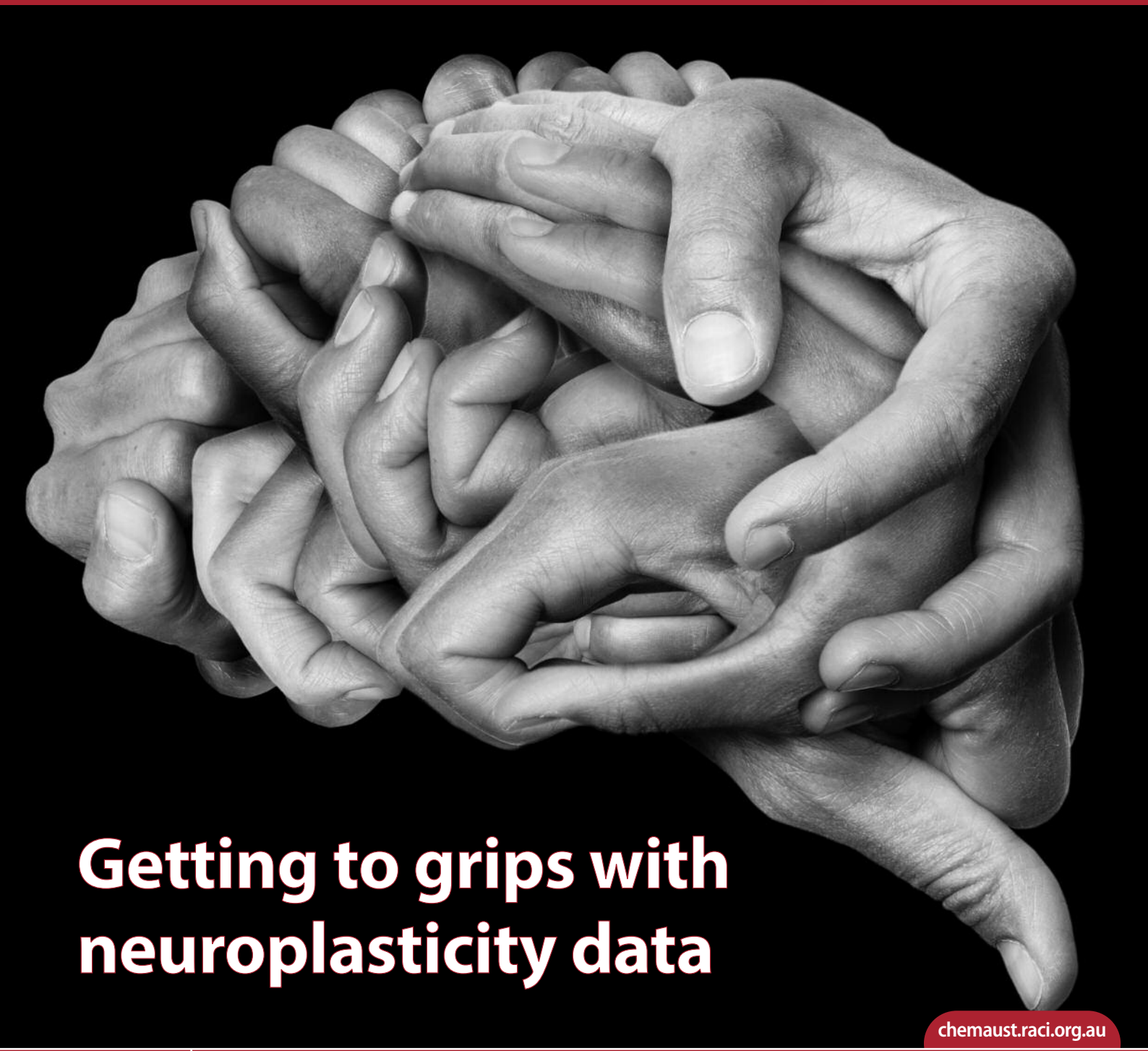
chemistry in Australia
February 2018



Getting to grips with neuroplasticity data

chemaust.raci.org.au

raci
Royal Australian Chemical Institute

- Pushing the boundaries of microscope resolution
- Metal–organic frameworks: a 'top ten' emerging technology
- The stories your chemistry teacher wouldn't tell you

ROWE SCIENTIFIC PTY LTD www.rowe.com.au

ADELAIDE | BRISBANE | HOBART | MELBOURNE | PERTH | SYDNEY

Quality System
Quality Endorsed Company
ISO 9001:2008
LIC 10372
SAI Global

VELP SCIENTIFICA

SALE ON NOW

On selected VELP Stirring equipment

PDF

SCAN CODE TO DOWNLOAD SPECIAL PRICES

https://goo.gl/NX72Jx

INTRODUCING THE NEW LINE OF

AREX-6

RANGE OF STIRRERS

Features include:

- Fast, precise and stable temperature control
- Ceramic coated, aluminium alloy hotplate
- Digital read-out of temperature and speed
- Timed operation
- Auto reversing function
- Stainless steel and glass probes available to suit a variety of mixing solutions
- Optional wireless temperature recording and ramping.

A 100% Australian owned company, supplying scientific laboratories since 1987.

Ajax Finechem | Bel-Art Products | chem-supply | cowie | CHROMACOL | Gilian | HACH | KartellLABWARE | SIGMA-ALDRICH AUTHORIZED DISTRIBUTOR | MN | MERCK | METTLER TOLEDO | OHAUS | SIMAX | Tarsons TRUST DELIVERED | TPS | Techno Plas | VELP SCIENTIFICA | witeg GERMANY

See our specials.

LABORATORY CONSUMABLES - CHEMICALS - INSTRUMENTATION - REPAIR SERVICES

Order online at your convenience at: **www.rowe.com.au**

New South Wales & ACT
Ph: (02) 9603 1205
Fx: (02) 9603 1084
rowensw@rowe.com.au

Queensland
Ph: (07) 3376 9411
Fx: (07) 3376 9455
roweqld@rowe.com.au

South Australia & NT
Ph: (08) 8186 0523
Fx: (08) 8186 0524
rowesa@rowe.com.au

Victoria & Tasmania
Ph: (03) 9701 7077
Fx: (03) 9769 2560
rowevic@rowe.com.au

Western Australia
Ph: (08) 9302 1911
Fx: (08) 9302 1905
rowewa@rowe.com.au

chemistry in Australia

February 2018

cover story

Making connections: from neuroplasticity data to treatment

A treasure trove of existing and emerging medical research findings beckons chemists to effect ground-breaking solutions to a wide array of medical issues.

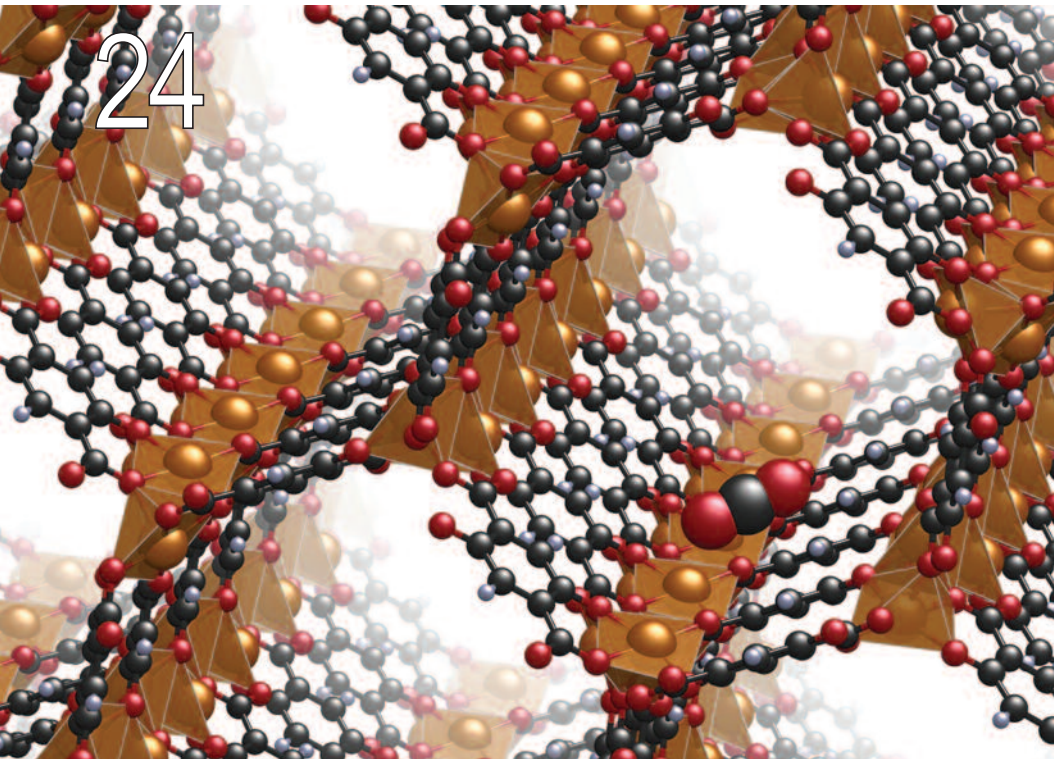
16

20 A cool visualisation breakthrough: the 2017 Nobel Prize in Chemistry. Part 1

The limits of microscopy resolution have been smashed as part of work recognised by the 2017 Nobel Prize in Chemistry.

24 Metal–organic frameworks: from laboratory to factory

Once thought of as the 'gunk in the bottom of the flask', metal–organic frameworks have emerged as a potential wonder material. Marta Rubio-Martinez and Matthew Hill present an Australian perspective.



news & research

5 News
10 On the market
12 Research
42 Cryptic chemistry
42 Events

members

28 Obituary
30 New Fellow
31 RACI news

views & reviews

4 Editorial
5 Your say
32 Books
34 Education
36 Economics
38 Science for fun
40 Grapevine
41 Letter from Melbourne

chemaust.raci.org.au

Movements and milestones

Part of my role as editor is commissioning contributors – making sure that we have enough content, as well as a good range of it. To start the new year, I'd like to report on a few movements and milestones within the pages of *Chemistry in Australia*.

Entrepreneur and technical consultant Dave Sammut has written more than 40 feature articles since he commenced contributing them in 2013. An active member of the RACI, Dave was thrilled to be involved in the 100 Reactions project during the RACI's centenary, and he is committed to helping young scientists transition from university to careers as part of the RACI's mentoring program. I am very grateful for his strong and enthusiastic support of the magazine.

Dave is co-authoring this year's features about the recipients of the 2016 Nobel Prize for Chemistry while our usual contributor, Peter Karuso, is taking a sabbatical. Peter volunteered to write Nobel prizewinner profile pieces for the magazine in 2009 and has been going strong ever since. He's introduced us to some very fine chemists and fascinating chemistry along the way. I wish him well on his sabbatical.

Also taking a break is environment consultant Paul Moritz. Writing the environment column since 2012, he has also contributed book reviews and a feature article on environment protection (November 2003). Paul has written more than 30 opinion pieces, and the editorial team particularly appreciates the time he has taken to complement his writing with interesting photos.

Science communicator Jeremy Just has been writing his 'science for fun' column since the beginning of last year. Jeremy is right at the end of his PhD, finishing off his thesis in organic chemistry. During his PhD studies, he has been investigating the use of a benchtop espresso machine to extract a diverse range of biologically interesting organic molecules from plants. The ultimate goal of this research is to develop a rapid and efficient extraction method (April 2017). He can regularly be seen around Tasmania presenting science shows and workshops, and in the media. Jeremy says he 'appreciates the opportunity to write general interest pieces for *Chemistry in Australia* as another outlet for engaging Australians in science'.

You may well remember contributions from a 'mystery' PhD and then postdoc diarist until mid-2016. That contributor was … cue drumroll … John Moraes. Writing from New South Wales and then from Switzerland and the US, John shared some candid accounts of his highs and lows as a chemistry PhD and postdoc, including the 'gentle art of quitting' (August 2016). That was his final contribution, in which his byline said that he was 'trying to break into the corporate world'. Here's a recent reflection and update from John:

> I found writing for *Chemistry in Australia* a valuable way to ruminate in public about the interesting career trajectory I had taken – from PhD student to postdoc to stay-at-home-dad to job seeker to corporate 9-to-5'er. I tried to provide insights into those particular snapshots of my life and guidance for those about to chart similar waters. It was fun. I hope it was useful. I now work for Nike in the USA. I don't do much with chemistry, but absolutely feel that each step I took in the circuitous journey was invaluable and helped me do what I do. And do it well.

These and all of our contributors are the pulse of our magazine. I admire all of you for sharing your knowledge and opinions with readers.

Sally Woollett (editor@raci.org.au)

chemistry in Australia
chemaust.raci.org.au

EDITOR
Sally Woollett
Ph (03) 5623 3971
wools@westnet.com.au

PRODUCTION EDITOR
Catherine Greenwood
catherine.greenwood@bigpond.com

ADVERTISING SALES
Mary Pappa
Ph/fax (03) 9328 2033/2670
mary.pappa@raci.org.au

BCA VERIFIED AUDIT

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

BOOK REVIEWS
Damien Blackwell
damo34@internode.on.net

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

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

PRESIDENT
Peter Junk FRACI CChem

MANAGEMENT COMMITTEE
Sam Adeloju (Chair) Sam.Adeloju@monash.edu.au, Michael Gardiner, Helmut Hügel, Colin Scholes, Madeleine Schultz, Pamela Sutton-Legaud, Richard Thwaites

CONTRIBUTIONS
Contributors' views are not necessarily endorsed by the RACI, and no responsibility is accepted for accuracy of contributions. Visit the website's resource centre at chemaust.raci.org.au for information about submissions.

ISSN 0314-4240 e-ISSN 1839-2539

raci

Visits and verses

Thank you for another year of *Chemistry in Australia* and in particular the November issue. I found many interesting articles, including the report on Sir John and Lady Cornforth (p. 16). This reminded me of his visits to the Department of Organic Chemistry (as it was then) at the University of Melbourne and the memorable poem, by Sir John, about Australia and Professor Arthur Birch of ANU. You may know it, but if not the first verse goes like this:

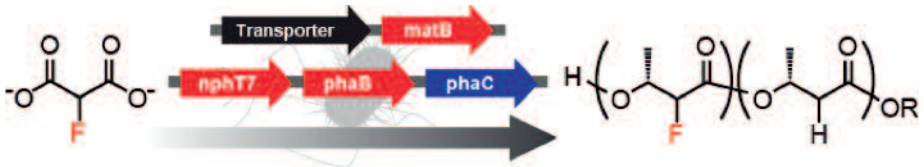
> That outpost of empire Australia,
> A land of the strangest mammalia,
> The kangaroo rat, the blood sucking bat
> And Arthur J Birch inter alia.

David Kelly FRACI CChem

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 wools@westnet.com.au.

Fluorine-containing molecules from cell culture



Natural organic compounds that contain fluorine are rare because living organisms – with a few exceptions – do not produce them. US scientists have now genetically engineered a microbial host for organofluorine metabolism, allowing it to produce a fluoridated intermediate known as a diketide. As reported in *Angewandte Chemie* (https://doi.org/10.1002/anie.201706696), the diketide could then be used as a monomer for the in vivo production of fluorinated bioplastics.

Unlike nature, chemists use fluorine often. Teflon coatings for pans and water-repellent Gore-Tex jackets, both based on polytetrafluoroethylene, immediately spring to mind. Fluorine is also found in many agrochemicals, and about 20–30% of modern pharmaceuticals, ranging from antimalarial and cytostatic drugs to inhalation anaesthetics, blood substitutes and liquid ventilation agents. Organofluorine molecules are also used in liquid crystals for displays, as well as in ozone-friendly refrigerants and propellants.

Given the potential for living systems to produce highly complex chemical compounds, researchers working with Michelle C.Y. Chang at the University of California, Berkeley, aimed to manipulate the biosynthetic machinery in cells to use simple fluorinated building blocks to make new organofluorine target molecules.

To achieve this, they introduced genes that code for three particularly efficient enzymes from a variety of other microorganisms into *Escherichia coli* to construct the diketide biosynthesis pathway. These enzymes are able to use fluorine-containing derivatives of their normal substrates. In addition, it was also necessary to introduce a gene for a transport protein that carries fluoromalonate – as fluorine-containing starting material – into the cell. The enzymes allowed the cells to use the biosynthesis pathway to make fluoromalonyl coenzyme A and convert it to the 2-fluoro-(*R*)-3-hydroxybutyrate diketide in high yield.

The researchers introduced yet another gene for an enzyme used by many bacteria to make polyhydroxyalkanoates (PHAs), which are polyesters used to store carbon and energy. Biodegradable PHAs are used in the production of bioplastics for applications such as food packaging and medical implants. The new, genetically engineered microorganisms incorporated the fluorinated diketides into the PHAs they produced, generating polymers containing 5–15% fluorinated monomers. The fluorinated bioplastics were less brittle than fluorine-free PHAs. Controlled incorporation of fluorinated monomers could allow for targeted variation of the properties of bioplastics.

The researchers also hope to use the key component fluoromalonyl coenzyme A to produce a broad spectrum of small fluorinated molecules in living cells for pharmaceutical applications.

Angewandte Chemie International Edition

Turning off the browning reaction

The anti-PPO gene blocks the production of polyphenol oxidase and therefore stops browning.

A special kind of sliced apple is now for sale at select US supermarkets, one that won't turn brown when cut, bitten or bruised.

Arctic® apples have been developed by Canadian biotech company, Okanagan Specialty Fruits Inc. (OSF). OSF is the first company to license CSIRO's non-browning technology.

Their first product is snack-sized bags of fresh Arctic® Golden apple slices, with more non-browning varieties expected in future years, including Granny Smith and Fuji.

Company founder Neal Carter began working on the apples in the mid-1990s.

'I came across research from CSIRO that had managed to "turn off" browning in potatoes', Carter explained.

'As an apple grower, I was very aware that apple consumption had been declining for decades while obesity rates had simultaneously been sharply rising.

'My wife and I felt that we could help boost apple consumption through a similar biotech approach with apples, as non-browning apples would be more appealing and convenient.

'We felt this could also significantly reduce food waste, as nearly half of all apples produced end up wasted, many due to superficial bruising', he said.

While there may be other sliced apple products already on the market, these are often coated with vitamin C and calcium to prevent browning and to preserve crispness, and this can change their taste.

Apples and other fruit and vegetables turn brown after they are cut or damaged because of a naturally occurring enzyme (polyphenol oxidase or PPO) that reacts with other components in the fruit cells when these cells are 'broken', producing a brown pigment.

CSIRO scientists constructed an anti-PPO gene which, when inserted into plants, blocks the production of PPO and therefore stops the browning.

Spoilage due to browning costs food-processing industries worldwide millions of dollars each year in wastage and costly chemicals to prevent the reaction.

This non-browning technology has potential to reduce waste, not only in apples and potatoes but also in other important horticultural crops, such as beans, lettuce and grapes where produce with only small injuries could still be sold.

CSIRO

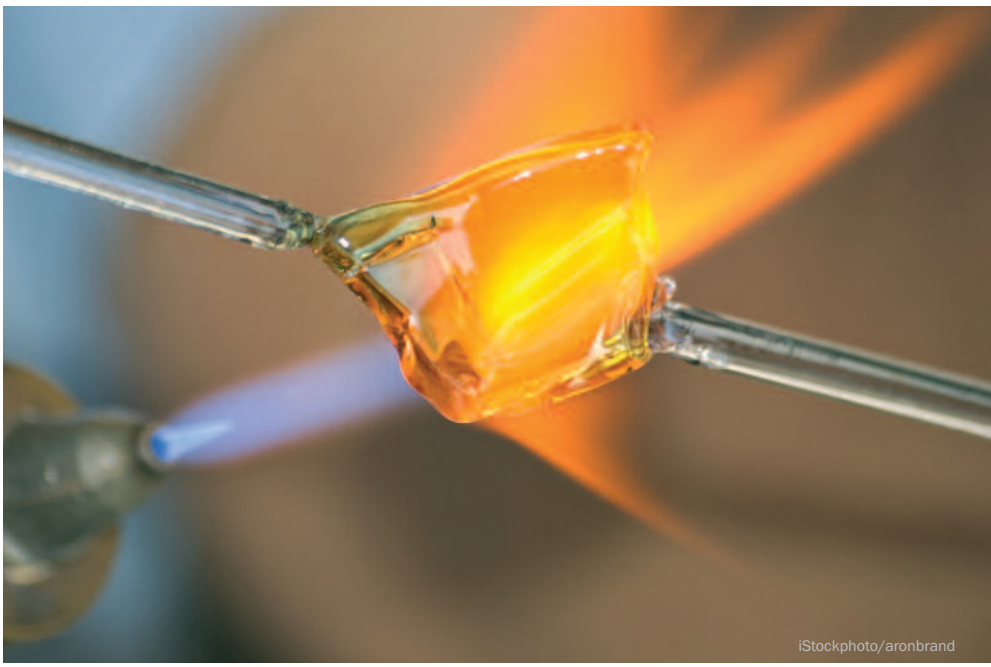
Scientists get to grips with a tricky liquid

When warm candy cools and solidifies, the mass of thick, viscous liquid sets to hard candy – an edible glass.

To physicists, glass is not just the stuff that we drink out of or look through. It is, more broadly speaking, a fluid that sets as a solid without crystallising. In a glass, molecules are arranged randomly, rather than in an ordered crystal lattice.

But what actually happens during the setting process? How do the mechanical properties change when viscous liquids cool and transform into glass?

This is what physicists at the research centre Glass and Time at Roskilde University (RUC), Denmark, are trying to find out in collaboration with scientists from the Massachusetts Institute of Technology in the US.



iStockphoto/aronbrand

Seven experiments planned

They designed seven experiments to measure the viscosity of the liquid as it cooled down, which are now published in the scientific journal *PNAS*.

'We're now able to measure the mechanical properties – flow properties – in a much larger area than was possible before. It's taken many years and a lot of work to reach this point', says lead author Tina Hecksher, an associate professor at the Department of Natural Science and Environment at RUC.

It is not easy to measure how fluids behave as they become increasingly viscous. There's a huge difference between measuring a thin liquid and one that is just about to turn to glass. It requires advanced measuring equipment, which the scientists first need to develop.

'The viscous liquids' dynamic properties are extremely dependent on temperature. But we used a host of different methods to measure a wide range of temperatures', says Hecksher.

Better cell phones and medicines

Understanding this transition has many applications; for example, in the manufacture of solid glass in consumer electronics, such as smartphones and flat screens. But there are other less obvious applications, says Hecksher.

'There's a lot of research into glass formation in medicine. It's easier for the body to dissolve medicine in glass form than medicine in the crystalline form, so it will be interesting to find out how we can produce medicine as a glass instead of crystals', she says.

Understanding the setting and formation of glass can also help geophysicists understand how magma flows and sets. The applications are numerous, but the basic research and theory needs to come first.

Viscous liquids resemble each other

The scientists studied silicone oil, but in principle, they could also have studied honey, tar, or another liquid that sets to glass as the temperature falls.

'All liquids can be supercooled. They can all form glass and behave surprisingly similarly when cooled', says Hecksher.

But not all liquids behave in exactly the same way, she says. 'It would be nice to have a universal theory for supercooled fluids. But perhaps we should develop a theory for particular simple fluids, which can be adjusted in various ways for more complex fluids.'

This is the hypothesis that Hecksher and colleagues will investigate.

'We'll try to find a theory for the simplest fluids, such as the silicon oil that we have used, and perhaps this can be the starting point. But theories need to be tested and this is what we've now shown we can do', she says.

Nice piece of work

The results will be compared with theories of what happens when fluids become more viscous.

Theoretical physicists need experimental basic research such as this, says Paolo Sibani, lecturer at the Department for Physics, Chemistry, and Pharmacy at the University of Southern Denmark.

'It's vital to develop new experimental techniques as they're doing in Roskilde. And theoretical physicists like me use these experimental results to develop theories. We need results that span over many orders of magnitude and it's always a challenge. What they've done here is very nice', says Sibani.

Science Nordic/Henrik Bendix

New method for identifying carbon compounds derived from fossil fuels

Scientists at the US National Institute of Standards and Technology (NIST) have developed a laboratory instrument that can measure how much of the carbon in many carbon-containing materials was derived from fossil fuels. This will open the way for new methods in the biofuels and bioplastics industries, in scientific research and environmental monitoring. Among other things, it will allow scientists to measure how much of the CO_2 in the atmosphere came from burning fossil fuels, and to estimate fossil fuel emissions in an area as small as a city or as large as a continent.

This is possible using carbon dating, but it requires extremely precise – and expensive – measurements. The new instrument, developed by NIST chemists Adam Fleisher and David Long and based on cavity ringdown spectroscopy (CRDS) technology, promises to dramatically reduce the cost of those measurements. This is described in the *Journal of Physical Chemistry Letters* (doi: 10.1021/acs.jpclett.7b02105).

The key to these measurements is carbon-14, a radioactive (yet harmless) isotope of carbon that is formed in the upper atmosphere. Carbon-14 is unstable, with a half-life of 5730 years.

But carbon-14 is extremely rare, and to use it for identifying fossil fuels, scientists need to be able to measure it at concentrations as low as one part in ten trillion, which requires an extremely sensitive measurement technique and a particle accelerator to separate carbon-14 from carbon-12. The CRDS instrument that Fleisher and Long have developed can sit on a laboratory benchtop and is relatively inexpensive to operate.

CRDS instruments analyse gases by detecting the wavelengths of light they absorb.

To measure the amount of heavy CO_2 in a CO_2 sample, the sample is injected into the instrument's measurement cavity, which is a tube with mirrors inside at either end. A laser of the exact wavelength that only heavy CO_2 absorbs is then shot into the cavity. As the laser light bounces between the mirrors, some of its energy is absorbed by the gas. The greater the absorption, the greater the concentration of heavy CO_2.

To achieve the required sensitivity, Fleisher and Long enhanced existing CRDS technology by engineering a system that chills the cavity to a uniform –55°C and minimises temperature fluctuations that would throw off the measurement.

This and other improvements boosted the instrument's sensitivity enough for accurate carbon dating.

Biofuels and bioplastics would be burnt, and the resulting CO_2 collected for analysis. This would allow you to test a fuel mixture to determine what fraction of it is biofuel. In the airline industry, for example, this would be useful because some countries require that aviation fuels include a specific biofuel percentage. Such tests could also be used to verify that bioplastics, which sell for a premium, do not contain petroleum-derived compounds.

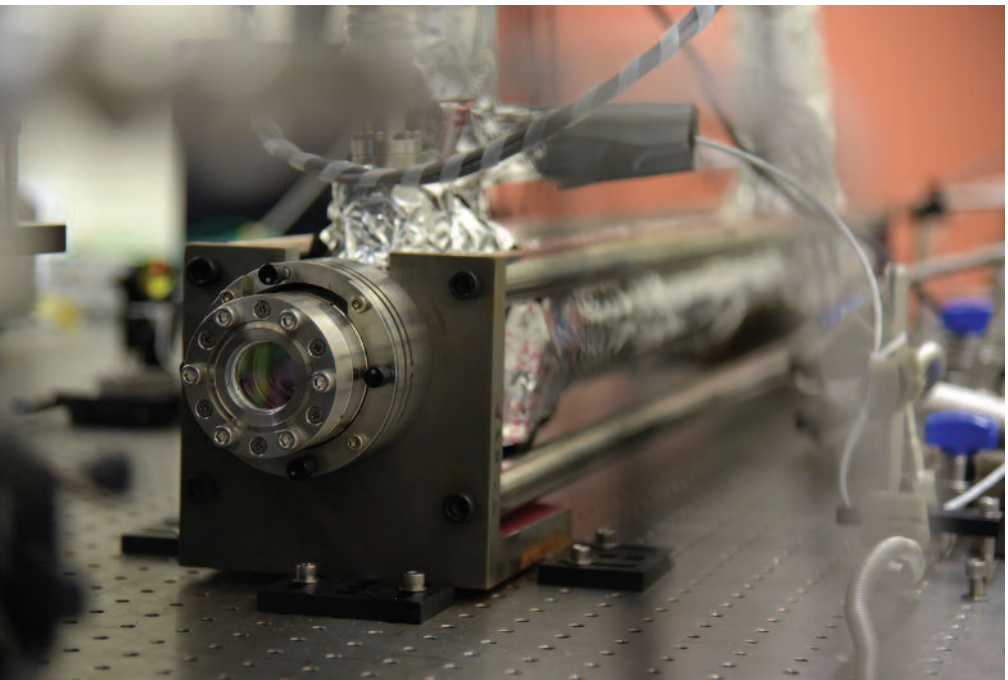
To estimate fossil fuel emissions in a geographic area, air samples would be analysed for the atmospheric CO_2. Areas with high fossil fuel emissions, such as cities and industrial zones, will have below-normal concentrations of heavy CO_2.

'Fossil fuel emissions dilute the concentration of heavy CO_2 in the air', said Fleisher. 'If we can accurately measure that concentration after it's been diluted, we can calculate how much fossil fuel emissions are in the mix.'

A report from the National Academy of Sciences estimated that 10 000 samples a year, collected at carefully chosen locations around the US, would be enough to estimate national fossil fuel emissions to within 10% of the actual value. Such a system of measurements can increase the reliability of national emissions estimates. This would be especially useful in parts of the world where high-quality emissions data are not readily available.

'There is a need for this type of measurement in many industries', Fleisher said. 'We've demonstrated a path to meeting that need in a cost-effective way.'

NIST



This NIST instrument that enables optical measurement of 'heavy' carbon dioxide ($^{14}CO_2$), showing the instrument's ultra-stable optical cavity and cold sample cell.

Rich Press/NIST

Missing atoms in a forgotten crystal bring luminescence

A little-studied member of the perovskite family of materials could find use in a range of electronic devices, after researchers at King Abdullah University of Science and Technology (KAUST), Saudi Arabia, discovered the secret of its strong photoluminescence.

Perovskites are a wide group of materials that are known to have remarkable optical and electronic properties. Perovskites with the general formula ABX_3, and particularly the perovskite methylammonium lead trihalide, have attracted almost all the research attention thanks to their great promise as low-cost, high-efficiency solar cell materials.

Other members of the perovskite family and perovskite derivatives are also worthy research subjects, says Michele De Bastiani, a postdoctoral researcher in Osman Bakr's group at KAUST.

De Bastiani and his colleagues have been testing Cs_4PbBr_6, a perovskite of the A_4BX_6 branch of the family. This material is noted for its strong photoluminescence – the ability to absorb light at one wavelength and re-emit it at another.

The material's potential applications include colour-converting coatings on LED light bulbs, lasers and photodetectors. But to be able to fine-tune the material's optoelectric properties for each application, researchers need to solve the mystery of why the perovskite photoluminesces so strongly.

'We investigated the structural and optoelectronic properties of Cs_4PbBr_6 to understand the origin of its photoluminescence', De Bastiani said. Subjecting the material to a barrage of tests, the team discovered that when a Cs_4PbBr_6 crystal was heated to 180°C, its photoluminescence was irreversibly destroyed.

Photoluminescence is a two-step process: absorption of light generates a pair of quasi-particles called excitons within the perovskite, which must recombine to re-emit the light. Using temperature-dependent X-ray diffraction to track structural changes to the material as heat was applied, the team discovered that at 180°C, $CsPbBr_3$ nanocrystals form within the mineral.

The heat-induced structural rearrangements that create these nanocrystals also swallow natural defects in the original crystal where bromine atoms were missing, the researchers concluded. These bromine vacancies act as traps for passing exictons. Confined in these traps, the excitons are much more likely to recombine and emit light.

'Now that we have this fundamental understanding, our next step is to move on to potential applications', De Bastiani said. 'The unique photoluminescence manifested by Cs_4PbBr_6 makes these perovskites compelling materials for electroluminescence devices, lasers and light converters.'

Meanwhile, many other little-explored members of the perovskite family with interesting properties are waiting to be revealed, De Bastiani added. 'One example is $CsPb_2Br_5$, a single crystal we recently synthesised for the first time with unseen optoelectronic properties.'

King Abdullah University of Science and Technology

Revolutionary SA asbestos testing tech set for world stage

South Australian company Frontier Microscopy has developed a fast and accurate way to test for airborne asbestos fibres, potentially making life safer for thousands of Australian families and workers.

Using artificial intelligence, advanced robotic microscopy and cloud-based software, this ground-breaking system known as Marvin will revolutionise the way the world monitors, detects and then stores the results of asbestos air monitoring on demolition and construction sites.

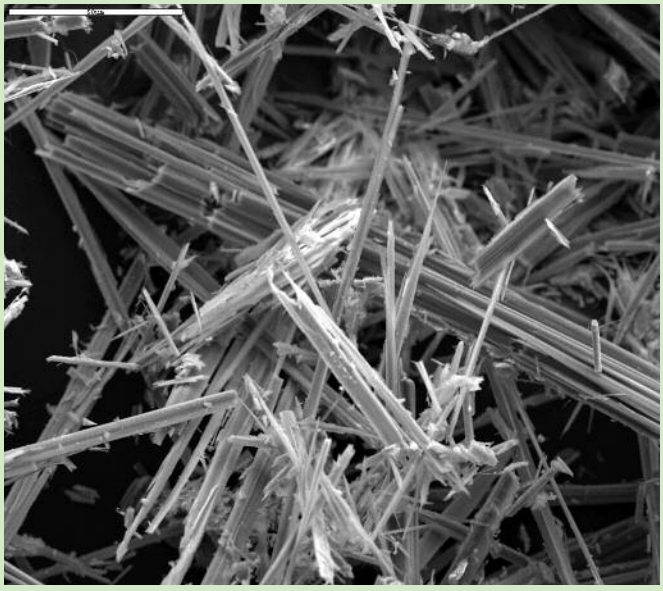
Frontier Microscopy Managing Director Jordan Gruber says there are two key components to the technology: a robotic microscope analysis system and a software management suite.

The management suite is a secure web and mobile software that has been designed for day-to-day asbestos air monitoring operations. It significantly increases air monitoring job efficiency by automating field data collection on demolition and construction sites, laboratory analysis, reporting and client communication.

Gruber said: 'We are currently piloting the management suite with Greencap, Australia's largest risk management and compliance company. Cutting edge technology is being applied to improve compliance, reduce risk and simplify information capture during air monitoring during asbestos remediation.'

'Asbestos is still a major issue across Australia, with one in three public buildings estimated to contain asbestos-based building materials. Asbestos-based materials must be respected, or else asbestos fibres can become airborne and pose serious risk to workers and the general public.'

About six times faster than a human, Marvin – which is patent pending – analyses air samples using a custom-built robotic microscope. The robotic microscope system takes several hundred photographs across an entire air filter sample in less than a minute. The images are then automatically uploaded to cloud software where they are analysed for signs of asbestos.



Scanning electron micrograph of asbestos fibres.
Courtesy of the US Geological Survey

'For labs there are significant benefits, as Marvin eliminates the manual processing of dangerous minerals and screens air samples for asbestos fibres in a fraction of the time it takes humans', Gruber said.

Marvin is expected to become commercially available worldwide in the next few months, following an extensive validation testing program in a commercial laboratory environment. In the meantime, air samples can be manually analysed through the management suite.

For more information, email jordan.gruber@frontiermicroscopy.com.

MEP Instruments becomes Metrohm Australia, Metrohm New Zealand

In response to changes in the ownership structure of the company and the successful expansion of its business operation, MEP Instruments has changed its name to Metrohm Australia and Metrohm New Zealand.

As of 1 January 2018, the distributor of leading analytical technology solutions started operating under the name of Metrohm, its sole parent company. The change reflects the close integration of the Australian and New Zealand operation under the global Metrohm brand.

Metrohm is a global market leader in the fields of titration and voltammetry, and a trend-setting innovator in ion chromatography, online analysis and laboratory automation, NIR Raman spectroscopy and electrochemical solutions for research and training.

MEP Instruments Australia and New Zealand was established by Metrohm Switzerland together with Anton Paar Austria nearly 20 years ago to strengthen support and service for their customer base in these countries.

The tremendous success over the past years and the enthusiastic acceptance by the scientific community in the region have led to the decision to change the name to Metrohm to reflect the commitment to the growing customer base in the region and to establish Anton Paar Australia and New Zealand as a separate entity.

Along with the name change, the company will adopt the corporate identity, including logo and visual identity of the parent Metrohm AG. All MEP/Metrohm office addresses and phone numbers will remain the same across Australia and New Zealand.

For more information, visit metrohm.com.au and mep.metrohm.com.au.

Machine learning uncovers large hidden job market for PhD graduates

iStockphoto/Murat Gocmen

Researchers have developed machine learning to scan tens of thousands of job ads and found a large hidden job market for PhD graduates.

The project, led by the Australian National University (ANU) and CSIRO's Data61, developed a job-searching machine to help universities prepare graduates for non-academic work and show industry the value of PhD graduate research skills.

One of the lead researchers, Dr Will Grant from ANU, said the machine read about 30 000 job ads, many of which were for non-academic work, and assessed the level of research skills required for each job.

'The PhD was originally designed to train the next generation of academics, but most graduates today find jobs outside of academia', said Grant from the Australian National Centre for the Public Awareness of Science.

'The machine found a large hidden job market in Australia for people with PhDs, with half of the job ads scanned specifying the need for a high level of education, including research skills.'

Grant said the job market was considered hidden because employers did not use 'PhD' as a keyword in ads.

He said highly skilled researchers working in a wide variety of industry sectors were important to Australia's future economic prosperity.

'We taught the machine to analyse job ads and tell us what skills were most important to employers. The problem is that industry employers in Australia – particularly in manufacturing, transport, logistics, marketing and communication – may not be aware that PhD graduates have the skill set they're looking for', Grant said.

He said Australian universities must do more to prepare PhD graduates for work outside of the higher education sector, while employers needed to be more receptive to people with PhDs.

'PhD programs still tend to favour skills required for an academic career over those demanded by industry', Grant said.

'There also seems to be a lack of trust in the PhD qualification as producing work-ready employees.'

Co-researcher Adjunct Professor Hanna Suominen, a natural language processing expert from CSIRO's Data61, co-invented the machine-learning algorithm and is optimistic about the potential of this tool to help find work for PhD students.

'Our researchers will continue to develop the machine into a web portal to support PhD graduates in their search for work', Suominen said.

The machine could be refined and used to track changes in industry demand for Australia's research skilled workforce.

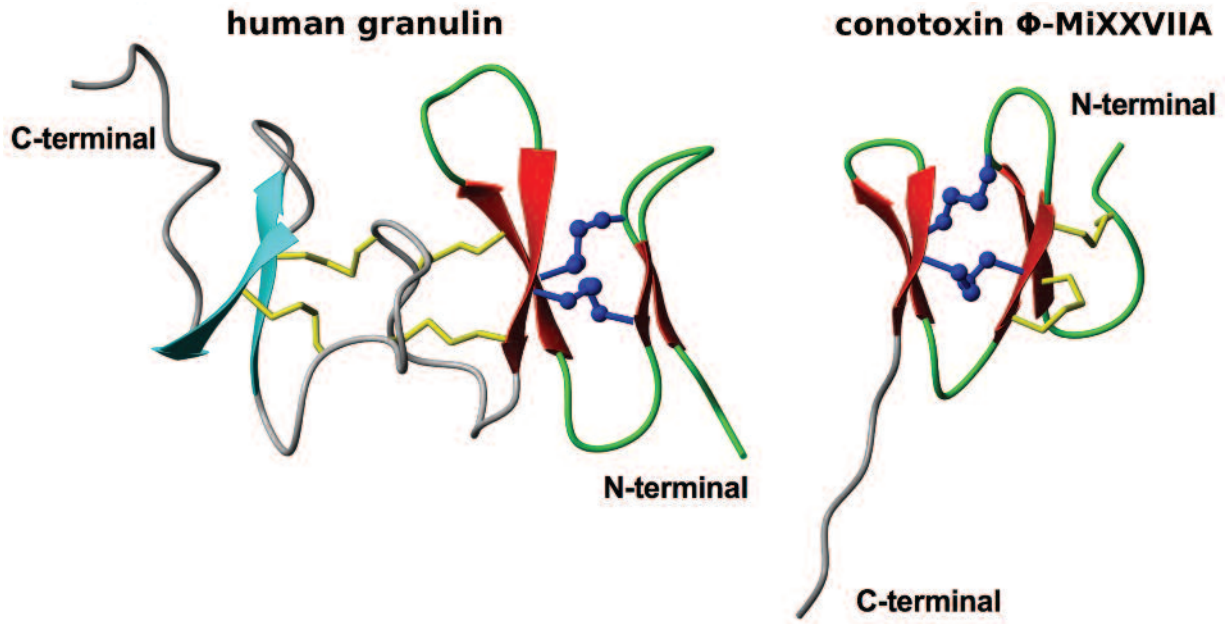
'It has the potential to connect PhD graduates with ideal jobs they may not have otherwise come across or considered.'

The research team has expertise in computer science, research education, linguistics and social science.

ANU

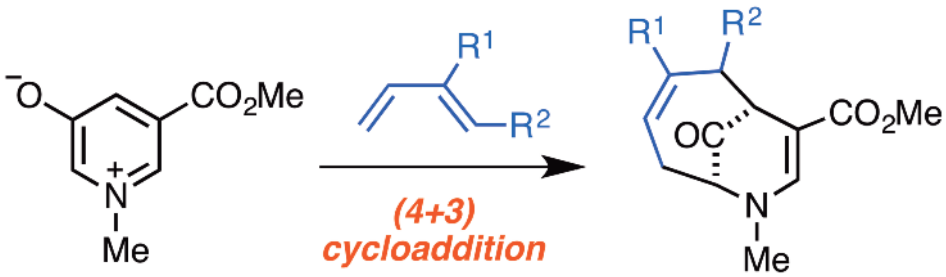
Uncovering activity of novel toxin

Venom-derived peptide toxins provide an abundant pool of molecules with diverse biological functions. Researchers from the University of Queensland and James Cook University have recently discovered another function of a large family of cysteine-rich peptide toxins from the marine cone snail *Conus miles* (Jin A.-H., Dekan Z., Smout M.J., Wilson D., Dutertre S., Vetter I., Lewis R.J., Loukas L., Daly N.L., Alewood P.F. *Angew. Chem. Int. Ed.* 2017, **56**, 14 973–6). Conotoxin Φ-MiXXVIIA contains a unique cysteine-rich motif comprising three consecutive cysteine residues and four disulfide bonds, which the researchers named as a new conotoxin framework XXVII (C–C–C–CCC–C–C) belonging to a new conotoxin superfamily G2. The researchers synthesised Φ-MiXXVIIA by using regioselective formation of 4 S–S bonds and determined its unique tertiary structure by 2D NMR spectroscopy. They found that the novel toxin is a structural mimic of the N-terminal domain of granulin, a human growth factor protein. Over extended periods, Φ-MiXXVIIA promotes cell growth and inhibits apoptosis, suggesting it acts as a granulin mimic.



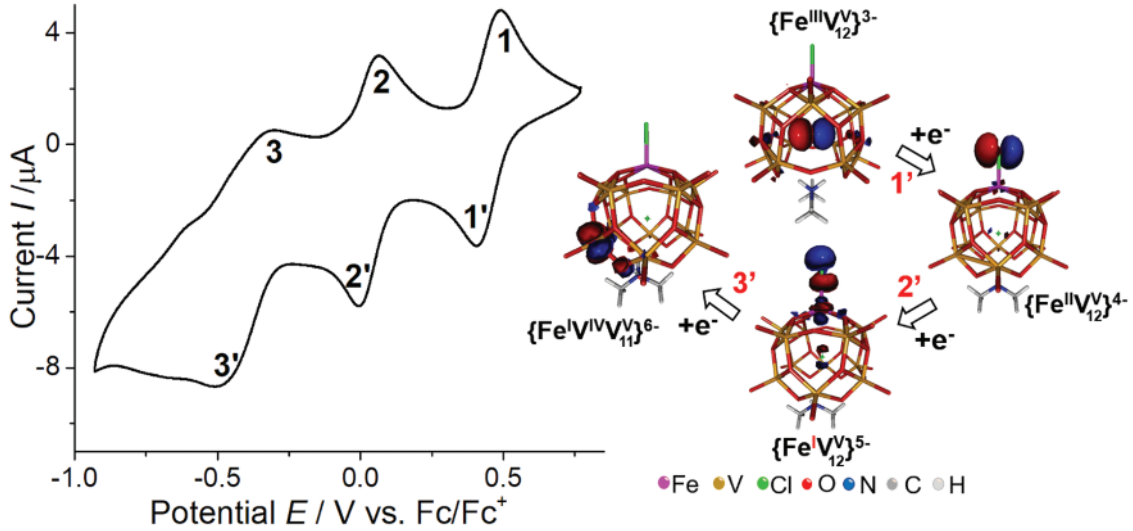
Rapid route to bicyclic nitrogen-containing frameworks

The cycloaddition between allylic cations and dienes provides rapid access to seven-membered rings. Recently, researchers from the University of Missouri-Columbia, USA, and the University of Queensland have examined a new substitution pattern of oxidopyridinium ions as a driving force for this reaction, in which these zwitterions act as dienes to produce the 7-azabicyclo[4.3.1]decane ring system in one step (Fu C., Lora N., Kirchhoefer P.L., Lee D.R. Altenhofer E., Barnes C.L, Hungerford N.L., Krenske E.H., Harmata M. *Angew. Chem. Int. Ed.* 2017, **56**, 14 682–7). This substructure is found in a number of different alkaloids. An intramolecular version of the reaction was also established. Density functional theory calculations showed that a concerted mechanism is favoured over a range of other mechanistic possibilities.



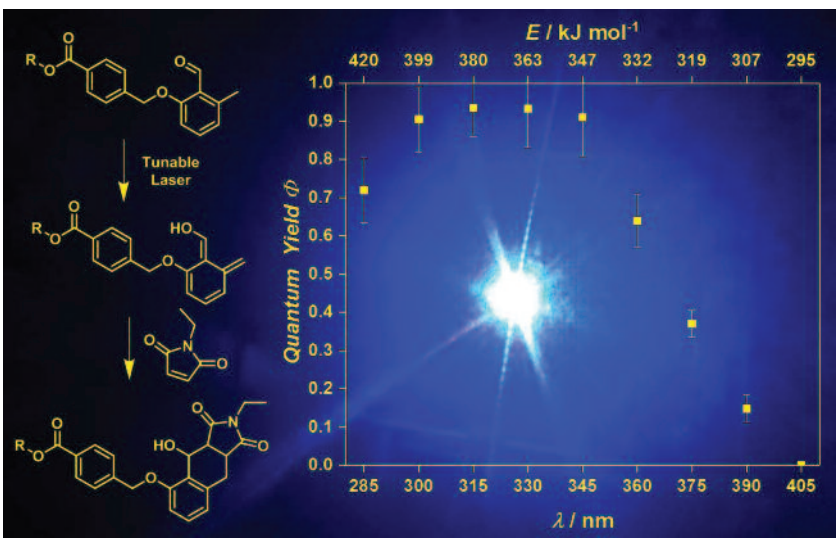
Regioselectivities were also generally high. The work holds promise for the synthesis of new molecular scaffolds to exploit unexplored chemical space as well as for the total and analogue synthesis of biologically active compounds.

Stabilising low-valent iron



Low-valent iron centres are critical intermediates in chemical and biochemical processes. An international collaboration led by Professor Carsten Streb of the Institute of Inorganic Chemistry at Ulm University, Germany, and Professor Alan Bond and Dr Jie Zhang of the School of Chemistry at Monash University has led to the discovery of the first example of a low-valent Fe^{I} centre stabilised in a high-valent polyoxometalate framework (Anjass M.H., Kastner K., Nägele F., Ringenberg M., Boas J.F., Zhang J., Bond A.M., Jacob T., Streb C. *Angew. Chem. Int. Ed.* 2017, **56**, 14 749–52). Detailed electrochemical and electron paramagnetic resonance studies and theoretical analyses provided insight into the reversible two-electron reduction of the native Fe^{III} species and the electronic features of the resulting Fe^{I} unit. Initial stability and reactivity analyses showed that the materials design approach could open new avenues for reductive electron transfer catalysis by polyoxometalates to achieve small-molecule activation and reversible electron storage for battery electrodes and molecular-magnet applications.

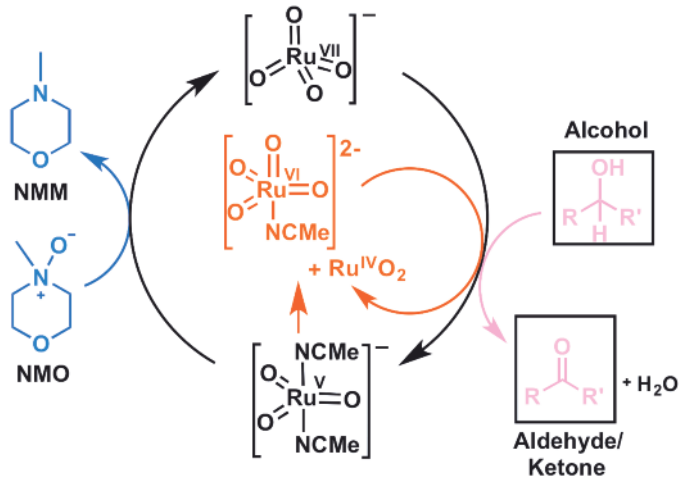
Light, reactivity, action!



Efficient light-induced ligation protocols are valuable tools for functional materials design. The teams of Christopher Barner-Kowollik and James Blinco, at the Queensland University of Technology and the Karlsruhe Institute of Technology, Germany, and Michelle Coote at the Australian National University have investigated two highly efficient photoligation reactions involving photoenols and nitrile imines in a combined experimental and theoretical study (Menzel J.P., Noble B.B., Lauer A., Coote M.L., Blinco J.P., Barner-Kowollik C. *J. Am. Chem. Soc.* 2017, **139**, 15 812–20). A unique tunable laser system was used to irradiate samples containing either *o*-methylbenzaldehydes or diphenyltetrazoles and *N*-ethylmaleimide at varied wavelengths and constant photon count to produce action plots of reactivity versus wavelength. The quantum yield of the nitrile-imine-mediated tetrazole ene cycloaddition was estimated to be higher than 0.55 ± 0.06 at 285 nm, while photoenol-ligation proceeded with quantum yields up to 0.91 ± 0.10, supporting theoretically established mechanisms via conical intersections. A combination of density functional theory and multi-reference calculations with precision photochemical analysis provided insight into the mechanisms and optimised reaction conditions for photoligation protocols. These findings will help to design advanced photoresists in which distinct material properties are encoded with different colours of light in 3D laser lithography.

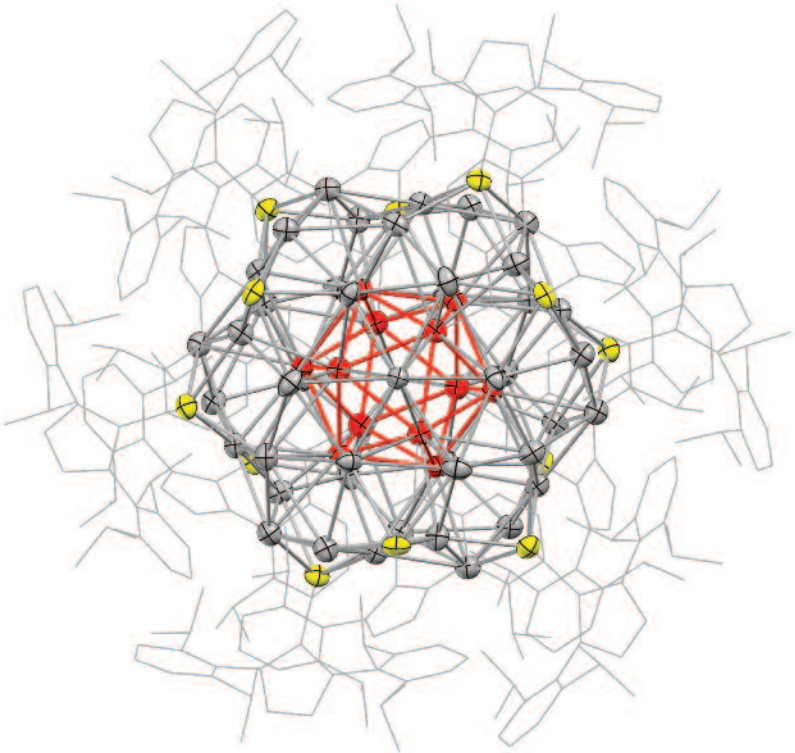
Aged catalyst improves alcohol oxidation

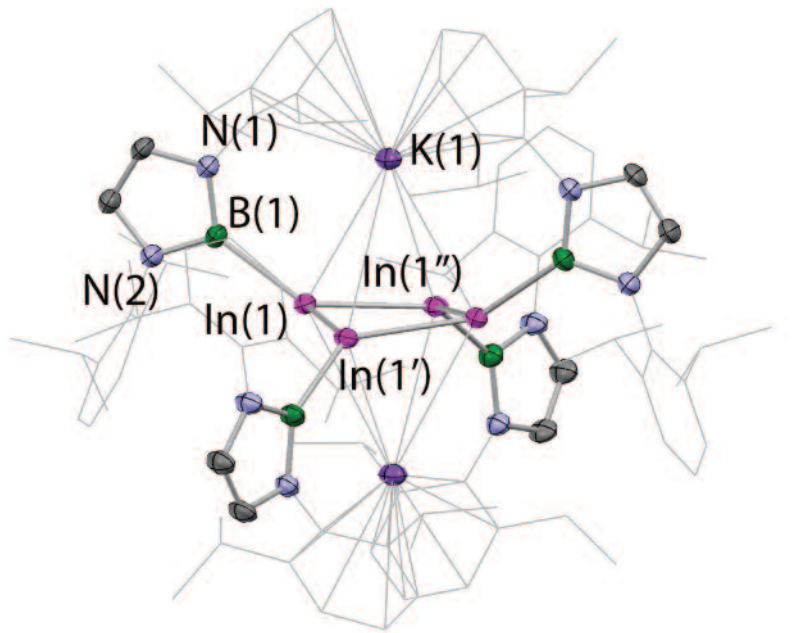
The selective oxidation of a primary alcohol to an aldehyde is a fundamentally important transformation in synthetic organic chemistry. Although many different reagents perform this type of oxidation, synthetic chemists tend to rely on only a few of these compounds in practice. Prominent among this suite is the Ley–Griffith catalyst TPAP (*n*-$Pr_4N[RuO_4]$), which is used in combination with the co-oxidant *N*-methyl morpholine *N*-oxide (NMO). The mechanism of this reaction has remained unknown since the seminal work of Ley and Griffith was published more than 30 years ago. Collaborators from the Universities of Queensland, Western Australia and Barcelona, Spain, thoroughly examined this reaction by using UV–visible, EPR and ^{99}Ru NMR spectroscopy, as well as isotopic labelling, in an effort to unravel the underlying mechanism (Zerk T.J., Moore P.W., Harbort J.S., Chow S., Byrne L., Koutsantonis G.A., Harmer J.R., Martínez M., Williams C.M., Bernhardt P.V. *Chem. Sci.* 2017, **8**, 8435–42). Their study unearthed the key finding that freshly prepared TPAP performs differently from the commercially available (or aged) catalyst. After a slow induction period with the fresh catalyst, the oxidation by-product water induces partial decomposition of *n*-$Pr_4N[RuO_4]$ to insoluble RuO_2. Serendipitously, small amounts of this RuO_2 impurity in aged TPAP enhances the rate of oxidation so that no induction period has been previously observed.



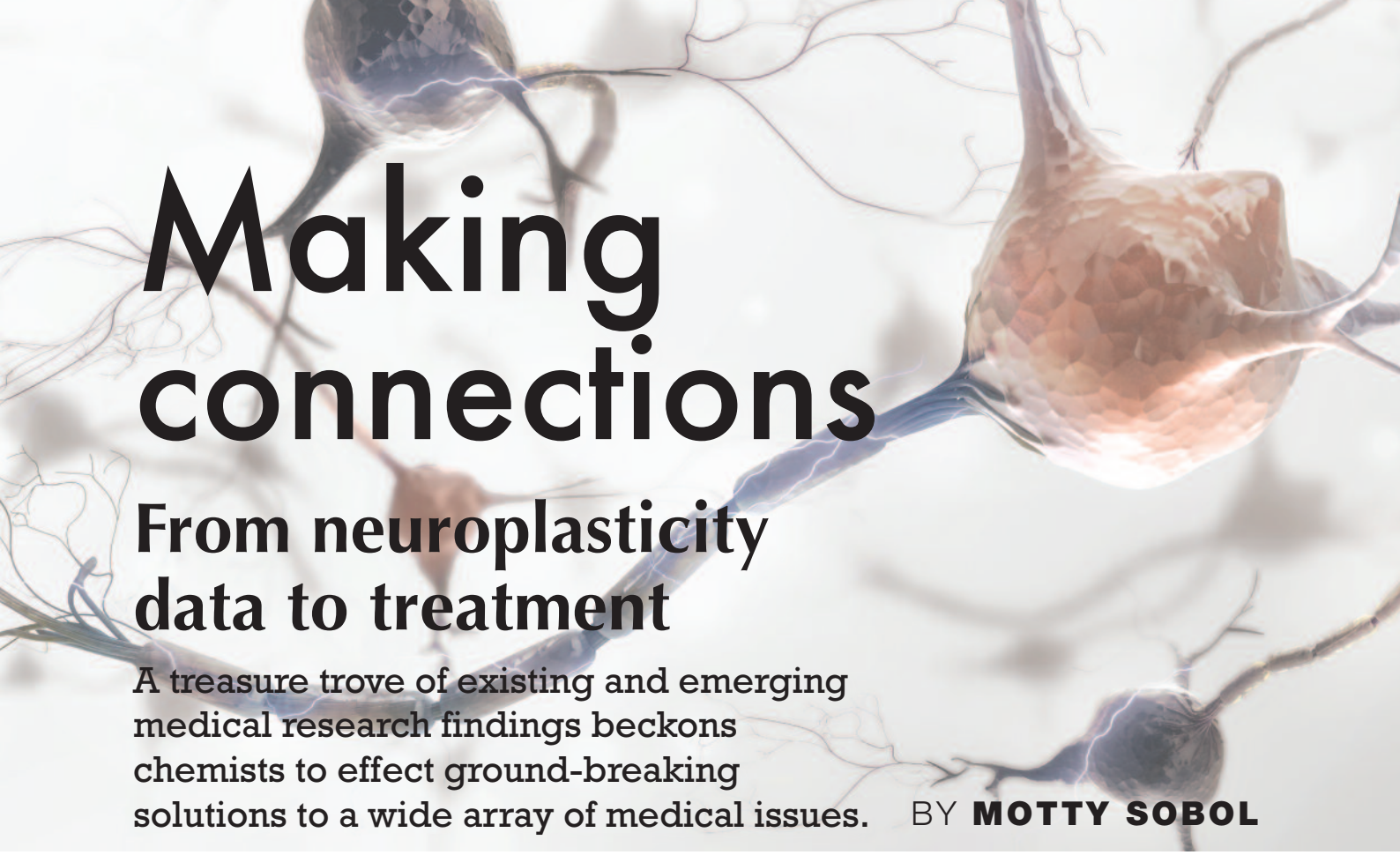
Aromatic indium

The chemistry of very low oxidation-state main group compounds has rapidly developed over the last two decades. One of the most formative early results in this field was Schnöckel's synthesis of the remarkable aluminium 'metalloid' cluster anion $[Al_{77}\{N(SiMe_3)_2\}_{20}]^{2-}$. Although gallium analogues have since been prepared, related indium clusters of a similar size have remained staunchly elusive. In their latest collaborative study, the teams of Professors Cameron Jones at Monash University and Simon Aldridge at the University of Oxford, UK, have rectified this situation with the synthesis of the indium metalloid cluster $[In_{68}(boryl)_{12}]^-$ (boryl = $-B(DipNCH)_2$, Dip = $C_6H_3Pr^i_2$-2,6) and the related planar four-membered cyclic dianion $[In_4(boryl)_4]^{2-}$, via the reduction of boryl boron(III) halide complexes (Protchenko A.V., Urbano J., Abdalla J.A.B., Campos J., Vidovic D., Schwarz A.D., Blake M.P., Mountford P., Jones C., Aldridge S. *Angew. Chem. Int. Ed.* 2017, **56**, 15 098–102). The cluster complex contains three concentric 'spheres' of indium atoms, $In_{12}@In_{44}@In_{12}(boryl)_{12}$, with 56 indiums only having bonds to other indium centres (average In oxidation state about 0.19). It is essentially a well-defined 'cut out' of indium metal with a boryl ligand coat. The smaller In_4 system is formally a 2π-electron cycle, which DFT studies show to have aromatic character. Such compounds could shed light on the mechanism of indium metal deposition in, for example, microelectronic devices.





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



Making connections

From neuroplasticity data to treatment

A treasure trove of existing and emerging medical research findings beckons chemists to effect ground-breaking solutions to a wide array of medical issues.

BY **MOTTY SOBOL**

In 1876, there were no effective treatment options for common bacterial infections, which were often lethal in the era before antibiotics. That year, John Tyndall published his findings that penicillin killed bacteria but his paper was ignored. In 1929, Alexander Fleming published his finding on penicillin and likewise it was initially ignored – until 1938 when Howard Florey came across his paper and decided to act. Until Florey proved otherwise, the prevailing attitude was that antibacterial drugs were a delusion. A similar attitude prevails today in relation to cures for neuroplasticity-related issues.

Until recently, neuroplasticity – the brain's ability to re-wire itself, in effect altering its own genetic operation – was firmly believed to be non-existent and impossible in adults. Like many widely held beliefs, it has now been shown to be false. We now know that many serious conditions could potentially be relieved or remedied by promoting, assisting and/or guiding the brain to re-wire itself and yet it is still a prevalent widely held conviction that drugs directing neuroplastic changes are a delusion.

The harsh reality is that there are no effective pharmacological means at present to neither significantly assist nor reverse existing damage, let alone cure the underlying causes of a wide array of intellectual disability, dementias, neurodevelopmental disorders (including autism and Down syndrome), age-dependent neurodegenerative diseases (including Alzheimer's and Parkinson's disease) and many other neurological-related applications.

Current pharmacological tools in psychiatry are effectively limited to symptom relief but are not in themselves curative. The current drugs often help and are needed for management and for other therapies to have a chance to work (e.g. psychotherapy). Schizophrenias, OCD, ADHD, anxieties and phobias, damage due to child abuse, neglect and trauma as well as many others, all potentially fall within the scope as being amenable to neuroplastic pharmacological curative tools yet to be created.

Additionally, injuries and afflictions relating to neural wiring such as vision impairment (whether it is congenital blindness, macular degeneration, injury or optical nerve atrophy), hearing impairment (either congenital or injury related), motor control (disease or injury), epilepsy and numerous others are currently beyond our ability to cure.

The potential scope of applications is much wider and can apply to healthy normal people such as enhancement of learning abilities (similar to that seen in very young children).

In the wider community (as well as within professional circles) there is a widely held hope that one day a 'miracle' discovery will be made and then these issues will be adequately dealt with. Reality and historical precedents say otherwise.

The disconnect between research and application, and thus a hurdle on the path to change, can be considered in terms of the maturity of technology, or technology readiness level (TRL).

iStockphoto/muzon

The mythology that medical researchers on their own and/or pharmaceutical giants will make this happen is fervently clung to by many.

No one in the private sector paid any attention to Tyndall's (TRL1) nor Fleming's (TRL1) work until Howard Florey serendipitously found Fleming's paper and showed that it works in practice having directed the efforts that isolated the active compound, purified it and manufactured in sufficient quantities to conduct initial clinical experiments (TRL3). Only then did industry (prodded heavily by the US government of the day due to its projected immediate wartime value) come on board and in record time bring it to TRL9 within four years. Nominally it takes 10–20 years to transition drugs from TRL3 to TRL9.

A golden opportunity for chemists in academia

Without chemists, especially tenured academics who in spirit and position are similar to Florey (who was able and willing to obtain and commit resources and skills to try something absolutely new and unproven) taking a leading role, medical theories and discoveries (TRL0–2) will very likely continue to be made but history continues to repeat as these are frequently seemingly ignored because they are not a viable commercial product (TRL9 or at the very least TRL3) as yet.

History and current practice remains that pharmaceutical companies do follow medical research and do conduct their own research internally (and/or sponsored); however, there is no denying that the industry has historically and consistently shown an apparently very strong preference to 'ambulance chase'. To minimise their risk envelope, they wait for someone else to make a commercially valuable proven product and then buy them out, copy them or use that as a 'lead' to either explore or use combinatorial libraries to try structurally related analogues. The prominent firms at the time all missed the boat in terms of both opportunity and staggering profits with cytokines (the genetic signalling molecules initially comprising G-CSF and GM-CSF) for cancer applications because it was outside the usual expectations for pharmacological entities.

Attitudes matter

The limiting step in paradigm change is perceptions and attitudes. If you fervently believe that it can't be done, then why would you even try?

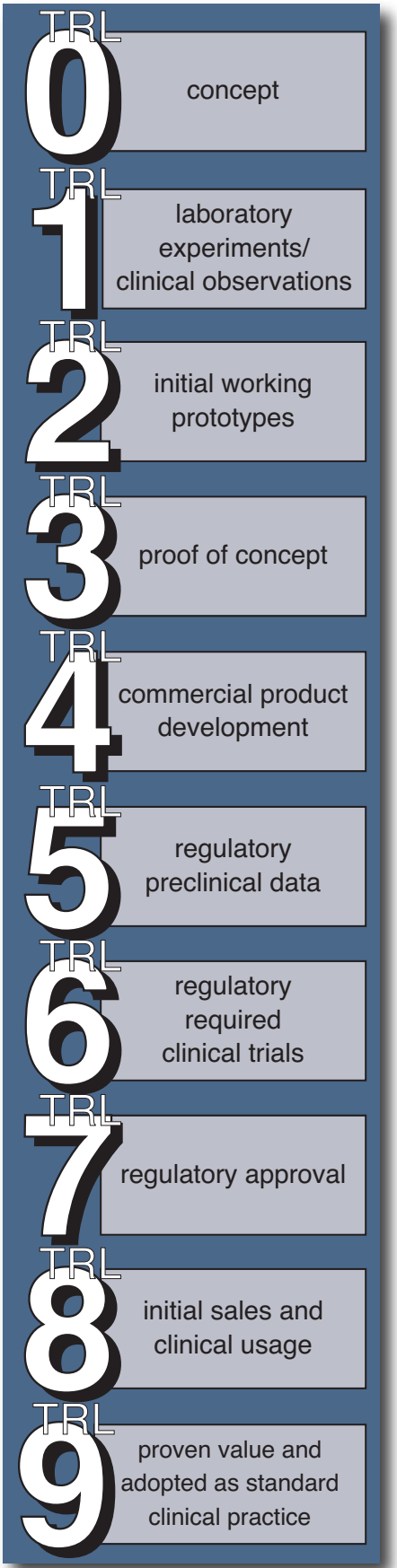
It would be very reasonable to assert that unless another 'Florey' comes along and takes the results of existing medical research results and transitions one or more of these into working prototype(s) that will prove the concept (at least to TRL3), then it is highly unlikely we will see the oft-hoped-for 'miracle cure(s)'.

To date, very little attention is seemingly being paid by applied chemists to a mountain of high-quality data (mostly TRL1) that hints at appropriate targets for drug design and development in the areas of dementias, neurodevelopmental disorders, psychological and neurological disorders, blindness, deafness and learning issues, which are all associated with neuroplasticity. Few chemists in academia and industry take much notice of research outside of their chosen areas of interest, and genetic research is often viewed as not being 'chemically relevant'.

Genetic experiments reveal targets for drug design

Oncology (cancer) research has made major contributions to date, but perhaps the most overlooked contribution is also the most important

Oncogenes are an inherently inbuilt system of 'master regulator genes'. When these go faulty, the result is cancer. They exist to control, monitor and regulate the operation of all other genes. They do this using a system of



Technology readiness level (TRL) ranges from concept stage (0) to adoption as standard practice (9).

receptors and messenger/signalling molecules. Thus, any research that shows activity/benefit by switching 'on' or 'off' various genes by means of genetic experiments using vectors (genetically modified viruses that either introduce and paste code or cut code out or a mix thereof) can translate to targets for drug design and development.

Every successful genetic experiment medical researchers report is an alert to the existence of targets that are pharmacologically amenable to getting the same end result using appropriately designed drugs. The precise biochemical mechanisms may not be known as yet, but there is potential to design drugs that either mimic or duplicate the messages or selectively block the relevant receptors. The key to success is knowing what the targets actually are.

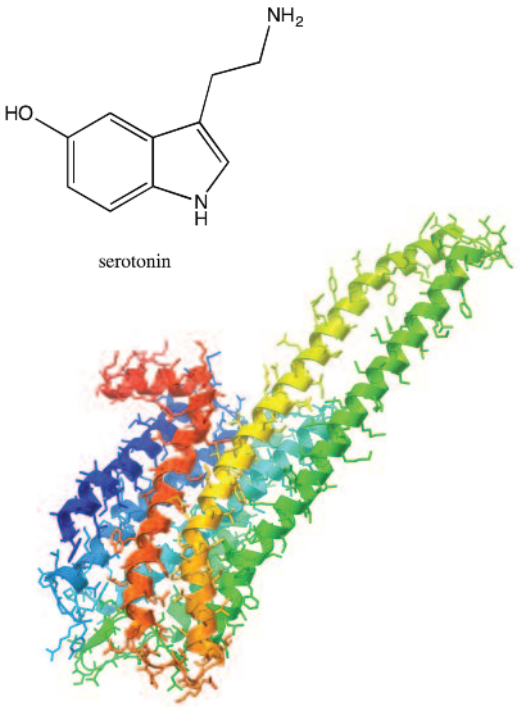
Knowing the precise and correct target is critical: the case of serotonin

Serotonin (5-hydroxytryptamine or 5-HT) modulates cortical function via widely projecting axons, which act on a diversity of receptor subtypes. Serotonin receptors are highly heterogeneous and they have been regrouped within seven different families (5-HT_1–5-HT_7). With the exception of the 5-HT_3 family, which is a ligand-gated ion channel, all others are G-protein coupled receptors, with each family sharing structural, pharmacological and transductional characteristics. 5-HT receptors have been implicated in the regulation of several psychiatric and neurological disorders related to serotonergic neurotransmission, and specific receptor subtypes have recently been associated with either the pathogenesis or the treatment of migraine headache. Current evidence continues to support the use of selective serotonin reuptake inhibitors as first-line pharmacologic interventions for OCD. Neuroplasticity modulation and enhancement via 5-HT agonists may well have a very useful role to play in chronic fatigue syndrome, fibromyalgia and irritable bowel syndrome as well as other implicated medically unexplained symptoms.

Following the amazing success of 5-HT_3 agonist ondansetron at changing the face of medical treatment of nausea and vomiting, attention turned to a spectrum of 5-HT receptors as potentially useful targets for drug design and development.

Between 2000 and 2007 Glaxo (UK) published their efforts to develop a novel (hopefully blockbuster class) rapid-acting antidepressant, having pinned their hopes and efforts on serotonin reuptake via a well-designed agonist initially for 5-HT_{1B}, then a dual-acting 5-HT_{1A}/5-HT_{1B} agonist (TRL5). A recent paper by Melburnian medical researchers suggest they may well have had far better results if they targeted 5-HT_{2A} receptors instead. It's now been demonstrated that 5-HT_{2A} agonists enhance functional connectivity between hierarchical brain networks, and modulate the influence of neural activity from lower-order upon higher-order regions (TRL1). The emerging data suggests that there may well be a useful role for these agents in the treatment for major depression, anxiety and drug addiction and in particular in some problematic circumstances where current treatment options are limited, prognosis is unfavourable, data suggests scant, if any, objective benefit of current therapy options and clinicians have historically adopted a distrustful attitude towards these difficult-to-treat patients.

Separating fervently held beliefs from objective facts is critical. This applies equally to the medical researchers conducting the genetic experiments and clinicians who treat diseases and conditions and to chemists who can assist by transitioning medical research data into practical pharmacological solutions.



The skeletal formula of serotonin, $C_{10}H_{12}N_2O$, and the human 5-hydroxytryptamine (serotonin) receptor 2A. DrLee/CCO

In schizophrenia for instance, initially the genetic operating basis was dismissed because the assumptions about which genes were responsible was out by a country mile and the conceptual basis itself was far too simplistic to prompt a search in the right direction.

Further studies revealed that schizophrenia is not one disease but several genetically distinct ones (and hence the way drugs work will differ among these). It is now known that a total of 42 genetic clusters working in tandem are responsible for the symptoms of eight distinct disorders, all falling under one clinical label. So far, this new data has not seemingly affected how psychiatrists prescribe drugs or how they treat these patients.

Beyond the 5-HT receptor class, there are a myriad of potential targeting systems emerging from medical research results.

Neuroplasticity in adults is possible

Neuronal plasticity peaks early in life during critical periods and normally declines with age. Neuroscientists recently showed that it's possible to return some of this plasticity to the

Brain development and epigenetic change

The Ancient Roman philosopher Seneca proposed that a human embryo is an adult in miniature and thus the task of development is simply to grow bigger. This idea was so appealing that it persisted for almost 2000 years. Only recently was brain development found to be a series of stages that can be broadly divided into two phases:

1. a genetically determined sequence of events in utero that can be modulated by maternal environment
2. a time (which is both pre- and post-natal in humans) when the connectivity of the brain is very sensitive, not only to the environment but also to the patterns of brain activity produced by experiences.

More importantly, however, it is now recognised that epigenetic changes, which can be defined as changes in developmental outcomes, including regulation of gene expression, are based upon mechanisms other than DNA itself and that gene expression can be altered by specific experiences, and this in turn can lead to organisational changes in the nervous system.

Neuroplasticity is now known to be affected by:

experience (both pre- and post-natal)

psychoactive drugs (e.g. amphetamine, morphine)

gonadal hormones (e.g. oestrogen, testosterone)

anti-inflammatory agents (e.g. COX-2 inhibitors)

growth factors (e.g. nerve growth factor)

dietary factors (e.g. vitamin and mineral supplements)

genetic factors (e.g. predisposition, strain differences, genetically modified mice)

disease (e.g. Parkinson's disease, schizophrenia, epilepsy, stroke)

stress (physical and/or psychological)

brain injury and trauma

brains of mice by tweaking a single gene (TRL1) (doi: 10.1073/pnas.1700866114). They targeted the expression of the Arc protein and genetically deleted its coding from DNA. This presents an enticing novel molecular target that could be used to fight age-related cognitive decline in humans. Moreover, the neuroscientists were able to restore the plasticity in the visual cortex of eyes of adult mice, potentially providing a gateway to developing means to restore sight, heal macular degeneration and correct age-related visual deficiencies. There are no effective treatment tools at present, and chemists are notable by their absence in this area.

The same result had serendipitously been obtained previously when neuroscientists (neuropsychiatrists) used a widely prescribed antidepressant drug called fluoxetine 'off-label' (TRL1) (doi: 10.1126/science.1150516). These researchers were able to restore the vision of adult rats while in the process of opening the door to unravelling new mechanisms for the therapeutic effects of antidepressants and for the pathophysiology of mood disorders.

Alessandro Sale, the co-author on this major paper was also the editor and co-author of the first chapter of *Environmental experience and plasticity of the developing brain* (see review December 2017/January 2018, page 32.)

A significant number of similarly identified targets have been reported. For example, the gene Lsamp regulates emotional and social behaviour (TRL1) and could potentially be the gateway to cures in a range of psychiatric illnesses and drug dependency.

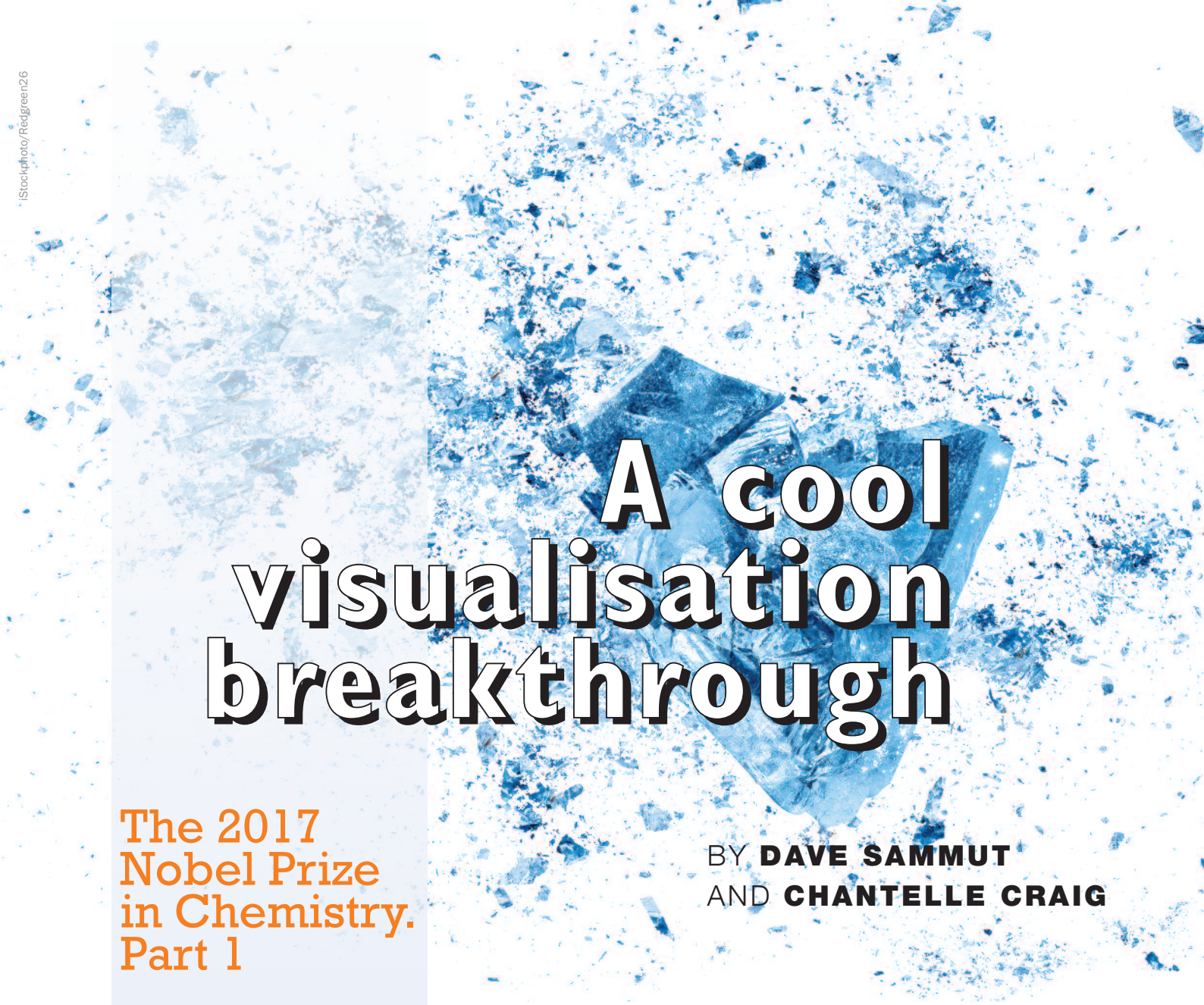
The potential targeting information available is at times very precise. For example, medical researchers are pinning down specific key molecules in the development and pathogenesis of emotion-related behaviour. One example is netrin-G1 which is a glycosyl-phosphatidylinositol-anchored synaptic adhesion molecule whose deficiency results in impaired fear-like and anxiety-like behaviours under specific circumstances. Genetic deletion of netrin-G1 in cortical excitatory neurons resulted in altered anxiety-like behaviour, but intact fear-like behaviour, whereas loss of netrin-G1 in inhibitory neurons resulted in attenuated fear-like behaviour, but intact anxiety-like behaviour.

From assumption to opportunity

We're starting to unravel the genetics of pathology in mental health and degenerative diseases among a plethora of neural-wiring-related applications potentially amenable via targeting the receptors used in the command and control of these pathways. This is the point where a gulf exists between existing medical researchers and those who can transform their discoveries into practical solutions. Many of our most cherished and widely long-held assumptions are proving to be false. We've never seriously looked at neuroplasticity because we haven't believed the possibilities.

'Use it or lose it' is the core operating principle of neuroplasticity. The same applies to these current and emerging golden opportunities.

Dr Motty Sobol FRACI CChem is a Neupogen award recipient (oncology research) and consultant to industry (chemical and allied industries).



iStockphoto/Redgreen26

A cool visualisation breakthrough

The 2017 Nobel Prize in Chemistry. Part 1

BY **DAVE SAMMUT** AND **CHANTELLE CRAIG**

The limits of microscopy resolution have been smashed as part of work recognised by the 2017 Nobel Prize in Chemistry.

Science is not the lonely profession that it used to be. Gone are the days of the misanthrope academics locked away in their ivory towers, in single-minded pursuit of arcane science. In the modern world, whole groups of academics cram into their ivory towers, collaborating to create the next leaps forward in scientific understanding. In 1675, Sir Isaac Newton wrote to Robert Hooke: 'If I have seen further than others, it is by standing upon ye sholders of giants'. Even then, he was adapting words that were already centuries old.

How, then, do we recognise achievement in the new era of science? Over the last 50 years, there has been a steady growth of the Nobel Prize in Chemistry being awarded jointly, and most particularly in the laurels being shared by the mandated maximum of three researchers. From 1968 to 1977, three researchers shared the prize just once. By contrast, the 2017 winners collected the eighth instance of a triple-shared prize in the last decade.

In 2017, the world's most famous prize for scientific merit was awarded to three researchers – Jacques Dubochet (University of Lausanne, Switzerland), Joachim Frank (Columbia University, USA) and Richard Henderson (MRC Laboratory of

Molecular Biology, UK) – 'for developing cryo-electron microscopy for the high-resolution structure determination of biomolecules in solution'.

This relatively new science for the visualisation of active molecules is creating significant excitement at the biochemical frontier. As just one example, the technique has already been used to create high-resolution, 3D images of the Zika virus in its natural state, identifying targets for a vaccine.

As is becoming common in modern science, the story of this breakthrough is one of separate, complementary developments coming together to create something outstanding.

The science

Let's start with the basics. For the purposes of this article, I'm going to follow the Royal Swedish Academy of Sciences in describing a fairly broad range of molecules, biological macromolecules and complexes under the generic term 'particle'.

The structure of particles influences their activity. This is particularly the case with biologically active particles, for which the structures can get *really* complex. Much more than just the issue of potential chirality of simple organic molecules, the complexity of particles only grows when you start to consider issues such as the folding of proteins (see May 2017, p. 26), or the physical interactions between particles and their environment.

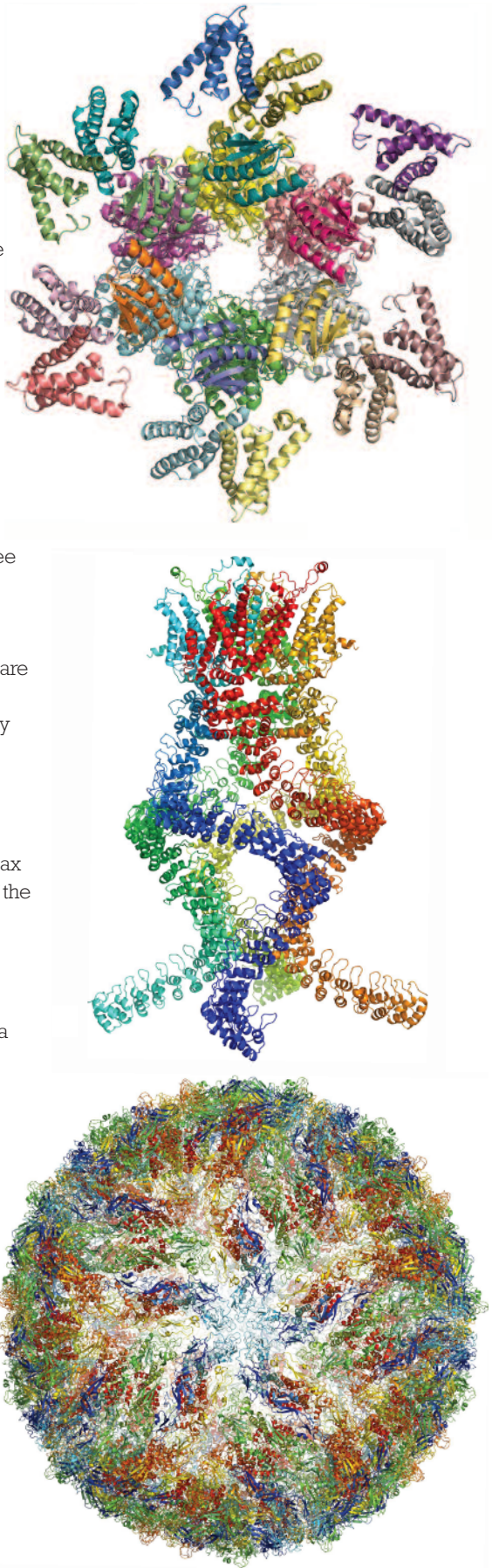
An early breakthrough in microscopy came when it was found possible to produce an image of an object by using an electron beam.

Learning about the structure of these particles tells us a great deal about their behaviours. Perhaps most famously, the 1962 Nobel Prize for Physiology or Medicine was awarded to Watson and Crick 'for their discoveries concerning the molecular structure of nucleic acids and its significance for information transfer in living material'. Their discovery crucially relied on X-ray crystallography results generated by Rosalind Franklin, who was only posthumously recognised for her contribution to this seminal work (see August 2014, p. 19).

Conventional microscopes fail at resolutions less than 400 nanometres, because molecules such as proteins are smaller than the wavelength in the visible spectrum. As demonstrated by Watson, Crick and Franklin, X-ray crystallography can assist with the visualisation of particles. X-ray crystallography was also key to the 1962 Nobel Prize in Chemistry, for Max Perutz and John Kendrew's studies of the structures of globular proteins.

However, X-ray crystallography suffers two substantial drawbacks. First, it only works for materials that will form crystals, which eliminates a significant portion of biologically active samples. And second, even when a crystal can be formed, this is often only possible by changing the matrix and/or state of the particle, so that the biological function or activity can't be assessed in context.

Nuclear magnetic resonance spectroscopy can assist in the characterisation of samples that are non-crystalline, but it is limited to very small particle sizes. Anything so large as a ribosome or an ion channel is prohibitive, let alone full cells.



Over the last few years, researchers have published atomic structures of numerous complicated protein complexes. From top to bottom: a protein complex that governs the circadian rhythm; a sensor of the type that reads pressure changes in the ear and allows us to hear; the Zika virus.

So an alternative technique was still needed. An early breakthrough in microscopy came when it was found possible to produce an image of an object by using an electron beam. With a significantly shorter wavelength, electrons offer a theoretical resolution as fine as about 0.1 nanometres, subject to quantum effect limitations.

Ernst Ruska constructed the first electron microscope in 1933, for which he (jointly) won the Nobel Prize in Physics in 1986. He went on to take part in the development of the first commercial mass-produced electron microscopes, which many consider to be the major breakthrough for this analytical technique.

However, electron microscopy (EM) also has a number of significant drawbacks. It has suffered long-term problems with sample preparation and stability, signal quality, and data analysis, and many of these problems were widely considered to be potentially insoluble.

Samples must be very thin to limit multiple electron scattering events, preferably only a single layer of the particles of interest. As well as this, even in crystalline samples the particles themselves can move due to temperature changes or interaction with the electron beam, and the movement further limits the resolution of the images. This effect is then influenced or limited by the speed of the detector.

And the problem is exacerbated for non-crystalline, asymmetric, randomly oriented particles.

Furthermore, EM requires vacuum conditions, which tends to vaporise water from samples, and which in turn can completely change their structure and/or chemistry. For EM to have wide applicability, it needed a technique to preserve water in the particles.

In transmission EM (of which cryo-EM is an improved version), only a portion of the high-energy electrons interact with the particle, yielding low contrast and in turn requiring high-intensity electron beams. But such intensive beams commonly destroy biological samples, and so the researcher was faced with the trade-off

Microscopy through the ages

13th–14th centuries — Lenses developed for use in spectacles.

Scheme I, *Micrographia*, 1665

1590 First microscope made by Dutch lens grinders Hans and Zacharias Janssen by placing two lenses in a tube.

1609 Compound microscope developed by Galileo Galilei.

1667 Robert Hooke published his microscope studies, including of cork, in *Micrographia*.

1675 Living cells seen by Anton van Leeuwenhoek using a simple, single-lens microscope. He achieved up to 300 times magnification of blood, insects and microorganisms.

18th century Technical advances improved microscopes and they became more common.

1830 Spherical aberration reduced by Joseph Jackson Lister, who combined several weak lenses to give good magnification with no blurring.

1878 Ernst Abbe's mathematical formula correlating resolution to the wavelength of light made it possible to calculate theoretical maximum resolution.

$$d = \frac{\lambda}{2n\sin\theta}$$

1903 Ultramicroscope developed by Richard Zsigmondy, which could study objects below the wavelength of light.

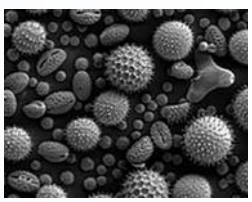
1932 Phase-contrast microscope invented by Frits Zernike, which could study colourless and transparent biological materials.

J. Brew/CC BY-SA 3.0

First transmission electron microscope built by Ernst Ruska. Using electrons, rather than light, greatly improves resolution.

1930s

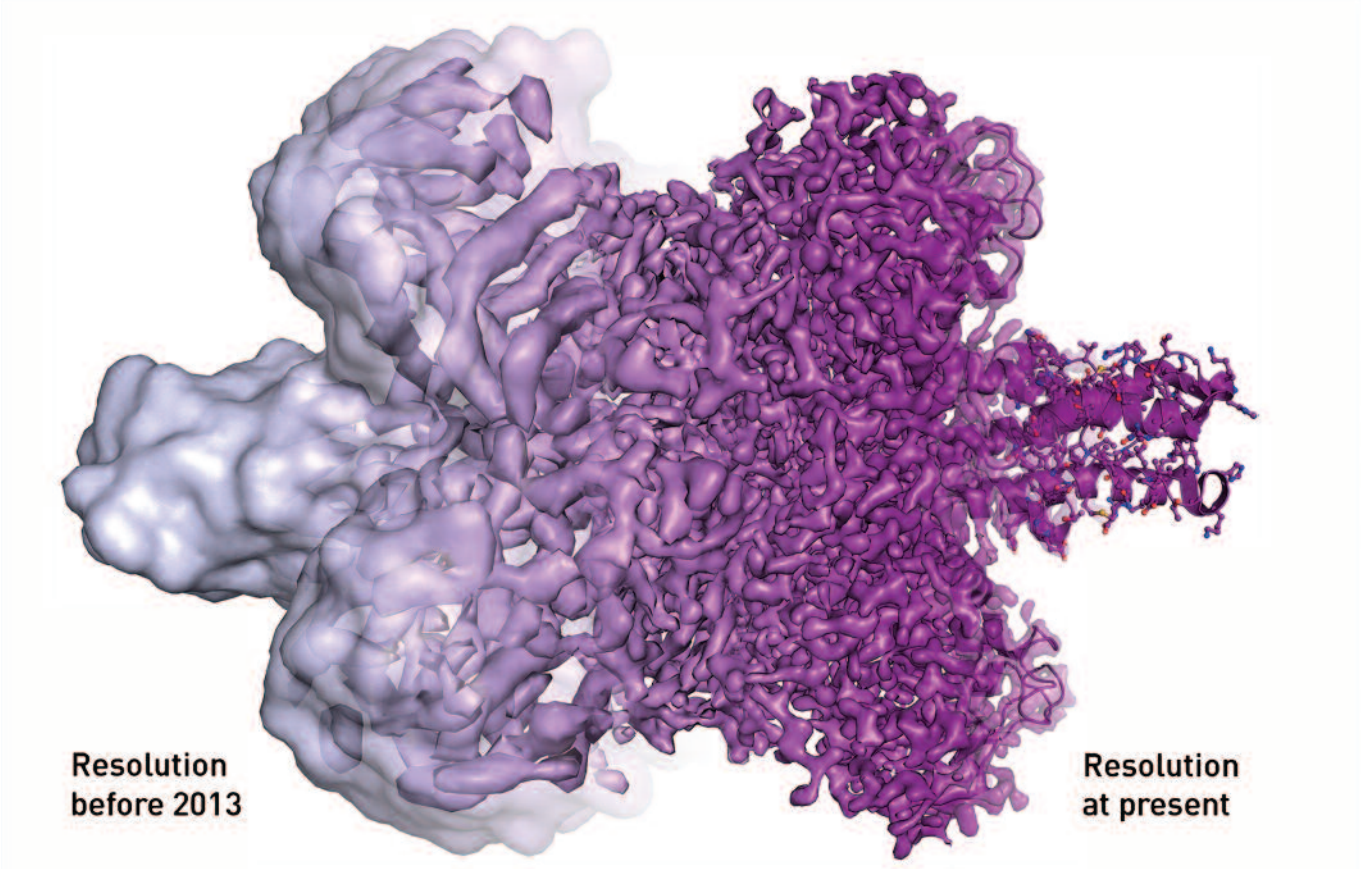
1942 First scanning electron microscope built by Ernst Ruska. It transmits a beam of electrons across specimen surface.



Dartmouth College Electron Microscope Facility

1981 Scanning tunneling microscope invented by Gerd Binnig and Heinrich Rohrer. It can give 3D images down to the atomic level.

2017 Cryo-electron microscopy allows high-resolution structure determination of biomolecules. Nobel Prize in Chemistry awarded to Jacques Dubochet, Joachim Frank and Richard Henderson.



The resolution progression of cryo-EM, illustrated by a representation of glutamate dehydrogenase with an increasing level of detail from left to right. For a protein of this size, 334 kDa, the 1.8 Å resolution to the right (38) could only be achieved after 2012/13. After an image by V. Falconieri (Merk A. et al. *Cell* 2016, vol. 165, pp. 1698–1707). Illustration: © Martin Högbom, Stockholm University.

between potential sample damage and limitation of resolution. EM has until now been generally only considered to be applicable to 'dead' samples.

Ultimately, this is a problem of signal-to-noise ratio. These effects typically limited EM to resolutions of a few nanometres, whereas cryo-EM potentially offers an extra order of magnitude of resolution.

Lastly, there are all the limitations of the data capture and analysis. The structure of the particles being analysed is three dimensional, and so the techniques that have been developed have had to be able to capture and then transform the electron scattering data, particularly given the complexities of low signal-to-noise ratio, randomly oriented particles, and the transformation of 2D sections into 3D visualisations.

The instrument

Collectively, the 2017 Nobel Prize represents the pinnacle of accumulated developments over decades, with individual inspiration and dedication that has combined to create a new analytical capability with revolutionary implications.

Cryo-EM uses the previously-unknown 'vitrified' state of water below around –160°C to effectively encapsulate and protect biological particles, both preserving them during analysis, and allowing virtually 'in situ' states to be analysed. It then applies some very sophisticated data capture and modelling to create very high-resolution visualisations.

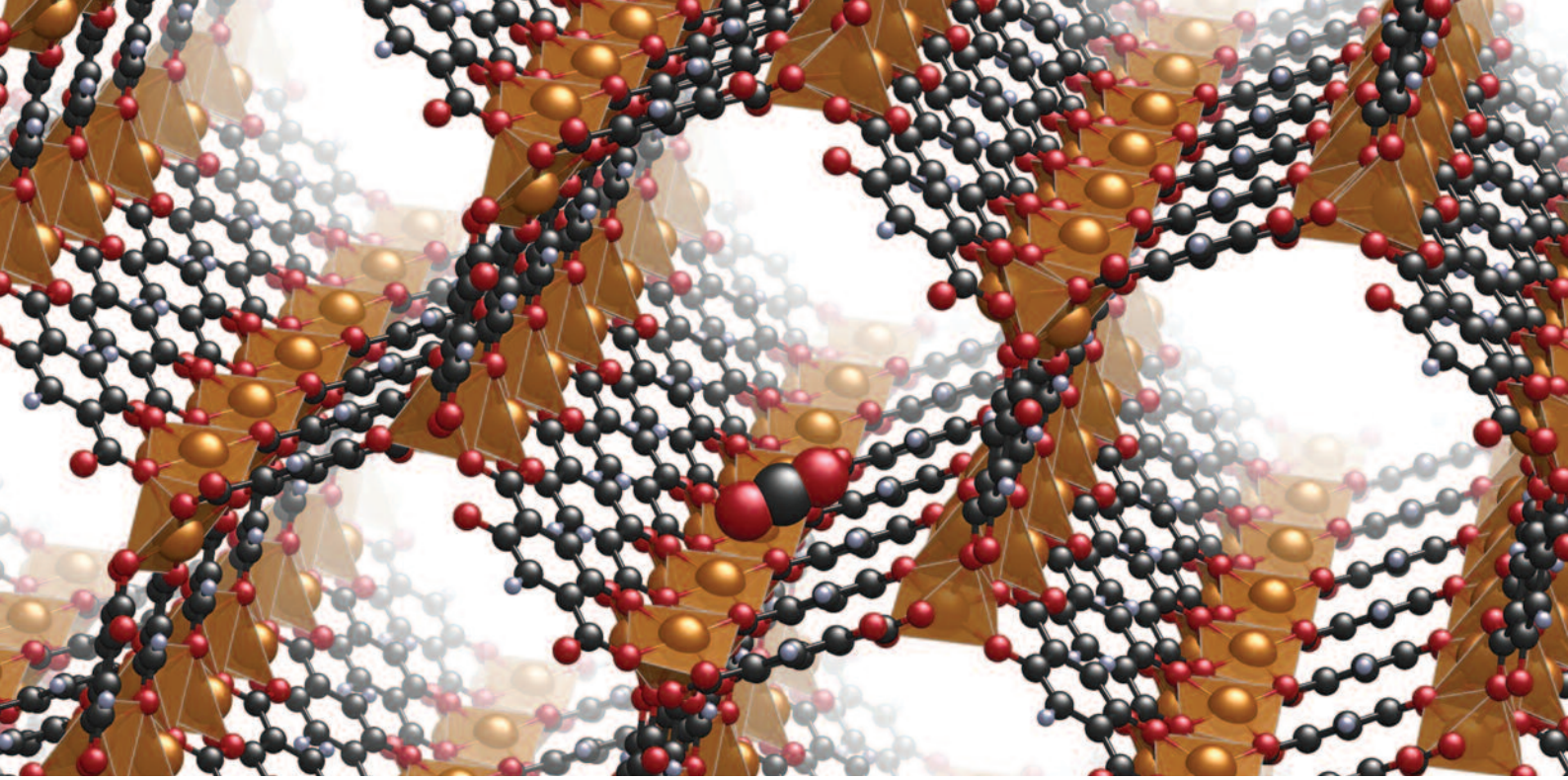
One of the most important aspects of cryo-EM is its ability to analyse very small sample quantities, effectively taking it closer to single particle analysis. But the technique is also versatile across a wide particle size distribution, from nano-scale to macromolecule complexes well over 500 000 daltons. In 1995, Henderson anticipated that enzymes might be analysed to as little as 52 000 daltons, and this has improved with ongoing developments in the technology.

Having come far from its early description as 'blobology', cryo-EM offers an unprecedented degree of resolution. In 2015, Dr Sriram Subramaniam, of the National Cancer Institute's Center for Cancer Research, imaged the enzyme beta galactosidase at a resolution of just 0.22 nanometres (bit.ly/2jPTway).

The technique is already proving to be a valuable tool across a range of biological fields: botany, biotechnology, zoology, pharmaceuticals, health care and cosmetics. Understanding how biomolecules function and interact is fundamental to the development of new innovations in any of these sciences. At this level of detail and resolution, it offers a powerful tool for understanding biochemistry in its dynamic states.

In the next article, we'll look at the individual contributions from Dubochet, Frank and Henderson.

Dave Sammut FRACI CChem and **Chantelle Craig** are the principals of DCS Technical, a boutique scientific consultancy, providing services to the Australian and international minerals, waste recycling and general scientific industries. Part 2 of this article will be published in the March issue.



K. Lee, J. Howe and J. Neaton, Molecular Foundry at Berkeley Lab/UC Berkeley

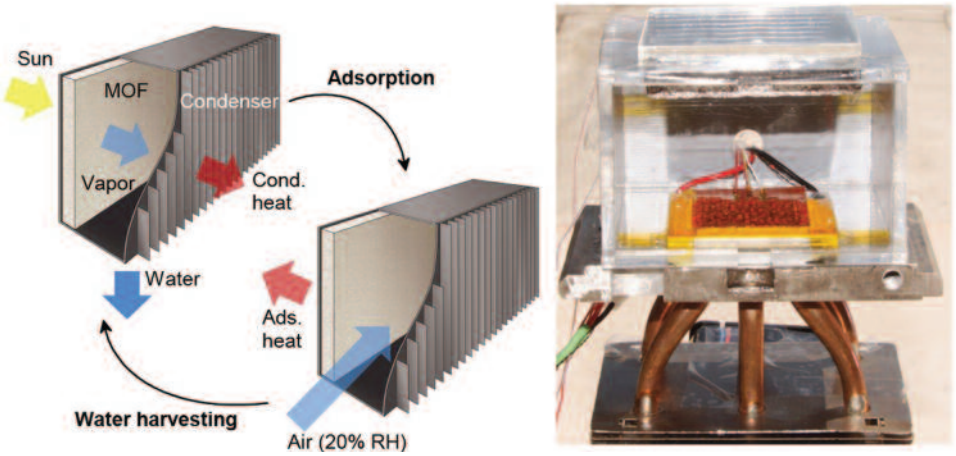
Metal–organic frameworks

From laboratory *to* factory

Once thought of as the 'gunk in the bottom of the flask', metal–organic frameworks have emerged as a potential wonder material. Marta Rubio-Martinez and Matthew Hill present an Australian perspective.

Metal–organic frameworks (MOFs), also known as porous coordination polymers, were first discovered by Professor Richard Robson at the University of Melbourne in 1989. Consisting of metal atoms or clusters joined to one another by organic molecules, their crystalline structures have unprecedented surface areas and uniform pore sizes. They may be capable of drastically enhancing the efficiency of a raft of processes that include separation, storage, detection and release of target molecules. MOFs have been selected by the World Economic Forum's Expert Network and Global Future Councils in collaboration with *Scientific American* and its Board of Advisors as one of the top ten emerging technologies of 2017 for their ability to harvest clean water from the air using no energy at all. The technology has been successfully tested by researchers from the University of California Berkeley, in collaboration with MIT, with a proof-of-concept device using a zirconium-based MOF, which showed that one

... in the past couple of years, the hurdles standing in the way of MOF commercialisation have been brought down, and new products are emerging.



Left: MOF water-harvesting device, composed of a MOF layer and a condenser. The high porosity of the MOF layer allows water to be captured from the ambient air. By placing the device in the sun, the MOF is heated and releases the captured water, which then condenses and is ready for collection. Right: Image of the device built for extracting drinking water from the air. First published in Rubio-Martinez M. et al. New synthetic routes towards MOF production at scale. *Chem. Soc. Rev.*, 2017, vol. 46(11), pp. 3453–80.

kilogram of the material could collect nearly three litres of fresh water per day – enough to supply drinking water for one person – from very dry air with a humidity of just 20%.

However, questions have arisen regarding the time taken for the tantalising properties reported under laboratory conditions to be realised in applied settings. Notably, the comparable material family of zeolites took several decades to find application, and MOFs are significantly more complex and varying materials. Nevertheless, in the past couple of years, the hurdles standing in the way of MOF commercialisation have been brought down, and new products are emerging.

The major challenge in making MOF application feasible is the cost-effective manufacture of MOFs on a large scale. Although many different MOF types with tailored functionalities have been developed in the laboratory, typically each of them requires a specific synthetic method or at least specific details. These laboratory reactions are quite slow, lasting up to several days, and yield only a few milligrams of high-quality crystals. To add to the challenge, these processes cannot be simply scaled up to produce more material. MOF crystals need a surface to nucleate, and using a larger reactor vessel dramatically reduces the surface to volume ratio, slowing down the synthesis or yielding poor-quality materials.

The use of solvents is another problematic aspect; many laboratory syntheses require large amounts of solvents, which are costly to obtain and costly to process as waste materials. Scaled up, these approaches would be economically unviable.

These hurdles have motivated many researchers and engineers to explore and develop novel and commercially viable routes to produce MOFs in an efficient, reproducible and cost-effective way.

Two promising strategies are mechanochemistry and flow chemistry.

The central idea behind mechanosynthesis is to promote chemical reactions by milling or grinding solids with no or minimal amounts of solvents (see image below left). This synthetic approach is restricted to the synthesis of only a few types of MOF structures, but is the most environmentally friendly process for producing MOFs, and could significantly lower the cost of production.

Flow chemistry, on the other hand, is a continuous processing technology that originated in the pharma and agrochemical sectors in the last two decades and which CSIRO has

From left to right: Mechanochemical synthesis of MOFs with a twin screw extruder. The CSIRO flow reactor capability used to fabricate MOFs at the kilogram scale. Seven kilograms of copper-based MOF synthesised by CSIRO flow reactor in six hours.
First published in Rubio-Martinez M. et al. New synthetic routes towards MOF production at scale. *Chem. Soc. Rev.*, 2017, vol. 46(11), pp. 3453–80.

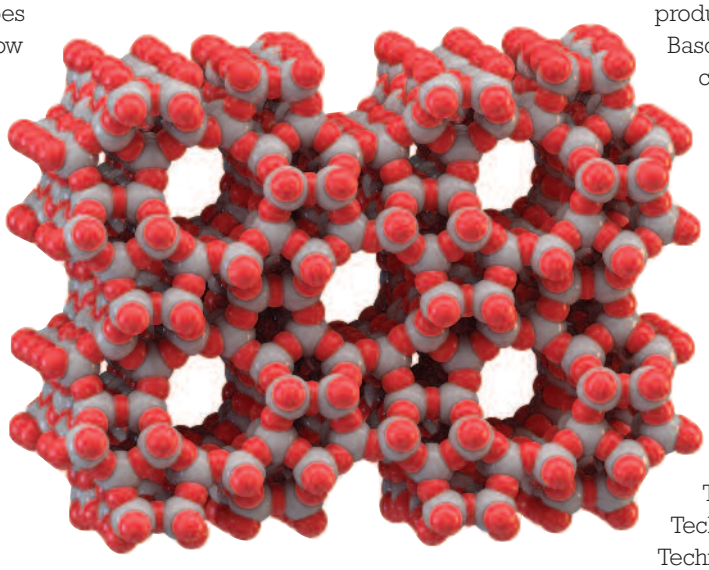
adapted as a new method to produce MOFs (see middle image bottom of page 25). Contrary to batch reactions, in a flow chemistry set-up, the chemical reactions occur in a continuously flowing stream in a tube or pipe rather than in a reactor vessel, solving the problem of surface area to volume ratio. This new method allows precise control over the reaction parameters and delivers an enormous throughput while maintaining the versatility to produce many types of MOFs. Reaction times in a flow reactor are dramatically reduced from days to minutes, without any loss in quality.

These two novel approaches to large-scale production are a complete game changer for MOFs, opening the way for commercial application that depends on a kilogram scale and above.

Despite these promising advances in production methods, MOFs still remain a niche product in commercial markets. This is in part due to the high cost of production, caused by expensive solvents and raw materials, but it is also a market phenomenon. At this stage, there is a low overall demand, which is typical for research applications, and commercial MOF synthesis is limited to small-scale batch production. Most MOFs are retailed at the gram scale by chemical suppliers such as BASF and STREM, and the cost is prohibitive for most industrial applications that require much larger amounts.

However, a recent study by Mosaic Materials, a spin-out from the University of California, in collaboration with the Ford Motor Company, reported that this scenario would dramatically change once market demand picks up. Their complete techno-economic analyses of four different MOFs with potential for hydrogen and natural gas storage assumed a high production of 2.5 Mkg/year. The study shows that, in this case, MOFs can be produced at scale economically if opportunities for further cost reduction are employed, such as using cheap and recyclable MOF precursors, reducing the amount of solvent and waste, and low energy consumption. In essence, this means a reduction from thousands of dollars to prices between $35 and $71 per kilogram, making the many potential applications feasible on a large commercial scale. Owing to the many applications, the growing market for MOFs will push MOF suppliers for further cost-efficiency to remain competitive. MOF production at scale is already underway, which will help secure customer confidence and open the door for other MOF-based products in the mid to long term.

… zeolites took several decades to find application, and MOFs are significantly more complex and varying materials.



The microporous molecular structure of a zeolite, ZSM-5. This aluminosilicate zeolite has a high silicon and low aluminium content. Thomas Splettstoesser/CC BY-SA 4.0

The first industrial company interested in MOFs was BASF, which has been exploring this topic for the last 15 years. During this time, the chemical giant has been working with leading researchers in the field and has developed a product portfolio of different MOF applications as well as selling six MOF products under the product names Basolite® and Basosiv™ to universities and companies for research purposes.

Since the first patent was filed in 1995 by the Nalco chemical company in the US, commercialisation of MOFs has progressed slowly. The first MOF-based products entered the market more than 10 years later in 2016 by MOF Technologies and NuMat Technologies. MOF Technologies, from Queen's University Belfast, developed a system called TruPick in collaboration with the fruit and vegetable supplier Decco Worldwide Post-Harvest Holdings. The product is a micro-adsorbent that holds methylcyclopropene – a gas that blocks the post-harvest ripening of fruit and vegetables, extending the storage life and quality of many fruits and vegetables. Another MOF-based product called ION-X, developed by US spin-out company NuMat Technologies, was launched last year. These gas cylinders are based on a proprietary set of MOFs for storing gases such as arsine, phosphine and boron trifluoride, which are important as dopants in the electronics industry.

In both cases, the companies were spun out of universities but other initiatives are also working towards the commercialisation of MOFs. For example, MOFapps aims to bring research and industry together by

The study shows that, in this case, MOFs can be produced at scale economically if opportunities for further cost reduction are employed ...

Left: TruPick technology from MOF Technologies based on NT-7815 micro-adsorbent for extending the storage life and quality of many fruits and vegetable. Right: Gas storage tank ION-X technology developed by NuMAT for storing speciality gases used in the electronics manufacturing industry. First published in Rubio-Martinez M. et al. New synthetic routes towards MOF production at scale. *Chem. Soc. Rev.*, 2017, vol. 46(11), pp. 3453–80.

identifying opportunities and developing commercially viable applications in the areas of gas storage, industrial cooling, toxic gas protection and health care. From an Australian perspective, CSIRO has created the spin-out entity MOFWORX, which is actively developing technology to directly capture carbon dioxide from the atmosphere for a myriad of uses. The potential for such technologies is based upon the discovery and development of continuous flow-based MOF production, underpinning the ability to access commercial scales of material in an economically viable fashion. MOFWORX will continue as a production house, developing MOF-based technology, targeting production in Australia.

Recent developments in the large-scale production and commercial application of MOFs leave the research field at a fascinating juncture. In future years, as more MOF-based products find their way into the marketplace, previously unknown challenges and opportunities will be surely uncovered. For chemistry researchers, this will spur additional fundamental research challenges. Scale-up production, while extremely promising, requires further development to improve efficiency and the overall economics. Chemists who are able to transition production to sustainable starting materials and solvents will find huge traction.

While many MOFs may appear fit-for-purpose, it is inevitable that new characteristics will be uncovered when they are put to the test in the field. From an Australian perspective, there is a remarkable strength of researchers in the field, going right back to the original inventor, and the team is globally recognised. They are well placed to lead in these new research opportunities as they arise, with the MOF2018 conference in Auckland an opportunity for this work to be showcased to the global community. Partnership with commercial interests in Australia, such as MOFWORX and other partners, is a key step to both enhancing scientific research and finding impact commercially.

Dr Marta Rubio-Martinez is a research scientist at CSIRO. **Professor Matthew R. Hill** is a principal research scientist at CSIRO and associate professor at Monash Chemical Engineering. A reference list is available from the author.

Peter W. Smith OAM

Generous and distinguished inorganic chemist

Dr Peter Smith was a much loved and revered figure in the close-knit Tasmanian chemistry and science communities. A champion for the advancement of science, and a most generous yet unassuming philanthropist, Peter died on 2 July 2017, aged 93.

Peter was born 30 June 1924, an only child. Young Peter excelled at primary school and later studied at the Hobart Technical High School. Upon completion, he found employment, working as a laboratory assistant for an arc welding manufacturer (1940–6). During this time, he studied part-time in the evenings at the Hobart Technical College, achieving diplomas in both chemical engineering and metallurgy (1945), and ultimately a Diploma of Applied Chemistry (1948). He had appointments with the Australian Aluminium Production Commission (1946–7), Murex Australasia – Chemical and Metallurgical Laboratories (1947–51), and then as an examiner at the Australian Patents Office in Melbourne and Canberra (1951–2).

He returned to Hobart, taking up a position as laboratory demonstrator in chemistry at the University of Tasmania in 1952, studying part-time for a BSc (awarded 1956, Honours 1957). Granted leave, he enrolled for his PhD at University College London, supported by a Du Pont Scholarship. Working under the supervision of Professor R.S. Nyholm, Peter was awarded his PhD in 1962 for his work entitled 'Aspects of the chemistry of molybdenum halides'. This interest in molybdenum chemistry stayed with him throughout his career.

Returning to the University of Tasmania, Peter progressed from lecturer (1962) to senior lecturer (1966) and ultimately reader (1971), serving for a time as Acting Chemistry Department Head (1981–2). Peter was a committed teacher, with responsibilities typically focusing around his expertise in classical inorganic and solid state chemistry. However, he was also innovative and forward thinking, modernising the curriculum in the inorganic program, as well as introducing new emerging topics such as Analytical Chemistry, Industrial and Applied Chemistry, and Chemistry for Engineers.

His research was productive, with a focus on the chemistry of intermediate oxidation state compounds of molybdenum, chromium, tungsten, vanadium and titanium, with particular reference to preparative, structural, magnetic and spectroscopic properties of some halides and pseudo-halides. This work proved fruitful, with around 40 papers being published, stemming from his supervision of approximately 25 honours and PhD students.

What set him apart from other educators was his consistent, sincere interest in the welfare of those students he taught or was associated with.

Recognising the importance of spectroscopy and instrumentation to university research, Peter was a key driver for the establishment of the Central Science Laboratory (1974).

Following his formal retirement in 1989, and with concerns about the future supply of scientists in Tasmania and Australia, Peter established his undergraduate scholarships in Physical Sciences at the University of Tasmania in 2002. A generous scholarship, Peter was at times supporting as many as 10 recipients. To date, approximately 30 students have benefited from Peter's generosity and support.

Outside the university, Peter made many profound contributions to professional life in Tasmania. Foremost among these was his support for the RACI. Peter joined the Institute as a Student member in 1940 and rose to Fellowship in 1972. He was a former Branch Secretary, Vice-President and two times President in the 1960s and 1980s. He was awarded a National Citation for his contributions to the profession in 1988, and was an Honorary Life Member. It was a privilege for some members of the local Branch to celebrate with Peter on the occasion of his 75th year of membership recently.

Peter also contributed in many other areas. He was a Life Member of the RSC (joining 1957), an office bearer and Past President of The Royal Society of Tasmania, an Honorary Life Member of ANZAAS (joining 1942), a much loved and distinguished Emeritus Fellow at Jane Franklin Hall residential college, a Branch member and State Chair of AUSIMM (joining 1969), and Tasmanian delegate to national council of AINSE (1982–9).

In his later years, Peter's many contributions were recognised and honoured through receipt of a University of Tasmania Distinguished Alumni Award (2005), an Honorary DSc (2011, coinciding with 50 years of Chemistry at the Sandy Bay campus), and in 2012 a Medal of the Order of Australia (OAM) 'for services to science, education and philanthropy'.

Peter never married, but in numerous conversations made clear he was never lonely. The countless students that came under his tutelage, his many colleagues, and his vast array of friends were his 'family' whom he kept in close contact with. Deeply loyal, he valued each, and kept close tabs on the lives of countless many. In return, Peter was embraced, honoured and cherished into broader family circles.

Peter is fondly remembered and held in the highest esteem by Tasmanian chemists across many generations. What set him apart from other educators was his consistent, sincere interest in the welfare of those students he taught or was associated with. He knew names, knew where each came from, met families, and was interested in individual journeys. He gave encouragement and, when necessary, rebuke to help make each student work and study harder. He organised excursions to Tasmanian chemical industries, helped students find vacation employment, and demonstrated the importance of contributing to a professional society. He was generous with his time and resources, and genuinely cared for the wellbeing of all.

The Australian chemical landscape has changed with the passing of Peter Smith. However, he has left us an amazing example, and an amazing legacy. We are thankful for his life and contributions, ever proper, ever distinguished, ever a scholar.

Ashley Townsend FRACI CChem, **Jak Denny** MRACI CChem, **Eoin Breen** and **Brian Yates** MRACI CChem

New Fellow

Jennifer Martin FAA is Director of the Griffith Institute for Drug Discovery (GRIDD, formerly Eskitis Institute). GRIDD is home to Compounds Australia, the nation's compound collection, and NatureBank – a unique drug discovery platform based on natural product extracts and fractions that have been derived from Australian plants, fungi and marine invertebrates. GRIDD also boasts unique resources for bioaffinity screening and high throughput screening/high content imaging.

Martin is one of Australia's foremost crystallographers, having made pioneering discoveries in protein crystallography and structural biology, specifically in the field of redox biology and drug discovery. She was the first to report a structure of an oxidative protein folding catalyst and to identify the evolutionary link between protein reductases and bacterial protein oxidases. She has reported structures of more than 130 proteins and protein–inhibitor complexes.

Martin is a former ARC Laureate Fellow, ARC Professorial Fellow, NHMRC Senior Research Fellow and ARC Queen Elizabeth II Fellow. She holds BPharm (Gold Medal) and MPharm degrees from the Victorian College of Pharmacy, and was an 1851 Scholar during her PhD research at the University of Oxford. She is currently President of the Asian Crystallography Association, and a member of the Executive Committee of the International Union of Crystallography.

Since establishing her laboratory 25 years ago, Martin has trained a generation of structural biologists. She is a strong advocate for women in science, and a founding member of the Australian Academy of Science 'Science in Australia Gender Equity (SAGE)' Committee that is implementing the Australian Athena SWAN pilot. She is a member of the NHMRC Women in Health Science Committee and was awarded the 2017 Wunderly Medal of the Thoracic Society for her work in gender equity.

Martin is passionate about raising awareness of science, and was inducted as a Bragg Member of the Royal Institution of Australia in 2017 for her contributions in this area. These include establishing Ångstrom Art to use stunning science images on free postcards; lobbying Australia Post to release a 2012 stamp of Lawrence Bragg in the centenary year of Bragg's law; and lobbying the Royal Australian Mint to issue a coin featuring crystallography in 2014, the UNESCO International Year of Crystallography.

Joseph Bevitt receives new ANSTO research award

Joseph Bevitt MRACI CChem is the inaugural recipient of ANSTO's Excellence in Science Communication and Outreach Award, for his skills in translating complex scientific ideas and concepts to broad audiences.

The Excellence in Science Communication and Outreach Award was introduced by ANSTO in 2017 to recognise an individual who has made an effort to inspire and nurture the future generation of scientists and engineers.

As ANSTO's Research Office Manager, Joseph is passionate about showcasing ANSTO's capabilities to students and tapping their curiosity to consider potential careers in the area of science, technology, engineering and mathematics (STEM).

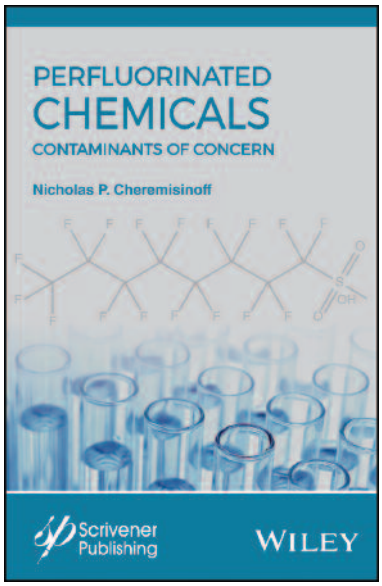
Michael Druce received the Sustained Contribution to ANSTO Award for his key role in Australia's advancement and manufacturing of molybdenum-99. This parent isotope of technetium-99m is used in many nuclear medicine procedures to diagnose diseases such as heart disease and cancer and to diagnose skeletal injuries. Druce was involved in the development of ANSTO's ^{99m}Tc generator.

Jessica Veliscek-Carolan received the ANSTO Early Career Award for her role in looking for improvements in the safe and sustainable management of radioactive waste.

The Australian Centre for Neutron Scattering Sample Environment team received the George Collins Award for Innovation for their ability to provide innovative solutions for challenging neutron beam experiments.

ANSTO CEO Dr Adi Paterson said it was a real privilege to work among such a talented cohort of individuals. 'Our people are our greatest asset and it's important to our organisation to celebrate their achievements and motivate them to be the best.'

ANSTO



Perfluorinated chemicals: contaminants of concern

Cheremisinoff N.P., Scrivener Publishing (John Wiley & Sons), 2016, hardback, ISBN 9781118363538, 272 pp., $321.95

Talk about good timing! Dr Nicholas Cheremisinoff (an experienced chemical engineer and technical editor of more than 145 books since the early 1990s) has provided yet another valuable guide to the environment industry. He has delivered another 'primer' with the right balance of the fundamental chemistry and environmental science of an emerging contaminant group, against practical guidance and related case studies.

Typical of such an emerging contaminant, the fluorine-based polymer group was initially described as 'perfluorinated chemicals' (or PFCs) as the book title notes, but the terminology for the environmental contaminant has quickly evolved to PFAS, now encompassing the broader range of both per- and poly-fluorinated alkyl substances. Cheremisinoff greatly helps to clarify such definitional issues, noting:

> PFASs comprise a large group of chemicals that are both chemically and thermally stable and are both lipophobic (have no affinity for oils) and hydrophobic (have no affinity for water), making them very useful in surfactants and as polymers. However, PFASs are composed of two main parts; one that is formed out of a hydrophobic alkyl chain and a hydrophilic (strong affinity to water) functional group. A total of 146 perfluorochemicals and 469 fluorochemicals are potentially able to degrade to PFCAs. The most investigated classes of PFASs are the perfluorocarboxylate acids (PFCAs) and perfluoroalkyl sulfonic acids (PFSAs). The most studied PFCA compound is perfluorooctanoic acid (PFOA) and for PFSA it is perfluorooctane sulfonate (PFOS).

PFAS is a highly topical, front-page issue across Australia and internationally, primarily due to the wide-spread historical use of these compounds, especially in aqueous fire-fighting foams (AFFF), for which PFAS compounds were an important ingredient. Again, Cheremisinoff notes:

> The most investigated classes of PFAS are the perfluorocarboxylate acids (PFCAs) and perfluoroalkyl sulfonic acids (PFSAs). The most studied PFCA compound is perfluorooctanoic acid (PFOA) and for PFSA it is perfluorooctane sulfonate (PFOS).

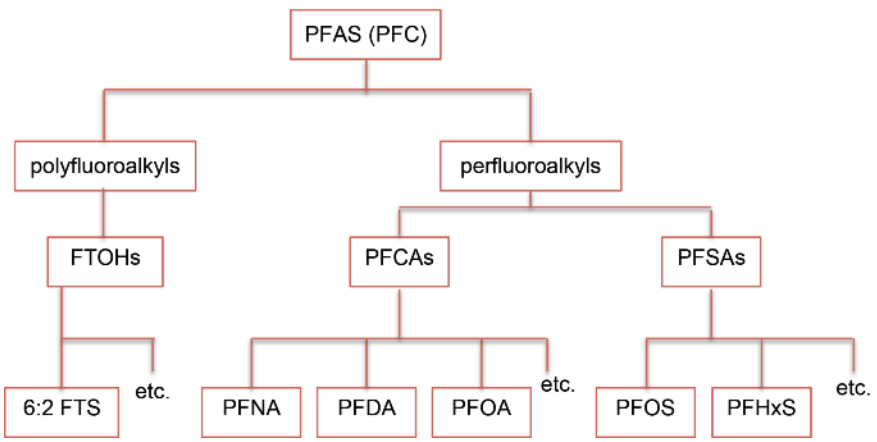
Indeed, because of its persistent, bioaccumulative and toxic (or PBT) characteristics, PFOS became a designated persistent organic pollutant, joining the better-known 'dirty dozen' identified at the 2001 Stockholm Convention.

Cheremisinoff's book is an excellent primer for environmental scientists and engineers currently involved in the assessment and management of this vexing and ubiquitous contaminant group. The book's well-designed table of contents takes readers from definitional challenges, through the vast uses of this group of complex chemicals, through the 'supply chain pathways', to its human and environmental risks and associated regulatory agency considerations. The latter part of the book provides an overview of treatment technologies and it rounds out with four case studies of PFAS-contaminated sites (all in the US).

Perhaps it was due to the rapid publication of this book to meet market demands, but one minor complaint in my reading of this book was the frequent duplication of information. This is most evident in relation to chapters associated with the health risk studies (Chapter 4), regulatory framework (Chapter 7) and the case studies (Chapter 10), although perhaps it was the author's plan to design these chapters to be able to be read in isolation, resulting in such duplication.

Of course, the pace of international research and development for PFAS has been nothing less than astonishing, and so it is to be expected that a book on PFCs would be quickly superseded. However, the currency of Cheremisinoff's book remains valid, especially in relation to the fundamental chemistry of this complex contaminant. Like any emerging

A family tree of perfluoroalkyl and polyfluoralkyl substances



FTOHs	fluorotelomer alcohols
6:2 FTS	6:2 fluorotelomer alcohol
PFAS	perfluoroalkyl substances
PFC	perfluorinated chemicals
PFCAs	perfluoroalkyl carboxylic acids
PFDA	perfluorodecanoic acid
PFHxS	perfluorohexane sulfonic acid
PFNA	perfluorononanoic acid
PFOA	perfluorooctanoic acid
PFOS	perfluorooctane sulfonic acid
PFSAs	perfluoroalkyl sulfonic acids

contaminant, standards, advisories and restriction (Chapter 7) and treatment options/technologies (Chapters 8 and 9) have become quickly dated and should be read with caution in light of significant international changes, especially in the last 12 months.

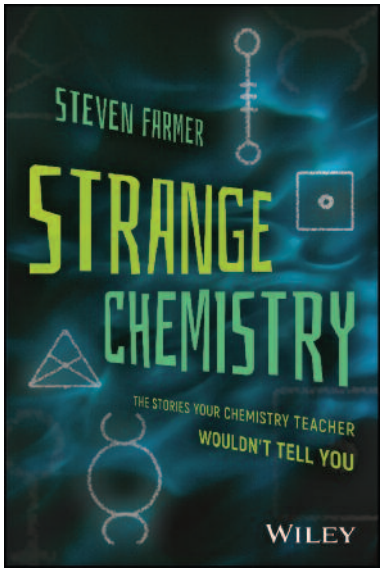
While not meaning to diminish the substantial value of this book, I wanted to identify two notable omissions. The first (at least in my biased analytical chemist's mind) was the lack of discussion of the analytical chemistry for this complex group of compounds, especially in relation to the challenges associated with analysing environmental levels for such a ubiquitous contaminant, as well as increasing interests in PFAS transformational and precursor compounds. The rapid development of analytical methods for total organic fluoride (TOF) and the total oxidisable precursor assay (TOPA) are quickly emerging to address so-called 'hidden PFAS', especially when the comprehensiveness and adequacy of remedial technologies are being evaluated. The second notable omission concerns linking of the compounds' environmental chemistry with their 'fate and transport', although this issue is tangentially discussed in Chapter 6 ('Supply Chain and Pathways to Contamination'). A second edition of the book would benefit from the development of a conceptual model that brings together the complex real-world environmental characteristics for these compounds.

Given the substantial international level of interest in PFAS, a second edition will probably be welcome. Such a revision could include updating of the compounds' regulatory status, more details on the increasing variety of remedial technologies for water, groundwater, soil and structures, and the addition of more case studies (noting that Australia has a wealth of examples to draw upon). As noted, the very recent and significant developments in analytical chemistry and a further expansion of the compounds' fate and transport may also prove sagacious for a second edition (please?)

In conclusion, I strongly recommend Cheremisinoff's 'primer' for those environmental chemists, environmental engineers, environmental regulatory agencies and the wider community who are involved in PFAS, as a very useful fundamental guide. The sheer novelty of this emerging contaminant group continues to cause confusion in relation to fundamental challenges such as terminology and basic chemistry and Cheremisinoff's book may help to address these issues and perhaps allow the debate to move into finding solutions to these vexing contaminants.

Ross McFarland MRACI CChem

Strange chemistry: the stories your chemistry teacher wouldn't tell you



Farmer S., Wiley, 2017, paperback, ISBN 9781119265269, 364 pp., $78.95

Strange chemistry: the stories your chemistry teacher wouldn't tell you is an exploration of science in the real world that is as gritty as it is informative. If you always wanted to learn the secret ingredient in Coca-Cola, the most toxic substance on Earth, or the most expensive, this book is a good place to start. In an effort to connect chemistry theory with the real world, these stories were created as part of author Steven Farmer's experiences teaching organic chemistry to university students. He had begun to include one of these real-world stories in each class, and then students started to admit that the stories were the only reason they attended classes.

An introductory chapter covers chemistry basics for anyone without a science background, or for those of us who are a bit rusty on organic chemical structures. The book's remaining chapters, including 'Why oil is such a big part of our lives', 'Why old books smell good' and 'The poisons in everyday things' contain a series of related stories. The book's stories also draw on popular media, including the TV series *Breaking Bad*, a program that has had a significant impact on how chemistry is viewed in society.

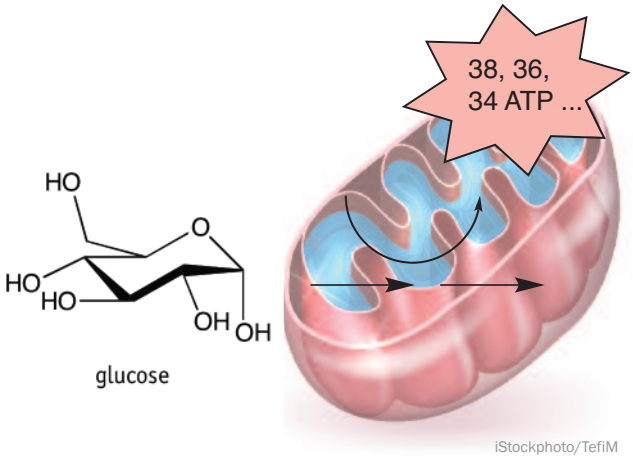
The book's pages are marked not only by chapter but also by story title, making it easy to flip through and find a good story. Despite this abundance of informative and entertaining stories, the book does not fall into the category of relaxing bedtime reading. However, for anyone interested in the science behind a specific story, the reading list at the end of each chapter offers the opportunity for further research on the topic. These reading lists are impressive – varying from books and journal articles through to recent US Government studies and publications.

One of the very few drawbacks of *Strange chemistry* is how the impact of many stories is reduced by the extensive use of trademark chemical names. Many of these brand names (for household chemicals and pharmaceuticals) are unfamiliar, diverting the reader towards Google to try and pick up momentum. Unless you have spent time in the US or are very familiar with these trademark names, some stories are a challenge to follow. The US-based statistics in many stories (not all of them recent) are also at times quite distracting.

Strange chemistry is not a cover-to-cover read, with the details of some stories being enough to make you put down your glass of wine or your coffee cup (at least temporarily anyway). Nonetheless, it's a great option for anyone looking for an entertaining story for a perhaps captive audience.

Samantha Profke MRACI

ATP and the textbook trap



iStockphoto/TefiM

Students often have an intrinsic belief in the infallibility of textbooks. It is in the textbook and so it must be right. These students worry when different textbooks give different information. For example, the production of adenosine triphosphate (ATP) in aerobic respiration is a key process in biochemistry. The reported number of ATP molecules produced per glucose molecule ranges from 30 to 36 in different textbooks. Some authors who write more than one textbook give different numbers in different books, published in the same year. Some books explain why there is uncertainty in the number, while others do not.

ATP production involves several interlinked steps, and some of these steps have alternative, parallel pathways that vary in the number of H^+ and/or other intermediates involved.

Earlier studies tried to study each step and each pathway within each step separately and obtained a maximum possible number of ATP produced per glucose molecule for each individual step or pathway. Then, assuming that if each step or pathway operated independently and at optimum efficiency, the researchers just added the maximum numbers for each separate step or pathway. This is the theoretical maximum number (approximately 40) in old textbooks. This is a theoretical maximum, not a real yield. Each pathway is linked to other pathways, so optimising one pathway decreases the efficiency of some other pathway, meaning this maximum possible number of ATP molecules produced per glucose molecule is not achieved.

In maths terms, this theoretical maximum is an upper bound or over-estimate. Scientists have tried to lower this upper bound in an attempt to get the lowest upper bound (decrease the over part of the over-estimation), which should (hopefully) be a better estimate for the real number.

More recent studies have tried to look at all steps and pathways in combination, to get a more realistic yield. The issue is whether laboratory conditions correspond to real physiology or biochemistry. As laboratory conditions are altered to better correspond to real physiology or biochemistry, the yield number is continually being revised downwards: 38, 36, 34, etc. Some latest reports have this number at 30 (or perhaps even 28). And there might be some disagreement about whether a particular set of test conditions corresponds better or worse to real physiology or biochemistry, meaning that some of the newer, lower numbers are not widely accepted.

Real processes are complex and have real-world limitations that limit the yield. This is true in all areas of science and technology, including chemistry.

Rote learning the number of ATP produced per glucose molecule is counter-productive because there is little understanding. (Changing what students should learn may have implications for the type of questions that can be asked in an examination, but that is a discussion for another occasion.)

The fact that different textbooks have reported different estimated numbers of ATP produced per glucose molecule is a great example of how knowledge in science has evolved and continues to evolve in response to new evidence and discoveries.

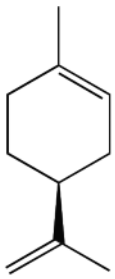
What is more important is that students develop 'an understanding of the nature of scientific inquiry', to be able 'to evaluate and debate scientific arguments and claims', and 'to appreciate the dynamic nature of science knowledge' (quotations from the Australian Curriculum: Science).

The fact that different textbooks have reported different estimated numbers of ATP produced per glucose molecule is a great example of how knowledge in science has evolved and continues to evolve in response to new evidence and discoveries. The various estimated numbers demonstrate the strengths and limitations of science as evidence-based conclusions continue to evolve based on new evidence.

Instead of focusing on a single number that is the most current estimate of the number of ATP produced per glucose molecule, students should focus on the fact that the downward revision of this number over time is a demonstration of the testable and contestable nature of science and the processes of science, including chemical science.

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

Oranges, lemons and limonene: addressing surprisingly persistent and enduring myths



R-(+)-limonene – the major enantiomer present in both oranges and lemons

iStockphoto/Kelenart

Introducing students (and non-scientists) to the concept of chirality is a fundamental aspect of science education. This often involves a discussion of chirality in nature and the implications of this molecular asymmetry, using real-world examples. Consistent with these objectives, one of the first laboratory experiments that second-year undergraduate chemistry students undertake at the University of Tasmania involves the steam distillation of *R*-(+)-limonene from lemons and oranges. *R*-(+)-Limonene is the major enantiomer present in these citrus fruits. As part of this exercise we have been somewhat surprised to find that some secondary sources (correctly) state that *R*-(+)-limonene is the major enantiomer present in oranges, while (incorrectly) claiming that *S*-(–)-limonene is the major enantiomer present in lemons. Moreover, it is also often erroneously suggested that *R*-(+)-limonene is responsible for the distinctive smell of oranges, while *S*-(–)-limonene is responsible for the characteristic odour of lemons.

It is difficult to pinpoint the origins of the myth that oranges and lemons contain opposite enantiomers of limonene in high enantiomeric excess. A 2004 review article, which discusses this topic, indicates that this may have originated from a paper published in *Science* in 1971 by Friedman and Miller. These researchers refer to two papers and suggest that these reports provide *evidence* that *R*-(+)-limonene from orange oil and *S*-(–)-limonene from lemon oil were used as starting materials in the semisynthesis of natural products *R*-(–)- and *S*-(+)-carvone, respectively. Interestingly, neither of the papers cited by Friedman and Miller discusses the synthesis of *S*-(+)-carvone from *S*-(–)-limonene or the use of lemon oil as a starting material. To this day, some chemistry textbooks still state that *R*-(+)-limonene is predominantly found in oranges while *S*-(–)-limonene is predominantly found in lemons, as does a webpage on the official website of the US National Museum of History – Smithsonian.

... the myth that *R*-(+)-limonene is responsible for the distinctive smell of oranges, while *S*-(–)-limonene is responsible for the characteristic odour of lemons, has also permeated the literature.

R-(+)-Limonene is often obtained from orange peel and it is described as possessing an orange or citrus odour. However, it is proposed that the components of orange oil that are responsible for this characteristic orange smell comprise less than 0.1% of the oil. This is consistent with the observation that high-purity *R*-(+)-limonene features a harsh turpentine odour. Notably, *S*-(–)-limonene has been described as having a harsh turpentine odour with a lemon note. Unfortunately, the myth that *R*-(+)-limonene is responsible for the distinctive smell of oranges, while *S*-(–)-limonene is responsible for the characteristic odour of lemons, has also permeated the literature. Currently, this includes chemistry texts, peer-reviewed articles, and, surprisingly, the 'Information for the Public' section for the 2001 Chemistry Nobel Prize on the official Nobel Prize website. Although these sources do not specifically state that *S*-(–)-limonene is the major enantiomer present in lemons, the mischaracterisation of the odour profiles of limonene enantiomers may lead people to make such an inference.

Relative to other myths that persist in the secondary literature, the above-mentioned issues arguably represent rather benign errors. However, by directly addressing and drawing attention to this particular issue, we aim to remind the chemical community (and highlight to students) how easily mistakes and misconceptions can propagate in science, and society more generally. This also reinforces the importance of testing theory in the laboratory and the need to preserve this feature at the core of chemical education, both now and in the future.

Christopher T. Desire MRACI (Australian Centre for Research on Separation Science), **Ross M. Deans**, **Robert A. Shellie** MRACI CChem (Australian Centre for Research on Separation Science), **Jason A. Smith** MRACI CChem and **Alex C. Bissember** MRACI CChem are at the School of Physical Sciences – Chemistry, University of Tasmania. Robert Shellie is now at Trajan Scientific and Medical, Ringwood, Victoria.

Carbon dioxide disposal

One of the main hopes for continuing the use of fossil fuels is that carbon dioxide resulting from combustion can be deposited in deep geological strata – so-called carbon geosequestration. In past issues of *Chemistry in Australia*, I have described the technology and economics of removing carbon dioxide from gas streams in the hydrocarbon processing industry and how these produce a concentrated stream that can be geosequestrated. I have also described the difficulties and costs of extracting carbon dioxide from flue gases, particularly from gas and coal power-generating facilities. There are also technology and cost issues associated with carbon dioxide disposal in storage facilities that need to maintain their integrity for hundreds of years.

The basic theory of carbon geosequestration comes from work in enhanced oil recovery (EOR) using carbon dioxide. In one method of EOR, carbon dioxide is injected into an oil reservoir, where it dissolves in the oil, lowering the oil's viscosity and allowing freer flow of oil to the producing well. For this to work, there has to a source of carbon dioxide, often remote process plants which means piping to the oil-field over long distances. This practice gives some reassurance that carbon dioxide pipelines and pipeline networks can be constructed safely and carbon dioxide transmitted over long distances. This is an important demonstration because most carbon dioxide emissions are remote from geological structures suitable for disposal.

An EOR project at Weyburn in Canada obtains carbon dioxide from a large lignite coal-to-gas plant in Dakota in the USA (Dakota Gasification Company). The EOR gas also contains hydrogen sulfide, which is also injected and disposed in the EOR project. The pipeline system for this is over 300 kilometres long. This project demonstrates that pure carbon dioxide is not required for geosequestration. The table lists methods that have been considered for long-term carbon dioxide disposal together with the typical pressure required to maintain carbon dioxide in the liquid state.

Methods for long-term carbon dioxide disposal

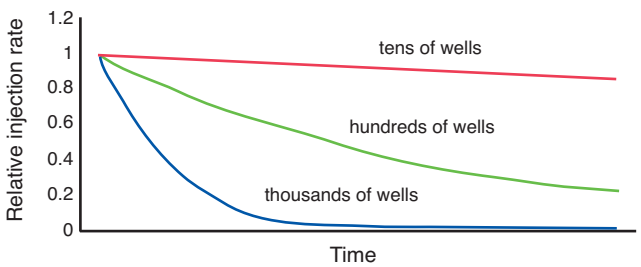
Method	Pressure required (bar)
Deep un-minable coal beds	80–100
Enhanced oil recovery	150–160
Deep saline aquifers	150–180
Abandoned oil and gas wells	150–180
Deep sea disposal	310 (3 km water depth)

Data source: Saxena and Flintoff, *Hydrocarbon processing*, December 2006

The methods listed are considered viable methods for disposing of carbon dioxide. In deep coal beds, the carbon dioxide is absorbed by the coal. In EOR, some of the carbon dioxide returns via the producing well dissolved in the oil but since the carbon dioxide is a valuable commodity, it is recovered and re-injected. Carbon dioxide can also be disposed of in deep sea trenches of static water and the like where the gas dissolves and remains in the cold water.

Deep saline aquifers and abandoned oil and gas facilities are the most studied. There are several issues to be considered. As noted above, the best sites are often remote from the emissions point, requiring a gas transmission pipeline, and because carbon dioxide is a heavy suffocating gas, leakage, especially near urban areas, will be cause for concern. Another issue is the dissolution of minerals causing, in the long term, caving and potential collapse and leakage from the storage site. The main worry is limestone (a very common mineral) but other minerals could also be attacked over the long times required for storage.

One of the main difficulties is identifying potential sites. For a greenfield site that is required to geosequestrate the emissions from a large coal-fired power station, the rate of carbon dioxide injection may be more than 10 million tonnes per year. Furthermore, this rate will be constant for the life of the power station. The rate of injection may be quite high on a newly drilled well but as more carbon dioxide is pushed down the well, resistance will build up and the rate will fall. This is illustrated in the graph. The top line shows an ideal situation where the rate of injection falls little with time but the more likely situation is with the lower lines. For a geological structure that is tight (highly compacted), resistance to injection may increase dramatically with time and in order to maintain a constant high injection rate thousands of wells may have to be drilled over the life of the project (lower line). This is analogous, but the inverse of, the production of gas from tight reservoirs or shale where many wells have to be drilled to maintain a constant overall production rate because the production rate of the individual wells falls dramatically with time.



Injection rate impact of reservoir properties.

The middle line on the graph is the intermediate case where increasing resistance can be overcome by drilling less but still hundreds of wells over the course of a major project. The geology will determine if a few or many wells will have to be drilled but whatever the case, it is certain that a geosequestration project will require an extensive area if large volumes of carbon dioxide from major power-generating facilities are to be disposed of; some estimates are in the thousands of square kilometres

... the best sites are often remote from the emissions point, requiring a gas transmission pipeline, and because carbon dioxide is a heavy suffocating gas, leakage, especially near urban areas, will be cause for concern.

So, for a carbon dioxide geosequestration project, assuming the costs of carbon dioxide extraction and compression is paid by the emitter (EOR experience indicates that this may be at least $20/tonne), the additional costs will be for transmission to the geosequestration site, possibly further compression costs at the injection site, and the cost of the well (typically $2–5 million each).

As can be deduced from the above, a major demonstration of this aspect of the carbon geosequestration will be costly. In a small project in Australia, the CO2CRC has demonstrated the injection of 65 000 tonnes of carbon dioxide in a depleted natural gas reservoir in the Otway basin in Victoria. The project has gone on to inject carbon dioxide into saline formations and to monitor movement of the gas in the underground reservoirs. A commercial carbon dioxide gathering system and pipeline network has been proposed for Victoria in the La Trobe Valley (known as CarbonNet) with carbon dioxide being geosequestrated in depleted oil and gas reservoirs in Bass Strait.

One of the largest projects is by Chevron in the Gorgon LNG project in north-west Australia. The LNG facilities on Barrow Island use gas from the offshore Gorgon gas field, which contains about 14% carbon dioxide. This is extracted prior to LNG production and is injected to a depth of two kilometres under the island using three compressor stations and nine injection wells supplemented with six water production/injection wells and two wells for surveillance. The project is said to dispose of 3.4 million tonnes of carbon dioxide per year when fully operational. However, this will only dispose of 40% of the facility emissions; most of the rest will probably be emitted in flue gas from power generation facilities to drive the refrigeration plant.

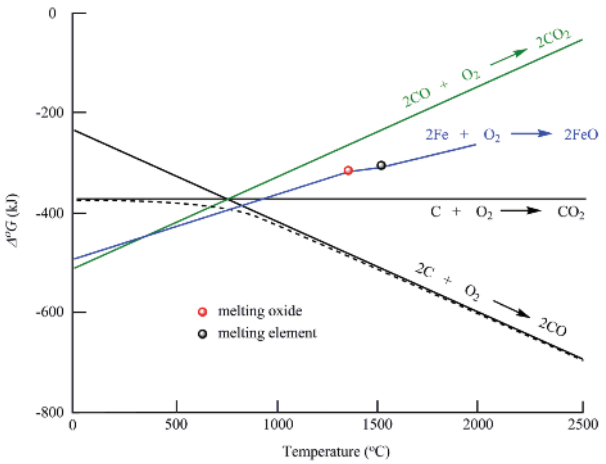
Duncan Seddon FRACI CChem is a consultant to coal, oil, gas and chemicals industries specialising in adding value to natural resources.

Ellingham and the iconic reactions of iron

The history of civilisation as we know it would have been quite different without the love affair between metallic iron and non-metallic carbon. A red-hot charcoal fire containing some nuggets of iron ore ushered in the Iron Age.

Ellingham and Gibbs free energy

Reducing iron ore to iron is possible because of a set of quirky chemical reactions, which can be shown on an Ellingham diagram. The diagram is named after Harold Ellingham (1897–1975) – a British chemist who first constructed the diagram in 1944. The diagram's use was explained by Ray Hodges in part 7 of his 'Back to basics' series (June 2012, p. 28).



Free energy as a function of temperature for three carbon and oxygen reactions and one iron and oxygen reaction. Graph created from data from Ives D.J.G., *Monographs for teachers*, No. 3, The Chemical Society (London), 1969

The horizontal axis is temperature and the vertical axis is $\Delta G°$ (Gibbs free energy), named after Josiah Willard Gibbs. Just as the bigger the voltage of a battery the bigger the energy it will deliver, the bigger the (negative) ΔG, the bigger the driving force for that reaction. Why negative? Sorry, the field just developed this way. The diagram shows that this driving force (think voltage) often changes strongly with temperature.

For any two reactions at a particular temperature, the one with the larger (negative) $\Delta G°$ will reverse the one with smaller (negative) $\Delta G°$. This has an exact parallel with battery voltages except that $\Delta G°$ in an Ellingham diagram has a very large dependence on temperature.

Talking about the voltage analogy, there *is* a direct correlation:

$$\Delta G° = -nFE°$$

where n is the number of electrons, F is the Faraday constant and $E°$ is the standard electrochemical potential. For electrochemical half-reactions, the reaction with the higher $E°$ drives the reaction with the lower $E°$ backwards.

Thus, the relative amount of electrical energy needed to refine metals electrochemically (at room temperature) parallels the $\Delta G°$ value for that metal.

Our interest here is in the reduction of iron oxide by carbon and its oxides and this occurs above about 720°C. The reduction reactions are the three reactions involving carbon and oxygen:

[1] $2CO + O_2 \rightarrow 2CO_2$

[2] $C + O_2 \rightarrow CO_2$

[3] $2C + O_2 \rightarrow 2CO$

[1] + [3] = [2]

- Note that the lines for $\Delta G°$ for CO and CO_2 cross at around 710°C.
- The equilibrium equation is $2CO \rightleftharpoons C + CO_2$ and is determined by equation [3] above 710°C and by equation [2] below 710°C.
- The dotted line is a composite curve connecting these two reactions.
- Above 710°C, CO is more stable than CO_2 and carbon dioxide will 'gasify' carbon.
- Below 710°C, CO can disproportionate into CO_2 and C (but this requires a catalyst).
- In practice, the gas CO generally does the contact work of reducing iron ore.

Kinetics overrules equilibrium

The Ellingham diagram shows the species at equilibrium. If the temperature is decreased suddenly, the time to reach a new equilibrium can be infinite. If the gases cool quickly, as in the exhaust from the hot cylinders of a car or from a gas-fired kitchen range, carbon monoxide is stable and remains in the burnt gases along with carbon dioxide, in spite of the lower temperature. Carbon monoxide poisoning can and does occur.

This was dramatically illustrated by Australia's biggest industrial accident. On 31 July 1902, an explosion killed 96 men and boys in a coal mine at Mt Kembla in New South Wales. Firedamp (mainly methane from the coal seams) in air at levels between its explosion limits catches fire when exposed to a naked flame. Afterdamp (mainly carbon monoxide) is found in the residual cooling gases.

Beware the occasional explanation that carbon monoxide is produced when there is insufficient oxygen. While it is true that the carbon dioxide–monoxide equilibrium is shifted to produce more monoxide at lower oxygen concentrations, this is relatively quite small compared to when a high temperature equilibrium mixture is cooled and locked in at ambient temperatures.

With increasing temperature, one line in the Ellingham diagram slopes up, another slopes down and the third is horizontal. The equilibrium of a reaction that produces more gas molecules than it starts with shifts to the right with increasing temperature. The equilibrium of a reaction that produces fewer molecules than it starts with shifts to the left with increasing

temperature. And a reaction in which there is no change remains virtually unchanged with temperature.

Gases are more disordered than solids (or liquids) and this drive to disorder (entropy $\Delta S°$) is the major temperature variable component of the chemical driving force $\Delta G°$ in the Ellingham diagram. The Ellingham diagram is determined by the equation $\Delta G° = \Delta H° - T\Delta S°$.

Abetxuko Bridge – a weathering steel bridge by J. Sobrino in Vitoria, Spain. Pontis21/CC BY-SA 3.0

Now for a phase diagram

Don't faint, yet.

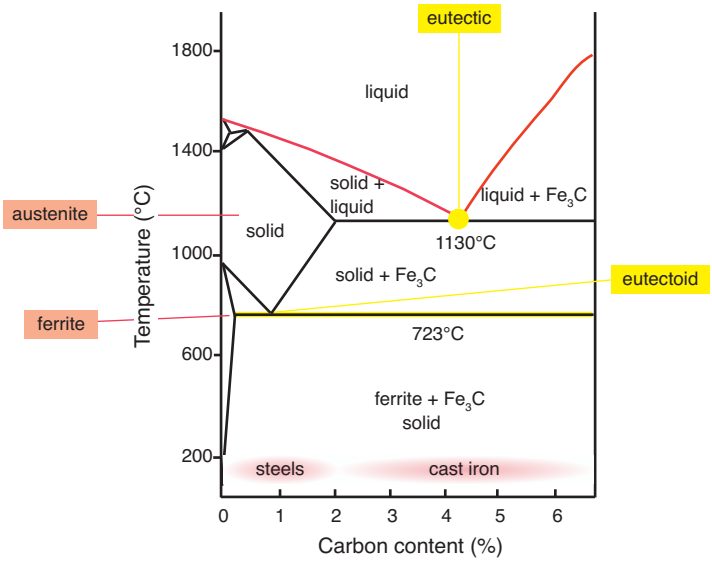
In the diagram below, keep your eyes peeled along the red line separating all liquid from solid plus liquid. This line reaches a minimum at the yellow dot. This occurs at a composition with a minimum and sharp melting point, just like a pure chemical. Carbon in iron can knock down the melting point from 1500°C to around 1100°C, making things a lot easier for blacksmiths at the start of the Industrial Revolution.

Now, look down.

To make steels, the amount of carbon in cast iron has to be reduced by burning it off. However, this also raises the melting point so it is easy to see why steel production came much later than iron production.

Think wrought iron and samurai swords. The beating and folding of the steel allows the carbon to come in contact with air and thus be burnt off. Iron becomes steel as the carbon content is reduced from 4% to 2% and below.

Remember, phase diagrams only represent equilibrium situations.



Iron iron–carbon phase diagram.

Consider any region in the diagram that represents a solid composition. If this material is suddenly quenched in water, this solid compound at equilibrium at high temperatures remains stable and non-equilibrium at ambient temperatures.

If clean water is dropped onto hot iron, the water just bounces off as bubbles (try this on your ironing iron). But dip that red-hot samurai sword instead into cold urine and the liquid sticks (don't try this) and the cooling is more efficient. Some iron nitride is produced on the surface, which provides a hard edge.

Adding chromium and nickel to steel makes stainless steel. Since the mid-20th century, many exotic metals have been added to form the stable rusty Corten™ (weathering) steel, currently the 'metal de jour' of sculptors by the sea and elsewhere.

Wood and trees in air are kinetically stable. A red-hot cigarette butt allows this system to move to thermodynamic equilibrium; that is, to carbon dioxide and water vapour accompanied by an output of extreme heat.

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

Wine under veil

Some years ago when I had my first opportunity to teach oenology in the Erasmus Mundus Master Vintage program, I came across the term 'vin de voile'. My initial reaction was to ask if this was a term applied to wine that created some sort of religious experience, but quickly came to learn that it was the French term for wine developed under a film or 'flor' yeast. The role of film yeast in the production of fortified dry white wines such as *fino* and *manzanilla* was well known to me, but the use of this type of yeast for ageing unfortified white wines was rather a surprise.

My first experience of dry, unfortified white wine developed using a film yeast was in Hungary. When I was teaching in the Vintage Master program at Corvinus University of Budapest, each Friday was set aside for an excursion to a wine region. In the Tokaj region, I was introduced to *Szamorodni száraz*. Apart from not being able to pronounce the name, I had some difficulty adjusting to the colour, aroma and palate of the wine. One fundamental issue was simply the presence of acetaldehyde, commonly used in the 'New World' as an indicator of a wine spoilt through oxidation. The grapes, mainly the Furmint cultivar, can give a wine of up to 14% alcohol. Without further alcohol addition, the wine is allowed to develop in barrel under the film or veil yeast. The descriptor of 'biological ageing' for this process is now in common use: biological, as the film yeast is active in development of the wine.

The wine of this style that perhaps is more widely known internationally is *vin jaune* (yellow wine) from the Jura region of France. Savagnin grapes, which can yield up to 14% potential alcohol when fermented to dryness, is the cultivar used for the production of *vin jaune*. The film yeast activity is critical to this wine style.

The image shows a *vin jaune* wine undergoing its 'biological ageing'. The thin film of yeast sits on the surface, creating the veil or voile effect. The barrel is a 228-litre aged oak barrel, selected so that it does not impart oak character to the wine. The headspace above the film allows contact with air, creating aerobic conditions, while anaerobic conditions exist under the film. While the wine in this image appears to exhibit a brown colour, the best wines are golden to deep gold in colour; hence the name *vin jaune*. Regulations require that a *vin jaune* is aged for six years and three months after grape harvest before it can be bottled. Some younger voile wines are aged for two and a half years only. Traditionally, a squat 620-millilitre bottle is used.

Major chemical changes occur during the ageing under veil process.

Arnaud 25/Wikimedia

The successful development of *vin jaune* is very much dependent on good cellar hygiene as well as the quality of the flor, film, veil, voile, vellum yeast – all these adjectives are used in discussions of the yeast in the literature. My experience in the production of '*apera*' wines, the name we now use for *fino*, was to try and maintain a permanent flor or film and remove wine or add new wine under the film with minimal disturbance. In the Hungarian and French styles of unfortified wines, the film yeast is allowed to develop over time in the barrel. For this to be successful, sugar fermentation must be complete and preferably malo-lactic fermentation finished. The developing film yeast then moves from fermentative to oxidative metabolism. This is a long story, about which I will write in a subsequent issue.

Major chemical changes occur during the ageing under veil process. Acetic acid (commonly referred to as 'volatile acidity') and acetaldehyde initially increase and then decrease in concentration. Both compounds along with glycerol are utilised in various metabolic processes linked to the ageing process; for example, condensation of glycerol with acetaldehyde can lead to the formation of acetals. Perhaps the most notable chemical change is the formation of sotolon from α-ketobutryic acid and acetaldehyde (Thuy et al. *J. Agric. Food Chem.* 1995, vol. 43, pp. 2616–19.). Sotolon is a powerful impact aroma compound that has a love it/hate it response by tasters. Its aroma is commonly ascribed to curry, burnt honey and fenugreek. Aged wines show a marked increase in neutral polysaccharides (Santos et al. *Vitis* 2000, vol. 39, pp. 129–34), which add to the viscosity and length of the mouthfeel.

Finding the traditional Jura wines in Australia can be a challenge with often only the younger two and a half year aged wines being available. The wines are great as an aperitif, and go brilliantly with Comté cheese, a so-called 'terroir cheese' made from unpasteurised cow's milk in the Jura region. A simple alternative, however, is to go to Kangarilla Road winery in McLaren Vale and get the 2015 The Veil (bit.ly/2BhSA21). A pleasant way to commence 2018.

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.

Plants to watch out for

The dandelion, *Taraxacum officinale*, flourishes in my garden but I enjoy the bright yellow flower so much that I often wait until the weed is in full flower before digging it out. I can't enjoy it for long because the fluffy seed head soon appears and the wind-blown seeds are sown to generate the next crop of dandelions. The common name of this plant is said to be derived from the French *dent de lion* – tooth of the lion – which refers to the shape of the leaves. I wondered what the French thought about this, but I got a surprise when I consulted my mini-Larousse and found *pissenlit* that translates as pee-the-bed.

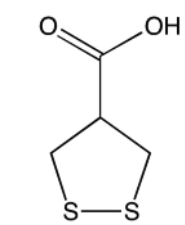
That's what we called it when I was a child. It was widely believed, at least among my peer group of neighbourhood kids, that picking the flowers, certainly holding a bunch of them, would inevitably lead to a nocturnal accident. I can't remember any evidence for this belief and I recall that I, even then a budding scientist, picked a few flowers and dared the plant to do its worst. Nothing untoward happened.

The purported diuretic effects of the dandelion could hardly have arisen from bunches picked by innocent children or the gardeners cursing its presence in their lawns so I undertook a little literature research. It revealed that various bits of the plant had been used for hundreds if not thousands of years in folk medicine and that diuresis was indeed among its pharmacological properties. The roots contain a number of sesquiterpene lactones and their glycosides, some triterpenes and phytosterols, and flavones. The aerial parts have flavones, too – hence the bright yellow colour – along with fructans, polyphenols and derivatives of hydroxy benzoic acids. It's not clear exactly which of these could be responsible, but an aqueous extract of the leaves is certainly diuretic. The leaves and stems are also very rich – 5% and 8% respectively - in potassium.

The purported diuretic effects of the dandelion could hardly have arisen from bunches picked by innocent children or the gardeners cursing its presence in their lawns so I undertook a little literature research.

Physiological effects produced by plants are nothing new, of course, but this was literally a 'backyard' example. Toxicity causing fatality would have to be the most extreme of the physiological effects, and just short of that the strange effects produced by opioid alkaloids can be quite scary. There are some less well known – but appreciated if you've been there – effects of the opioids, such as their propensity to induce constipation.

I turned to *Chemistry in the market place* (sixth edition, Ben Selinger and Russell Barrow, 2017) – CiM6, as the authors call it – to check out my asparagus knowledge. When we eat asparagus, the cyclic disulfide contained in it, asparagusic acid, is converted in the body to thiols that are rapidly excreted in the urine, giving it a strong, unpleasant smell. It was my understanding that only some people's metabolism worked that way so stinky pee wasn't guaranteed, but Ben and Russell are up to date with the four classes of asparaperson: those who excrete but can't detect, neither excrete nor detect, detect but don't excrete, detect and excrete (the category in which both authors, and I, fall). A game of perms and pongs, to paraphrase those mathematics lectures.



asparagusic acid

Inulins are fructans, sugar polymers consisting of chains of fructose units with some glucose end groups, which are regarded as 'dietary fibre'. They are soluble, so 'fibre' seems to be stretching it a bit (no pun intended), but that's the way dietary nomenclature works. Health food shops stock dietary fibre concoctions, and you can find them in the 'alternative' section of most pharmacies. That's for deliberate ingestion, but inadvertent ingestion can occur, too, if the food contains the carbohydrate inulin. Inulin makes up about 75% of the tubers of the Jerusalem artichoke *Helianthus tuberosus* – nothing to do with Jerusalem and not even an artichoke. Once planted, these things grow like weeds in Melbourne gardens and produce kilograms of tubers that are edible, with a sweet, delicate flavour ... but watch out. I used to be able to eat them with no ill effects, but now in my mature years even a small amount of Jerusalem artichoke produces copious amounts of intestinal gas, courtesy of an over-active biome.

Ian D. Rae FRACI CChem (idrae@unimelb.edu.au) is a veteran columnist, having begun his Letters in 1984. When he is not compiling columns, he writes on the history of chemistry and provides advice on chemical hazards and pollution.

events

6th International Conference and Exhibition on Materials Science and Chemistry
17–18 May 2018, Rome, Italy
materialschemistry.conferenceseries.com

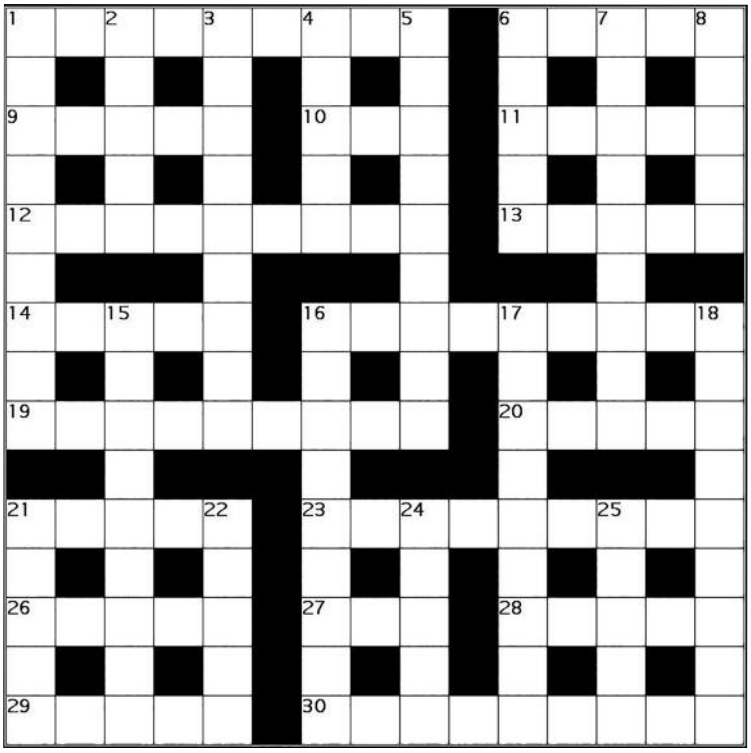
ALTA 2018 – Nickel-Cobalt-Copper, Uranium-REE & Gold-PM Conference & Exhibition
19–26 May 2018, Perth, WA
altamet.com.au/conferences/alta-2018

AOCRP-5 – 5th Asian & Ocean Regional Congress on Radiation Protection
20–23 May 2018, Melbourne Vic.
aocrp-5.org

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

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

cryptic chemistry



Across

1 Made Spooner very busy. (9)
6 See 28 Across, 2 Down and/or 25 Down.
9 Sneer at iodine trapping scale. (5)
10 Rent permit. (3)
11 $Al_2SiO_4(F,OH)_2$ is best from beginning to end. (5)
12 Benzene, for example, is like clockwork around oxygen. (9)
13 Calls may be 12 Across. (5)
14 Less sugar here? (5)
16 C_4H_4S is not 12 Across. (9)
19 Pick 10 Across cosine error. (9)
20 Our inclusion of a metalloid surface. (5)
21 Bring together a band. (5)
23 Gathering one tricep hurt. (9)
26 Born earlier; back in the days when secured loans were safe. (5)
27 Even anomers get used in spectroscopy. (1.1.1.)
28 & 6 Across Make up proteins from calcium, molybdenum, iodine and silicon. (5,5)
29 1613117 compounds. (5)
30 Bones of knees lost flexibility. (9)

Down

1 See 15 Down.
2 & 6 Across Chair stood to reveal the most hydroxylated of the set. (5,5)
3 Flame with oxygen every so often outside the ring. (9)
4 Silly radical: $R_3Si–$. (5)
5 Enticed to circumvent discovery. (9)
6 Looking for posterior. (5)
7 Bumping up against pigment in transition. (9)
8 Scopes how big they are. (5)
15 & 1 Down Old capillaries clot badly: size is important and so is a phase boundary. (9,9)
16 Episulfides near this iodine reaction. (9)
17 PH_3 happens to react with HO–. (9)
18 Destroy or reuse on invalid. (9)
21 Cultivates sprouts. (5)
22 Scrutinises small apertures. (5)
24 Change of direction: hyperbola, perhaps. (5)
25 & 6 Across Iron lost as NaI modifies C compounds containing both =CNH and –COOH groups. (5,5)

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

raci

Royal Australian Chemical Institute

PLAN YOUR NEXT TRIP WITH YOUR RACI MEMBER BENEFITS

Regardless of your destination, your RACI Member Advantage benefits can help you save, so you can spend more time doing the things you love.
Access savings on accommodation, dining, flights, car hire and much more.

Flights
Get 3% discount on pre-purchased Flight Centre e-gift cards and use them on flights, accommodation or tours.

Hotels & Accommodation
Access over 100,000 promotional deals and competitive rates on accommodation options worldwide.

Travel Insurance
Ensure a great trip for you and your family with premium travel insurance.

Car Hire
Obtain either reduced car hire rates or excess in Australia and New Zealand with Hertz, Europcar or Avis/Budget.

Dining
Enjoy great savings on dining at selected restaurants nationally. Offers include 2 for 1 dining or discounts off the total bill.

Entertainment
Save on pre-purchased admission tickets for museums, animal sanctuaries, cruises and other popular Australian attractions.

www.memberadvantage.com.au/RACI

For more information: email info@memberadvantage.com.au or call 1300 853 352

Member ADVANTAGE®

raci
Royal Australian Chemical Institute

Focus on your health this summer with incredible discounts on a range of health benefits including:

HCF Health Insurance
Access great discounts on health insurance premiums with Australia's largest not-for-profilt health fund.

Goodlife Active Plus Membership:
Get fit this summer with 15% off membership making it easier to stay motivated.

Specsavers Premium Club:
Get offers not available to the public and 1000s of frames to choose between.

Discover all your benefits at:
memberadvantage.com.au/raci
or call 1300 853 352

Member ADVANTAGE®