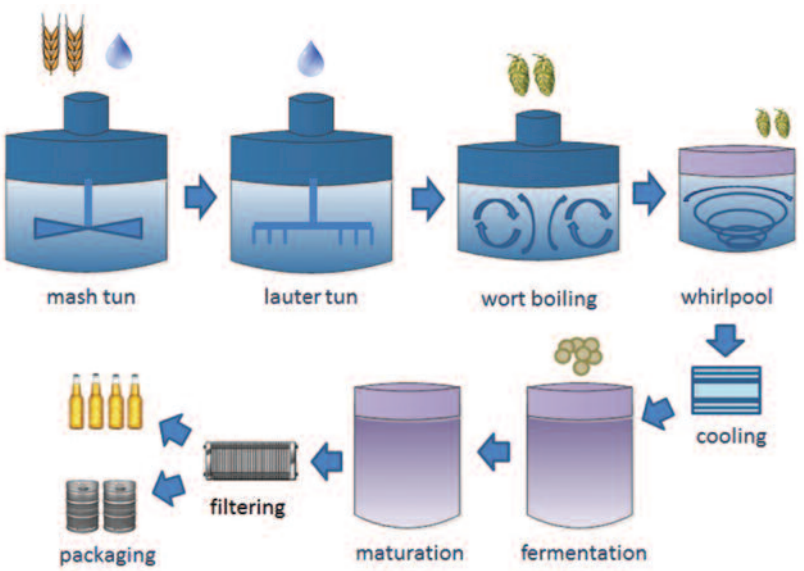
Hops are added to the wort kettle as cones or pellets (a compressed pelleted hop flower). It is the alpha-acids in the hops that are extracted into the wort and isomerised during the boil to the more soluble iso-alpha-acids, which provide the characteristic bitterness. A series of hop additions are made to the kettle, which is maintained as a rolling boil. This process depends on temperature and concentration since the hop compounds are barely soluble. In addition to alpha-acids, hops also contain essential oils, contributing to the sensory characteristics, such as hoppy, resinous, floral, fruity and spicy aromas to name a few. Most of these compounds are highly volatile and can therefore be lost by evaporation during wort boiling. In order to obtain a suitable compromise between sufficient boiling to coagulate protein, isomerisation of the hop acids, and retaining aroma, the brewer may add part of the hop addition later to the whirlpool (late hopping) or even much later during the maturation process (dry hopping).

Hop varietals used in the beer have become of increasing interest as consumer's interest in raw material provenance grows. For the brewer and the brewing chemist, the addition of hops opens up a plethora of chemical reactions that determine not only the characteristic bitterness of the beer and beer foam improvement, but also the flavour profile and quality of the sensory bitterness achieved. It is important to note that the aromatics of the raw hop may not necessarily directly predict the final aroma in beer. Aroma hop compounds (ppt–ppb range) can be analysed during the brewing process or in beer itself by gas chromatography with solid-phase micro-extraction. In our laboratories, analytical profiles of raw hop pellet slurries have revealed very different essential oil and thus olfactory profiles from those present in the final product. However, each hop variety will produce specific flavour profiles in finished products that are somewhat related to the original composition when considering expected losses of volatiles and more importantly the addition point of the hops. This is a complex process, and often hops are added at several stages during brewing, further complicating the elucidation of the origin of the aromatic contributions produced. Besides addition point, one must also consider the effect of yeast fermentation on the production of hop aroma, where aroma compounds are bio-transformed during fermentation by yeast.

Wort boiling fulfils many other functions like stripping of undesirable volatiles such as dimethyl sulfide, which can produce a corny, vegetal aroma. Dimethyl sulfide is continuously produced in hot wort from the sulfur-containing amino acid *S*-methylmethionine, which originates from the malt. Wort is chilled as quickly as possible after the boil to prevent further dimethyl sulfide production and prepare the wort for fermentation.

The unique character of beer as opposed to other alcoholic fermented beverages is due to the subtle interaction between carefully selected 'brewing strains' of yeast and the malt and hops that come together as wort. Beer fermentation involves the conversion of sugars, derived primarily from malt, into ethanol by the yeast. Cooled and aerated wort is

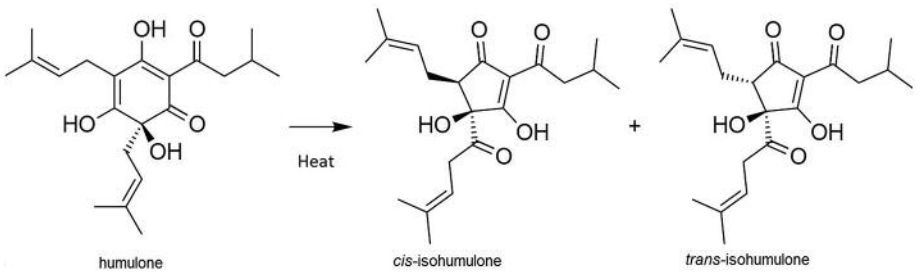
The brewing process: where tradition meets technology



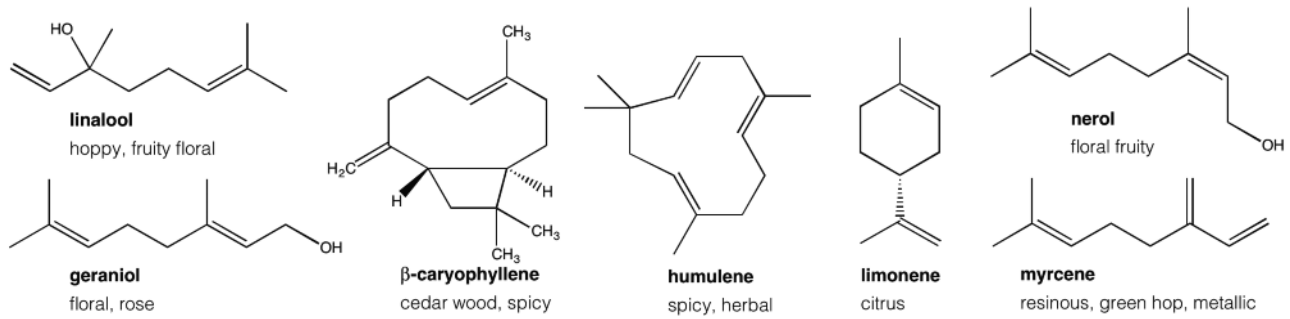
The author and analytical chemist Ian McInerney at the GC-MS.

mixed rapidly with yeast ('pitching') and the cells multiply, take up sugar and produce ethanol, carbon dioxide and energy. Fermenters may be open or closed. The temperature of fermentation determines the rate and amount of the side reactions generating small quantities of hundreds of compounds such as diacetyl, higher alcohols and esters that contribute to the beer's flavour, some desired and others not so. The level of higher alcohols or 'fusel oils' produced are monitored as these compounds can negatively affect flavour. One important family of compounds produced are the esters, which strongly influence the organoleptic properties of beer due to their presence at threshold concentrations, and therefore small changes in concentration have a large impact. The main representatives are ethyl acetate (solventy) and iso-amyl acetate (fruity). Lager beers, fermented at low temperature with bottom-fermenting yeast, usually have low ester concentrations, producing a characteristic clean flavour. Ales, which are fermented at higher temperature with top-fermenting yeast, often have the fruity or flowery notes characteristic of esters. This is a clear example of the diversity of beer styles. Flavours that are appropriate and desirable in one style of beer may be considered defects in another style.

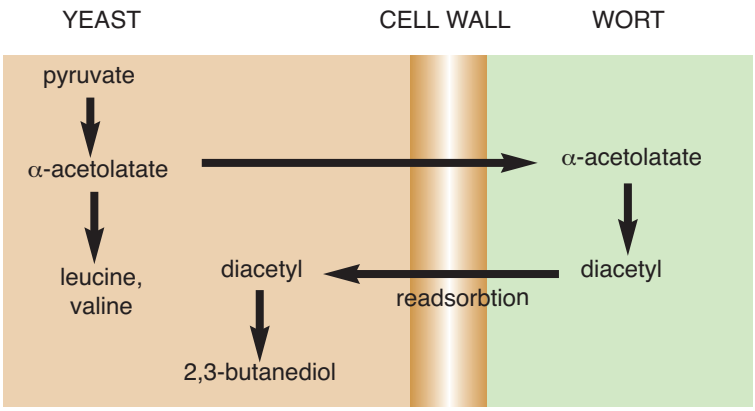
During fermentation, the pH of the beer drops, which inhibits infection. A subsequent maturation period allows time for any residual sugars to be fermented while non-desirable compounds such as aldehydes and



Isomerisation of isohumulone



Key hop aroma compounds



Diacetyl formation and removal by yeast.

sulfur compounds are removed by the carbon dioxide produced. Maturation also serves to degrade diacetyl (2,3-butanedione)) and α-acetolactate (the precursor). Diacetyl and related 2,3-pentanedione are known as vicinal diketones (VDKs). Diacetyl is characterised by a butterscotch aroma and flavour and is considered undesirable in lager beers. VDKs are generated by yeast as it synthesises the amino acids valine and leucine, the reaction accelerated by higher temperature and lower pH. Diacetyl is later converted to 2,3-butanediol by the yeast, which has a lower flavour impact. The presence of sufficient healthy yeast during maturation promotes diacetyl removal. Thus, diacetyl is a key parameter monitored during maturation and it must reach the desired level before chilling and filtration of the matured beer can commence.

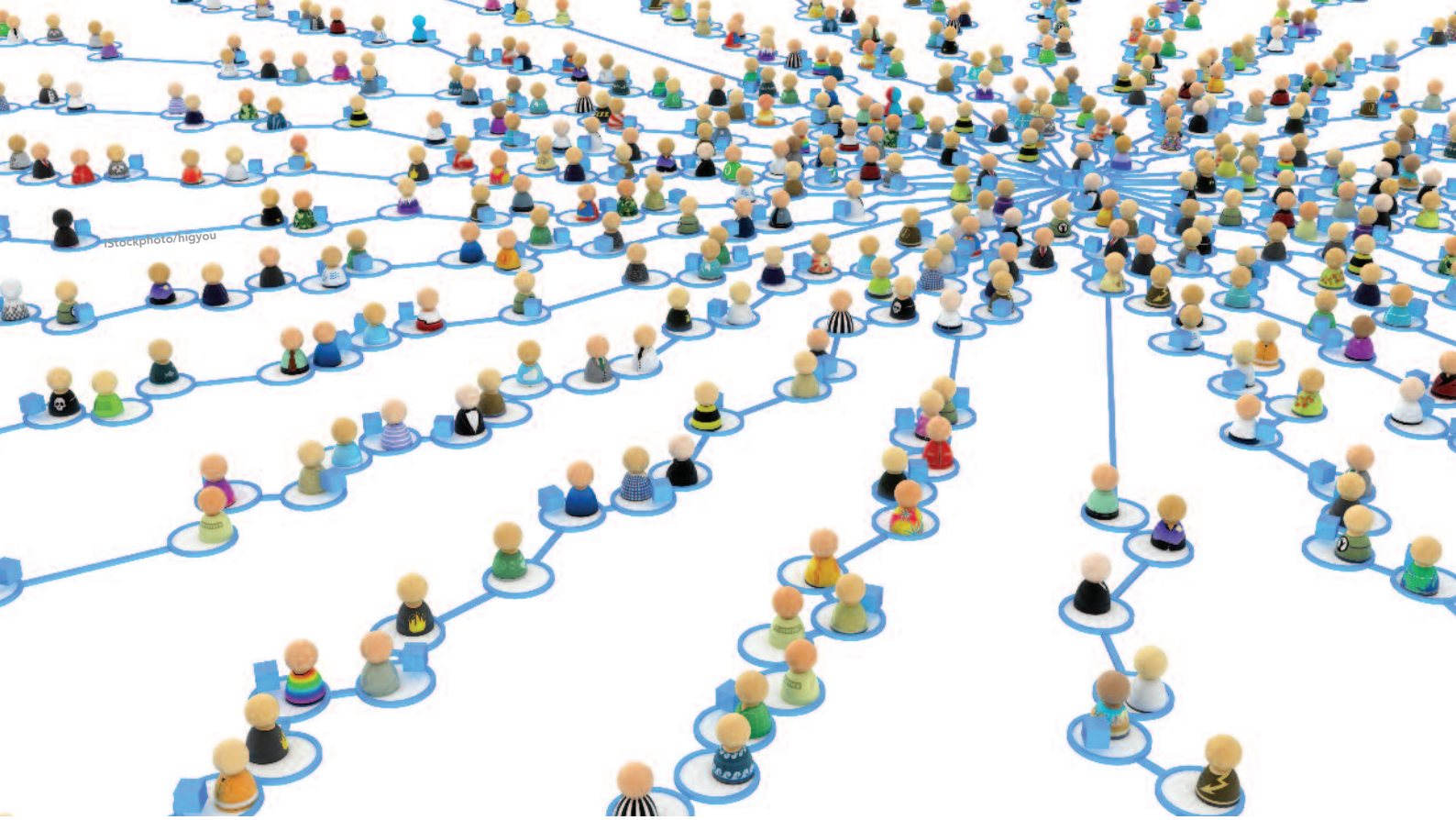
A key challenge for the brewer is the physical and chemical stability of the product. Matured beer is filtered to remove turbidity due to the presence of residual yeast and colloidal haze, and stabilised to promote flavour and foam stability. Final pasteurisation or sterile filtration ensures microbiological stabilisation.

Beer is best consumed fresh with very few exceptions. As consumer preferences shift towards packaged products and away from on-premise consumption, an understanding of the stability of the product and how to control and lengthen its shelf life is essential. The main catalysts for development of aged characteristics are oxygen and temperature. Packaging of beer must be carefully controlled to avoid oxygen pick-up. Initially, chemical reactions develop fruity flavours (fruity 'ribes'), but progress to papery (*trans*-2-nonenal) and waxy characteristics, as bitterness decreases.

As a chemist or microbiologist in brewing all processes are closely monitored from raw materials to packaged products. When I started working as a chemist in brewing, one of the first things I noticed was the high level of analytical technology and complex chemistry that was being investigated. From dissolved gases, flavour and aroma profiles to sugar spectrums, there are always problems to solve, new varieties of hops to discover and processes to improve. Sensory evaluation is required throughout and tasters undergo rigorous sensory training of flavour and aroma attributes with continual assessments and re-familiarisation to maintain accreditation and alignment in scoring. For a brewer, the interdependencies of the various chemicals derived from the natural ingredients, as well as those produced during the different stages, and their subsequent interaction with yeast and each other is what makes brewing so fascinating and technically challenging. Yet, at the end of the day, the sheer variety of delicious, thirst-quenching and wholesome beers that can be produced makes all the effort worthwhile.

The foam head of a lager contributes to its aromatic qualities.

Dr Melinda Christophersen is Analytical Services Manager at Carlton and United Breweries, where she manages the National Laboratory function and support services to the production breweries. The laboratory specialises in flavour and aroma analyses for brewing and beverages.



Citizen science

The New Enlightenment

BY **DAVE SAMMUT**

Riding on the ICT revolution, recruiting public help for research is on the rise, bringing benefits for both scientists and non-scientists.

In the wave of scientific advancement through the Renaissance, through the Enlightenment and extending into the 19th century, independent science was an inspiring movement. Our history is replete with men and women – for example Antoine Lavoisier, Henry Cavendish, Mary Anning and Charles Darwin – whose innate curiosity translated to their direct dedication to scientific endeavour, using whatever resources were available to them at the time.

As the 19th century progressed, the increasing complexity and cost of research saw the process become more institutionalised, and by the 20th century independent science was virtually extinct.

It might be argued (albeit simplistically) that by taking science and sequestering it behind ivy-covered walls, we have done it a disservice. By reserving scientific advancement and recognition largely to an academic elite, perhaps we have disenfranchised a significant portion of the population. In a recent article (May issue, p. 18), I wrote about the direct consequences of poor communications of science prior to the L'Aquila earthquake, which is at least partly a consequence of disparity in understanding and expectation.

In the past 5–10 years, an emerging paradigm – citizen science – is showing promise in bridging the gap. Its participants are different from the earlier independent scientists because the former were scientists first, by inclination and training. By contrast, the participants in the modern citizen science or crowdsourcing projects come from as wide a range of backgrounds as can be imagined.

As with any relatively new field, the terminology is evolving, but a good working definition of citizen science is provided by Dr Philip Roetman of the Australian Citizen Science Association. He describes citizen science as projects where scientists work with the community to conduct research. Roetman emphasises that a good citizen science project must include three key components: research, engagement and education.

Perhaps the biggest driver in the rapid growth of citizen science projects in the 21st century has been computing and communications technology, which has become cheap, rapid and ubiquitous. Information has become democratised, readily available to all, in a manner in which the creation and distribution of information is no longer 'top-down', but much more shared. Roetman notes that the IT revolution has been 'the catalyst for the explosion of citizen science around the world.'

One of the key advantages of citizen science is that it offers the potential to gather significantly greater quantities of data, numerically, spatially and temporally, than would be achievable using paid field staff.

Earlier citizen science projects involved the sharing of computational resources as 'distributed computing', particularly for intensive calculations such as astronomy. However, in Roetman's opinion, this lies at the edge of the field, because it can lack participant engagement. More recent projects such as those within Zooniverse (www.zooniverse.org) provide better examples within astronomy. Among these projects, amateurs were encouraged to assist in laborious tasks such as examining astronomical images for galaxies and undiscovered planets. Moving beyond astronomy, zooniverse has a range of interesting projects, such as 'Old Weather', which asks volunteers to transcribe the weather observations from historical ship logs, valuable data that could help us understand how the climate has changed. Critically, it was found that not only did amateurs enthusiastically participate in the requested work, but they also formed forums in which they interacted with each other to conceive and contribute their own hypotheses to carry the research forward.

A good Australian example is the Explore the SeaFloor project (exploretheseafloor.net.au). Nearly 10 000 citizen scientists are helping to analyse nearly 400 000 images, initially to spot a northern sea urchin species invading Tasmanian waters as part of an investigation into the effects of climate change on local kelp and seaweed ecosystems. Participants are given online tutorials and support to identify urchins in images captured by a robotic underwater vehicle, so that researchers can then assess the depths and locations of the urchins, their number and range. There is feedback on the progress, and the opportunity to win a small prize as reward.

In the National Koala Count, selected and trained citizen scientists are provided with a mobile phone app, and in a ten-day annual program they locate and photograph koalas across a wide geographical distribution. Importantly, these photos are automatically geo-tagged using the phones' GPS location features, so that the data can be verified and analysed for bias (such as a predominance of sightings along roads).

One of the key advantages of citizen science is that it offers the potential to gather significantly greater quantities of data, numerically, spatially and temporally, than would be achievable using paid field staff. It therefore lends itself particularly well to environmental and ecological studies, where the greater sampling also increases the chance of capturing rare or sporadic events.

Ornithology is particularly benefitting from citizen science, drawing on a substantial established resource of enthusiastic hobbyists. However, flora and fauna studies and ecology more generally also gain substantial participation, and it is notable that such studies offer great examples of the multiple models for citizen science. In 'Contributory' models such as the Koala Count, the research is designed and conducted by scientists, with data input from the public. In 'Collaborative' models, the public may help refine the project design, analyse data or disseminate findings. In 'Co-created' models, the public are active in all phases of the research from initiation. This is particularly the case for local ecological projects such as studying contaminated aquatic ecologies.

Across all of these models (most obviously the co-created projects), engagement is a crucial component. This extends beyond the choice of research topics and emphasis to engage the interest of the participants, but also to the use and sharing of the

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Other citizen science projects

If you are interested in the opportunities, practice and successes in Australian Citizen Science, check out the Australian Citizen Science Association website (www.citizenscience.org.au), which will be celebrating the success of its July 2015 inaugural conference.

Links to various projects here and internationally include:

- Streamwatch (bit.ly/1C9LmHb)
- Who's Living on My Land? (bit.ly/1ej29Tj)
- Weather Detective (bit.ly/1MY1Ybo)
- Donating computer downtime (stanford.io/1QzTywn)
- National Geographic citizen science (bit.ly/1GoZ39c)
- scistarter.com

Current citizen science projects in chemistry seem to be relatively scarce. The RACI is spreading the word among chemists by sharing the ABC's call for citizen science project proposals for National Science Week in August (bit.ly/1K8zVqd).

interim and final results. As such, this also shows the importance of good project design and clear definition of goals, because in a local ecological project, for example, the community's emphasis might be on gathering data to support or precipitate early action or intervention, whereas the scientists' emphasis might instead be on longer-term evaluation and/or analysis in a wider context.

The educational component of good community science is similarly important. The integrity of the data captured by citizen scientists is for preference verifiable, and the use of technology has been of significant assistance in this regard. However, proper training and support for citizen scientists is important to minimise observer bias or sampling error, most particularly as the degree of complexity in field work increases.

As noted by Janis Dickinson et al. (*Front. Ecol. Environ.* doi: 10.1890/110236), 'A critical component of this effort is the creation of educational materials, including background information that allows the participants to understand the theory and ideas behind the research, a comprehensible description of the research questions, and clearly described, tested protocols for how to carry out observations.'

This reliance on technology means that citizen science can't simply be assumed as a source of 'free data'. The growing literature on the subject routinely emphasises the importance of good project infrastructure design, including the website for engagement,

... proper training and support for citizen scientists is important to minimise observer bias or sampling error, most particularly as the degree of complexity in field work increases.


iStockphoto/Mouse-ear

Citizen science during times of war

In World War II, decoding of the Enigma machine, one of the notable successes at Bletchley Park, was a massive group project, involving hundreds of codebreakers (contrary to the story in the recent film on the topic), including civilian amateurs who had been recruited through a newspaper competition. Although necessarily secret at the time, this is an example of success in citizen science.

However, citizen science hasn't always been successful. In 1941, actress Hedy Lamarr conceived an approach to protect wireless communications from jamming by 'frequency hopping', synchronised between the transmitter and receiver. The idea was rejected by the US Navy, who told her that she could better serve the war effort by using her status as an actress to sell war bonds. But it was eventually taken up during the Cuban Missile Crisis in 1962, and the idea has served as a basis for the modern spread-spectrum communication technology, used in Bluetooth and other wireless communications. She was inducted into the Inventor's Hall of Fame in 2014.

interaction and easy data entry, and (if appropriate) a mobile phone app for field use.

The establishment costs for a citizen science project may be appreciable, and it is important to factor in the costs of the appropriate support, oversight and engagement/education resources throughout the tenure of the project. However, the answer to this may at least partially lie in the crowdsourcing model itself. Already there are specialist sites through which researchers can pitch their ideas for crowdsourced funding, often in return for project trinkets or outputs.

In an era when academic institutions are under increasing pressure for funding, citizen science may be an opportunity for efficiency in larger projects, particularly where these involve certain types of labour-intensive data input (such as weather observations or image analysis), or expensive field trials. However, more importantly than just project efficiencies, I believe that the inclusion of the wider public in scientific endeavour can only lead to improved outcomes for the communication and general understanding of science more generally.

By participating in the scientific process, community members can become more familiar with the rigours of the scientific method, the importance of repeatable experiment over anecdote, the importance of uncertainty and the timeframes of the development of knowledge. They will surely become more alert to scientific news, and more receptive to informed discourse.

By engaging more directly with the public, we as scientists should also become more adept at explaining our work, more inclusive in our thinking and (perhaps most importantly) better at the art of listening, regarding and adapting to the needs of the community that supports us. After all, that hasn't always been our strong suit.

Dave Sammut FRACI CChem is Principal of DCS Technical, a boutique scientific consultancy, providing services to the Australian and international minerals, waste recycling and general scientific industries.

Your science career

Making a strategic plan

BY **MARGUERITE V. EVANS-GALEA**

iStockphoto/GlobalStock

Our working lives can seem simpler when we have a career plan – a timeline with goals and outcomes. In reality, the path can be far from clear.

Science is undergoing a significant transformation, moving away from the traditional silo-style research laboratories to larger consortia-style 'conglomerates' that operate more like small companies than small businesses. Group leaders have evolved into group coordinators who pull in the funding, sell the product at international meetings, liaise with multiple collaborators and manage several teams led by postdoctoral fellows. Postdocs too have greater responsibilities – supervising students, managing lab administration, balancing budgets, serving on committees, writing papers and leading their own projects – akin to group leaders of small laboratories 20 years ago.

Convergence, collaboration and communication are the latest buzz words. Today's scientists are urged to develop interdisciplinary cross-sector collaborations, attract industry partners, patent and translate their basic discoveries, diversify their funding portfolios, contribute to policy development and effectively communicate their research to politicians and the public.

With all of this change, it can be challenging to plan ahead and know your next move.

There are certain milestones every scientific researcher is expected to achieve – and the bar gets higher every year. There will always be a small percentage of 'high flyers' who go far and above such expectations to dizzying heights, where *Nature* and *Science* papers abound, and funding and awards are plenty.

Failing to make strategic moves, however, can leave you stranded in a holding pattern or 'pushed out' – at any stage. Exciting opportunities can arrive at any time, so how can you best prepare yourself to recognise them?

1 STAY FOCUSED

But don't lose sight of the big picture. Defining your mission will help you to work harder and stay focused on your goal(s). As a graduate student, your goal was to get a PhD. Goals are less black-and-white as we progress, especially in science where the career structure is undefined for most of the research workforce. Our goals can blur to 'doing good science' or 'contributing to the greater good' – still excellent goals, but much less defined. Only a small percentage of researchers will experience the linear academic career path to professor. If that is your primary goal, however, it is important that you keep this in mind during the day-to-day grind of negative data, failed funding applications and rejected manuscripts.

2 TICK BOXES

Consistently. Like your research, develop an 'operational mode' that is reproducible and consistent. Tick the boxes routinely on your list. If you agree to meet with someone, be there. Follow up with emails and stick to deadlines. Know your stuff – and get known for it. Instead of brushing over the abstracts, actually read the literature. Try not to spread yourself too thin. Become a productive recognised expert in your research area. While 'publish or perish' is the academic's mantra, publish quality over quantity. A highly cited paper of significance carries more weight than one that gets lost in the noise. Make first- or senior-author papers your priority, but demonstrate collaborations with 'other author' papers as well. Speak whenever possible – this is great experience and also gets you and your research known. Importantly, be financially responsible. Be strict with your budget and a good steward of funds – public and private. If you perform consistently and develop good habits, you will be reliable – and people will be more forgiving when you need to divert your efforts for unexpected reasons.

iStockphoto/devseren

3 SEEK SUPPORT

Personal and professional. No one is an island. As much as we think we are invincible and can do it all ourselves, this is an unrealistic view. A research career is rewarding, but it is also highly demanding. Do not be afraid to ask for help and guidance. Our family and friends celebrate our successes, commiserate our failures and cheer us on. A team of mentors, including senior investigators and/or peer mentors, can share their experiences and provide advice on different aspects of your research and career. A strong support network, at home and at work, will make the tough times less challenging and enhance your ability to perform at your best.

4 GET CONNECTED

'It's not what you know, it's who you know'. In science, this is a false statement because if you do not know your stuff (see point 2), you will not be respected. This does not mean who you know is unimportant. It is critical to extend your professional network by getting out and meeting people. This can include attending social events in your organisation, sitting next to someone new at the next seminar, speaking with presenters at a poster session or working the room at an international meeting. Social media has added another layer to networking since it is an excellent tool for connecting with people anywhere in the world. Networking enhances our skills, exposes us to new people and professions, and ensures we are always thinking 'outside the box' and ready for opportunities.

5 BUILD A WINNING TEAM

Even a team of one. Develop your leadership style by being the change you want to see. While you do not need to become Gandhi, visionary leaders with a strong ethical compass attract followers in droves. Be consistent in your approach. Praise in public and critique in private – with one critical exception (bit.ly/1M6JVzb). Disrespectful behaviour or commentary should be called out diplomatically and promptly. Fully acknowledge those who did the work. It is common to see a group leader's presentation consistently use the royal 'we'. Particularly in smaller group meetings or in media releases, be inclusive and take the time to say 'well done'. Respect and reward your team with simple acts: check in with them occasionally, ask how you can help move their work forward, spend time with them and say goodbye at the end of the day. Support their professional development – be a leader of leaders.

6 SYNERGISE

Collaboration (bit.ly/1eMPOGM) is at the heart of research. So is healthy competition. With dwindling funds, research has become hyper-competitive. Funding bodies and the public are keen to see researchers collaborating more – young researchers want to work this way too. Collaborating is also a plus in a tight fiscal environment since sharing resources and talent reduces cost. We can encourage collaboration within our own team, but importantly within our own organisation. Do a quick assessment of the research teams on your floor. How many do you know? How many do you collaborate with? Does your team know the other teams – do they know what techniques and equipment they have? Consider co-supervising a student or fellow on a novel project. Cross-fertilise ideas by hosting joint group meetings. These are simple ways to extend your research capacity and network in-house. Beyond your institute, reach out to colleagues with similar over-arching research goals even if they are in a different discipline or field. Find common ground and work towards a shared goal by complementing and utilising each other's expertise.

7 PLAN AHEAD

But be prepared for anything. Develop a strategy to achieve your goals. This will involve breaking things down into smaller bite-size triumphs. When we aim high, we are setting ourselves aspirational goals – and these can seem far off, and on a bad day, unattainable. By mapping things out and setting achievable goals, like planning a long-distance road-trip, these goals become more realistic.

Imagine that you want to build your international profile. Sounds big, but a good way to move towards this goal is to speak at an international meeting. Plan backwards and set realistic achievable goals that lead up to abstract submission and the meeting itself. This could include presenting your research within your institute and seeking feedback on both the quality of your work and your presentation. You are then in a stronger position to develop a high-impact publication. Promote your work through a blog, attend a national meeting and do a 'speaking tour' in different institutes. Speak with your colleagues, collaborators and mentors often – and consider their counsel. Importantly, revise your research plan as you go to increase the quality of your work. Once your paper is ready, it is time to submit your abstract, and click 'oral presentation preferred'. This obviously takes time, but before you know it you will be the invited speaker.

This strategy can be applied to almost any goal. If you want a promotion, then research the requirements for the next level and work at or above this level. If you want to increase your public profile, write a blog every time you publish and share it via social media. Work with your organisation's public relations team to engage positively with the media.

Looking five years ahead is constructive and motivating. Have an individual development plan (http://myidp.sciencecareers.org). Revisit what is important to you both personally and professionally, then map it out – while expecting the unexpected.

8 BUILD RESILIENCE

Let's face it, scientific research can be a roller-coaster ride. You need to have confidence, be persistent and know you can do it. Researchers are typically self-motivated individuals with a hunger for success. Eureka moments are few and far between, and high-achieving researchers can sometimes struggle with these long periods. Find a way to ride the wave. This is different for everybody: keep a 'good moments' folder on your desktop (filled with acceptance letters, awards and friendly emails), practise mindfulness, do kick-boxing or go for a walk. Ensure your inner voice speaks kindly. Imposter syndrome (bit.ly/1BGupnv) and negative self-talk are both common, especially in women, but both are unhelpful. Work on strengthening the skills you need to develop, but have confidence in what you do well.

9 CREATE OPTIONS

We now tell students that a PhD provides excellent training and skills for any career, and the UK Royal Society recently developed guidelines for doctoral student career expectations (bit.ly/1KAz8fM). So we must inherently believe and practise this ourselves. Attend workshops to nurture, update and polish these skills, which include critical-thinking, problem-solving, trouble-shooting, project management, public speaking, leadership and management, finance, writing and debating skills. Develop a teaching philosophy, write a teaching statement and teach or tutor whenever possible. Stay current with your techniques and expertise, and accept opportunities to contribute beyond the research sector. This will develop new skills and networks that may be needed and useful when you least expect.

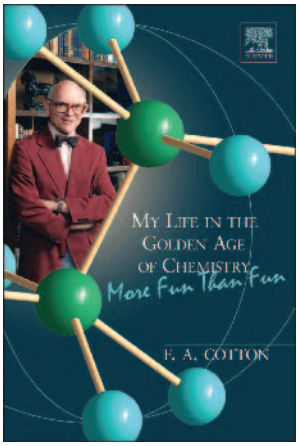
10 HAVE AN EXIT PLAN

Today's scientific research environment requires an element of entrepreneurial savvy. So as with any good business plan, there must be an exit strategy. Have a back-up plan (bit.ly/1dIMIU0). This is where all of the elements in the previous nine points come together to provide you the skills and know-how of transitioning to a different organisation or another professional career (in or out of science) if required, or if desired. We all have limits and over time we get firmer on where those limits lie – on our time, expertise, finances, heart, body and mind. You will know when you are close to reaching your limits. It is up to you what your exit plan looks like and when it needs to engage, but at least look beyond the bench to what else is out there. You don't want to miss any exciting opportunities.

So can you really 'strategically plan' a career in science?

For success in any career, it is perhaps less about having a plan and more about 'being strategic'. Of course timing and luck also play a role. Developing the skills and applying the strategies outline here will strengthen your ability to never run low on fuel, avoid holding patterns and take flight to succeed in science!

Dr Marguerite V. Evans-Galea is at the Bruce Lefroy Centre for Genetic Health Research, Murdoch Childrens Research Institute and the Department of Paediatrics, the University of Melbourne. She is co-founder of Women in Science Australia.



My life in the golden age of chemistry: more fun than fun

Cotton F.A., Elsevier, 2014, hardcover, ISBN 9780128012161, 344 pp. + appendices, $77

Though not an avid reader of autobiographies, I jumped at the opportunity to review *My life in the golden age of chemistry*. Every inorganic chemist over the past 60 years has heard of Frank A. Cotton. I have often referred to his books and papers, but knew little about him, so was eager to learn more.

Frank Albert ('Al') Cotton was one of inorganic chemistry's giants. His research output exceeded 1600 publications in both coordination and organometallic chemistry, he was co-author of the standard textbook on inorganic chemistry for well over two decades (I have three editions) and he authored *Chemical applications of group theory*. He also supervised 119 postgraduate students and nearly 150 postdocs (all listed in the appendices), many of whom went on to distinguished academic positions.

Sadly, Cotton passed away on 20 February 2007, while this book was being prepared, as a result of injuries sustained during a brutal assault while walking near his house.

The timeline of the book traces Cotton's periods at high school, then as an undergraduate in Philadelphia and postgraduate at Harvard, followed by his academic career at MIT and then Texas A&M University.

Cotton arrived at Harvard in 1951 and decided to work with a new assistant professor, Geoffrey Wilkinson. Shortly thereafter, Kealy and Pauson published their seminal paper on the synthesis of bis(cyclopentadienyl)iron(II), now known as ferrocene (so named by Mark Whiting, a postdoc of Robert Woodward). Wilkinson and Woodward's deduction of ferrocene's correct structure and their discovery that E.O. Fischer in Berlin was working in the same area led to a veritable frenzy of activity in the nascent area of organometallic chemistry.

Following his PhD, Cotton transferred to MIT where the years 1955–71 were spent rising from instructor to full professor. He subsequently joined Texas A&M University to occupy the Robert A. Welch Chair.

Part of this book's fascination is that Cotton's career coincided with the renaissance of inorganic chemistry, to which he made fundamental contributions concerning both its synthetic and theoretical aspects. Many of these were 'firsts', such as:

- application of group theory to metal carbonyl compounds
- application of crystal field theory
- X-ray crystallography
- metal–metal bonds and clusters
- dynamic NMR spectroscopy and fluxional molecules
- agnostic interactions.

Cotton knew and interacted with all the big names of the époque; some are mentioned in the book's various sections and others are grouped in a separate chapter near the end (this includes his thoughts on Geoffrey Wilkinson).

The appendices include details about Cotton's publications, postgraduate students and postdoctoral fellows. Particularly germane to the present dire research climate is Appendix D, which contains the text of his presentation for the 1998 Priestly Lecture, entitled 'Science Today – What Follows the Golden Age'. I concur with his sentiments expressed therein, namely that the days of curiosity-driven research are over. Nowadays, the obsession is with applications or usefulness. Funding is tight and controlled by administrators with short-term perspectives. You need look no further than the proliferation of journals to see that everybody is riding on the same few bandwagons. Academics spend much of their time chasing their next grant instead of focusing on and enjoying the chemistry.

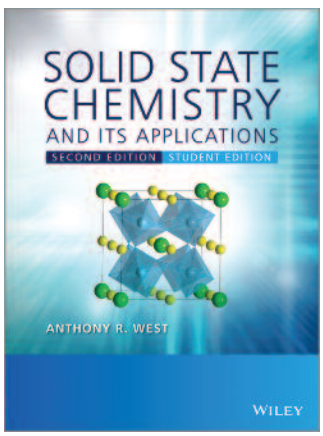
I find the book's title especially apt. The 'golden age' of research is well and truly over, golden in this context meaning the period of generous funding for pure research.

The style is easy to read. Naturally, as Cotton was a chemist, there is a solid amount of chemistry among his reminiscences. This gives him the opportunity to acknowledge those who contributed to the research.

I highly recommend this book without any hesitation to anyone with an interest in inorganic chemistry.

Franz Wimmer FRACI CChem

Solid state chemistry and its applications (student edition)



West A.R., John Wiley and Sons, 2nd edn, 2014, paperback, ISBN 9781119942948, 556 pp., $77.95, ebook $62.99

The first edition of *Solid state chemistry and its applications* by Anthony West appeared in 1985. You can still buy it from the publisher in print-on-demand format for a mere $964.95! This 2014 version is a slimmed-down, student edition of the eponymous book, which is scheduled for re-publication in 2015/2016. Essentially, it is an update on West's related work *Basic solid state chemistry*, first published in September 1988 with a second edition paperback published in May 1999. If you are confused, then so am I. It appears the aim is to meld two titles into one, distinguished by the term 'student edition'. This book is not the 'real deal', but an abbreviated version of the yet-to-appear major work. Either way, it is an impressive work with a wide and up-to-date coverage.

Solid state chemistry is an interesting 'beastie' and a very, very important area both economically and intellectually. Yet,

perhaps because the teaching of chemistry traditionally divides into four main segments (physical, organic, inorganic and analytical), while the solid state spans the field (and so belongs to none), it is probably under-studied, under-appreciated and largely unloved in undergraduate chemistry courses. West advances a cogent argument, slightly tongue-in-cheek, for dividing chemistry into two areas, *molecular* (liquids and gases) and *non-molecular* (solid state). Though probably a good idea, I can't see it happening any time soon. Meanwhile, materials scientists, chemical engineers, geologists and sundry other 'apostate chemists' have largely claimed this section of our noble chemical heritage!

This book is very well written and logically developed. After developing crystal structures and crystal chemistry, then bonding in solids, very interesting sections on synthesis and fabrication of solids and techniques for analysing them ensue. This is all really well done, but if I have to single out one bit for special mention, then the discussion of defects in solids would be it.

The book's concluding chapters concentrate on the electric, magnetic and optical properties of solids, bringing the reader up to speed on areas including superconduction, fibre optics, phosphors, photodetectors and solar cells. Much of this is very topical and directly relevant to our lives today. The explanations are clear and the book is splendidly colour-illustrated. Since crystal structures are usually three dimensional and bits of paper essentially two, the use of colour to illustrate structures is superbly beneficial, although I don't know whether a phase diagram gains all that much. The accompanying website (www.wiley.com/go/west/solidstatechemistrystudent) is a mine of freely available and useful information, including a downloadable CrystalMaker viewer program (Windows and Mac) and a library of 100 or so crystal structures to access and manipulate on your computer. The website also hosts PowerPoint slides of diagrams from the book, answers to questions and so on.

So what is missing? The earlier 'full' edition contained chapters on glass, cement and concrete, refractories and organic solid state chemistry. These topics receive minimal coverage in this edition but will, presumably, be treated in the new 'full' version. They are, after all, major areas of solid state chemistry, albeit perhaps lacking the glitz of the more recent developments discussed.

If you read this book (and it is a very good book), then you will ensure you have a very fine grounding in all the fundamental aspects of the chemistry of solids, plus a good grasp of some of the more recent developments in the field. If you lecture and seek a good book to underpin a course in solid state chemistry, then you have found it! All in all, I recommend this book most highly as a well-thought-out, well-written tome, pitched at undergraduate to postgraduate level, about a fundamentally important area of chemistry and materials science.

R. John Casey FRACI CChem

Open-source lab: how to build your own hardware and reduce research costs

Pearce J.M., Elsevier, 2013, hardback, ISBN 9780124104624, 271 pp., $65

Open-source lab is a very enthusiastic book. Using open-source microcontrollers (the book concentrates on one variety, Arduino, costing US$20-50*) and 3D printing (using a RepRap, or self-replicating rapid prototyper), plus freely available software, author Joshua Pearce claims you can considerably cut research costs. He's probably right. However, if you do decide to DIY, the time spent sourcing the hardware and software you need, fathoming out whether you need to adapt the latter and, if so, *how* (these devices operate on a LINUX platform and a bit of programming knowledge in C++ is also useful), or using your 3D printer to produce bits of hardware, again from downloadable open-source software, could make the economics less favourable. You will probably also need to be a proficient at soldering (and this can take practice too!).

... *Open-source lab* is for enthusiasts who like tinkering about with clever devices, enjoy a bit of programming and know a bit about assembling circuitry.

The notion that there are all these goodies on the internet, freely available to share and develop in an evolutionary way so you can re-share anew with others, is very appealing. The idea of building your own lab-jack, spectrophotometer, reaction vessel or Buchner funnel using software someone else is happy to give you is also very exciting, particularly if you think it will save you money too. But it gets better! The 3D printer is one you have made yourself. The text devotes a lot of effort to describing exactly what parts are needed, where to buy them, and how to assemble your RepRap for about US$600. Intriguingly, the RepRap is capable of making over 50% of its own parts. Well, I guess the moral is 'don't be first', or at least have a friend with a 3D printer.

You can see, I hope, that *Open-source lab* is for enthusiasts who like tinkering about with clever devices, enjoy a bit of programming and know a bit about assembling circuitry. They also quite enjoy soldering components onto circuit boards

*Australian enthusiasts may be more familiar with, for example, Raspberry Pi.

(made with their RepRap?) and are looking for cheap ways to facilitate their work. To build your own RepRap is a great temptation, but it does mean backing your own ability to the tune of US$600 odd. What if it doesn't work? Well, there's plenty of help out there on the internet, but for not a lot more you could buy a commercially available printer (although I have no idea of performance comparisons) which is, more or less, guaranteed to work. If you do want to build your own, then Pearce's text looks like a good guide to follow.

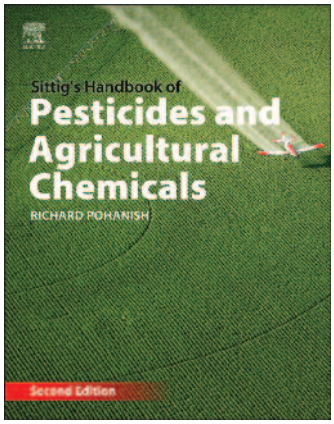
I think you could have a lot of fun with your Arduino, without (even) blowing the petty cash budget. There are lots of interesting bits and bobs you can build, some of which could be very useful in teaching laboratories where you might be looking at 'class sets'. There are big savings to be had in making your own pH meter, potentiostat or fluorimeter (to name three I've seen in action) and getting them to work. While costing labour into the mix might turn your savings ephemeral, if it is fun, then enjoy. In a research environment, the possibilities are limited only by your own imagination. Like the TV program *Yes Minister*, if you want the answer to your problem, then you have only to ask. If you don't know what questions to ask, then I guess you buy this book, grub around the web, buy yourself an Arduino and have a play. It just might pay off big-time.

I can see a role for 3D printing in chemistry, but my vision is limited. It may be more productive to take your ideas to a laboratory craftsman to realise than to reinvent the wheel. Again, if it is fun, then applications will surely follow.

Overall, I enjoyed this book. It is enthusiastic and encouraging and will point you in the right direction if you enjoy tinkering. As a burnt finger survivor, my advice is *festina lente*. Treat the exercise as good fun, but don't expect miracles.

R. John Casey FRACI CChem

Sittig's handbook of pesticides and agricultural chemicals



Pohanish R.P., Elsevier, 2nd edn, 2015, hardcover, ISBN 9781455731480, 973 pp. (including 105 pp. of synonyms and 124 references), $531.95

When I agreed to be a book reviewer for the RACI, I expressed a preference for the traditional hardcopy rather than the new e-book format. Having since received this 2.6 kg reference, perhaps I should have considered my request more carefully! However, despite its relative mass, *Sittig's handbook of pesticides and agricultural chemicals* was certainly easier to 'use' than if it were in electronic format. Being able to thumb quickly to other pesticides and between cross-references is best performed with a hardcopy, rather than the cumbersome scrolling demanded by the 'newer' electronic format.

As an environmental chemist of more than 30 years' experience, it has been a long time since I actually needed to read the 'How to Use this Book' section of a reference work like this. But with a complex reference tool like *Sittig's handbook*, such reading is mandatory. The 14 pages of 'how to use' details the systematic methodology applied to organise and describe the more than 450 pesticide and agricultural chemicals included in the handbook. Some 40 sections describe key information such as chemical name, use type (of which there are 28, including fertiliser and fungicide), CAS number, formula and synonyms (which proves especially useful for pesticides) through to regulatory and advisory agency trigger values, physical properties and, importantly, incompatibilities and storage recommendations. Personal protective equipment (including respirator selection), medical surveillance, first aid,

points of attack on the human body and (finally!) disposal methods round out the range of information sections presented.

As noted in the preface to this second edition (hopefully with no pun intended), the handbook is described as an important tool for 'all who come in contact with pesticides and agricultural chemicals at work or at home'. Sittig reports that the world's top ten pesticides consumed in 2007 (based on mass used) in an agricultural market dominated by the US were the herbicides glyphosate, atrazine, metolachlor-S, acetochlor, 2,4-D and pendimethalin; and the fumigants metam-sodium, dichloropropene, methyl bromide and chloropicrin. Sittig also notes that an estimated 80% of all US pesticide usage in 2007 was in agriculture. Between 2000 and 2007 (the most recent year reported in Sittig for this data), the world's total mass of pesticides consumed was reported to have actually decreased by 8%, from 1.2 billion pounds to 1.1 billion pounds (though still more than 500 000 metric tonnes!), commanding a value of more than US$12.5 billion.

As a reference, *Sittig's handbook of pesticides and agricultural chemicals* has considerable value. I would recommend it to those chemical industry practitioners who need quickly accessible data at their fingertips. Notwithstanding today's electronic database society, such hardcopy references still remain a much more user-friendly and accessible means for complex data inquiry (or am I just getting old?).

Ross McFarland

Online magazine discount

The quality of our monthly magazine *Chemistry in Australia* has never been better thanks to the professionalism of the editorial team, the many regular columnists and guest authors. Unfortunately, the costs of printing and posting hard copies of the magazine have continued to rise and they are placing increasing pressure on the RACI's finances and thus membership fees. Compounding the problem is the increasing trend of advertisers moving away from in-print advertising to online advertising. For these reasons, it has been necessary for the RACI Board to put in place a strategy to address the results of declining advertising income and rising printing and postage costs.

To ensure that the quality of the magazine continues to improve and that all members continue to have access, we have recently established a dedicated website (chemaust.raci.org.au) for *Chemistry in Australia*. All members are encouraged to visit the website to appreciate the work that has gone into making this magazine even more accessible. The online issue is also available earlier than the printed copy.

Many RACI members are already choosing the online version of *Chemistry in Australia* but they have not received any financial incentive for this until now. The Board has decided to introduce a membership fee differential where members taking the online only version of *Chemistry in Australia* will receive a $15 discount from their membership fee from the next renewal cycle.

Those members who wish to continue receiving their hard copy will still be able to do so at the standard member rate.

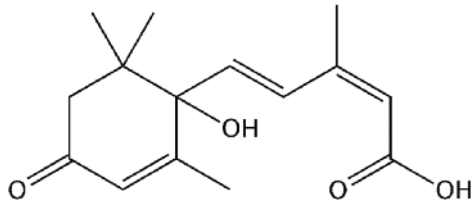
Honorary life members, who pay no subscription, will continue to receive the hard copy free of charge if they wish.

Paul Bernhardt FRACI CChem, RACI President

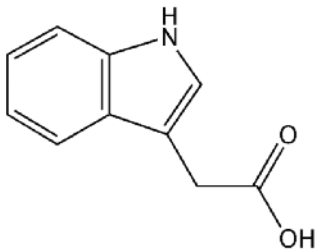
Memoir: Stephen Angyal

Under the auspices of the Australian Academy of Science, a biographical memoir that will be of interest to chemists was published in the latest issue of *Historical Records of Australian Science* (vol. 26, no. 1, pp. 84–91): 'Stephen John Angyal 1914–2012'. Many members will have access to the journal via institutional subscriptions. Others can obtain a pdf copy by contacting the author at johndstevens@yahoo.com. Accompanying the online publication is a complete publication list for this important Australian chemist.

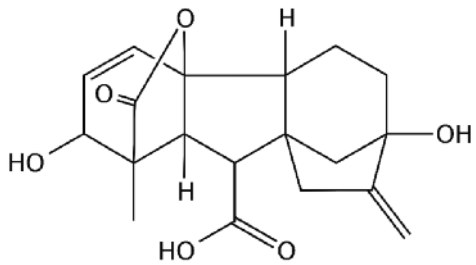
Chemistry happens underground where no one is looking



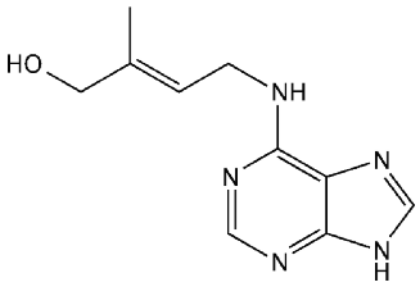
abscisic acid



indole acetic acid



gibberellic acid



zeatin

Since proteins are zwitterions, they have a high affinity for water, so seeds with higher protein content will imbibe more water than those whose major energy-storage compounds are starch or lipids.

This is a true story.

There once a lovely gentleman who was so old that he had been one of the Rats of Tobruk. He was, and still is, a gardener, a storyteller and a poet.

Just before his 100th birthday, he reluctantly moved into a nursing home, where he arranged for one of the raised garden beds in the courtyard to become a vegetable garden, partly for therapy for the other 'sick' people in the home. He planted some seeds and sat in the Perth autumn sun and waited. All his relatives arriving for his birthday celebrations waited with him.

And chemistry happened, down in the soil where no one could see.

Dry seeds are in a state of quiescence, maintaining a minimum (but not zero) level of metabolic activity. Everything is there ready for them grow, but there are also hormones such as abscisic acid that inhibit the initiation of germination. This is just a common example – there is a wide variety of inhibitory compounds in different plants.

When the seed 'feels safe' – usually where it is damp and dark, there is a Goldilocks ('just right') temperature for that particular species, there is adequate oxygen circulation and not too much carbon dioxide – then water penetrates the semipermeable membrane of its hard coat. Since proteins are zwitterions, they have a high affinity for water, so seeds with higher protein content will imbibe more water than those whose major energy-storage compounds are starch or lipids. (This is neither good nor bad, it is just something else that differs between plants.) Once the critical water concentration has been achieved for that particular seed, germination proceeds and the process cannot be turned back.

Water deactivates (or sometimes washes away) the inhibitors and activates other hormones such as gibberellic acid A that modulate chromosomal transcription and initiate some of the enzymes that break down the nutrients stored in the seed into simpler sugars and amino acids. All the other metabolic processes that ensure the development of the seed into a plant are also stimulated. Giberellic acid concentrations typically rise as abscisic acid concentrations fall.

Eventually the hard seed coat ruptures and the little radicle (root) emerges. At the same time, the developing embryo takes in even more water and increases its respiration rate. The root shuns light, and, under the influence of gravity, it moves down through the soil. The gardener could not see this, but from his long experience he knew it was happening. He sat and waited some more.

After this phase, when nutrients are being metabolised and ATP produced like mad, the epicotyl (shoot) pushes out of the ground, moving towards the light and away from the force of gravity – as each generation of primary-school students continues to affirm. Each plant is now an autotrophic organism … the process of 'germination' is complete. Hormones called

auxins, such as indole-3-acetic acid, promote cell growth in certain ways, and cytokinins (such as zeatin) influence cell division and shoot formation in other ways.

But more chemistry needs to happen before the vegetables grow and can be harvested. The first leaves to appear are the cotyledons (seed leaves). Dicotyledons and monocotyledons differ in both physiology and biochemistry, and there are also some plants whose cotyledons stay beneath the earth. But all these fat little leaves have a reserve of partially hydrolysed nutrients, a source of quick energy for the newly growing plant to use before the real leaves develop and can start photosynthesising.

And the day that our gardener's vegetables first showed their beautiful little green shoots to the onlookers was 1 April – my Uncle Colin's 100th birthday. This was not one of his usual practical jokes, nor was it an April Fool's prank played back on him. This really is a true story.

Dr Deidre Tronson FRACI CChem used to be a mad scientist, but is now the Good Little Banksia Lady who, in retirement, is an enthusiastic member of Scientists and Mathematicians in Schools at a local primary school. She has proudly raised three science graduates. She has had separate careers in research and teaching, culminating in a position as part-time senior lecturer at the University of Western Sydney, Hawkesbury campus.

(PS. My previous article (May issue, p. 40) was about plant communication. If you want to follow that up and see that I was not totally talking through my hat, see the set of Smithsonian (US) videos at bit.ly/1cXv1yM.

Uncle Colin next to his raised vegetable garden bed.

Australian inherency – the devil is in the detail

Inherency is a complex issue that often arises in patents relating to the life science technologies. In the appeal decision in Bristol-Myers Squibb Company v. Apotex Pty. Ltd. [2015] FCAFC 2, the issue of whether or not a particular chemical property of a particular drug was inherently disclosed in a prior art document was considered.

Brief background of the invention

Australian Patent No. 2002334413 in the name of Otuska Pharmaceutical Co. Ltd. and assigned to Bristol-Myers Squibb Company (BMS) is titled 'Low hygroscopic aripiprazole drug substance and processes for the preparation thereof'. The claimed invention relates to a chemical compound, generically called aripiprazole, in a crystallised form. Aripiprazole is an atypical antipsychotic drug useful for treating schizophrenia and is the active ingredient in Abilify, which is supplied by BMS Australia. This crystalline form of aripiprazole was shown to have low hygroscopicity. Such an improved form of aripiprazole would allow ease of handling during manufacture, improved shelf life, and improvements in the preparation of accurate dosages.

The patent claim under consideration recites:

> Anhydrous Aripiprazole Crystals B wherein said crystals have low hygroscopicity wherein said low hygroscopicity is a moisture content of 0.40% or less after placing said drug substance for 24 hours in a closed container maintained at a temperature of 60°C and a humidity level of 100%; have a powder x-ray diffraction spectrum which is substantially the same as the following powder x-ray diffraction spectrum shown in Figure 5; have particular infrared absorption bands at 2945, 2812, 1678, 1627, 1448, 1377, 1173, 960 and 779 cm^{-1} on the IR (KBr) spectrum; exhibit an endothermic peak near about 141.5°C in thermogravimetric/differential thermal analysis (heating rate 5°C/min); and exhibit an endothermic peak near about 140.7°C in differential scanning calorimetry (heating rate 5°C/min).

Prior art

One of the prior art documents, which was also discussed in the patent specification, detailed in its examples how one form of anhydrous aripiprazole crystals can be made. This prior art exemplified recrystallisation of aripiprazole from ethanol to form anhydrous aripiprazole as a specific type of crystal, designated as Type-I.

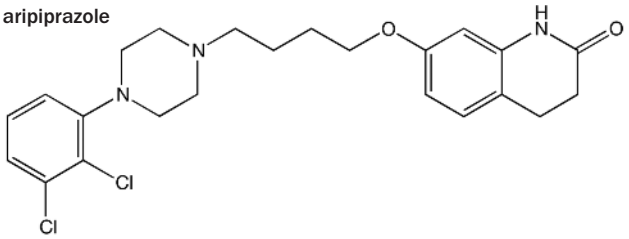
The prior art further exemplified that aripiprazole was subsequently used in pharmaceutical testing on mice, but the document did not state the form of the chemical used.

Apotex's submissions

Apotex made several submissions. These included that:

1 a particular crystalline form (a polymorph) was claimed
2 the crystalline form was not limited to any particular environment
3 the crystalline form was not limited to any particular process of manufacture

aripiprazole



This decision confirms that a document would be considered to inherently disclose a feature if the skilled person would, as a result of following the instructions, inevitably obtain the claimed invention.

4 hygroscopicity is an inherent property of a polymorph and the claim refers to a single unique polymorph
5 the skilled person would remove ethanol as a matter of routine from the crystals when following the procedure described in the prior art.

Inherent disclosure?

Apotex's position was that the prior art disclosed a method of making a crystal form of aripiprazole as claimed in the patent. In order to demonstrate its position, Apotex directed its expert witness to follow the experimental procedure as outlined in Example 1 of the prior art document. Apotex's expert completed the experimental procedure, but he additionally dried the crystals at between 80°C and 100°C overnight in an oven to remove ethanol bound within the crystals of aripiprazole. Ethanol was removed in line with the motivation to prepare aripiprazole suitable for pharmaceutical testing. Apotex's expert's procedure resulted in the formation of the claimed crystals, having the specified hygroscopic property.

BMS similarly instructed its expert witness to follow the prior art method. However, its expert did not dry the crystals formed. The crystals formed by BMS's expert did not have the specified hygroscopic property.

It was submitted by Apotex that a drying step would be a routine step conducted by any chemist at the priority date and would have been done as a matter of course.

A question to be considered by the Court was whether Example 1 of the prior art inherently disclosed the low hygroscopic crystalline form of aripiprazole, when the skilled person followed the instructions, even though a drying step was not disclosed.

What causes the low hygroscopic nature of aripiprazole?

The experts were questioned on the role of the crystal structure on hygroscopicity. The evidence suggested that crystal structure was not the sole contributing factor and that other physical properties, such as crystal size and the surface properties of the crystal, also played a role. BMS's evidence suggested that a specific drying step, as disclosed in the patent, resulted in modifying the physical characteristics of the crystal surface, which in turn, resulted in reduced hygroscopicity. This reasoning was approved by the Court and it agreed that the unique surface properties of the crystal structure were imparted as a result of the drying step.

The evidence also showed that a broad range of drying procedures was available as options for removing ethanol. Since Apotex failed to show that a different drying step to that conducted by its expert would also result in crystals with reduced hygroscopicity, it did not show that any drying step would result in the claimed hygroscopic property. Therefore, the Full Court determined that the skilled person, in following the experimental procedure, might have obtained the claimed crystals serendipitously, but it was equally possible that they would have obtained conventional crystals without the reduced hygroscopicity. Since there were no clear and unmistakable directions to do what the patentee claimed to have invented, the Court considered that the prior art did not inherently disclose the low hygroscopic feature.

Take-home message

This decision confirms that a document would be considered to inherently disclose a feature if the skilled person would, as a result of following the instructions, inevitably obtain the claimed invention. Although Apotex had shown that drying a compound was a routine step, it did not show that other drying methods would result in aripiprazole having low hygroscopicity.

Elizabeth Houlihan FRACI CChem (elizabeth@houlihan2.com) and **Jim Y. Onishi** (jim@houlihan2.com) are patent attorneys at Houlihan^2, Patent & Trade Mark Attorneys.

Biodiesel and by-products – glycerine

In a chemical process, if by-products have no or little value, then processes should be refined to minimise their production and eliminate waste disposal costs. For many processes, by-products are a significant outcome that cannot be eliminated. The essence of many a successful chemical business is maximising the sales revenue from such by-products.

The impact of the value of by-products is well illustrated in the production of biodiesel from vegetable oils and fats. Biodiesel is a mixture of fatty acid methyl esters (FAME) produced by the trans-esterification of oils and fats using methanol. The by-product is glycerine (glycerol).

Regional agricultural considerations tend to determine the source of FAME. In the US, soybean is a major source, in Europe it is rape (canola) and in our region palm oil is a major feedstock. Many other seeds can be used if available. Another source in our region is tallow (beef and lamb fat) produced from meatworks.

From seeds, the first step in the process is milling (crushing of the seed) to produce the vegetable oil and a by-product meal used as cattle feed. So at this first stage, the ultimate production cost of the biodiesel depends on three variables – the cost of the seeds (farm economics, seasonal influences), the value of the vegetable oil and its alternative use as a foodstuff, and the value of cattle feed. Clearly the processing margin at the mill will influence the price paid for the vegetable oil for biodiesel.

Oils and fats are triglyceride esters of fatty acids. Although many enthusiasts use these oils as diesel fuel, the high viscosity and contaminants make them unsuitable for use as quality biodiesel. The oil produced is trans-esterified with methanol to produce FAME and glycerine. The process removes impurities and reduces the viscosity, making the produced FAME a suitable diesel fuel, especially when blended with conventional diesel to produce a blend such as B5 or B20 (5% and 20% blend of biodiesel and petroleum diesel respectively). Higher blends are possible but the use of high levels of FAME is generally not recommended by vehicle manufacturers without changes to engine components such as pumps and injectors.

The inputs are oil and methanol and the outputs are FAME and crude glycerine. Methanol prices are sometimes quite volatile and this volatility has to be accommodated in the process economics.

Refined glycerine has a large demand in food, cosmetics and other high-added-value industries. There are several grades, with some grades such as kosher being exclusively produced from vegetable oils. In the early days of biodiesel production, glycerine was a by-product of quite significant value. However, as the biodiesel industry has expanded, so has the production of glycerine and this has seen the relative price of glycerine fall.

Palm oil is derived from the fruit pulp of oil palms, predominantly *Elaeis guineensis*.

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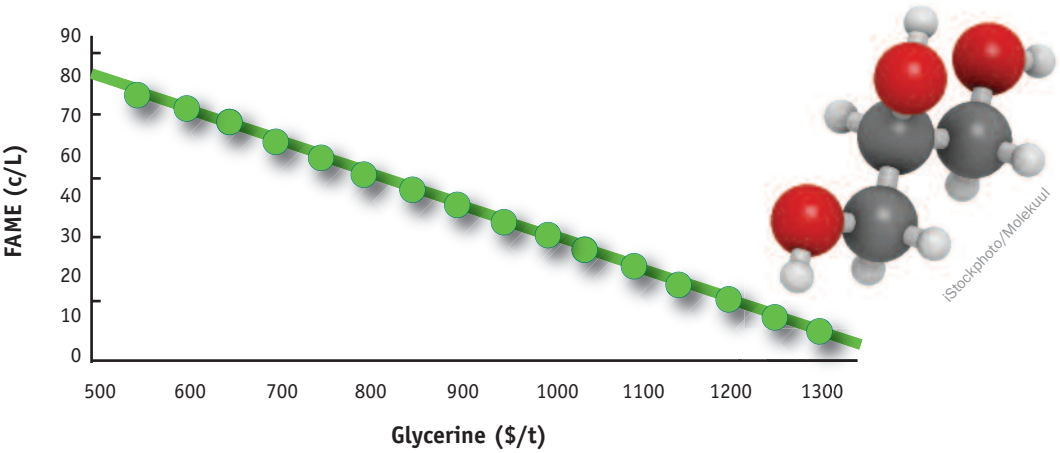


Effect of price of glycerine on price of FAME.

The declining profit of biofuel operations in the face of declining glycerine prices and the glut of glycerine on the market has sparked research into alternative uses for glycerine.

The fall in the price of glycerine has had a major impact on the production cost of FAME. This is illustrated in the graph, which takes account only of the feedstock (in this case canola oil at $500/t) and methanol costs ($300/t); operating and capital costs are not included.

This graph illustrates the dramatic dependence of the cost of biodiesel production on the achieved value of the by-product glycerine. At current oil prices, diesel is traded at about 50c/L, which requires crude glycerine prices in excess of $800/t compared to recent prices below $500/t.

The declining profit of biofuel operations in the face of declining glycerine prices and the glut of glycerine on the market has sparked research into alternative uses for glycerine. One is the selective hydrogenation to produce 1,2-propanediol, which is a highly valued product produced from propylene oxide. This is having some impact on the 1,2-propanediol market but it is not a perfect substitute, with preference for some uses still favouring the relatively expensive propylene oxide route. Another idea is the selective hydrogenation to 1,3-propanediol, another highly valued chemical.

A consequence of poor FAME economics is the promotion of an alternative approach to biodiesel, so-called 'green' diesel. In this process, the vegetable oil or tallow is treated at high temperature and pressure with hydrogen over a catalyst to hydrogenate and decarboxylate the glycerol esters to produce paraffins and propane. For example, a C18 fatty acid ester produces a mix of C17 and C18 paraffins and propane. These products are completely compatible with mineral diesel and LPG (propane). This route avoids the compatibility issues of FAME and conventional diesel as well as avoiding the production of crude glycerine.

Green diesel can be produced in small-scale plants producing 100% biofuel for blending or use. It can also (with a bit of adaption) be utilised in a conventional refinery hydro-treater, producing diesel and directly produce a blend of biodiesel and mineral diesel; for example, B5 can be produced by hydro-treating conventional gas-oil with 5% vegetable oil or tallow added to the hydro-treater feed. Using a conventional oil refinery process unit avoids the capital cost of building and operating a bio-fuel facility. The economics are almost entirely determined by the price of the vegetable oil relative to that of diesel and LPG.

This route can also be used to produce bio-jet fuel by choosing oils with high C14 and C15 ester content such as coconut oil.

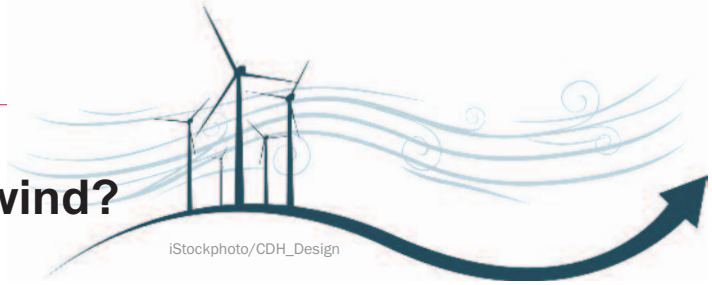
The concept of green diesel has gone further to the concept of bio-refinery in which vegetable oils and tallow are hydro-treated to produce 100% bio-jet, biodiesel and bio-LPG.

As various jurisdictions legislate for the inclusion of more renewable fuel in the conventional fuel mix, the concept of a bio-refinery is of increasing interest. For example, the Italian company ENI has converted its refinery near Venice to produce more that 300 000 t/year of 100% renewable fuel.

The major downside for this process is the source of the feedstock. The preferred feed (because of relatively low price as a consequence of high crop yields) is palm oil. This is now being shipped in large parcels to bio-refineries in Europe and around the region for the production of bio-fuels so as to achieve government-legislated mandates. This is adding considerably to the demand for palm oil, leading to the destruction of tropical rain forests for increased oil production.

Duncan Seddon FRACI CChem is a consultant to coal, oil, gas and chemicals industries specialising in adding value to natural resources. He is indebted to CRU International Limited (www.crugroup.com) for market information on bauxite, alumina, anode carbon and metal prices.

Is the answer blowin' in the wind?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Renewable energy and energy policy have been in the news lately. Just before writing this, the federal government and opposition were engaged in negotiations over the revised Renewable Energy Target (RET). The RET was intended to, among other things, encourage the generation of electricity from renewable resources and reduce greenhouse gas emissions. However, the negotiations have refocused to a reduction of the target. Once again, the 'policy' debate has been mainly about a very large number, which can't be comprehended by most people, and is measured in units that many in the media seem unable to get right.

The RET was adjusted because, although the previous GWh number had been set at 20% of anticipated electricity production in 2020, reduced electricity demand meant that the previous figure would likely be 23% of production. For some reason this was not acceptable to the federal government. Perhaps this was due to the perception that renewable energy was causing an increase in electricity prices. However, this perception is countered by the findings of the RET Review, which concluded that the RET was exerting some downward pressure on wholesale electricity prices. This begs the question of why the government wasn't happy with the previous target.

However, just when it seemed that an agreement was possible to allow the new RET to be implemented, the idea was floated that electricity generation from burning wastes from native forest logging should be included in the amount of electricity generated to count towards meeting the target. While the timber industry has long used wastes and off-cuts to provide heat and electricity for its own operations, it would be hard to argue that native forests are a renewable resource. Certainly, plantation timber is renewable within a period of less than about 20 years, but selectively harvesting a native forest takes out the largest trees that have been growing for some 30 years or more, and these can't be 'renewed' within an economic time period. In any case, the amount of electricity generated this way is likely to be small. The electricity industry recognised in the late 1800s that coal was a better fuel than wood.

Recent media debate has also cast light on the performance of the coal-fired electricity industry. Newspaper reports have commented that in the absence of a price on CO_2 emissions, the proportion of electricity generated by burning brown coal has increased, mainly at the expense of black coal. Almost perversely, brown coal, which has a lower energy density than black, and which we probably couldn't give away, has an advantage in the domestic market. The explanation is that black coal is priced according to the world price, and local buyers have to compete with export customers. To someone like me who has been exposed to the process industries, this is a contradiction. But life can be stranger than fiction.

Almost perversely, brown coal, which has a lower energy density than black, and which we probably couldn't give away, has an advantage in the domestic market.

Turning our attention back to renewables, recent debates in the press have discussed the role of solar-generated electricity. Several state-based schemes provided generous feed-in tariffs to encourage the uptake of solar power, and the industry has blossomed. One school of thought says that subsidies spent on these schemes have resulted in very expensive CO_2 abatement. For example, I have heard that Germany spent some €70 billion subsidising solar power and yet replaced only 1.5% of their generating capacity. I thought it was bad news, personally, to read that all mainland capitals, *except* Melbourne, are well placed for household solar electricity. That may be the case, but I have recently established that at home we are on track to achieve the seven-year payback we were told to expect when we installed solar panels in 2011.

In contrast to the federal government, the New South Wales and Victorian state governments have been keen to promote the benefits of emerging battery technology to boost solar generation. Both governments have been talking up the Tesla battery from the US, produced by the maker of electric cars of the same name. The Powerwall battery is just that, a unit about the size of a suitcase mounted on the outside of a house. However, the governments' timing seems to be unfortunate. Within days of the Victorian pronouncements on this topic, an online discussion group for environmental professionals carried a report that even Tesla considered the Powerwall not up to the task for which the local ministers were advocating. It seems that Tesla's domestic units are intended mainly as back-up to the grid, and are designed for only about 50 charge cycles a year. They aren't yet up to the task of daily charge and discharge needed by household solar installations. Back to the drawing board for the ministers.

All of this focus on renewable energy and battery storage reminded me of a neighbour when we arrived in Melbourne in 1992. He had a small wind turbine above his house, and the basement was filled with batteries. He installed this unit to supply all his electricity needs because, when he built his house, it was going to cost him nearly as much to connect to the grid as to install the turbine and batteries. It sounds like there is really is nothing new under the sun (or in the wind).

Paul Moritz MRACI CChem (Paul.Moritz@douglaspartners.com.au) is a Principal Contaminated Land Consultant with Douglas Partners, and an EPA-appointed Environmental Auditor in Victoria, New South Wales and the Northern Territory. He acknowledges the assistance of his colleague, Alan Lee, in the preparation of this article.

Astringency and phenolic conformations

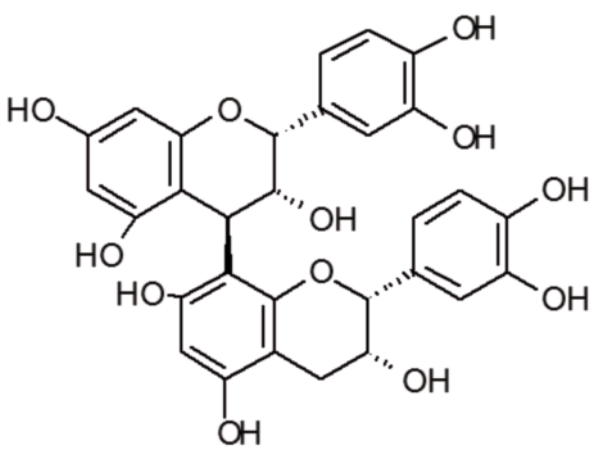
A vast body of research has attempted to identify the compounds in a food or beverage that contribute to the astringent response. Consumers generally do not like highly astringent beverages: adding milk to tea is a good example of 'softening' the mouthfeel. On the other hand, polyphenolic compounds are often claimed to show health-promoting effects. Perhaps the rhesus monkey that chooses food based on its phenolic content has a better understanding of astringent response than we do and I wonder if a new fad, the rhesus diet, could be established!

In wine research, two general strategies have been used to try and understand what compounds contribute to astringency. One involves adding a compound to a wine or model wine and then assessing the change in astringency. This process is slow, simply due to the large number of compounds that are involved, but it does generate a lot of data for doctoral programs.

The second strategy involves size fractionation of the wine followed by tasting the reconstituted fractions or taste dilution analysis of the fractions. Taste dilution analysis involves sequential dilution of the fractions, each sub-fraction being tasted to identify which sub-fraction contains the most astringent compounds. Chemical analysis of each fraction or sub-fraction is then used to identify compounds that appear to contribute to the astringent response. The limitation to this second approach is that the tasting is no longer occurring in the wine matrix so that any important molecular interactions will be missing.

Not surprisingly, the two approaches give different results. The 'compound addition' method has shown that the monomeric flavan-3-ols, (+)-catechin and (-)-epicatechin, contribute to astringency. This has not been observed in wine fractionation studies. Rather, hydroxybenzoic acids and hydroxycinammic acids together with polymeric compounds have been seen to be important. More detail on these studies is set out in our review on red wine astringency (*Trends Food Sci. Nutr.* 2012, vol 27, pp. 25–36).

Procyanidin dimer B2
(−)-Epicatechin-(4β→8)-(−)-epicatechin



In addition to perturbation of the wine matrix in these experimental approaches, the fascinating conformational chemistry of phenolic compounds makes astringency assessment difficult. The flavan-3-ols readily polymerise through the C4 to C8 or C4 to C6 positions. The dimer shown here is (−)-epicatechin-(4β→8)-(−)-epicatechin, usually abbreviated to procyanidin B2. There are three other C4–C8 isomers, depending on the arrangement of catechin and epicatechin in the dimer. Further, there are four C4–C6 isomers, giving B1 to B8, all of which have the same molecular mass, which makes identifying them in a wine matrix a challenge.

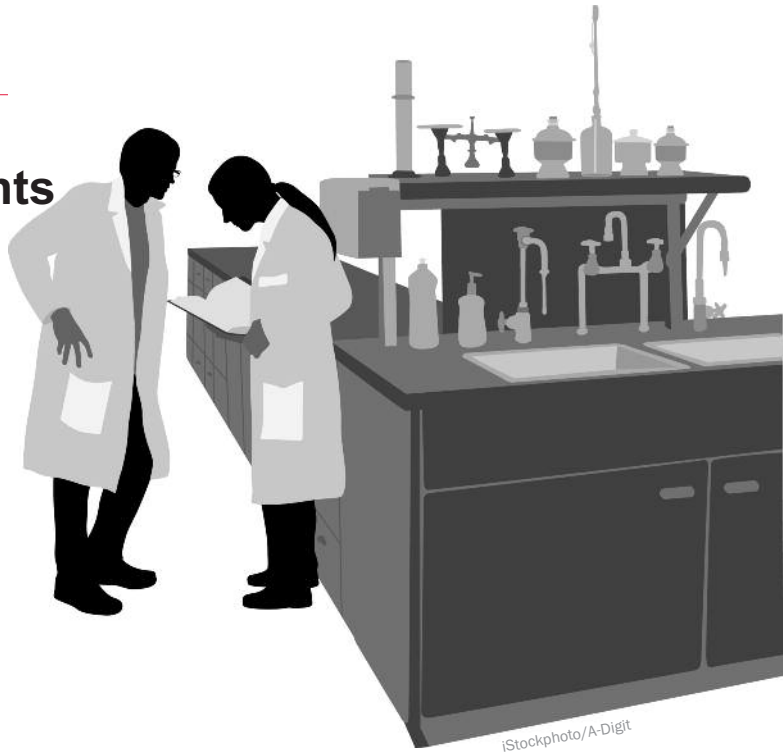
Stereoselective synthesis allows some isomers to be prepared. Isabelle Pianet and her team from the University of Bordeaux have looked at the dimers B1 to B4 as well as the trimer C2 (three catechins linked C4 to C8) using diffusional NMR (DOSY). Aggregation or self-association of the flavan-3-ol monomers is efficient, much more than for the procyanidin dimers. This high affinity for monomer self-association was supported by dynamic simulations (see *Langmuir* 2008, vol. 24, pp. 11 027–35). These results imply that the monomers are more likely to form hazes or precipitates and not interact with proteins.

To assess the potential interaction between procyanidins and proteins, the interaction between B1 to B4 and C2 with the proline-rich peptide, $IB7_{14}$ (14 amino acid residues), was examined by the Bordeaux team using DOSY and other analytical techniques. C2 was found to have the highest affinity for $IB7_{14}$, followed by B2 > B4 > B1 > B3 (Carla et al., *FASEB J.* 2010, vol. 24, pp. 4281–90). Extending this work, the Bordeaux group (*Planta Med.* 2011, vol. 77, pp. 1116–22) found that the procyanidin's conformation played a critical role. One can imagine the dimer to be like a pair of tweezers, hinged at the C4–C8 bond. The lowest energy conformation for B2 is an open tweezer, while B3 is closed. The open-tweezer structure allows binding to two proline-rich peptides, whereas the closed structure, with a significant degree of intramolecular binding, interacts with only one proline-rich peptide.

While the implications of these results for astringency assessment are still to be evaluated, it is now clear that there is highly specific chemistry affecting the tannin-protein response. I confess that I would never have imagined isomer and conformer chemistry to be so exciting!

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.

Of thee I sing (part 1): students



As the new semester begins, public transport gets clogged and carparks on campus disappear. As we drown in the deluge of students, I often parry my colleagues' complaints about the crowds with: 'Yeah, this would be a great university if it wasn't for all the students.'

The truth is that I consider students an essential part of the life of an academic researcher. If funding is the lifeblood that keeps the group running, then students are the heart through which this blood pumps. So although many of my colleagues look at taking on part-time students as a hindrance to their workflow, I welcome the challenge of training up a newbie and enjoy watching them grow into a competent researcher. I'd like to talk about a few of my students here, just to illustrate the great experiences I've had and all we've accomplished together.

The first student I mentored was Christian. Christian hailed from Germany and I designed a perfect research project for him. It was simple, but he could work on it independently and it would generate useful data for the group. My supervisor insisted that we dial down the skill level required for the project because we're never sure of the ability of short-term visitors. Christian turned out to be amazing in the lab. He quickly worked out that my idea was less solid than I'd originally thought and he had a much better one. His idea turned out to be so good, that a postdoc took over the project and we eventually published the paper in the *Journal of the American Chemical Society* (no small feat for a simple visiting student).

After Christian came Hedi. Hedi was from Tunisia and hadn't really spent any time in a chemistry lab so I couldn't expect Christian-level work from him. I designed a project for him based on polymerisation kinetics with an emphasis on ^{1}H NMR analysis. I spent the first few weeks teaching him polymerisation methodology, how to operate the NMR spectrometer and interpret the data. Then I left him to his devices. Hedi promptly went and broke his foot that weekend playing football. So all those NMR spectra that I wanted him to run would no longer be run (the NMR spectrometer is a 10-minute walk from the lab). I wanted to re-design the project, but Hedi would have nothing of it. He insisted on working and corralled me into walking to the spectrometer for him. In the end, he completed his project and we published the work this year after running 121 ^{1}H NMR spectra!

At the same time as I was running NMR spectra for Hedi, I also started mentoring Seb. Seb came from Italy, looked at the project I proposed and suggested we do something entirely different. I wanted him to work on polymer functionalisation reactions, but he said he'd rather work with cancer cells. So together we learned about culturing cells and measuring their properties using flow cytometry. As Seb analysed the cells, more questions were raised so we planned more and more experiments, which he ran with ever-increasing adroitness. Every time we planned an experiment, he ended up analysing 690 000 cells. Eventually we analysed enough cells to temper even Seb's seemingly boundless enthusiasm. He collapsed into a seat in the office and begged me never to plan another experiment again. I agreed and he breathed an audible sigh of relief.

If funding is the lifeblood that keeps the group running, then students are the heart through which this blood pumps.

Despite my apparent taskmaster-like attitude, Seb still pops into my office every now and then to find someone to grab a beer with. He even gave a glowing report of me as a supervisor to Muriel (a Swiss-German). Muriel took over where Seb had left off. She scoured the literature, optimised procedures, planned experiments and executed them flawlessly (Swiss precision and German efficiency, I guess). Five months after she saw her first cell (and her first Erlenmeyer flask) she was engaged in a vigorous debate with my supervisor, gallantly defending her results. That and the 1 350 000 cells she analysed earned her the best grade in the class.

I could go on about the great students I've encountered, like Michael (who did about four times the amount of work I wanted him to do while sorting out his future internship at MIT), or Henri (the second-year student who was so pleased with his two weeks in the lab that he begged to come in in his spare time and continue his tinkering), or Joan (who somehow managed to make amazing polymer brushes while learning Spanish so that he could volunteer in Ecuador). But at this stage you get the point: students have absolutely been the highlights of my research career and I have been in great universities *because* of them.

Decapilated oat coleoptile

When I was a third-year student in the late 1950s, Professor 'Old Bill' Davies lectured on heterocyclic chemistry. It was mostly about the syntheses of nitrogen heterocycles that came with the names of their authors – pyrroles by Knorr, isoquinolines by Bischler–Napierelski and by Pictet and Spengler, and indoles by Fischer (yes, it was Emil, he of the sugars). Curiously, none of these heroes is memorialised in *Organic chemistry: the name game* (Nickon and Silversmith, 1987), but the names dot the pages of innumerable texts on heterocyclic chemistry.

Davies never lost his strong Yorkshire accent, nor the limp that derived from some childhood illness, but it was his lecture performance that sticks most strongly in my memory. Drawing structures on the blackboard, he would speak about the chemical change taking place in the next step, pull down the sleeve of his jacket and use it to erase part of the structure, and then chalk in the new atoms. It made note-taking a difficult task, which most of us managed by scribbling in the new bit and leaving space so that the whole structure could be written in later. Good revision, I suppose, although I didn't think of it that way at that time.

Davies spent quite a while on indole chemistry and in particular on indole-3-acetic acid and its action as a plant hormone, showing pictures of growing plants and speaking of what I heard as 'decapilated oat coleoptile'. 'Coleoptile' was clearly a technical term but since I judged that the material was probably not examinable, I never looked up its meaning. Likewise, I accepted that 'decapilated' might have meant some kind of trimming of the plant tissue. When I came to write this Letter I found that what he said was probably 'decapitated' so I was more-or-less correct, albeit uninformed. And as for the coleoptile, it is the sheath covering the growing shoot.

What none of us students realised at the time, and what I have only recently discovered, is that Davies had done research in this field, in conjunction with his student Philip Hudson, and George Atkins, a tutor in Philosophy and 'researcher in Botany' at the university. Their work was reported in a short note to *Nature* in 1936 and a full paper the following year in *Annals of Botany*. In the few years before and after 1930, Kögl, Erxleben and Haagen-Smit had extracted from human urine three substances that exhibited plant growth-promoting activity and were known generically as auxins. The most potent of them, heteroauxin, was shown to be identical with indole-3-acetic acid. This started a hunt for other auxins, and in 1933 others reported that the juice of oranges and lemons promoted plant growth in oats (*Avena sativa*) and speculated that ascorbic acid (vitamin C) might be the active principle. Experiments over the next few years produced mixed results, and that is where the Davies team began their work.

Davies and his collaborators found that indole-3-acetic acid promoted root growth in willow shoots. Ascorbic acid in low concentrations did, too, but stronger solutions caused retardation, and that was puzzling. The researchers purchased their ascorbic acid but synthesised the indoles they used in their experiments. Indole-3-acetic acid was synthesised from the anion of indole by reacting it with chloracetonitrile before hydrolysing the nitrile group to COOH. The Fischer indole synthesis was used to prepare indole-3-propionic acid, as well as the corresponding malonic acid and 3-ethylindole. All were tested as very dilute aqueous solutions but olive oil was used as solvent for more concentrated solutions. In a series of experiments, the substances were applied to one side of the petioles (stalks connecting leaf blades to the stems) of tomatoes and castor-oil plants (*Ricinus communis*). Only for indole acetic and propionic acids was the petiole 'curved readily downwards' – that is, gave positive results. Ascorbic acid was ineffective but the researchers went to extraordinary lengths to confirm this negative result. As well as simply wiping the solution onto the petiole, they tried with small pads of cotton wool soaked in the test solution and renewed frequently. Worrying that the ascorbic acid might have been destroyed by aerial oxidation, they tried excluding air by coating the pads with paraffin wax, and even administered ascorbic acid mixed with adrenalin, which was expected to preferentially absorb oxygen. It was possible, they concluded, that there was no effect or, alternatively, that translocation of ascorbic acid was so rapid that differential action could not be observed.

Auxin A and auxin B ... belong to a series of natural product structures ... that were fantasies of someone's imagination.

Auxin A and auxin B were supposed to be cyclopentenes with short, hydroxylated side chains, but they probably never existed. Instead, they belong to a series of natural product structures identified in Kögl's laboratory that were fantasies of someone's imagination. It is widely believed that Erxleben produced the evidence confirming Kögl's hunches and that he uncritically accepted these 'proofs' of structure.

Davies' co-workers subsequently went on to interesting careers. After wartime work for the defence industries, Hudson worked in chemical industry and spent some years with Monsanto in Melbourne. Atkins, who already had his MA at the time of the plant research, went on to earn his MSc, then worked at Defence Standards Laboratories in Maribyrnong as a mycologist investigating attack on fabrics by a range of microorganisms and fungi.

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.

Southern Highlands Conference on Heterocyclic Chemistry
30 August – 1 September 2015, Bowral, NSW
www.chemistry.unsw.edu.au/news-events/latest-news/conferences-and-workshops/2015-southern-highlands-conference-heterocyclic

13th Conference on Laser Ablation (COLA-2015)
31 August – 4 September 2015, Cairns, Qld
http://cola2015.org

13th Annual UNESCO/IUPAC Workshop and Conference on Macromolecules and Materials
7–10 September 2015, Port Elizabeth, South Africa
http://academic.sun.ac.za/unesco

22nd International Clean Air and Environment Conference
20–23 September 2015, Melbourne, Vic.
http://casanz2015.com

4th Federation of Asian Polymer Societies – International Polymer Congress
5–8 October 2015, Kuala Lumpur, Malaysia
www.4faps-ipc.org.my

2015 Sustainable Industrial Processing Summit and Exhibition
9 October 2015, Turkey
www.flogen.org/sips2015

Pacifichem 2015
15–20 December 2015, Honolulu, Hawaii
www.pacifichem.org

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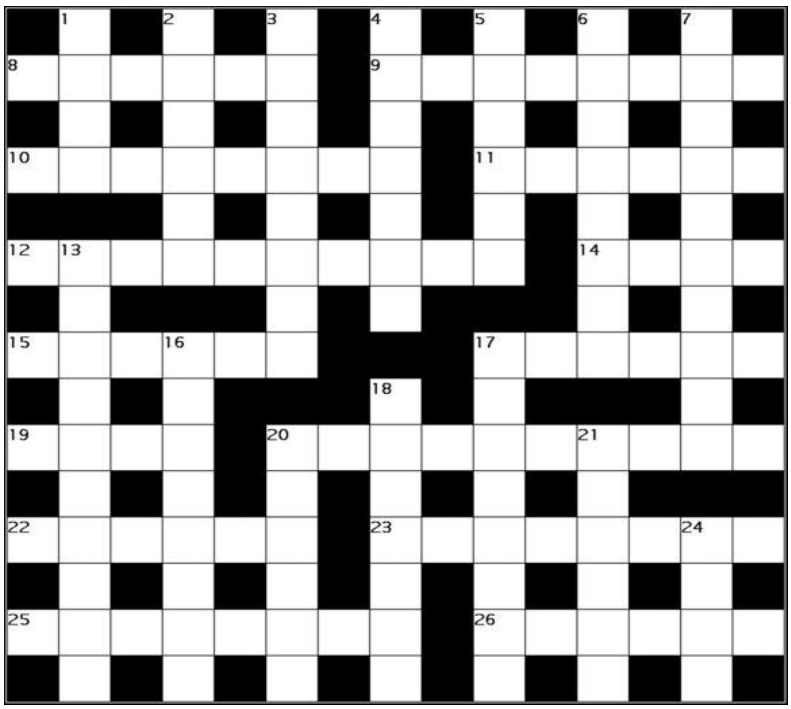

Across

8 First and last, exact heavy negligence for compound. (6)
9 Giving off gem tin it made. (8)
10 Pertinent to horizontal software? (8)
11 11 and 16 subjected to hatred. (6)
12 Do aluminium practical. (10)
14 Taking interest in, being indebted. (4)
15 Saturated 8 Across beneath structure with no boron. (6)
17 Lymphocyte immune globulin initiates and forms a complex. (6)
19 50% of the all AFL seconds. (4)
20 Production facilities with reference to great duds. (10)
22 Indicates scores. (6)
23 Remove charge discharge. (8)
25 Unconnected specific. (8)
26 Tight limit. (6)

Down

1 Stage walk. (4)
2 Recurrent 639636. (6)
3 Exact detail about it. (8)
4 It causes reactions about a bloke. (7)
5 Oil Spooner's eye valley. (6)
6 Looking at hitting the books. (8)
7 Dance cut-in riot by which an electromotive force is created. (10)
13 Lutetium comes back with cast iron breaking up above 20 kHz. (10)
16 Liking similarity. (8)
17 Rant: lens rotates lights. (8)
18 Property results. (7)
20 Frankincense and myrrh, perhaps, feature in stores in summer. (6)
21 Give back soak boiler. (6)
24 Instrument to sort out Be/O_2 reaction. (4)

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