NZIC Chemistry IN NEW ZEALAND

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Articles and Features

Other Columns

Comment from the President

Here at Waikato, we recently held the annual Open Day (targeted at secondary school students) and a Community Open Day to celebrate the 50th anniversary of the University. At events such as these, it is always gratifying to see people's engagement and delight in chemistry, whether it be using liquid nitrogen to freeze foliage, "flashes and bangs" or something as simple as a magnetic stirrer in a large flask of fluorescent solution. Simple demonstrations such as these seem to entertain young and old alike. It is a shame that the general public perception of chemistry is not always so positive! One of the things that always surprises me is how non-scientific people are fascinated by something as simple as a rotary evaporator! Blasé to us but we all have our own chemical delights. For me, it may be an aesthetically pleasing NMR spectrum while to others it may be a crystal structure or a particularly elegant calculation!

I would like to draw the attention of members to the Prime Minister's Science Prizes. These are New Zealand's pre-eminent annual awards for excellence in science (prize money totals $1 million) and aim to raise the profile and prestige of science in New Zealand. The prizes include the following:

The Prime Minister's Science prize: To an individual or team who has made a transformative discovery or achievement in science that has had a significant impact on New Zealand, or internationally

The Prime Minister's MacDiarmid Emerging Scientist prize: To an outstanding emerging scientist undertaking research for a PhD in New Zealand, or within five years of the date of the award of their PhD

The Prime Minister's Science Teacher prize: To a teacher for outstanding achievement in teaching Science

The Prime Minister's Science Media Communication prize: To a practising scientist who is an effective communicator; this prize provides them with an opportunity to further develop their knowledge and capability in science media communication.

The Prime Minister's Future Scientist prize: This prize is automatically awarded to the Supreme Award recipient from the Royal Society of New Zealand's 'Realise the Dream' competition for outstanding achievement in carrying out a practical and innovative research or technology project.

The prize round closes on **4 August.** For more information or to enter, go to *www.pmscienceprizes.org.nz*

The recent budget actually held some good news for science and education. For the tertiary sector, $83.3 million was allocated to lifting tuition subsidies in disciplines including science (8.5% increase), agriculture (8.5% and selected health sciences (pharmacy 16.4% and physiotherapy 12.4%). An additional $53 million over four years was also allocated to establish another three Centres of Research Excellence (CoREs), which will bring the total number to ten. Details of these and other initiatives can be found on the website *www.beehive.govt.nz*

Finally, I hope that everyone took a few minutes to complete the recent short survey on the current format and content of *Chemistry in New Zealand*. The results of this survey will be made available when they have been analysed fully.

Michèle Prinsep
NZIC President

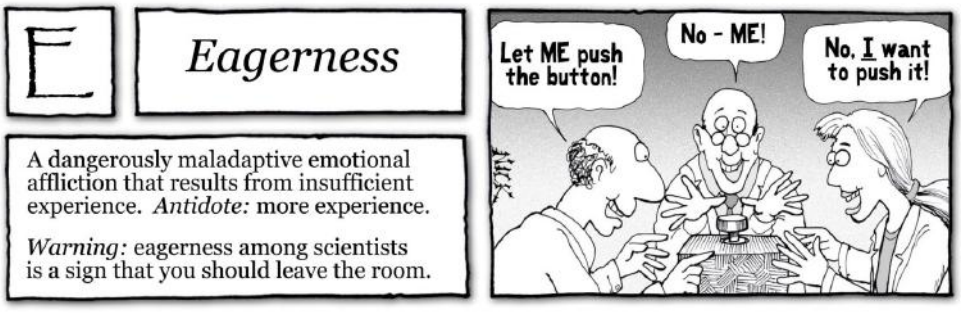
From the Editor

Thank you to everyone who took the time to respond to the *Chemistry in New Zealand* reader survey and particularly those who provided thoughtful feedback and comments. As the survey was still open as this issue went to print, a summary of the results will be published in the October edition of the journal.

One of the most enjoyable aspects of my career as a chemist has been working alongside colleagues who are passionate about their job, who bring their enthusiasm for science to the lab and the lecture room, and who inspire the next generation of young people. I recently came across this wonderful cartoon by Nick Kim (*http://www.lab-initio.com/*) which reminded me of why I chose the career pathway I did.

Of course there are many times when experiments go wrong, papers are rejected, funding proposals are declined and yet more changes or cuts are made in the science sector, provoking feelings of cynicism and despair with "The System". However, I hope we are all helping to promote the same eagerness and excitement in our undergraduates, new postgraduates and early-career researchers that will lead them to pursue a satisfying and ultimately rewarding career in chemical science that many of us currently enjoy.

Catherine Nicholson
Editor



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New Zealand Institute of Chemistry

supporting chemical sciences

July News

Branch News

AUCKLAND

The University of Auckland

ACS Medicinal Chemistry Award

Distinguished Professor *Bill* ***Denny***, Director of the Auckland Cancer Society Research Centre and Honorary Professor in the School of Chemical Sciences, was presented with the 2014 American Chemical Society Division of Medicinal Chemistry Award at the ACS 34th National Medicinal Chemistry Symposium, held in Charleston, South Carolina 18-21 May. Following the presentation of the award, Bill gave the Award Address entitled *Drug development in a university setting*. Professor Denny is the first non-American recipient in more than 30 years of the biennial Medicinal Chemistry Award, made by the world's largest scientific society, the American Chemical Society.

Prof Denny delivering the award lecture

Maurice Wilkins Centre re-funded

The Maurice Wilkins Centre, an existing CoRE hosted by the University of Auckland, has been approved for further funding by the Tertiary Education Commission in the recent funding round. The University of Auckland hosts the Maurice Wilkins Centre in partnership with the universities of Otago, Canterbury, Victoria and Waikato, and the Malaghan Institute of Medical Research. The Centre will specifically target three groups of diseases that pose grave threats to New Zealand society; cancer, diabetes and infectious disease.

Vice-Chancellor's Commercialisation Medal

Professor *David* ***Williams***, from the School of Chemical Sciences, was awarded the 2014 Vice-Chancellor's Commercialisation Medal at the University of Auckland's Research Excellence Awards on 2 May.

Chemistry quiz

The Auckland Branch held its second chemistry pub quiz in April 2014. The event was well attended with 70 participants making up 15 teams. The winning team, *Oxidants Happen,* was represented by *Katie* ***Lin***, *Aaron* ***Tay***, *Mario* ***Kubanik***, *Mathew* ***Graham*** and *Stefanie* ***Maslek***.

The event was organised by our student volunteers *Charles* ***Kong*** (student representative), *Nelson* ***Lam*** (Quiz Master), *John* ***Arabshahi*** and *Shama* ***Dissanayake***. The chemistry pub quiz was a great fun event and an opportunity for networking and has now become an annual event for the Auckland branch.

The New Zealand Institute of Advanced Study, Massey University, Auckland

Peter Schwerdtfeger gave a public lecture at the Max-Planck Institute for Complex Systems in Dresden on *The end of the Periodic Table: going for superheavy elements*.

He co-organised (together with *Sergeij* ***Flach*** and *Joachim* ***Brand***) a workshop on *Nonlinear physics at the nanoscale*.

Auckland Branch Chemistry Quiz 2014 winning team "Oxidants Happen"

Student volunteers of the Chemistry Pub Quiz

A position in organic chemistry is going to be advertised soon, and there will be more positions in chemistry over the next few years to cater for the increasing number of chemistry students at the Albany Campus. A new science building is planned and student accommodation is currently being built on the Albany campus.

CANTERBURY

University of Canterbury

Sad news

The Department was saddened by news of the death of *Alan R.* ***Katritzky*** in February, at the age of 85. Alan was born in London, completed his DPhil (1954) at Oxford with Sir *Robert* ***Robinson*** and then took up a postdoctoral position at Cambridge. He returned to a lectureship at Oxford until 1963, when he was appointed Professor of Chemistry and Dean of the School of Chemical Sciences at the newly established University of East Anglia. In 1980 he moved to the University of Florida in Gainville, where he set up the Centre for Heterocyclic Compounds, which he ran until his death. Alan is best known for his work in heterocyclic chemistry, for which he received numerous awards and honours. He was a prolific publisher, having published over 2200 papers (that equates to one every ten days for 61 years) and over 200 books. He had a strong connection with Canterbury through a 25 year collaboration with Peter Steel, with whom he published over 100 papers.

Postgraduate research showcase day

The Department came together on 28 April to celebrate the research endeavours of 2nd year PhD students. The day was split into four sessions chaired by members of the postgraduate committee. With 15 speakers, there was a wide range of excellent science on show, and the professional standard of the slides and presentations was obvious from the start. All speakers did an excellent job of keeping the audience entertained, educated and enlightened about their research. Presentations were given by *David* ***Lim****, Lita* ***Lee****, Kalib* ***Bell****, Will* ***Kerr****, Eric* ***Lang****, Govind* ***Singh****, Andrew* ***Wallace****, Logan* ***Heyes****, Gert-Jan* ***Moggre****, Rasika* ***Kariyawasam****, David* ***Young,*** *Michael* ***Weusten****, Sandra* ***Atkinson****, Fatemeh* ***Tavakolinia*** and *Gerd* ***Mittelstaedt***. At the conclusion of the day the judges (*Sally* ***Gaw****, Andrew* ***Watson*** and *Penel* ***Cross***) deliberated for rather a long time over the winner of the *Ralph H. Earle Jr. Seminar Prize*. This prize results from a generous bequest given to the Department by the late Ralph H. Earle Jr., (Ralph was a Postdoctoral Fellow in the Department during 1965), because of his strong belief that chemists should appreciate the importance of being able to verbally communicate their subject. The prize is now awarded annually *for the best review seminar presentation given in the Department of Chemistry by a second-year postgraduate student*. This year the recipient was Gerd Mittelstaedt from the Parker group for his presentation entitled *A long story cut short – investigation of the regulation of adenosine triphosphate phosphoribosyl transferase (ATP-PRT).* Gerd was a very worthy winner, with a fantastically enthusiastic and clear presentation which held the audience's attention to the very end. Having said that, the deliberations took time due to the excellent standard set by the speakers and the panel agreed that all of them would have done the Department proud had they been at an international conference. Kalib Bell from the Downard group was also given an honourable mention for his presentation entitled *Nanoscale modifications of metal oxide materials*. At the end of the presentations there was a drinks reception very kindly sponsored by the Canterbury Branch of the NZIC. It was a lovely way to end the day with everyone enthusiastically discussing the presentations whilst mingling over nibbles and wine.

Visitors

We welcomed *Stephen G.* ***Withers***, Professor of Chemistry and Biochemistry at the University of British Columbia. He is a native of South West England and obtained his BSc and PhD at the University of Bristol, UK. He then moved to Canada in 1977 as a Postdoctoral Fellow at the University of Alberta using protein NMR approaches to probe mechanisms of glycosyltransferases working with Brian Sykes and Neil Madsen. In 1982 he joined the University of British Columbia as Assistant Professor. His research interests centre on understanding how the enzymes that form and degrade glycans work as such efficient catalysts. Using the tools of chemistry, biochemistry and microbiology, and many collaborations, his work led to the uncovering of several 'new' mechanisms for glycoside cleavage, the development of new classes of enzymes for synthesis (glycosynthases), as well as to potential new therapeutics for influenza, diabetes and Gaucher's disease.

Welcome also to *Richard L.* ***McCreery***, currently Professor of Chemistry at the University of Alberta, with a joint appointment as Senior Research Officer at the National Institute for Nanotechnology (NINT). Until 2006, he was Dow Professor of Chemistry at Ohio State University. He received his BS in chemistry from the University of California, Riverside, in 1970, and PhD under Ralph Adams at the University of Kansas in 1974. His research involves spectroscopic probes of electrochemical processes, the electronic and electrochemical properties of carbon materials, and carbon-based molecular electronics. Much of the new research involves collaborations with materials scientists and engineers, as well as surface scientists and electrochemists. He leads an effort at NINT and the University of Alberta to investigate hybrid devices for molecular electronics, which combine existing CMOS technology with new electronic and optoelectronic devices containing active molecular components. McCreery has written over 230 refereed publications, including one book and has ten US patents, with three of those extended to Europe and Japan. He has served as an Associate Editor for the American Chemical Society journal *Analytical Chemistry* since 2004.

Finally, *Dr John* ***Brown***, a Manchester graduate who did his PhD with Professor *Arthur* ***Birch*** on metal-ammonia reductions. This was followed by postdoctoral work with Professor Ronald Breslow at Columbia and then a Research Fellowship at the Australian National University in Canberra. His first academic post was at the then new University of Warwick, for eight years, which was followed

by a move to Oxford in 1974, to a lectureship associated with a tutorship at Wadham College until 2008. For that period his main research involved catalysis by transition-metal complexes with emphasis on understanding their mechanisms and contributing to synthesis, particularly asymmetric synthesis. More recently he has held a Leverhulme Emeritus Fellowship (2008-2010). Prior work in catalysis has led to the award of the TSC Tilden Lecture in 1991, the RSC Prize in Organometallic Chemistry in 1993, election to the Royal Society in 1996, a share of the Descartes Award 2001, the Pracejus Prize in 2005 and the RSC Robert Robinson Award in 2013. He has held short-term visiting professorships in several universities across Europe.

Annette ***Steward*** has recently joined Emily Parker's group as a Research Assistant to study bacterial enzyme evolution; this will involve molecular biology, protein expression and purification. Annette will be spending half of her time with the Parker group and half at AgResearch in Lincoln until September 2015. She has a biochemistry degree from the University of Newcastle, UK and previously worked in a research group in Cambridge, UK, studying protein folding.

R.H. Stokes Medal awarded

Alison ***Downard*** has recently been awarded the R.H. Stokes Medal of the Electrochemical Division of the RACI. The medal is awarded for distinguished research in the field of electrochemistry carried out mainly in Australasia. Past recipients include three former Erskine visitors to our Department: Alan Bond, Stephen Fletcher and Justin Gooding.

MANAWATU

Massey University, Institute of Fundamental Sciences

Mark ***Waterland*** attended the 10th Australasian Conference on Vibrational Spectroscopy in April and presented recent work on characterisation of graphene nanoribbons. In June, *Ashley* ***Way*** attended the Quantum and Computational Chemistry Student Conference (QUACCS), which was organised by *Deborah* ***Crittenden*** from UC, and gave a presentation on computational studies of graphene and graphene analogues. *Eileen* ***Obben*** has started as a PGDipSci student in the Waterland group. Her project is Raman and infrared microscopies for the pathohistological identification of skin cancer. *Maaruthaah* ***Senilnathan*** is carrying out her final year engineering research project in the Waterland group, investigating perovskite-based solar cells.

Other new postgraduate students are *Natalia* ***Olivecrona***, *Lily* ***Lian***, and *Leonie* ***McKenzie***. Natalia will be studying NMR-based metabolomics under the supervision of *Pat* ***Edwards***. Lily is studying collagen-based biomaterials in conjunction with LASRA under the supervision of *Bill* ***Williams***. Leonie is studying disubstituted paracyclophanes and the conservation of helical asymmetry under the supervision of *Gareth* ***Rowlands***.

Jamie ***Withers*** successfully defended his PhD study entitled *Supramolecular assembly and metal-coordination in G-quadruplex structures* on 11 March (supervisors: Dr *Vyacheslav* ***Filichev*** and Associate Professor *Shane* ***Telfer***). A recent article published by the group of Vyacheslav Filichev was chosen to be featured on the front cover for the first issue of ChemPlusChem published by Wiley in 2014. Cover Profile accompanies the cover picture and describes research efforts towards sequence-specific gene labelling in live cells. *Amy* ***Toms*** started her technician position in Vyacheslav's group on 1 March 2014.

Professor *Carlos* ***Gonzalez*** (Instituto de Quimica Fisica Rocasolano, Madrid, Spain) visited IFS-Chemistry for two weeks in April 2014 as a part of collaboration with Vyacheslav Filichev and Patrick Edwards on *NMR-based studies of modified G-rich sequences* supported by an International Mobility Grant from the Royal Society of New Zealand.

In April, *Jana* ***Filitcheva*** started working on the establishment of G4-DNA-specific helicase assay as a part of a collaborative project between several research groups at IFS. The initiation of this project has been supported by the grant from the Palmerston North Medical Research Foundation awarded to Vyacheslav Filichev and *Gill* ***Norris***.

Recent talks by visitors to Massey University have included *Olivier* ***Van Wuytswinkel*** from Université de Picardie in France, who spoke about the roles of pectin structure modifications in plant development. *Chris* ***Easton*** talked about a radical approach to enzyme biotechnology in a joint NZIC/IFS seminar. *Gareth* ***Rowlands*** talked about his work on chirality.

OTAGO

The Branch organised a 'Beer and Posters' social event in April which was well attended by staff and students from around the Otago campus. The poster prize was awarded to Department of Chemistry PhD student *James* ***Wright*** for his presentation on *Hexaphenylbenzene and hexa-peri-hexabenzocoronene "click" 1,2,3-triazole ligands*.

Guy Jameson presents James Wright with his poster prize.

University of Otago, Department of Chemistry

Rob ***Middag*** has been awarded the Royal Netherlands Academy of Arts and Sciences 2014 Heineken Young Scientists Award for Environmental Sciences for his highly productive research into trace metals in the world's oceans. Rob will travel to The Netherlands in October to receive his award.

Brookers Bunch recently expanded, with new PhD student *Stuart* ***Malthus*** having started on 1 May. *Sébastien* ***Dhers*** submitted his PhD thesis in April so is now on a publishing bursary and awaiting his oral exam, after which he will return to France to take up a postdoctoral fellowship with Jean-Marie Lehn (Strasbourg). We heartily congratulate *Humphrey*

Feltham and his partner Katie on the safe arrival of baby Fraser Feltham on Anzac Day.

Annie ***Powell*** (Karlsruhe Institute of Technology) was with us for a fortnight in May, on the last of her Julius von Haast Fellowship visits. PhD student *Reece* ***Miller*** headed to Europe in mid-June to visit collaborators and returned after presenting his research at the International Conference on Coordination Chemistry (ICCC) in Singapore in mid-July. *Sally* ***Brooker*** travelled to Europe in late June. She presented a lecture at the Challenges in Inorganic and Materials Chemistry conference in Dublin in early July and visited her collaborator *Martin* ***Albrecht*** (UCD). She then travelled to Edinburgh, Durham and ICL to present department seminars and visit collaborators, before flying to Germany to visit Annie Powell (KIT) and *Eva* ***Rentschler*** (Mainz). Sally returned to Dunedin via the ICCC in Singapore at which she presented a keynote lecture.

David ***Savory****,* under the supervision of *Jim* ***McQuillan****,* has recently completed his PhD requirements and awaits graduation at the next ceremony. His thesis on *ATR-IR studies of trapped electrons in titanium dioxide* was assessed as being among the top 10% of theses examined. Jim gave an invited talk on IR studies of electron trapping in anatase TiO_2 aqueous photocatalysis at the 10th Australasian Vibrational Spectroscopy Conference held in Adelaide 13-16 April.

Keith ***Gordon*** has been associated with three successful Centres of Research Excellence bids in NZ and Australia. *Sara* ***Fraser*** (now Miller) recently married fellow chemist *Ben* ***Miller***. She and *Stasi* ***Elliott*** have also recently submitted their PhD theses. *Geoff* ***Smith*** has received a scholarship from the conference organisers to attend the International Conference on Raman Spectroscopy (ICORS) in Jena, Germany; fellow Gordon group students *Greg* ***Huff*** and *Holly* ***van der Salm*** will also be in attendance. *Chris* ***Larsen*** has been accepted to attend the electron donor-acceptor interactions Gordon Research Conference in Rhode Island, USA. Chris and Holly have also recently published their work in *Inorganic Chemistry* and the paper was highlighted as a featured article.

Welcomed to the research groups of *Bill* ***Hawkins*** and *Dave* ***Larsen*** in April were *Etienne* ***Decaudin*** and *Sebastien* ***Maugin*** who were visiting on a 12-week work placement from the ESIREM Materials Engineering School in Dijon, France, where they are studying 4th year Materials and Sustainable Development.

In March, the Department hosted Collette Boskovic (University of Melbourne) to present her RACI Alan Sargeson Lecture during the NZ leg of her lecture tour.

WAIKATO

A recruitment evening for prospective Branch members was held at the University of Waikato. Members and prospective members enjoyed pizza and drinks whilst *Kyle* ***Devey*** of Hill Laboratories spoke about his recent conference trip, which was partially funded by an NZIC Waikato Branch travel grant.

Hill Laboratories

Hill Laboratories has appointed Dr *Matt* ***Glenn*** as the new General Manager of Operations and Analytical Technology. Dr Glenn brings to Hill Laboratories almost two decades of executive management experience in the biotechnology, biopharmaceutical, food ingredients and chemicals industries. In 1995, after completing a PhD in molecular biology at the University of Leeds, he moved to New Zealand from England and began his career as a scientist at Genesis Research and Development Corporation Limited in Auckland. He was head of the Company's Genomics Division, looking after the biggest DNA sequencing facility in the southern hemisphere and has since worked in management roles for some of New Zealand's most successful companies, including Fonterra as Portfolio Manager for its Marketing and Innovation group, and Ballance Agri-Nutrients in Tauranga as General Manager of Research and Business Development. For the five years prior to his appointment at Hill Laboratories, Dr Glenn was the Founder and Principal of Idea Partners, a specialist management consultancy company.

NIWA

Bob ***Wilcock***, Principal Scientist in Water Quality, NIWA, retired at the end of June after 39 years as a scientist working for DSIR (Chemistry, and Marine and Freshwater Divisions), Ministry of Works and Development Water Quality Centre, and NIWA. We wish Bob a very pleasant retirement.

University of Waikato

Open Day at the University of Waikato was held on 16 May. Graduate students *Lewis* ***Dean*** and *Steven* ***Salmond*** from the Chemistry Department did displays of liquid nitrogen and fluorescent dyes and *Bill* ***Henderson*** gave Chemistry's mini lecture, *What can molecules do for you?*

In April, *Michael* ***Mucalo*** and his student *Jacob* ***Jaine***, who is undertaking a PhD in the development of immobilised colloidal catalysts, visited the Australian Nuclear Science and Technology Organisation (ANSTO), Lucas Heights, where they were hosted by Dr *John* ***Bennett***. They visited the Open Pool Australian Lightwater (OPAL) neutron reactor where a number of Jacob's catalyst samples have been submitted for NAA (nuclear activation analysis) to provide accurate elemental information on loading of metal content in the catalyst materials. The trip and project were funded by an AINSE grant awarded to Michael last year and the work done will provide some essential data for Jacob's PhD.

Obinna ***Okpareke*** has started a PhD with Bill Henderson and *Jo* ***Lane***, looking at MOF chemistry and *Sangata* ***Kaufononga*** has started a PhD with *Sarah* ***Finch***, and *Alison* ***Popay*** (AgResearch) and *Michèle* ***Prinsep*** looking at indole-diterpenoid secondary metabolites produced by a fungal-ryegrass symbiosis.

We have had a number of seminars from visiting speakers recently. Emeritus Professor Richard Field of the University of Montana, Missoula, USA, gave two seminars entitled *Deterministic chaos in chemical systems* and *Modelling of the dynamic of social support for moderation of stress in individuals*, Professor Chris Easton, ANU, Canberra, Australia, gave his RSC Australasian Lecturer

talk *A radical approach to enzyme biotechnology*, visiting Erskine fellow at Canterbury, Professor Phil Gale, University of Southampton, UK, spoke on *New anion receptors and transporters* and Professor Garon Smith of the University of Montana gave a talk entitled *Honey bees: flying chemical detectors at the ppq*.

WELLINGTON

The March Branch meeting took the form of the 2nd Ferrier lecture given by Professor *Jef* ***De Brabander*** entitled, *Natural products: discoveries in chemistry, medicinal chemistry and biology* early in the month. Jef is Professor of Biochemistry at the University of Texas Southwestern where he has taught since 1998. He serves on the Science Advisory Board of Reata Pharmaceuticals and SynAlpha Therapeutics – companies which he co-founded. He has been a collaborator of *Peter* ***Northcote*** for some time and it was especially good to have him visit Victoria. His lecture attracted a large audience to the Memorial Theatre where he spoke on drug studies that could provide new treatments for life-threatening infections; with the frequency of antibiotic-resistant bacteria currently rising at an alarming rate, the need to identify new antibiotics has reached a critical level. He specifically discussed a unique drug development aimed at the treatment of pneumonia and other infections.

In April Drs *Rebecca* ***Priestley*** and *David* ***Bibby*** of VUW spoke on *Nuclear New Zealand: the history and future of nuclear power*. The first part of the seminar saw Rebecca overview New Zealand's 20th twentieth century plans for nuclear power and then outlined why the decision not to proceed to building a nuclear power plant was made. David then discussed the basics of nuclear reactors and some of the many different avenues that have been explored in developing applications of nuclear fission. At the end of the month Professor Chris Easton (RSC, Australian National University) gave his RSC-RACI-NZIC 2013 lecture *A radical approach to enzyme biotechnology* as the Wellington component of his NZ lecture tour. As described elsewhere, he outlined his group's fundamental studies of free radical reactions of peptides and proteins in the context of regulation of hormone production in human cancers. This led to their enzyme biotechnology for sustainable agriculture and manufacturing, developing enzyme biotechnology for the conversion of biomass to liquid transport fuels, and in collaboration with the Grains Research and Development Corporation, towards enzyme-catalysed production of crop nutrients.

On May 14, following the VUW Science and Engineering graduation ceremony, Dr *Paul* ***Croucher*** of The Croucher Brewing Co., Rotorua, provided a survey of his work as a chemist and brewer under the title *My battle with drugs and alcohol: a chemist's journey to the alchemy of brewing*. This was an enlightening discourse on his career pathway that took many twists and turns prior to becoming a commercial brewer. Following this there was time for a tasting of the company products.

Victoria University – SCPS

Associate Professor *Richard J.* ***Payne*** (Chemistry Department, University of Sydney) visited the School in early April to conduct a PhD oral and then gave a lecture on his recent and impressive work entitled *Synthesis of therapeutic glycopeptides and glycoproteins via novel synthetic strategies*. He reminded the audience, made up of organic and biological chemists, that glycopeptides and glycoproteins are ubiquitous in nature and possess a range of biological activities that make them attractive targets for the development of novel therapeutics and for applications in biomaterials. He showed that much of the work in his laboratory has overcome many of the difficulties associated with assembling these complex biomolecules ranging from the development and application of novel chemical ligation methodologies to developing molecules up to 19.5 kDa in size. The development of synthetic glycopeptide cancer vaccine candidates, together with their potential application as materials and therapeutics, were also described.

PhD students *Janice* ***Cheng*** (Stocker-Timmer), *Angelique* ***Faramus*** (Tilley) and *Sarah* ***Hoyte*** (Spencer) successfully completed their doctoral degrees shortly before the last issue of *CiNZ* appeared in print and together with *Hemi* ***Cumming*** and former chemistry student *Catherine* ***Davis*** (now Cell and Molecular Bioscience) they all graduated at the May 14 ceremony. These chemists currently remain in the School on contracts, writing papers and seeking more permanent appointments. *Michelle* ***Cook*** (Supervisor: Professor Johnson) and *Struan* ***Cummins*** (Dr Fulton) both graduated MSc with 1st Class honours while *Lucy* ***Gloag*** (Dr Tilley) and *Stephen* ***Tat*** (Dr Harvey) gained BSc (Hons) 1st Class degrees. Lucy was also awarded the prestigious *University Medal for Academic Excellence in Science* by the Chancellor. Riyad Mucadam successfully completed his PhD studies with *Kate* ***McGrath*** in late May with a thesis entitled: *Architecture of a nanocrystalline biomineralised shell***.**

PhD candidate *Marjorie* ***Griffiths***, studying under the supervision of Professor *Kate* ***McGrath*** and Associate Professor *Bill* ***Williams*** (Massey University) won first prize in the ATA Scientific Study Award (AUD$1000). Marjorie and the team's work focuses on the development of state-of-the art tools to study structure, dynamics and interactions of macromolecular assemblies. Janice Cheng attended the 6th Hope Meeting held in Tokyo in mid-March. There were five students from each of the Asia-Pacific countries represented who met with a variety of Nobel Laureates that included chemist Ei-ichi Negishi.

In June, Professor *Ken* ***MacKenzie*** and two of his PhD students, *Mahroo* ***Falahpoor*** and *Mohammad* ***Alzer***, attended the 13th International Conference on Modern Materials and Technologies (CIMTEC 2014) held in Montecatini Terme, Italy. Ken presented a keynote paper entitled *The secret life of inorganic polymers: more than simply ecologically-friendly cements*. As a rare honour both students were invited to present oral papers on their work. Mahroo's lecture was entitled *Photoactive inorganic polymer composites with oxide nanoparticles* and Mohammad spoke on *Inorganic polymers (geopolymers) as novel catalysts for organic reactions*.

Ms *Susanna* ***Leung*** accepted the recently advertised technician position in chemistry and is now running the introductory laboratory.

Article

Prussian Blue: Its accidental discovery and rebirth of interest

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Keywords: Prussian Blue, cyanotype process, caesium entrapment, nanoparticles

Introduction

The Prussian Blue (PB) story is one of the most interesting in the history of chemistry. It was discovered over 300 years ago and yet new discoveries about its properties and potential use continue to intrigue.[1] The conventional story[2] began in 1704 with Heinrich Diesbach, a Berlin colourmaker, attempting to make a red pigment based on cochineal red from crushed beetles. Normally this was done by precipitating an extract of cochineal containing carminic acid with alum, iron(II) sulfate and potash (K_2CO_3). Being short on potash, he borrowed some from the alchemist Johann Dippel in whose laboratory he was working. The potash had been used to make 'medicinal' animal oil from a distillate of animal carcasses, horns, blood, bones and offal. Diesbach must have been surprised when he saw an intense blue-black precipitate upon addition of the potash which we now know was contaminated with $K_4[Fe^{II}(CN)_6]$ and its Fe(III) analogue. The cyanide ion and other species containing C-N bonds, such as those in pyrrole, are produced when organic matter containing C-N bonds is fused with potash and the mixture heated and ignited. After burning, the black product was extracted with water, filtered off and the above cyano complexes formed by the reaction of the CN^- with iron present from the blood. This product then reacts with the added iron to give PB. A similar but effective reaction for the formation of NaCN occurs in the well-known Lassaigne sodium test[3] where organic nitrogen compounds are heated with molten sodium.

The nature of PB was a mystery at this time and it is interesting that the element nitrogen was not to be discovered until 1782 by Daniel Rutherford. Scheele discovered hydrogen cyanide in the same year by reacting PB with diluted sulfuric acid, and in 1811 Gay-Lussac's determination of its composition led to the conclusion that PB contained cyanide.[4] A detailed structure of PB was not elucidated until 1977 by Ludi *et al*.[5]

The nature of Prussian Blue

Syntheses and redox properties of PB

Difficulty has been reported in obtaining pure PB, as it is known to exist in two forms. One is the so-called 'insoluble' form obtained from the reaction of Fe^{3+} with the hexacyanoferrate(II) ion in a 4:3 ratio according to the equation:

$$4Fe^{3+}_{(aq)} + 3[Fe^{II}(CN)_6]^{4-}_{(aq)} \rightarrow Fe^{III}_4[Fe^{II}(CN)_6]_3{\cdot}xH_2O_{(s)}\ (x = 14\text{-}16)$$

Aqueous solutions of the pale-coloured reagents, when added together, produce an intensely coloured, colloidal suspension of an inky blue-black compound, which is truly a marvelous reaction to observe. A broad visible absorption band appears at 680 nm with an extinction coefficient of 10^4 M^{-1} cm^{-1} which has been assigned as a transfer of electrons from the Fe(II) to Fe(III) in an intervalence charge transfer transition.[6] However, upon reduction of all of the Fe(III) to Fe(II) in PB to give Berlin white, $Fe^{II}[Fe^{II}(CN)_6]^{2-}$, the color changes from blue to colourless as the intervalence charge transfer is eliminated. This compound is easily oxidised by air, back to PB. Alternatively PB can be oxidised to Prussian Yellow, $Fe^{III}[Fe^{III}(CN)_6]$, which is a powerful oxidant, being reduced back to PB.

The so-called 'soluble' form of PB is obtained by the reaction of Fe^{3+} with the hexacyanoferrate(II) ion in a 1:1 ratio according to the equation:

$$K^+_{(aq)} + Fe^{3+}_{(aq)} + [Fe^{II}(CN)_6]^{4-}_{(aq)} \rightarrow KFe^{III}[Fe^{II}(CN)_6]_{(s)}$$

Once again a deep blue-black coloured colloidal suspension is obtained. Reduction of the Fe(III) in this form is accompanied by the insertion of one monovalent cation into the cavities of the colorless PB as shown:

$$KFe^{III}[Fe^{II}(CN)_6]_{(s)} + K^+_{(aq)} + e^- \rightarrow K_2Fe^{II}[Fe^{II}(CN)_6]_{(s)}$$

In contrast, oxidation of the 'soluble' PB is accompanied by the expulsion of the cation from the solid to give a yellow product:

$$KFe^{III}[Fe^{II}(CN)_6]_{(s)} \rightarrow Fe^{III}[Fe^{III}(CN)_6]_{(s)} + K^+_{(aq)} + e^-$$

The essential lattice structure is not changed as electrons are added or removed and the cations move in or out of the lattice to balance the change in electric charge that occurs. When an electric potential is applied across an electrode that contains a thin film of 'insoluble' PB it becomes electrochromic, owing to the above changes in colour on reduction and oxidation, leading to a possible application in smart windows.

The structure of PB

The structural basis for all the PBs is a cubic lattice with the framework consisting of Fe^{II}-CN-Fe^{III} sequences. In the 'insoluble' PB, eight lattice water molecules are found in the large cavities created by the scaffold, with tunnels going in three directions in the lattice. However, the lattice is imperfect since the ratio of Fe^{III}:Fe^{II} = 4:3, hence a quarter of the Fe^{II} as $[Fe(CN)_6]^{4-}$ is absent and the Fe^{III} coordination sphere contains coordinated H_2O with an average composition $[Fe(NC)_{4.5}(H_2O)_{1.5}]$. In 'soluble' PB, the ratio of Fe^{III}:Fe^{II} =1:1 and the lattice is more perfect. The low spin Fe^{II} centres bind with the C of the CN groups octahedrally and the high spin Fe^{III} centres bind with the N of the CN groups octahedrally. Half of the cubic sites are occupied by K^+ ions or other ions or molecules with a radius of no bigger than 182 pm.[5,7,8]

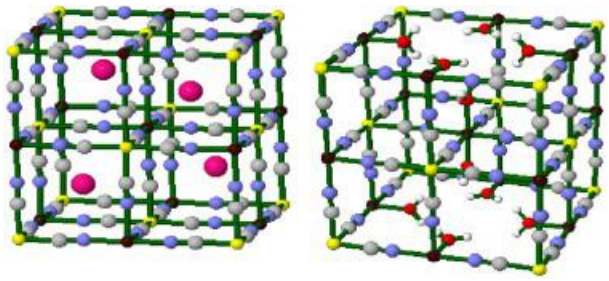

Fig. 1. Structures of 'soluble' PB (left) $KFe^{III}[Fe^{II}(CN)_6]$ and insoluble PB (right) $Fe^{III}_4[Fe^{II}(CN)_6]_3 \cdot 14H_2O$. The Fe(II) ions are yellow, the Fe(III) ions are black, the C atoms are grey, the N atoms are blue and the large mauve atoms in the cavities in the left hand diagram are K^+. The coordinated water molecules are seen in the right hand diagram. The O atoms are red and the H atoms are white.[7] (Reproduced with permission)

Early uses of Prussian Blue

PB as a pigment

After its discovery in 1704, PB was used as a blue pigment by artists and it replaced the more expensive ultramarine. Canaletto, Watteau, and Picasso incorporated it in their works but Renoir was horrified by the colour. It was also used in the blue Prussian military uniforms from 1746 to1756 and the blue wallpaper from the Banqueting Room at the Royal Pavilion in 1817-1820.[9]

Holocaust deniers claim that PB should have appeared in the gas chambers at Auschwitz and Birkenau as a by-product of the interaction between HCN and the iron in the walls of the chambers, but its formation is quite sensitive to the concentration of the CN^- ion and the pH. In the Majdanek chamber PB residues were clearly seen on the walls as it was in the disinfection chambers at Birkenau (Fe extracted from the bricks).[10]

PB and the blueprint process (cyanotype)

The blueprint process which was invented by Sir John Herschel in 1842, just three years after the discovery of photography in silver, has been well documented.[11] A Herschel's cyanotype paper consists of a mixture of a light-sensitive iron(III) carboxylate, such as ammonium ferric citrate or ammonium ferrioxalate and potassium ferricyanide. The photodecomposition of ammonium ferrioxalate offers some advantages over the use of ammonium ferric citrate in that it is more light sensitive, is not a nutrient for mould growth and its solution better penetrates cellulose fibres and mordants well on to fabrics.

$$h\nu + 2[Fe^{III}(C_2O_4)_3]^{3-}_{(aq)} \rightarrow 2[Fe^{II}(C_2O_4)_2]^{2-}_{(aq)} + C_2O_4{}^{2-}_{(aq)} + 2CO_2$$

The Fe(II) photoproduct is in equilibrium with the aquated ferrous ion and this reacts with the ferricyanide anion to precipitate PB:

$$Fe^{2+}_{(aq)} + [Fe^{III}(CN)_6]^{3-}_{(aq)} \rightarrow Fe^{III}[Fe^{II}(CN)_6]^-_{(aq)}$$

The excess chemicals are washed out of the sensitiser paper and photographic negatives when contact-printed give positive prints (see experimental details below).

Stamps and banknotes printed with PB

The first British Colony to issue postage stamps was Mauritius. A two pence blue Mauritius stamp from 1847 was printed in PB and this rare stamp, one of which is held by the British Library, has realised up to about one million pounds at auction. During the siege of Mafeking in the Boer War in 1900, the military commander Robert Baden-Powell had cyanotype bank notes and stamps made. On these special stamp issues it was surprising that his head appeared rather than that of Queen Victoria.[12]

Fig. 2. (a) The rare blue two pence Mauritian stamp of 1847. (b) The stamp authorised by Robert Baden Powell during the siege of Mafeking. (c) The one pound note with a design based on a sketch by Baden-Powell during the siege of Mafeking (images reproduced from ref. 12).

Experimental details for making a cyanotype print

The first step is to prepare an A4 copy of a negative print. Take a digital photograph and download this to a computer. A black and white image with good contrast is best but a colour image can be used. Open the image in Picasa; this is freeware which can be downloaded from the internet. If the photo is in colour, convert it back to a black and white image using the *B&W* icon in the *Fun and useful image processing* menu, then crop the image, if desired, using the *Crop* feature in the *Commonly needed fixes* menu. Increase shadow setting, to improve contrast, using the *Shadow* slide-bar in the *Finely-Tuned lighting and colour fixes* menu then further enhance the contrast using the *Auto contrast* icon in the *Commonly needed fixes* menu. Flip the image using *Ctrl-Shift-h*, convert the image to a negative using the *Invert Colours* icon in the *More fun and useful image processing* menu then save the image with a new file name. Exit Picasa then copy the manipulated image to Microsoft word and resize as required. Finally print the image onto an A4 acetate sheet. This sheet will be the negative for the cyanotype.

The sensitiser is prepared as described by Ware.[13] In a darkened room, with dim incandescent lighting, paint the sensitiser on to a medium weight water colour paper using a paint brush then leave in the dark to dry. In an A4 photo frame lay the acetate sheet against the glass then lay the coated paper onto the acetate sheet so the ink side of the acetate is in contact with the sensitiser. Attach the backboard of the frame so the acetate sheet and the paper are pressed firmly together. The cyanotype can now be exposed to light. Two to five minutes in direct sunlight is enough but a longer exposure time will be needed with a less intense UV light source. Fluorescent lights can be used with an exposure time of approximately 90 minutes. After exposure the cyanotype is removed from the frame and washed in a basin of ~ 0.7% nitric acid for 1-2 minutes then washed under running water to remove all the unexposed sensitiser from the paper. The paper is then hung to dry. Fig. 3 is a cyanotype produced by this method.

Fig. 3. A cyanotype image of a spotted-necked dove produced in an undergraduate laboratory at Massey University, Palmerston North.

Newer discoveries involving Prussian Blue

PB nanoparticles (PBNPs) as an MRI contrast agent and delivery vehicle for small molecules

Biocompatible, superparamagnetic PB nanoparticles have been made by adding citric acid to mediate the nucleation reaction of $FeCl_3$ with $K_4[Fe^{II}(CN)_6]$ and to prevent the nanoparticles (NP) from aggregating in solution. The citrate was covalently attached to the surface of the NP to the Fe(III) and this also provided a functional group for further conjugation of molecules (such as drugs) to their surfaces. The NPs were internalised by cells and displayed neither detectable cytotoxicity nor production of reactive oxygen species (ROS). The average load of citrate was 7.4 wt% and the NP size distribution range was 8 -16 nm.[7,14]

The following properties of this PB make it suitable as a MRI contrast agent. The Fe(III) centres are high spin (S = 5/2) and this is coupled to a symmetric electronic ground state derived from the ^5S state of the free ion. Additionally, these centres have water coordination so the inner sphere relaxation mechanism is active and this shortens the longitudinal relaxation time T_1 of protons from bulk water. Finally, high spin Fe(III) complexes generally have low to modest thermodynamic stabilities and are kinetically labile, so *in vivo* free aquated Fe(III) ions are usually inevitable and, if reduced to $Fe^{2+}_{(aq)}$, could possibly catalyse the generation of ROS. However, these NPs cause no measurable increase in ROS production, suggesting little ionisation to free $Fe^{3+}_{(aq)}$. Also, the NPs are stable in HCl solutions with concentrations of less than 1M and it was concluded they are resistant to attack by an acid stronger than gastric acid (~ 0.16 M). (The FDA has approved the use of PB capsules as an oral antidote for the treatment of radioactive caesium and thallium poisoning.) The ability of PBNPs to penetrate cells and show no detectable cytotoxicity is critically important if they are to be used intravenously as MRI contrast agents.[7,14]

Currently the great majority of contrast agents consist of the paramagnetic Gd^{3+} ion chelated to polyaminopolycarboxlate ligands, but there is concern because the components exhibit high *in vivo* toxicity. The relaxivity values of PBNPs are lower than those found in the commercial Gd^{3+} based T_1 contrast agents, and incorporation of Gd^{3+} into PBNPs to give $Gd_{0.1}Fe^{III}_{3.9}[Fe^{II}(CN)_6]_3$ has been carried out. It has the same face-centered structure, and the longitudinal and transversal relaxivity values for Gd^{III} are higher than those for Fe^{III}. Further studies on the use of PBNPs to act as stable carriers of Gd^{III}, but with less toxic side effects, are underway.

PBNPs as photochemical ablation agents for cancer therapy

PBNPs prepared in the presence of citric acid have a strong absorption peak at about 712 nm, with a high molar extinction coefficient, and aqueous dispersions of 500 ppm showed a dramatic increase in temperature to 43°C during irradiation with 808 nm light for three minutes. This ability of PBNPs to act as a photothermal agent to convert NIR light into heat is sufficient to kill cancer cells. The NPs showed stable temperature elevation during 4 cycles suggesting their reuse during practical applications. For a 16 ppm dispersion the cell viability was less than 10% after 10 minutes irradiation.[15] Efforts are still required to study the intracellular effects for intravenous administration.

Single crystals of $Fe^{III}Fe^{III}(CN)_6$ nanoparticles with a high capacity and high rate cathode for Na ion batteries

$Fe^{III}Fe^{III}(CN)_6$ nanocrystals with cubic geometry have been studied as a model compound of the PB type and explored as a Na storage cathode in Na ion batteries. It was used as a cathode and working electrode and a Na disk as a counter electrode. As before, the crystal structure consists of a three-dimensional network of Fe^{III}–N–C–Fe^{III} chains, forming a large cubic inner space to allow facile insertion and extraction of Na^+. $Fe^{III}Fe^{III}(CN)_6$(yellow coloured) can be first electrochemically reduced to $Na^+Fe^{III}Fe^{II}(CN)_6$ (PB) with one Na^+ intercalated and then reduced to $Na^+_2Fe^{II}Fe^{II}(CN)_6$ (white coloured) with another Na^+ ion intercalated. This system has a good rate capability at 20°C and cyclability with 87% capacity retention over 500 cycles; this results from the highly stable framework of $Fe^{III}Fe^{III}(CN)_6$ with large channels which avoids structural distortion and collapse. The lattice parameter

alpha was found to increase from 10.18 Å in the fully charged state to 10.41 Å at the completely discharged state, showing a reversible expansion and contraction.[16]

PB modified γ-Fe_2O_3 magnetic nanoparticles and their high peroxidase–like activity

The peroxidase-like activity of γ-Fe_2O_3 is very weak due to the lack of ferrous ions at the NP surfaces, but when modified with PB enough ferrous ions could be provided to contribute to the catalytic reaction between Fe^{2+} and H_2O_2 (Fenton reaction) to produce hydroxy radicals which can oxidise 3,3',5,5'-tetramethylbenzidine to give a blue product.[17] The formation of the PB modified γ-Fe_2O_3 NP occurs in dilute HCl solution, where the negative charge on the $[Fe(CN)_6]^{4-}$ ion is attracted to the positively charged surface of γ-Fe_2O_3, and the CN^- ion can form a complex with the ferric ions at the surface of the γ-Fe_2O_3 to form PB coatings.

Cyanide-based magnets

In the 'insoluble' PB, the Fe(II) centres are low spin but the Fe(III) centres are high spin (S = 5/2). These latter centres are about 10 Å apart and the exchange mechanism would be very weak, yet it becomes a molecular magnet with a blocking temperature of 5.6K.[18,19] The ferromagnetism between the high-spin Fe(III) centres is due to the admixture of the low-lying intervalence Fe(II)-Fe(III) excited state with the ground state.

By preparing other metal-substituted analogs of PB in which every metal centre is paramagnetic and the through–bond distance is reduced from 10 Å to 5 Å, the exchange coupling should be stronger than it is in PB and have a higher ordering temperature. A variety of magnetic behaviours has been achieved. Ferromagnetic coupling occurs when the spins on nearest-neighbour metal sites reside in orthogonal orbitals, e.g. d^8 ($t_{2g}^6e_g^2$) and d^3 (t_{2g}^3), as found in $CsNi^{II}[Cr^{III}(CN)_6]$. $2H_2O$ but when the magnetic orbitals are not orthogonal e.g. for d^5 ($t_{2g}^3e_g^2$) and d^3 (t_{2g}^3) (both sites contain spins in the t_{2g} or e_g orbitals) as found in $CsMn^{II}[Cr^{III}(CN)_6]\cdot H_2O$, the three unpaired spins in each of the two sets of t_{2g} orbitals couple antiferromagnetically, but the electrons in the e_g orbitals couple ferromagnetically to give a ferrimagnet. Each complex had a T_c value of 90 K.[20,21]

The compounds $K_{0.2}Co_{1.4}[Fe(CN)_6]\cdot 6.9H_2O$[22] and $Rb_{1.8}Co^{III}_{3.3}Co^{II}_{0.7}[Fe^{II}(CN)_6]_{3.27}\cdot 13H_2O$[23,24] contain large amounts of Co(III) (d^6) low spin and Fe(II) (d^6) low spin but when illuminated with a red light at -150°C the compounds shift from being essentially a weak paramagnetic material to a ferrimagnetic one. The change is stable, but can be reversed with heat. These effects are caused by an internal photochemical redox reaction and the oxidation states change from Fe^{II}-CN-Co^{III} to Fe^{III}-CN-Co^{II}. The contribution from the $Fe^{II}(t_{2g}^6, S = 0)$CN-$Co^{III}(t_{2g}^6, S = 0)$ state is now much reduced and that of the new state of $Fe^{III}(t_{2g}^5, S = ½)$-CN-$Co^{II}(t_{2g}^5e_g^2, S = 3/2)$ is increased by red light irradiation. For the latter state an antiferromagnetic interaction between the cobalt and the iron ions leads to ferrimagnetism. Such compounds which can memorise binary information could be used as storage bits for future computers and may have applications in magneto-optical devices.

Functionalisation of single-walled carbon nanotubes (SWNTs) to PB

SWNTs have been successfully functionalised with 'insoluble' PB. It was invoked that they were held together by electron donation from the SWNT to the CN acceptor to give a p-p stacking interaction coupled with an ionic interaction. This decreased the n(C-N) stretching frequency by 11 cm^{-1} and increased the negative charge on the N atom. A SWNTs-PB modified glassy carbon electrode was prepared[25] and maintained good electrochemical activity of PB and may find applications in electrochemistry.

PB inks and electrocatalytic water oxidation

The 'insoluble' PB pigment can be dispersed by an organic solvent, e.g. toluene, by surface modification with aliphatic amines, e.g. oleylamine, or water-dispersible by the addition of further $Na_4[Fe(CN)_6]\cdot 10H_2O$. Both reactions involve the displacement of surface water bound to the Fe(III) of 'insoluble' PB with the aggregation of the NPs being inhibited.[26]

The insoluble pigments $K_{0.14}Ni_{1.43}[Fe(CN)_6]\cdot 5H_2O$ and $K_{0.1}Co_{1.45}[Fe(CN)_6]\cdot 5.5H_2O\cdot NH_3$ were also converted to toluene-dispersible NP inks Ni-PBA (yellow) and Co-PBA(red) respectively in the same way as for PB above. The three primary coloured nanoparticle inks may possibly be used in ink-jet printing and they offer a low cost but simple way for mass production.[26] Also, a similar Co^{II} compound, $K_{2x}Co_{(2-x)}[Fe(CN)_6]$ ($0.85 < x < 0.95$), has been shown to be a heterogeneous water oxidation catalyst after deposition as a film onto a fluoride-doped tin oxide coated glass electrode. Cyclic voltammetry displays a quasi-reversible one-electron redox couple assigned to the $Co^{II}Fe^{II}$-$Co^{III}Fe^{II}$ couple and at higher oxidation potentials a catalytic water oxidation wave appears. It maintained constant catalytic rates for weeks.[26]

PB as an ion exchanger to reduce radioactive caesium contamination on territories affected by the Chernobyl and Fukushima nuclear accidents

The accident at the Chernobyl nuclear power plant in 1986 led to the dispersal of radioactive material such as ^{137}Cs over many countries. PB was used to reduce the ^{137}Cs levels in a range of animal products such as milk and meat and PB was found to have no adverse effects on animal and human health. The PB compounds bind Cs ions (from pasture and water) in exchange for monovalent cations such as Na^+, NH_4^+ or K^+. The colloidal particles of PB provide a large surface area for Cs^+ binding which is bound 10^3 to 10^4 times more efficiently than NH_4^+ or K^+ at physiological pH. Binding of Cs^+ occurs in the gut (the PB remains intact at the pH of the gut) and these particles are too large for absorption and are excreted. In soil, plant roots do not take up Cs^+ quickly from the PB.[27,28]

After the Fukushima Daiichi nuclear power plant was crippled by an earthquake and tsunami, Japan was faced with the most difficult task of cleaning up vast amounts of land and water contaminated by radiation. An acid

washing method was trialed to remove the radioactive caesium from the top 3 to 4 cm of soil and the Cs cations were removed from the acid with PB. Fundamental studies showed that the 'insoluble' PBNPs more efficiently adsorbed hydrated Cs^+ ions than 'soluble' PBNPs. The former has many lattice 'defect' sites of $[Fe(CN)_6]^{4-}$ that contain coordinated water, and the hydrated Cs^+ ions are exclusively trapped by chemical adsorption *via* the hydrophilic lattice defect sites and accompanied by proton-elimination from the coordinated water.[29]

PB as a gas capture agent

Dehydrated cobalt analogues of PB of the type $Co_3[Co(CN)_6]_2$[30] have been shown to capture gases such as CO_2 (20-30 wt%) under standard conditions. H_2 is adsorbed (1.2 wt%) at 77 K by $M^{II}_3[Co^{III}(CN)_6]_2$.[31] Another study has shown that some CO_2 molecules bridge between two 'bare' Fe(II) sites in $Fe_3[Co(CN)_6]_2$ which have had coordinated water removed by heating.[32]

Conclusion

PB can claim to be the first synthetic coordination compound and synthetic coordination polymer. Although it was first prepared in 1704, interest in its properties and potential uses is still increasing and will do so for many years to come. At first it was its intense blue colour that gave rise to its use as a pigment in paints and it is the traditional blue in "blueprints". More recently it has been used in medicine as an antidote for metal poisoning and has possible uses as an MRI contrast reagent and in cancer therapy. Other potential uses stem from its magnetic and redox properties and it may have applications in nanoscience.

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Article

Recent developments in metal-organic framework (MOF) chemistry

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Introduction

The combination of divergent ligands and metal ions or clusters produces polymeric materials.[1] In ideal cases these polymers are both crystalline, so their atomic coordinates can be revealed by X-ray crystallography, and porous, so they are able to host small guest molecules. In 2010 we provided an overview of MOFs in this journal.[2] Research in the field has gathered further steam over the past few years and in this account we provide selected highlights of recent progress.

Interpenetration control in MOFs

Interpenetration, or catenation, in MOFs can have a significant effect on the key properties. While interpenetration can increase the stability of the framework, it reduces the pore volume and tends to reduce capacities for absorbing guest molecules (Fig. 1).[3] On the other hand, by reducing the pore size the selectivity for certain guests can be improved.[4] It is therefore desirable to gain control over whether interpenetration occurs, and to what degree. As summarised below, control over interpenetration has been achieved through careful adjustment of the reaction conditions,[5] by attaching bulky substituents to the ligand struts,[6] or through removal of ligands/solvent.[7] These are useful tools in realising the potential of MOFs as ultraporous functional materials.

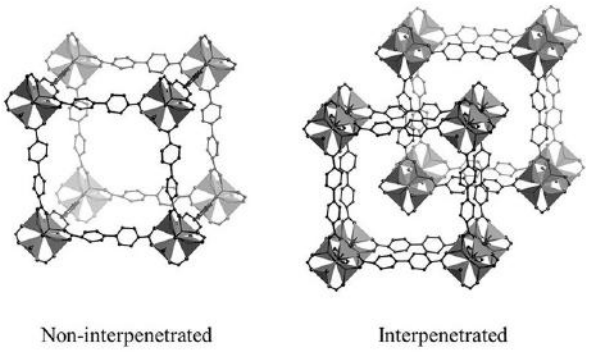

Fig. 1. Examples of non-interpenetrated (*left*) and interpenetrated (*right*) MOFs.

Control by reaction conditions

There have been several examples in recent years of interpenetration control by alteration of the reaction solvent, temperature and concentration. The solvent employed can have a templating effect during MOF synthesis and as a result, bulky solvents can block interpenetration or reduce the level of interpenetration observed. Sumby and co-workers have recently reported evidence for this templating effect.[8] They have synthesised a MOF containing alcohol substituents on the ligand, which can be prepared as the interpenetrated or non-interpenetrated phase through solvent control. Using dimethylformamide (DMF) as the reaction solvent produces the interpenetrated phase, while diethylformamide (DEF) gives the open non-interpenetrated phase. Yang *et. al*. have also recently shown that both the interpenetrated and non-interpenetrated forms of an IRMOF-20 (IRMOF = isoreticular MOF) derivative can be isolated by simply altering the solvent from DMF to DEF.[9] This resulted in an increase in the gravimetric surface area from 430 $m^2 g^{-1}$ for the interpenetrated phase to 1504 $m^2 g^{-1}$ for the non-interpenetrated phase. Although the lower density of non-interpenetrated phases inherently leads to higher gravimetric surface areas, this large difference reflects the shielding of accessible surface area by neighbouring lattices in interpenetrated MOFs. In this case the more open form was used as a chromatographic column for separating transition metal ions.

Reaction temperature has also been shown to have an influence over interpenetration.[10] A partially interpenetrated MOF has recently been reported,[11] where the high temperature synthesis produced a mixture of phases, one partially interpenetrated, the other 4-fold interpenetrated. At lower temperatures only the partially interpenetrated phase is formed, which upon activation, shows excellent selectivity for CO_2.

A further experimental variable that impacts on interpenetration is concentration. There are a few examples in the literature where a concentrated reaction solution produces an interpenetrated phase, while a dilute reaction solution allows isolation of the non-interpenetrated phase.[12] The most prominent example of concentration-controlled interpenetration is within the IRMOF family.[13] In this family the carboxylate linkers are sequentially extended in length to produce MOFs with larger and larger pores, with the non-interpenetrated, highly porous frameworks being accessed via dilute reaction conditions.[14]

Control by steric bulk

The introduction of bulky substituents to the ligand struts of MOFs has proven a successful method to inhibit interpenetration.[14] Hupp and co-workers have recently shown that interpenetration can be blocked through addition of azolium moieties to the dicarboxylate ligand backbone.[15] A ligand with only one azolium group attached produced an interpenetrated framework when combined with $Cu(NO_3)_2 \cdot 3H_2O$. However, when a second azolium group was added to the starting ligand a non-interpenetrated framework was produced.

Our own group has used the bulky Boc (Boc = *t*-butoxycarbonyl) protecting group not only to produce open

non-interpenetrated frameworks, but also to mask active groups that can be revealed through deprotection once the MOF has formed. In the first example a Boc protected amino group was attached to a biphenyldicarboxylate ligand to give a non-interpenetrated cubic framework.[16] The MOF crystals were then subjected to heating above 150°C to remove the protecting group in a single-crystal-to-single-crystal transformation. The thermolysis step increases the free volume and pore size within the framework (Fig. 2). This technique has also been used to synthesise a non-interpenetrated MOF which contains a catalytically active group.[17] A Boc protected proline substituent was attached to the ligand strut, with the Boc group again being removed by thermolysis after the MOF had formed. Blocking interpenetration with the bulky ligand substituent ensured free space around the catalytically active proline group, allowing the MOF to catalyse aldol reactions within the pores. Preparation of the catalytically active MOF with a naked proline group attached to the ligand is not possible due to interference from the proline nitrogen atom during MOF synthesis.

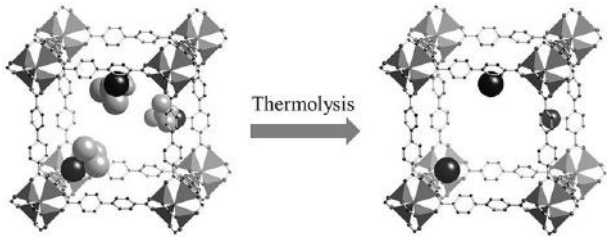

Fig. 2. Use of the bulky NHBoc group to suppress framework interpenetration followed by thermolysis of the Boc group to reveal a porous functionalised framework.

Control by post-synthetic removal of ligands or solvent

The strategies detailed above all focus on control of interpenetration during the synthesis. In a small number of recent reports it has also been shown to be possible to control the degree of interpenetration following MOF formation through removal of ligands or solvent.[18] One impressive recent example shows that removal of DMF ligands from a non-interpenetrated framework by heating leads to an interpenetrated framework in a single-crystal-to-single-crystal transformation.[7] The transformation is accompanied by a change in the coordination geometry around the zinc centres and is fully reversible upon exposure of the crystals to DMF. The authors were also able to isolate intermediate phases during the transition from non-interpenetrated to interpenetrated, with the gas sorption properties changing noticeably at different points along the transformation. The most recent example of post-synthetic interpenetration is by Barbour and colleagues.[19] They have shown that a doubly interpenetrated structure converts to a triply interpenetrated structure upon loss of the solvent molecules from the pores. This irreversible change in the degree of interpenetration was characterised by single-crystal X-ray diffraction as it occurs via a single-crystal-to-single-crystal transformation. This result may help explain the reduction in porosity upon activation of many previously reported frameworks and also contribute some answers to the question of how interpenetration occurs in MOFs.

Multicomponent MOFs (MMOFs)

Research into multicomponent MOFs (MMOFs) has developed rapidly in recent years and has expanded the complexity and diversity of known porous materials.[20] This section aims to provide an overview of zinc(II) and carboxylate ligand based MMOFs.

MMOFs constructed from ligands with the same geometry

It is known that reacting terephthalic acid (H_2BDC, Fig. 3) with zinc nitrate produces MOF-5[21] while reacting aminoterephthalic acid ($H_2BDC\text{-}NH_2$) with zinc nitrate produces IRMOF-3.[13] Matzger *et al.*[22] and Baiker *et al.*[23] used H_2BDC and $H_2BDC\text{-}NH_2$ to synthesise MMOFs where the two ligands are randomly dispersed. Matzger *et al.* also found that reacting these two ligands stepwise with zinc nitrate can form core-shell MOF@MOFs.[22] Including MOF-5 crystals in the synthesis of IRMOF-3 produces an IRMOF-3 shell layer outside of MOF-5 core. This core-shell IRMOF-3@MOF-5 could be further coated with a third layer of MOF-5. Core-shell strategy enables the synthesis of MMOFs with well-defined macroscopic domains of each ligand component.

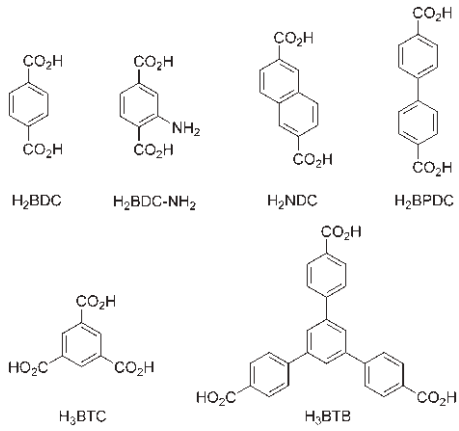

Fig. 3. Structures of ligands used in MMOF syntheses

Yaghi *et al.* reported a series of MMOFs synthesised with up to eight variously-substituted terephthalic acid ligands.[24] Ligand composition and their ratio of different single crystal segments are the same, implying macroscopic homogeneous ligand dispersion. Further analysis by solid state NMR and computational studies allowed them to conclude that microscopic inhomogeneity presents in some of these MMOFs.[25] One of these MMOFs shows a four-fold enhancement of selective adsorption of CO_2 over CO compared to MOF-5.

MMOFS constructed from ligands with different geometries

MMOFs that that are built up using ligands with different geometries usually form well-defined lattices since the ligands can be differentiated from one another during MOF formation.

The first ternary (MMOFs containing two distinct ligands) zinc carboxylate MOF was reported in 2003, where benzene-1,3,5-tricarboxylic acid (H_3BTC) and H_2BDC were used.[26] This family of MMOFs didn't arouse too much

attention for half a decade until 2008, when Matzger *et al.* reported a ternary MOF synthesised with zinc nitrate, H_2BDC and 1,3,5-tris(4-carboxyphenyl)benzene (H_3BTB), also known as UMCM-1 (UMCM = University of Michigan Crystalline Material, see Fig. 4).[27] BDC is ditopic ligand, i.e. a linear ligand which has two carboxyl groups, whereas BTB is a tritopic ligand, i.e. planar ligand with a three-fold rotational axis which has three carboxyl groups. Combining these two ligands with different geometries afforded a highly ordered and periodic framework. UMCM-1 has a BET (Brunauer–Emmer–Teller) surface area of 4160 m^2g^{-1}, which exceeded any other porous materials at that time.

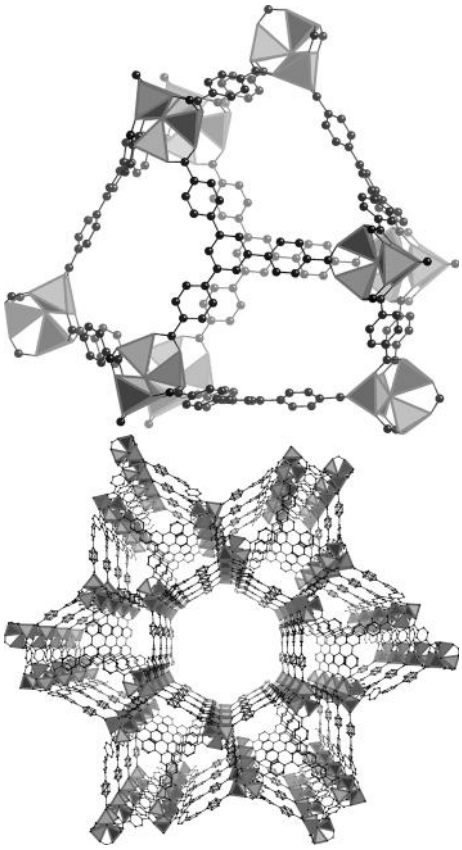

Fig. 4. X-ray single crystal structure of UMCM-1. Top: a microporous pore of UMCM-1. Bottom: A one-dimensional mesoporous channel of UMCM-1.

A practical challenge faced when synthesising ternary MOFs is that the individual ligands can independently form MOFs. This introduces at least two competing phases during the synthesis of a ternary MOF. The production of phase-pure UMCM-1 requires careful adjustment of the feed ratio of H_3BTB and H_2BDC. High H_3BTB / H_2BDC ratio produces phase pure MOF-177 [$(Zn_4O(BTB)_2$][28] or a mixed phase of MOF-177 and UMCM-1, while a lower ratio produces phase pure UMCM-1. If this ratio is too low, a mixed phase of UMCM-1 and MOF-5, or a phase pure MOF-5 could form.

Since the discovery of UMCM-1, many more ternary MOFs with a ditopic and a tritopic ligand have been reported.[29-33] Interestingly, new examples often surpass previous records for the most porous known material.[29,31]

Instead of using a tritopic and a ditopic ligand as described above, is it possible to use two ditopic or two tritopic ligands to synthesize ternary MOFs. SUMOF-4 [$Zn_4O(BDC)_{3/4}(BPDC)_{3/4}$],[34] UMCM-8 [$Zn_4O(BDC)_{3/4}(NDC)_{3/4}$],[35] and UMCM-9 [$Zn_4O(BDC)_{3/4}(NDC)_{3/4}$][35] are three examples where two ditopic ligands of different lengths build up ternary MOFs. Lah *et al.* reported an anionic MOF, $(NH_2(CH_3)_2)_3[Zn_6(BTC)_4(BTB)]$, which used two tritopic ligands, BTB and BTC.[36]

We now turn to quaternary MOFs, which are constructed from three distinct ligands to make quaternary MOFs. In a recent review article, Yaghi *et al.* proposed that the materials beyond should have *multiple kinds of building units* (ligands), and the arrangement of these building units within crystals should have *specific sequences*.[1] MMOFs with distinct ligands are the most promising candidates to achieve sophisticated applications which require high complexity in highly ordered crystalline materials. However, they realised that it is *an outstanding challenge* to make MMOFs with *as few as three or four* distinct ligands because they believed that such chemistry will give a mixed phase of binary and ternary MOFs rather than a single phase of quaternary or quinary MOF. We note that for a quaternary MOF there are six competing phases (single-ligand MOFs and ternary MOFs).

Our group recently reported the first quaternary MOF, MUF-7a (MUF = Massey University Framework, Fig. 5).[37] MUF-7a was synthesised from a tritopic ligand and two ditopic ligands with different lengths, which has a formula of $Zn_4O(BTB)_{4/3}(BPDC)_{1/2}(BDC)_{1/2}$. Phase pure MUF-7a was made by careful adjustment of the ligand feed ratio to suppress the formation of six known competing phases, which are MOF-177, IRMOF-9,[13] IRMOF-10,[13] MOF-5, UMCM-1 and SUMOF-4. Different functional groups were also introduced onto each of the ligands and a family of eight quaternary MOFs, MUF-7a-h, was synthesised. Through the combination of different ligand sets, we can program the MOF pore environment. Within some complex pores, different functional groups work synergistically to enhance CO_2 uptake of the MOF by almost 100%.

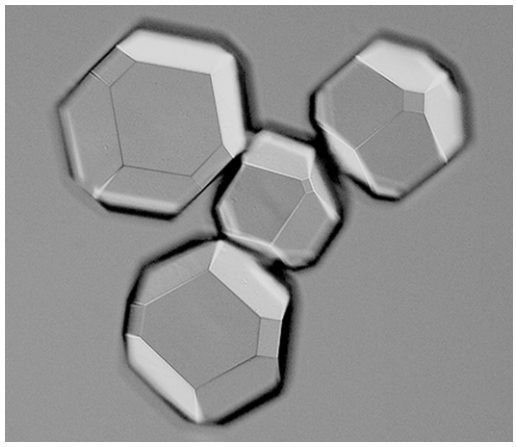

Fig. 5. A photograph of MUF-7a crystals prepared in our laboratory.

Nitrogen-donor ligands for MOFs

While carboxylate ligands are prevalent in MOFs[21,28] nitrogen-donor ligands (Fig. 6) expand the scope and diver-

sity of this class of porous materials. Numerous examples of both single-ligand and mixed-ligand MOFs with these N-donor type ligands have been synthesised and characterised. The section below will highlight a selection of these materials.

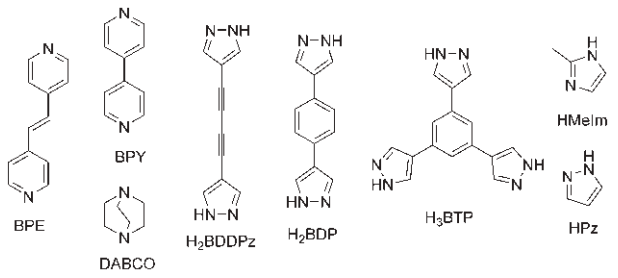

Fig. 6. Examples of N-donor type ligands used in MOFs (BPE: 1,2-bis(4-pyridyl)ethylene; BPY: 4,4'-bipyridine; DABCO: 1,4-diazabicyclo[2.2.2]octane; H_2BDDPz: 4,4'-buta-1,3-diyne-1,4-diylbis(3,5-dimethyl-pyrazole); H_2BDP: 1,4-benzenedipyrazole; H_3BTP: 1,3,5-tris(1H-pyrazol-4-yl)benzene; HMeIm: 2-methylimidazole; HPz: pyrazole.

N-donor single-ligand MOFs

Zeolitic Imidazolate Frameworks (ZIFs), developed in the early-mid 2000s, comprise imidazole based ligands [38-40] ZIFs exhibit a wide range of framework topologies; the 12 ZIFs prepared by Yaghi *et al.* in 2006 having 7 different zeolitic nets between them. ZIF-8 (Fig. 7), constructed from 2-methylimidazole (MeIm), has shown particular promise as a molecular sieve. The durability of this material compliments its ability to separate compounds such as propylene and propane, and hydrogen and oxygen.[41-42]

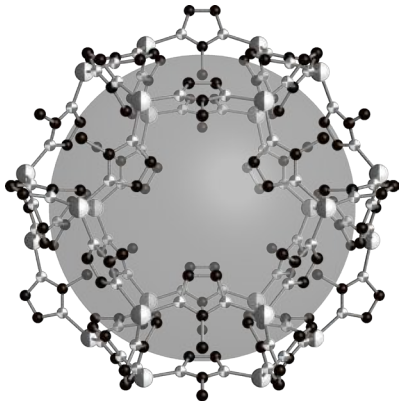

Fig. 7. Crystallographic structure of a ZIF-8 cage.

A family of materials derived from copper hexafluorosilicate and pyridyl ligands has been developed by Zaworotko *et al.*.[43] These frameworks exhibit interesting gas sorption selectivities: whilst neither CH_4 nor N_2 were taken up to any great degree, the CO_2 uptake was quite dramatic, with loadings up to nearly 25% by weight. Properties such as these could potentially be of use in extraction of CO_2 from flue gas, air-recycling apparatus, or other such areas with high concentrations of CO_2.

There are also examples of single-ligand MOFs containing pyrazolate ligands. In 2011, the Long group used tritopic 1,3,5-tris(1*H*-pyrazol-4-yl)benzene (H_3BTP) to generate MOFs using nickel, copper, zinc, and colbalt (Fig. 8).[44] These materials show many interesting properties, including high thermal stabilities in air of up to 510°C, and resistance to boiling in aqueous acid/basic solutions. These characteristics would allow these materials to be employed in environments that would destroy other MOFs. Ditopic versions of pyrazolate ligands have also been used. Colombo *et al.* in 2012 used 1,4-benzenedipyrazole (H_2BDP), as well as substituted analogues to generate nickel and zinc containing MOFs, and the Long group developed an iron containing MOF in 2013.[44-45] These materials appear to have promising futures in chemical separation, with Long's iron MOF being able to separate numerous hexane isomers, an ability that has strong potential in the petrochemical industry. Procopio *et al.* in 2013 produced a cobalt MOF containing 4,4'-buta-1,3-diyne-1,4-diylbis(3,5-dimethylpyrazole) (BDDPz), whose topology, aside from the interpenetration, is analogous to MOF-5 synthesised by Yaghi.[46-47] It is interesting to note that, again, the pyrazolate ligands have increased the chemical stability of the material, with the MOF having an increased resistance to hydrolysis than its carboxylate based counterparts.

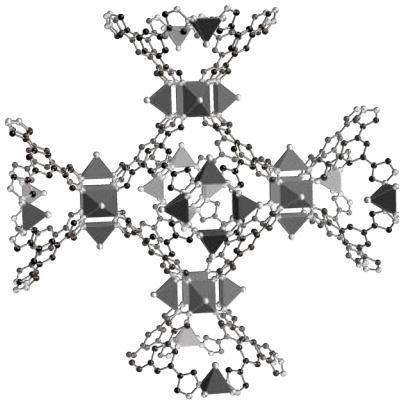

Fig. 8. Crystallographic structure of Long's nickel-pyrazolate MOF ($Ni_3(BTP)_2.3H_2O$).

N-donor mixed-ligand MOFs

Often in mixed-ligand MOFs, the N-donor type ligand is combined with a carboxylate ligand, which can result in the formation of 'paddlewheel'-like metal centres. An example of this is the work carried out by Cohen *et al.* in 2012 with their combinations of 4,4'-biphenyldicarboxylate (BPDC) with 4,4-bipyridine (BPY) or 1,4-diazabicyclo[2.2.2]octane (DABCO).[48] These are examples of pillar-layer structures (Fig. 9), where the BPDC and zinc form 2D sheets or 'layers' which are connected by BPY/DABCO 'pillars'. Shear deformations are often seen in pillar-layered structures, where an alteration in the angle of the nitrogen-metal bond reduces the distance between the 2D sheets. This can lead to changes in the internal surface area and/or volume of the materials. Breathing can be seen in the [Zn(1,4-BDC)$_2$(DABCO)] MOF developed by Kim *et al*. in 2004, in which the framework shrinks upon the uptake of guest molecules, but expands upon their release.[49] This remarkable property of these structures can create interesting properties, such as hysteresis in gas absorption and gate-opening effects (changes in porosity which are usually triggered by pressure).[48,50] An excellent example of gate-opening effects can be seen in the mixed-ligand MOF developed by Kitagawa *et al.* in 2009. Using a combination of 2,5-bis(2-hydroxyethoxy)-1,4-

bis(4-pyridyl)benzene (BPB-HE_2) and 2,3-pyrazinedicarboxylic acid (H_2PzDC) with cadmium, Kitagawa was able to block the pores within the MOF through the hydrogen bonding that occurred between the hydroxyl groups of adjacent BPB-HE_2 ligands.[51] These 'gates' remain closed until the concentration of guest molecules is sufficient to disrupt the hydrogen bonding keeping the gates closed. With the bonding disrupted, the BPY-HE_2 pillars are free to rotate, and thus the guest molecules are able to enter the previously inaccessible space and prevent the gates from closing again. In this MOF this results in a large increase in capacity for guest molecules, from ~6-7 molecules per formula unit with closed gates to ~12-13 molecules per formula unit when the gates are open, over a P/P_0 range of ~0.2. These sharp, dramatic changes are useful for the reactivation/recycling of materials used in gas separation/storage applications, where it is desirable that the rejuvenation of the material can be carried out with minimal energy expenditure.[52]

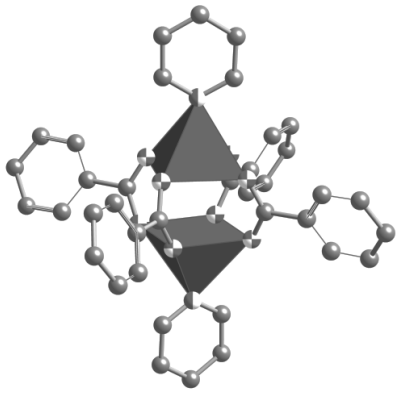

Fig. 9. Example of a paddle wheel metal centre. Solid Spheres: Carbon, Half spheres: Nitrogen, Quarter Spheres: Oxygen, Tetrahedra:Zinc.

Hupp has used the redox active *N,N*'-di-(4-pyridyl)-1,4,5,8-naphthalenetetracarboxydiimide (DPNI, Fig. 10) as a MOF ligand on multiple occasions.[53,54] The mixed-ligand interpenetrated MOF [Zn_2(2,6-NDC)$_2$(DPNI)] exhibited promising selectivity of CO_2 over CH_4, as well as a gate-opening effect for H_2 and N_2 adsorption caused by the reduction of the ligand framework when exposed to Li^+.

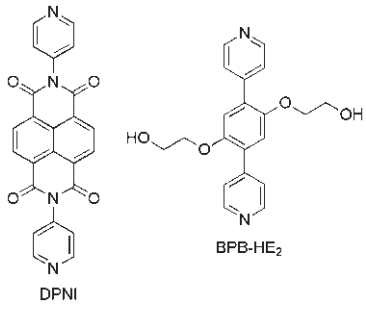

Fig. 10. DPNI: *N,N*'-di-(4-pyridyl)-1,4,5,8-naphthalenetetracarboxydiimide; 2,5-bis(2-hydroxyethoxy)-1,4-bis(4-pyridyl)-benzene : BPB-HE_2

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Pacifichem conference 2015

The Organising Committee of the 2015 Pacifichem Conference held its third meeting 12-16 June in Queenstown. This was the first time that a meeting of the Pacifichem Organising Committee has held a meeting in New Zealand. As one of the sponsoring societies of Pacifichem, the NZIC provides one member of the Organising Committee. This role was established by Brian Halton (Wellington), and continued by Rob Smith (Otago) until 2010. Mark Waterland (Manawatu) is the current NZIC representative. Pacifichem is held in Hawaii during December every five years, and it attracted over 12,000 delegates in 2010. It uses a symposium structure where delegates propose symposia topics that are approved by the Organising Committee. The symposium structure allows the focus of a small conference but on a scale of large national meetings such as the ACS or MRS meetings in the US.

Symposia organisers independently determine the speaker list for their symposia. The Symposia organisers must include members from at least three of the seven sponsoring chemical societies. The NZIC is one of the seven sponsoring societies. The American Chemical Society, Canadian Society for Chemistry, Chemical Society of Japan, Chinese Chemical Society, Korean Chemical Society and the Royal Australian Chemical Society are the other six sponsoring societies. NZIC members are often involved in organising symposia at Pacifichem. The NZIC also provides symposia reviewers for the 11 topic areas ranging from fundamental areas such as analytical and organic chemistry to newer areas such as materials and nanoscience and chemical biology, as well as chemical education and chemistry in industry. The symposia titles for 2015 were approved at the Queenstown meeting and symposia organisers have begun organising their sessions.

The Conference Chair for 2015 is Prof Peter Stang from the ACS (the conference chair cycles between the original sponsoring societies; the ACS, CSJ and CSC). The theme is Building Bridges Across the Pacific. Prof Stang has visited New Zealand as an Erskine Fellow at the University of Canterbury and he encouraged the Pacifichem Organising Committee to come to New Zealand to increase the profile of Pacifichem outside of the US, Canada and Japan.

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Polysaccharide hydrogels for colon-targeted drug delivery

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Keywords: polysaccharide, hydrogels, drug delivery, colon

Introduction

Hydrogels are three dimensional, hydrophilic, polymeric networks capable of imbibing large amounts of water or biological fluids**.** Since the pioneering work of Wichterle and Lim in the 1960s on the crosslinked three-dimensional polymers obtained by the copolymerization of hydroxyethylmethacrylate (HEMA) with ethylene dimethacrylate (EDMA), polymeric hydrogels have attracted tremendous research interest.[1] Stimuli-responsive hydrogels, which are also called intelligent, smart or environmentally sensitive hydrogels, are defined as polymer networks able to respond to small environmental changes resulting in abrupt changes in their swelling behaviour, network structure, permeability and/or mechanical strength.

Applications of hydrogels in drug delivery

Controlled release systems were first used in medical research in the 1960s. The earliest drug delivery systems were first introduced in 1970s and were based on polymers formed from lactic acid.

With conventional dosing formulations, the drug level in the blood often exceeds the toxic level immediately after each administration of the drug and then declines sharply below the minimum therapeutic level until the next administration.[2] This bolus administration of drugs is therefore far from ideal, not least of all in pain relief therapies. Controlled drug delivery systems are designed for long term administration where the drug level in the blood remains constant, between the desired maximum and minimum, for an extended period of time (Fig. 1).

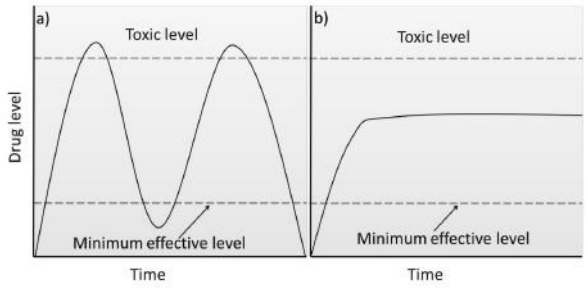

Fig. 1. Drug level in blood with a) traditional drug administration and b) controlled drug delivery.

Due to their attractive physicochemical and biological characteristics, hydrogels have attracted a lot of attention as they are excellent candidates for delivery systems of therapeutic agents. Hydrogel-based delivery devices can be used for ocular, transdermal, subcutaneous, rectal and oral delivery (Table 1).[3-9]

Oral drug delivery

Administering drugs orally is by far the most widely used route which helps eliminate the pain caused by injection, psychological barriers associated with multiple daily injections and possible infection from injection sites.[10] Almost 90% of all medicines are oral formulations. However, it is important for oral drug administration to overcome several different obstacles during delivery through the gastrointestinal tract (Fig. 2). The barriers can be morphological barriers such as mucus layers and microvilli as well as physiological factors such as a wide range of pH conditions and enzymatic activities.[11]

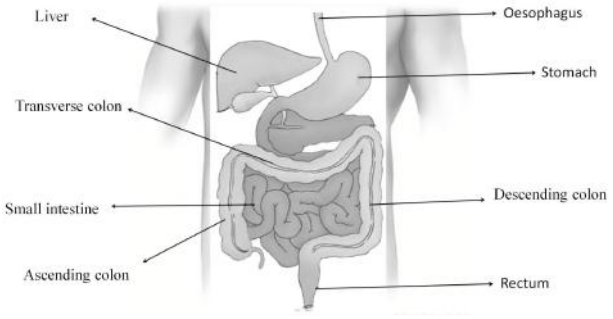

Fig. 2. Anatomy of gastrointestinal tract.

Site-specific drug delivery

Drug discovery and development involves highly challenging, laborious, and expensive processes which take an average of 15 years and a cost of about US $1 billion for a drug to travel from the research lab to the patient. However, most of the drugs fail to achieve favourable clinical outcomes because they do not have the ability to reach the intended targets.[12] Therefore, aggressive research efforts have recently focused on development of new strategies for delivering drugs to the required site of action.[13]

Table 1. Examples of stimuli-responsive hydrogel systems used for drug delivery

Hydrogel	Stimuli	Application	Drug
Poloxamers[3]	Temperature	Ocular delivery	Liposomes
Xyloglucan[4]	Temperature	Ocular delivery	Timolol/pilocarpine
Chitosan[5]	pH	Ocular delivery	Ofloxacin
Ethylene-co-vinyl acetate[6]	Magnetic field	Oral drug delivery	Insulin
Poly(2-hydroxyethyl methacrylate)[7]	Electric field	Oral drug delivery	Propranolol hydrochloride
Polyethylene glycol[8]	Temperature	Nasal drug delivery	Mucin
Carboxymethyl Chitosan[9]	pH	Intestinal drug delivery	Methyl prednisolone

Colon-specific drug delivery

Absorption and storage are the two main functions of the colon which lead to a lower water content and fluid mobility than other areas of the gastrointestinal (GI) tract. These conditions mean drugs can have higher residency times which will allow for the maximum possible drug uptake efficiency in patients. Therefore, the colon as a site for drug delivery has received a good deal of interest for the treatment of localised diseases such as irritable bowel syndrome, colon cancer, and inflammatory bowel disease (IBD) including Crohn's disease and ulcerative colitis.[14-17] Oral colon-specific drug delivery of protein and peptide drugs has also attracted the attention of worldwide drug delivery scientists due to the relatively low proteolytic enzyme activity in the colon compared to the small intestine.[18]

Factors affecting the design of colon-specific drug delivery systems

a) pH of the colon

The pH of the GI tract is subject to both inter- and intra-subject variations. The highest pH levels were measured by radiotelemetry and were found to be 7.5 ± 0.5 in the terminal ileum. On entry into the colon, the pH drops to 6.4 ± 0.6. The pH in the transverse colon was measured at 6.6 ± 0.8.[19]

b) Transit time to colon

Arrival time of a drug or drug composite in the colon depends on the rate of gastric emptying and intestinal transit time. The movement of materials through the colon is slow, tends to be highly variable and influenced by a number of factors such as diet, stress, disease state and presence of drugs.[20]

c) Colonic microflora and their enzymes

The sluggish movement of material through the colon provides perfect conditions for bacterial growth with over 400 resident species and a range of 1011-1012 colony-forming units (CFU)/g in comparison to the stomach (102 CFU/g) and the small intestine (104-107 CFU/g).[21] The colonic microflora are able to break down polysaccharides by producing a large number of reductases and carbohydrases.[22]

Polysaccharide-based colon-targeted drug delivery systems

Polysaccharides have gained much attention in developing colon-specific drug release systems because of their flexibility in obtaining a desirable drug release profile, cost effectiveness, ease of modification, biocompatibility, biodegradability and ability to form hydrogels (Table 2). Polysaccharides are widely distributed natural polymers. They are formed by condensation reactions of monosaccharides that result in glycosidic linkages. Hydrolysis of the glycosidic linkages on arrival in the colon triggers the release of the entrapped bioactive.

The death rate from bowel cancer in New Zealand is one of the highest in the developed world. At least 2,700 people are diagnosed with bowel cancer every year and more than 1,200 die each year as a result, equivalent to more than 100 New Zealanders every month. Because a high intracolonic drug concentration is required for the treatment of diseases associated with the colon, a considerable amount of research work has been carried out to develop colon-targeted drug delivery systems.

The main benefits of colonic delivery as a site for drug delivery are:

a) Proteolytic activity of colon mucosa is less than that observed in the small intestine, thus the colon may be helpful in achieving a reasonable absorption of certain drugs that are enzymatically labile in the small intestine

b) The colon provides a longer retention time and appears highly responsive to agents that enhance the absorption of generally poorly absorbed drugs

c) The colon is rich in lymphoid tissue which can take absorbed antigens into the mast cells of the colonic mucosa. This leads to rapid local production of antibodies which can help in efficient vaccine delivery.[19]

d) The colon continues to attract interest as a site where poorly absorbed drug molecules may have an improved bioavailability

e) The colonic region has a somewhat less hostile environment with less diversity and less intensity of activity as compared to the stomach and small intestine.

To achieve successful oral colonic delivery, a drug needs to be protected from the absorption and degradation pathways of the upper gastrointestinal tract and then achieve abrupt release into the colon.

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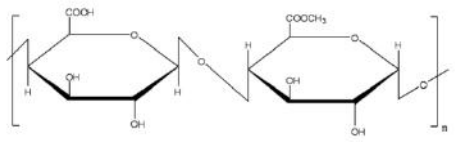
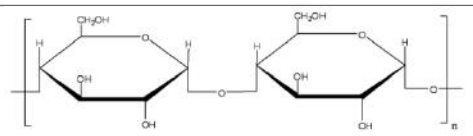
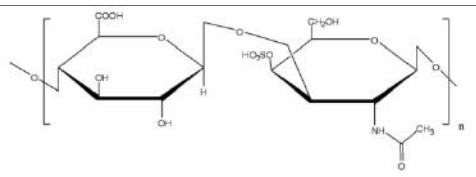
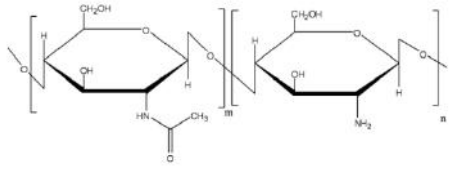
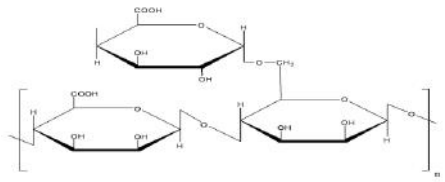
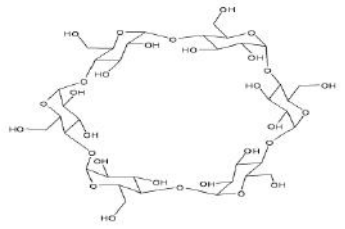
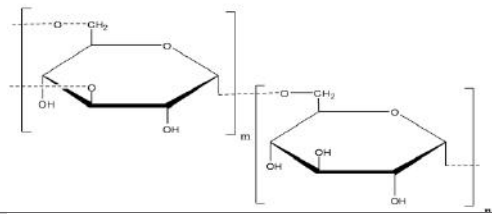
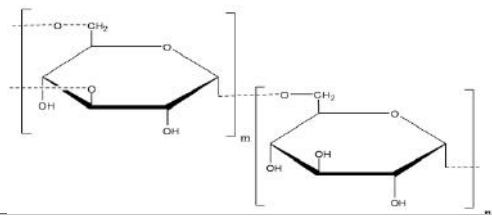
Table 2. Polysaccharide-based colon-targeted drug delivery systems

Polysaccharide	**Structure**	**Source**	**Bacterial species that degrade polysaccharide**
Pectin		Citrus peel and apple pomace	Bacteroids, Bifidobacterium, Eubacterium
Amylose		Plant	Bacteroids, Bifidobacterium
Chondroitin sulfate		Animals and humans	Bacteroids
Chitosan		Exoskeleton of crustacean and insects	Bacteroids
Guar gum		Seeds of plants	Bacteroids, Ruminococcus
Cyclodextrin		Plant	Bacteroids
Dextran		Microbial (bacterium Leuconostoc mesenteroides)	Bacteroids
Cellulose		Plant, microbial (Acetobacter xylinum)	Bacteroids

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Article

The effects of high pressure and pH on the hydrolysis of cytosine at high temperatures

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Keywords: Origin of life, nucleotide stability, high-pressure, high-temperature

Abstract

There has been much speculation regarding the environment in which life originated but it has still to be determined what environmental chemical and physical conditions were necessary for the evolution of self-replicating chemical systems. Opinion is strongly divided on whether life arose on earth under hot or cold conditions; the hot-start and cold-start scenarios respectively. While it has been determined that DNA, RNA and their components are chemically unstable at high temperatures, there have yet to be studies into the role of high pressures. We report experimental results showing that high pressures *increase* the rate of hydrolysis of cytosine to uracil. The results have been obtained with a specialised high-pressure NMR cell. These results provide evidence of a low pressure/low temperature environment being necessary in the origin of life, at least for RNA-based life forms.

Introduction

There are many, varied and hotly debated scenarios for the origin of life on earth. Most scenarios have RNA-based life forms preceding the extant protein-based life forms but this is also vigorously disputed.[1] There are hot-start[2] *versus* warm-start[3] *versus* cold-start[4] scenarios with hot-start scenarios popularistically featuring the energy- and chemically-rich deep ocean black smokers where hyperthermophiles from the kingdoms Archaea and Crenarchaea, often taken as the closest living descendants of the first protein-based life forms,[5] thrive at temperatures between 80°C and 110°C and at high hydrostatic pressure. However, it is well known that at least at ambient pressure of one atmosphere (0.1 MPa), folded RNA structures denature at temperatures less than 70°C *in vitro*.[6] A pioneering study on the chemical stability of RNA components by Levy and Miller[7] found that the nucleobase cytosine hydrolysed to uracil (Fig. 1a) with a half-life of just 19 days at 100°C and ambient pressure, compared to 340 years at 25°C. This rate of hydrolysis is at least 15 times faster than the rates of decomposition of other nucleobases (guanine, 0.8 year and adenine, 1 year at 100°C). Assuming that earliest life forms were rather inefficient and not adapted and stripped down for speedy turnover, in the manner of many extant Prokarya, Crenarchaea and Archaea, these seminal results rendered unlikely a hot-start scenario for RNA-based life forms.

However, these studies did not address the effect of pressure, and whether or not high pressure countered or exacerbated the deleterious effects of high temperatures on the physical and chemical stability of RNA. It is believed that high pressure may have had an important role in the development of life on earth.[8] We report here a comprehensive study on the effects of high hydrostatic pressure on the chemical stability of cytosine and cytidine at 100°C along with brief studies on the effects of pH on chemical stability under high pressure. We show that the rate of hydrolysis of cytosine and cytidine at 100°C increases with increasing pressure and, further, that this rate is minimised for cytosine at pH ~7.

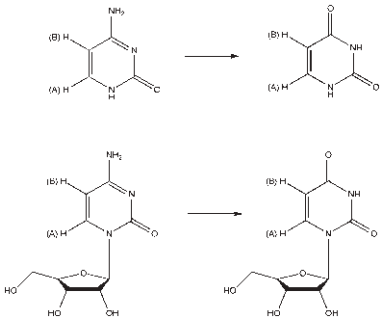

Fig. 1. The hydrolysis of (a) cytosine and (b) cytidine to uracil and uridine respectively. The atom labelling scheme is shown for H(A) and H(B).

This increase in the rate of hydrolysis of cytosine at high pressure may lead to the rethinking of high temperature/high pressure origin of life theories which involve cytosine in genetic coding.

Materials and methods

High pressure NMR apparatus

The commercially available on-line high pressure NMR cell was purchased from Daedalus Innovations. The high pressure cell consists of a zirconia tube (inner diameter 3 mm, outer diameter 5 mm) attached to an aluminium manifold, connected to a long stainless steel tube, connected to a remote hand pump. Pressure is applied to the aqueous sample in the NMR cell *via* an immiscible hydraulic fluid (paraffin oil). This setup allows the pressure on the sample to be set at any value between 0.1 and 250 MPa (measured with a HiP Bourdon Gauge). A specially designed rig allowed the NMR cell to be reproducibly positioned in the spectrometer and to be safely moved under pressure from an external oil bath at temperatures up to 373 K to the spectrometer, allowing other users to access the instrument over the time course of experiments. The cell was interfaced

with a Bruker Avance 500 MHz NMR spectrometer. The sample was positioned in a commercial 5 mm ^{1}H-detection inverse probe with an *x, y, z*-field gradient coil.

Samples

A stock solution of cytosine or cytidine (Sigma), 3-(trimethylsilyl)-2,2',3,3'-tetradeuteropropionic acid (TMSP-d4) (Merck) and sodium azide was added to a phosphate buffer in H_2O/D_2O (90:10 v/v) to give a final solution of 1 mM cytosine, 0.05 M phosphate buffer, 0.02 mM sodium azide and 0.2 mM TMSP-d4. The ionic strength of all solutions was adjusted to 0.2 M with NaCl. The TMSP was added to act both as an NMR reference and as an internal concentration reference. Due to the effect of pressure on pH in a phosphate buffer, the pH values at atmospheric pressure for the high pressure samples were corrected to give the true pH at 298 K while under pressure.[9] Table 1 details the incubation conditions of the individual samples.

Hydrolysis measurements

Samples were inserted into the high pressure cell and brought up to pressure. A ^{1}H NMR spectrum was recorded and the sample was then incubated in an oil bath at 373 K for a period of at least 135 hours while maintaining the pressure at the target value (no leaks were observed over periods of weeks). During this time further ^{1}H NMR spectra were recorded periodically at 298 K after which the sample was promptly restored to 373 K. All NMR spectra were recorded with 64 scans and a relaxation time of 10 s with a presaturation pulse to suppress the water peak. The integrals of the NMR peaks corresponding to protons H(A) and H(B) for both cytosine and uracil (Fig. 1a) were measured for each spectrum using the TMSP peak as a reference. From this, a plot of ln concentration *versus* time was used to determine the rate constant for hydrolysis, *k*, for each sample.

Results

The hydrolysis of cytosine was monitored at 373 K and at pressures of 0.10, 50, 100, 150 and 200 MPa (Fig. 2a). The corresponding data for hydrolysis of cytidine at 373 K at pressures of 0.1 and 150 MPa are shown in Fig. 2b. The processes are first order in all cases, as all plots of ln [cytosine] *versus* time are linear. The NMR spectra, especially of cytidine, were closely inspected for evidence of decomposition additional to the deamination to uracil. No evidence was found by way of peaks not assignable to uracil and cytosine (or cytidine). Moreover, the integrals of the H(A) and H(B) proton signals for uracil and cytosine (or cytidine), normalised to those of TMSP, were constant within 4.0% over the time course of the experiment.

The rate constants and associated estimated standard deviations derived as the slope of these plots are tabulated in Table 2, alongside the half-lives, for cytosine (or cytidine). The half-life decreases monotonically as the pressure increases from 0.1 to 200 MPa, from 19.3 ± 1.6 days at 0.10 MPa to 9.1± 0.4 days at 200 MPa. The half-lives for cytidine at 0.10 MPa and 150 MPa and 373 K are 1.89 ± 1.6 days and 9.3 ± 0.8 days, respectively (no measurements taken at 200 MPa). The half-lives for hydrolysis of cytidine at both low and high pressures are shorter than those for cytosine, which lacks the ribose group attached to the nucleobase.

Table 1. Pressure and pH incubation conditions for individual samples including corrected pH values at 0.1 MPa

	Pressure / MPa	pH under pressure	pH at 0.1 MPa
Cytosine	0.1	6.00	6.00
	0.1	7.00	7.00
	0.1	8.00	8.00
	50	7.00	7.20
	100	7.00	7.39
	150	6.00	6.56
	150	7.00	7.56
	150	8.00	8.56
	200	7.00	7.71
Cytidine	0.1	7.00	7.00
	150	7.00	7.56

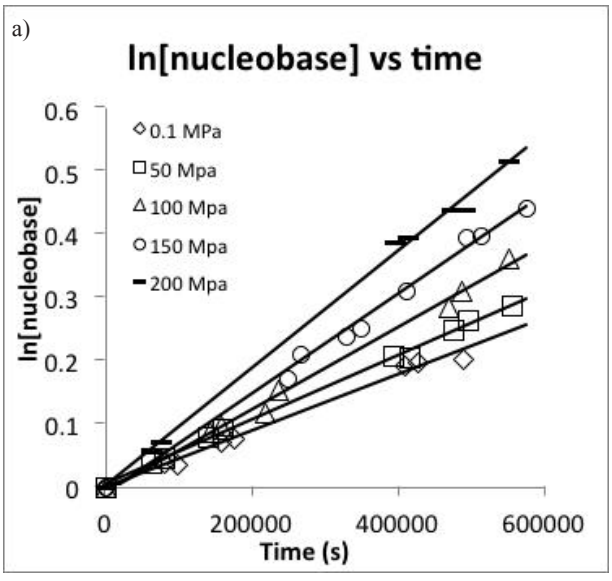

Fig. 2. Plot of ln [nucleobase] *vs* time at 373 K for (a) cytosine at various pressures and (b) cytidine at 0.10 MPa and 150 MPa. The rate constant for hydrolysis of cytosine to uracil is given by the slope of the fitted line

Table 2. The rate constants and associated estimated standard deviations for each incubation condition from Table 1. Half-lives are displayed below each rate constant in square brackets.

	Pressure (MPa)				
	0.1	50	100	150	200
	k / s^{-1} x10^{-6} [$t_{1/2}$ (/day)]	k / s^{-1} x10^{-6} [$t_{1/2}$ (/day)]	k / s^{-1} x10^{-6} [$t_{1/2}$ (/day)]	k / s^{-1} x10^{-6} [$t_{1/2}$ (/day)]	k / s^{-1} x10^{-6} [$t_{1/2}$ (/day)]
Cytosine pH 6.0	0.59 ± 0.07 [13.55]			0.87 ± 0.07 [9.261]	
Cytosine pH 7.0	0.42 ± 0.04 [19.29]	0.49 ± 0.04 [16.45]	0.62 ± 0.03 [13.04]	0.72 ± 0.06 [11.13]	0.88 ± 0.04 [9.141]
Cytosine pH 8.0	0.42 ± 0.03 [18.91]			0.78 ± 0.04 [10.34]	
Cytidine pH 7.0	0.44 ± 0.04 [18.22]			0.87 ± 0.08 [9.254]	

The pressure profile of the rate constants for cytosine at 373 K is shown in Fig. 3, as a plot of ln k *vs.* pressure p,

$$\frac{\partial lnk}{\partial p} = -\frac{\Delta V^{\ddagger}}{RT} \qquad \text{Equation 1}$$

where R is the gas or universal constant and T is the absolute temperature in K. From this the value of the reaction volume of activation, $\Delta V^{\ddagger}$, was calculated to be: for cytosine -11.7 ± 1.2 cm^3 mol^{-1}, and for cytidine, -14.6 cm^3 mol^{-1}. These values are similar in magnitude to the molar volume of water, 18.01 cm^3 mol^{-1}.

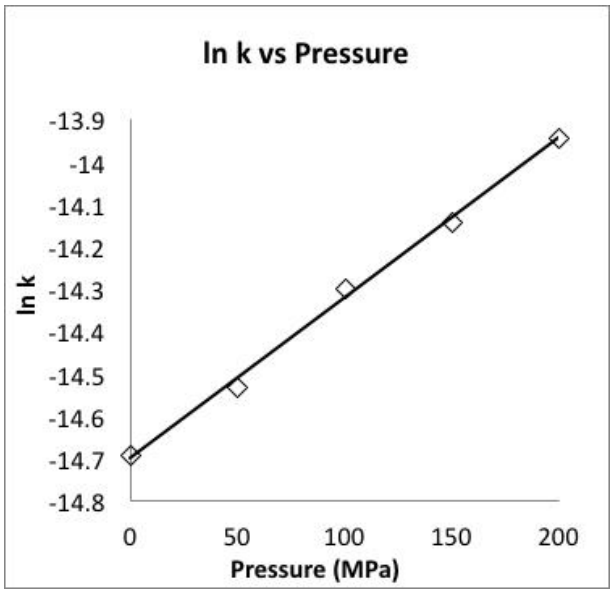

Fig. 3. Plot of the log of the rate constant k for the hydrolysis of cytosine *vs.* pressure p. From the slope of the line $-\Delta V^{\ddagger}/RT$ the activation volume $\Delta V^{\ddagger}$ can be derived.

A brief examination of the pH dependence of cytosine hydrolysis was carried out at pressures of 0.1 and 150 MPa (Fig. 4). It is seen in both curves that the rate of hydrolysis is the slowest in the region of pH 7. Initial measurements made at pH 4.00 and 373 K (data not shown) were consistent with this, as the rates calculated were much larger than those at pH 7.

Discussion

The relatively fast rate of hydrolysis of cytosine to uracil at

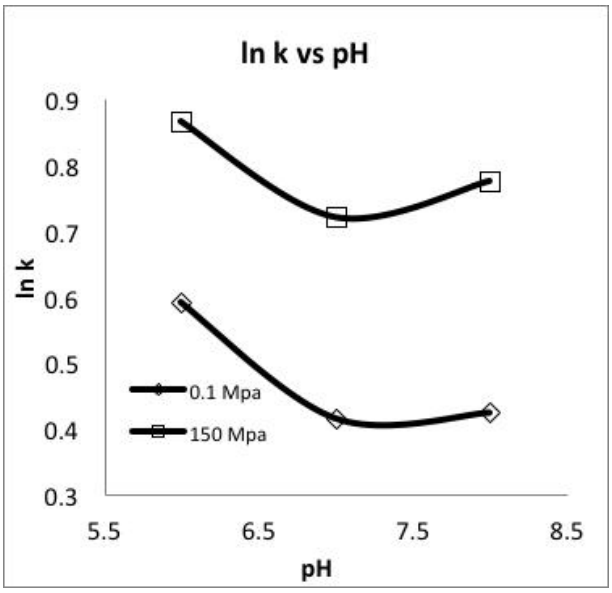

Fig. 4. The pH profile for the hydrolysis of cytosine at 0.1 MPa and 150 MPa. pH values shown at 150 MPa are those corrected for pressure effects. It can be seen that there is a minimum in the rate of hydrolysis just above pH 7. The lines are for visual reference only.

100°C and ambient pressure, compared to geological time scales, has previously been cited as a limiting factor for the evolution of life at high temperatures.[7] With regard to all the possible locations for the development of life, there is a wide range of different conditions to consider, from acidic high pressure, high temperature deep sea black smokers to alkaline low pressure, moderate temperature saline springs. Because of this, we have examined the effect of pressure and pH on cytosine hydrolysis to determine whether there is any possibility of high pressures offsetting the negative effects of high temperatures on nucleotide chemical stability.

Somewhat counter to our expectations, the rate of hydrolysis of cytosine increases with pressure such that at 200 MPa the rate constant for deamination is doubled compared to that measured at an ambient pressure of 0.10 MPa. The half-life determined at 0.10 MPa and 100°C in our measurements of 19.3 ± 1.6 days compares well with that of 19 days determined by Levy and Miller[7] at 0.10 MPa 100°C

for cytosine at pH 7 under the same conditions (0.05 M phosphate buffer at an ionic strength 0.2 M). We observed that under the same conditions, the rate of hydrolysis of cytidine is faster than that of cytosine, the difference being more pronounced and significant at higher pressures. Respectively, the half-lives for hydrolysis at 100°C are; for cytosine, at 0.10 MPa, 18.9 ± 1.6 days and 19.3 ± 1.6 days, and for cytidine, at 150 MPa, 9.3 ± 0.8 days and 11.1 ± 0.9 days. This shows differences of 0.4 days to 1.8 days. Similar differences were observed for results obtained at pH 4.8 (data not shown).

From the plot of ln k vs p, the activation volume, $\Delta V^{\ddagger}$, for the hydrolysis of cytosine and cytidine at 100°C was calculated to be -11.7 ± 1.2 $cm^3\ mol^{-1}$ and -14.6 ± 1.4 $cm^3\ mol^{-1}$. Respectively, these results appear to be typical for biochemical processes, where the magnitude of values for $\Delta V^{\ddagger}$ are within the range of 0 to 50 $cm^3\ mol^{-1}$.[10] Our negative value corresponds to an increased rate of deamination with increasing pressure. The difference between the two results for cytosine and cytidine indicate that the hydrolysis rate for cytidine, which has the attached ribose ring, is slightly more susceptible to the effects of pressure.

Compared to the half-life at 0.1 MPa (atmospheric pressure) of 19.3 days, the value of the half-life, calculated via equation 1, is 13% lower at 38.2 MPa, the pressure corresponding to the mean ocean depth of 3790 m.[11] At the deepest ocean pressure of 110 MPa, corresponding to a depth of 10920 m,[12] the half-life is 33% shorter than that at atmospheric pressure. Here, the result is significantly different but applies to only a small portion of deep sea environments.

The examination of the pH dependence of the hydrolysis of cytosine has shown that the pH dependence of hydrolysis at high pressures is similar to that at ambient pressure (Fig. 4). Both plots indicate that the pH that will result in the lowest rate of hydrolysis is located somewhere just above pH 7. At atmospheric pressure this result is to be expected since the nucleobases are the most stable at pH 7.[13]

The instability of biomolecules has long been recognised as a weakness in the argument for a hot-start origin of life theory.[14] Cytosine has been observed to be the least stable of all the nucleobases having a half-life of 340 year at 298 K (compared to ~ 10000 year for adenine and guanine at 298 K) but having a half-life of only 19 days at 373 K (compared to ~ 1 year for adenine and guanine). These half-lives are very short on the geological time scale and therefore decrease the likelihood of a high temperature origin of life involving cytosine. It had been argued that the instability of RNA and its components at high temperatures may be offset by high pressures in a high temperature/high pressure theory.[8] Our results show that this is not the case and that it is in fact the opposite for the hydrolysis of cytosine and cytidine. This is a solid argument against a high temperature/high pressure origin of life theory involving cytosine or derivatives. There is also a possibility for an origin of life theory that does not involve cytosine as a nucleobase, in genetic material that is either two base coded with just adenine (A) and uracil (U) or where the cytosine-guanine (CG) pair has been substituted for an alternate base pair (isoguanine and isocytosine, diaminopurine and U, diaminopyrimidine and xanthine).[7] However, numerical simulations indicate that a model containing only A and U does not lead to the unique stable folded RNA structures necessary for catalytic functions.[15,16] This would be an important limitation if proteins had yet to be used for catalytic function.

Conclusions

As previously indicated, the rate of hydrolysis of cytosine at 100°C is relatively short on the geological time scale. Our data on the chemical stability of cytosine and cytidine under high pressure conditions at 100°C indicates that both cytosine and cytidine have significantly faster rates of hydrolysis at high pressure. Data also show that there is a rough translation of the pH dependence on the rate of hydrolysis for cytosine at both 0.10 MPa and 150 MPa. These results favour a low temperature/low pressure origin of life theory over a high temperature/high pressure theory.

What still remains unknown is the effect that specific adjuvants, such as amino acids, short peptides, and magnesium ions may have on the chemical stability of cytosine and its derivatives while under pressure. There is also the question of the chemical stability of cytosine within folded RNA/DNA molecules under pressure. A study of the chemical and physical stability of RNA/DNA molecules is to be a major part of current work.

Acknowledgements

We gratefully acknowledge funding from the Marsden Fund of the Royal Society of NZ (grant 09-MAU-140) for a PhD scholarship to CPL and support of this project, from the Allan Wilson Centre for Molecular Ecology and Evolution for the high pressure/high temperature NMR cell, and from the Lottery Health Board for an Autotune-and-Match module for the 500-MHz NMR spectrometer.

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Article

Flag the Periodic Table

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I was searching the web for a plain unadorned Periodic Table and came across this representation created by Jamie Gallagher at Glasgow University. The source is: *http://www.smithsonianmag.com/smart-news/the-periodic-table-of-elemental-discoveries-1773011/* or just google "periodic table flags". It is anything but plain and unadorned and gives an intriguing perspective on the elements. It provides another opportunity to discuss the human dimension of the Periodic Table. Since locating this I have found there are other slightly different versions depending on how the discovery is interpreted, but I'll stay with this version as it is the one Jamie has given me permission to use.

The first thing that surprised me was that Sweden came in at number two for the number of elements discovered. My immediate justification was the Ytterby elements and Carl Wilhelm Scheele. But no. Scheele is only directly credited with two: chlorine in 1774, but not recognised as an element until Humphry Davy isolated it in 1808, and molybdenum, discovered as a new entity by Scheele in 1778 and first isolated by his countryman Peter Jacob Hjelm in 1781. The selection is based on the country in which the element was isolated, not where the source sample came from so only four of the seven elements identified in the tailings of the Ytterby mine are credited to Sweden (terbium, holmium, erbium and thulium). Of the others yttrium is credited to Finland (at an institution which was part of Sweden at the time of discovery), and gadolinium and ytterbium to Switzerland.

Sweden and France are distinct from the other major players in element discovery in that their elements are spread throughout the Periodic Table, whereas the UK, Germany and USA discoveries tend to be grouped.

In the 18th and 19th centuries, chemistry was a young science with limited techniques and although it might be apparent that a new substance had been found, identifying it as a new element was a different matter. Part of the problem was the definition of an element as *a substance that cannot be broken down into anything simpler*. This is a negative definition and it is interesting to discuss the implications of negative definitions with students. In this case the question is: "Have you tried hard enough?" Lime (CaO) and magnesia (MgO) were originally classified as elements because neither strong heating nor chemical reducing agents such as carbon would break them down into anything simpler. The later (positive) definition that an element was a substance that contained only one type of atom could not be implemented until atomic structure discoveries of the early 1900s made it clear what "type of atom" meant.

Scheele had produced chlorine by the action of HCl on the ore pyrolusite (MnO_2):

$$MnO_2 + 4HCl \rightarrow MnCl_2 + Cl_2 + 2H_2O$$

This is still a standard method for preparing chlorine in the laboratory. Scheele was aware that pyrolusite contained a new element but was unable to isolate it. This was achieved by fellow Swede, Johan Gottlieb Gahn, in the same year (1774) when he reduced the MnO_2 with carbon to obtain manganese.

The discovery of oxygen is clouded by the phlogiston theory and the tardiness of publishers. The phlogiston theory was essentially an "anti-oxygen" theory. In attempting to explain burning, it proposed that combustible substances contained *the* component of fire naming it phlogiston. When these substances burned they lost phlogiston which was why carbon lost weight when it burned. Breathing was thought to remove phlogiston from the body. When ignited in a closed container the substance stopped burning because the air became saturated with phlogiston. A mouse in this container died because it could not get rid of its phlogiston (since the air was already saturated with it).

In 1772 Scheele discovered oxygen by heating mercury(II) oxide and "various nitrates", presumably KNO_3 and $NaNO_3$. The account of his studies was not published until 1777. In the meantime Joseph Priestley in England had done much the same experiment and called the gas "dephlogisted air" because candles burned much longer in it than in ordinary air. Antoine Lavoisier in France was instrumental in unravelling the confusion, recognising that the phlogiston theory was unsatisfactory in many instances and firmly denouncing it. He named the gas "oxygène", meaning acid generator, believing it to be a component of all acids, so there was still a way to go in understanding. Scheele, Priestley and Lavoisier all effectively discovered oxygen hence the three flags in the oxygen space.

Vanadium was first discovered by a Spanish-Mexican mineralogist, Andrés Manuel del Rio, in 1801, but other chemists convinced him that all he had was impure chromium and he retracted his claim. It was subsequently isolated in 1831 by Nils Gabriel Sefström in Sweden. Later Frederich Wöhler confirmed del Rio's work.

Jon Jacob Berzelius, Georg Brandt, Carl Mossander, Per Theodore Cleve and their co-workers account for many of the other discoveries attributed to Sweden.

The clusters of elements with the same flag can generally be traced to the development of particular techniques. The earliest example of such a cluster is the Group 1 and 2 metals. Chemists had been aware of the elements but it wasn't until Humphry Davy got his hands on a voltaic pile (electrochemical cell) and electrolysed the molten salts that the metals themselves were isolated. In a two year burst in 1807-08 he produced samples of the metals sodium, potassium, magnesium, calcium, strontium and barium.

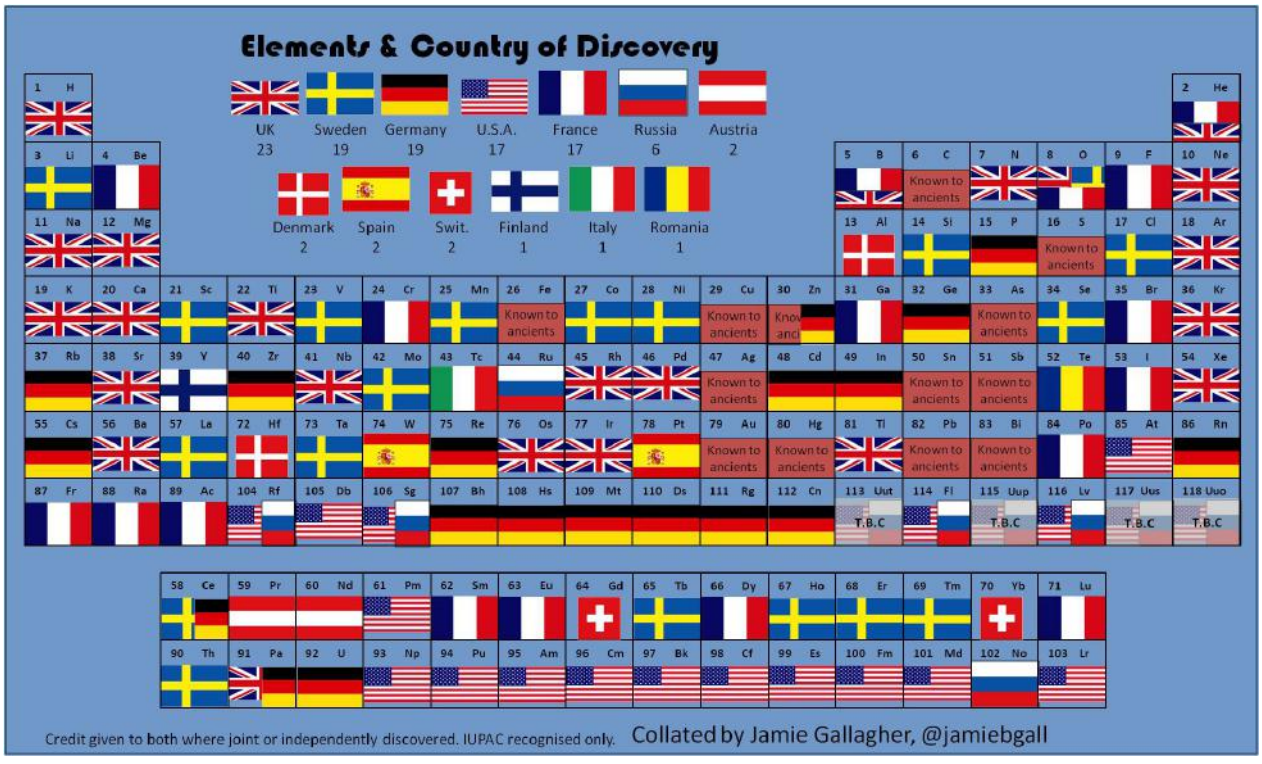
Almost a century later, English physicist Lord Raleigh and Scottish chemist William Ramsay confirmed the existence of a whole new group of elements – the noble gases. They were investigating discrepancies between the density of nitrogen gas obtained from air and nitrogen obtained from chemical reactions. They suspected that atmospheric nitrogen contained another gas.

Careful fractional distillation of air yielded not one but several gases that they named krypton, neon and xenon as Group 18 elements in addition to helium and argon that had been isolated earlier. In 1868, previously unseen spectral lines were detected in the analysis of light from the sun during an eclipse and indicated the presence of a new element. It was named helium (after *helios,* Latin for sun). Various studies showed evidence of helium on earth but it was not finally confirmed until William Ramsay isolated it in 1895.

USA, "the new world", didn't feature on the Periodic Table until 1940 when astatine was discovered. They made up for lost time by harnessing the cyclotron particle accelerator at the University of Berkeley, California, to bombard atoms and under Glen Seaborg generated synthetic elements 93 to 103 with the exception of nobelium, element 102, which was created at the Flerov Laboratory of Nuclear Reactions in Dubna, Soviet Union. A group at the Society for Heavy Ion Research in Darmstadt, Hessen, Germany were responsible for elements 107–112 and Russian/US laboratories have collaborated to produce elements 113 -118.

It is a rule that elements are not named after living people. This rule has been broken once when element 106 was named Seaborgium in 1997, having been created in 1994. The naming honoured Glen Seaborg's life-long contribution to science including leading the team at Berkeley that produced so many transuranium elements. The naming caused heated debate among chemical societies. Seaborg died in 1999. A similar rule applies to people's images on banknotes. New Zealand broke this rule when Sir Edmond Hilary featured on the $5 note in 1992. He died in 2008.

This article merely scratches the surface of a few of the many fascinating stories around the discovery of the elements, particularly those discovered pre-1900. The Wikipedia entries for each element and the chemists and physicists involved are good starts for information. *The Disappearing Spoon (and other true tales of madness, love and the history of the world from The Periodic Table of the Elements)* by Sam Kean is another good source, although some of his chemical statements are what you might expect from a physics major – which he is.



Feature Series

Some unremembered chemists

A series of articles that explores the lives and work of selected chemists who have made a significant contribution to the advancement of the discipline, the profession and well-being of mankind, yet who are little remembered.

William Henry, MD, FRS (1774-1836)

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William Henry by James Lonsdale (© National Portrait Gallery, London, with permission)

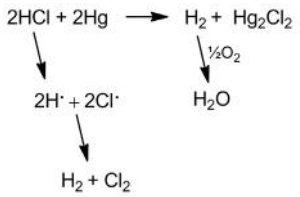
William Henry was born on December 12 in 1774 at 19 St. Ann's Square, Manchester. He was the third son of Thomas Henry and his wife Mary (née, Kinsey).[1-3] The Henry family hold the distinction of having three generations of chemists, Thomas (1773),[1] William (1809)[4] and William's son (William) Charles (1834),[5] holding Fellowships of the Royal Society continuously for close on one hundred and twenty years from 1773.[5]

Henry senior (1734-1816) was a surgeon and apothecary (a trading chemist) who taught himself chemistry from the traditional eighteenth century text *Elementa Chemiae* written in 1732 by Dutch chemist Boerhaave. Although a surgeon, Thomas Henry was not an MD as, in those days, the majority of surgeons qualified by apprenticeship through an apothecary. However, it was Thomas Henry's chemical acumen that placed him among the more affluent members of Lancashire society. This came from the manufacture of magnesia – magnesium oxide – for which he devised an industrial process and gained the name *Magnesia Henry*. Although little is known about the education of his elder sons, Thomas and Peter, William was privately educated by the Rev. Ralph Harrison who taught Latin and Greek at the nearby Unitarian Cross Creek Chapel, the Dissenters' Meeting House. When the Manchester Academy (which Thomas Henry had helped establish) opened in 1786, Harrison was appointed Professor of Classical Literature[3,4] and William, although only eleven years old and below entry age, was permitted to follow his tutor there. The academy was run by English Presbyterians as one of several dissenting academies that provided religious nonconformists with higher education – the English Universities of Oxford and Cambridge took only Anglicans. As a young boy, William suffered serious injury when a heavy beam fell on his right side. The consequential acute neurological pain he suffered remained with him throughout his life and turned him to study since normal physical boyhood activity was limited. In 1790, at the age of sixteen, he left the academy to become secretary-companion to Thomas Percival, a colleague of his father and the leading physician in Manchester, perhaps best known for crafting the first modern code of medical ethics published in 1794. Percival had poor eyesight and suffered violent headaches, and William's job was to read aloud to him, keeping him familiar with developments in medicine and science, and then taking whatever dictation was required. Thus, William Henry became familiar with Percival's correspondence with the noted men of science and literature of the day. During his time with him, William began to study medicine and he entered Edinburgh University for a medical degree in the winter of 1795.

Edinburgh was the centre of modern medical education in the UK as Oxford and Cambridge held strong to classical medical tradition. While there, the young Henry attended lectures in chemistry given by Joseph Black (1728-1799) who, though old and frail, was still the Professor of Chemistry.[4] He became more drawn to science than medicine and he performed his first piece of serious scientific research there – studies of carbonated hydrogen gas. This was read to the Royal Society by his father on June 29, 1797.[6] After a year of medical school, Henry senior recalled William to Manchester to help run the family businesses as his elder brothers had little appetite for business and lacked the aptitude to assist. William became central to the family affairs,[1,5] and after a short time, he was taken into partnership by his father. He ran the magnesia factory, the mainstay of the family fortune, under the name T & W Henry from 1797. It survived under this name until the end of 1933. Late in 1805, William returned to Edinburgh to complete his studies, leaving the factory in the hands of a manager. His two years there gave him his only period freed from commercial responsibilities and he graduated MD with a thesis on uric acid (*De acido urico et morbis a nimia ejus secretion ortis*), a substance that continued to hold his interest.

William Henry had a natural talent for experimental study and it was over the ten years following his first return from Edinburgh that he made his major contributions to chemistry, carrying the skills he learned as a manufacturing chemist to the research bench. Apart from magnesia, the other major activity of the Henrys was the production of aerated waters – soda water with or without added flavouring. Thus, William Henry had a life-long interest in gases, their essential properties and their chemical behaviour,

and, later, he became actively involved in the gas lighting industry in Great Britain. His interest in gases led him to work with his father on pneumatic medicine - the inhalation of gases to treat disease and especially consumption - at the Royal Manchester Infirmary and it directed much of his early work. In this, William studied the composition and decomposition of muriatic acid gas (HCl) which, like all acids at that time, was thought to contain oxygen. He came close to solving the problem of its composition in 1800, some ten years ahead of Humphrey Davy. His results appeared in the *Philosophical Transactions* of the Royal Society in 1800.[7] Henry repeatedly exposed HCl to electric discharges and when performed over mercury he saw a volume reduction and the formation of a white solid [now recognised as mercury(I) chloride].

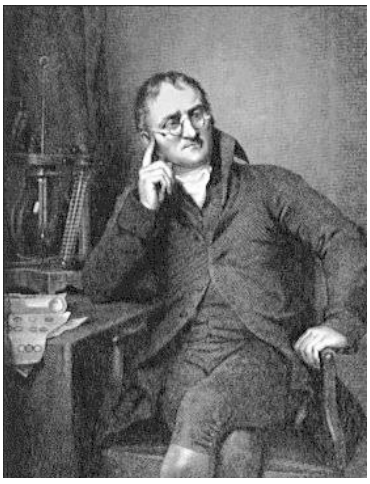


Scheme 1. Electric discharge of hydrogen chloride

When repeated with HCl in the presence of O_2, a greater volume drop was seen as water is formed from reaction of the liberated hydrogen with the oxygen, and in the absence of mercury, chlorine was produced (Scheme 1). When Davy finally showed that muriatic acid was comprised of hydrogen and chlorine only, Henry supported him and provided additional evidence in 1812.[8] Although Henry was unable to come to the correct conclusion regarding HCl until after Davy's paper, it is clear that his results are correct and of significance. However, the work for which he is best known is on the solubility of gases.

Henry's studies on gas solubility gave rise to what we now regard as Henry's law. It also led to a friendship and collaboration with the teacher John Dalton, most notably from 1800-1805.[9] He helped the colour-blind Dalton with his experiments and, while Dalton subsequently became world-famous for his theories, his practical abilities were less enduring. Thus, Dalton and Henry shared an interest in the chemistry of gases and liquids. Understandably, William Henry approached his study of them from the viewpoint of an industrialist who manufactured soda water and hoped to use gases in medicine. Dalton, on the other hand, came to chemistry from a metrological background.

By about 1800 Dalton saw the atmosphere as comprising four types of particle – the atoms of oxygen and nitrogen and the compound atoms of water and carbonic acid (carbon dioxide) that were motionless. He could not understand why a puddle of water could diffuse into the atmosphere or why the air did not separate into layers. His discussions with Henry as to what might cause these effects were probably important in the development of his atomic theory. In 1801 Dalton formulated the concept that there was a repulsive force between particles of the same kind in a gas,[10,11] viz. like repels like, and that this resulted in every particle of water in air getting as far from another as possible so that the whole would be evenly distributed throughout the available space. William Henry, initially



John Dalton (1766 – 1844) (from *http://www.wpclipart.com/famous/science/science_2/John_Dalton.png.html*)

opposed to this, converted to acceptance by 1804 saying every gas is a vacuum to every other gas.[12] The change stemmed from his and Dalton's experiments on gas solubility, notable over 1801 and 1802 when both worked on the solubility of gases in water. Because most previous study had been with carbonic acid (carbon dioxide), Henry chose this as his first target and he reported his results to the Royal Society (London) just before Christmas in 1802 and published them in the *Philosophical Transactions* early in 1803.[13] Dalton read his studies to the Manchester Literary and Philosophical Society some ten months later, on October 23, 1803, and published them in the Memoirs of the Literary and Philosophical Society of Manchester in 1805.[14] Henry's conclusion, which appears in an appendix to the original paper,[13] became known as Henry's law and for this he was awarded the Copley Medal in 1808. The law, one of the fundamental gas laws, states:

> *At a constant temperature, the amount of a given gas that dissolves in a given type and volume of liquid is directly proportional to the partial pressure of that gas in equilibrium with that liquid.*

An equivalent is:

> *The solubility of a gas in a liquid is directly proportional to the partial pressure of the gas above the liquid.*

Not surprisingly, the most common practical illustration of Henry's law is provided by carbonated soft drinks. Before the container of carbonated drink is opened, the gas above the drink is almost pure carbon dioxide at a pressure slightly higher than atmospheric. The drink itself contains dissolved carbon dioxide. When the bottle or can is opened, some of this gas escapes, giving the characteristic hiss (*pop* in the case of sparkling wines). Because the partial pressure of carbon dioxide above the liquid is now lower, some of the dissolved carbon dioxide comes out of solution as bubbles. Obviously, when a glass of the drink is left in the open, the concentration of carbon dioxide in solution equilibrates with the carbon dioxide in the air, and the drink goes flat. A more complex example of Henry's law is in the bends that can be suffered by underwater divers.

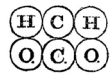
Dalton's experiments on the solubility of gases provided a mechanical model of it and led to his conclusion that the differences in the solubility of different gasses depended on the weight and number of the ultimate particles of the several gases,[13] a generalisation that is now known as Dalton's law of partial pressures.[14] Henry was much more concerned with the facts associated with his studies than with theory, but when they fitted to a theory he was delighted. Thus, Henry began his study from the knowledge that the solubility of CO_2 in water was increased with increased pressure. However, in 1801, the preparation and handling of pure gases was essentially unknown and his work used gas mixtures – almost always containing amounts of air. This led to the overlap of his and Dalton's studies and Henry's 1802 presentation on the quantity of gases absorbed by water was possible only after taking into consideration the mixed gases and Dalton's law of partial pressures known to him but unpublished at that time. The nature of the experiments and the rather crude equipment then available has been nicely described by the Farrars and Scott[9] and does not justify further discussion here. Suffice to say that the true solubility of CO_2 could only be determined from an analysis of the undissolved gas and applying the law of partial pressures to it. This only became apparent to Henry after he had read his paper and presented his manuscript for publication. It was clarified in the appendix where he says that the absorption of gases by water is a purely mechanical effect and that the amount is exactly proportional to the density of the gas, independent of any other gas with which it may be mixed. The result of some 50 experiments on CO_2, H_2S, N_2O, O_2 and N_2 led to the formulation of Henry's law.

William Henry's subsequent work with gases included the electrolysis of ammonia in order to assist in determining its composition.[1] Here, a series of experiments led to the conclusion that dry ammonia doubled in volume (1 volume increased to 1.98 volumes) from electric discharge. We now know that two volumes of N_2 are replaced by four volumes of gas as per:

$$2NH_3 \rightarrow N_2 + 3H_2$$

However, it is his studies on the destructive distillation of coal and oil that led to his involvement with the gas lighting industry and it provided the only fundamental research in that industry until the mid-1800s.[15] His papers on this were published over the 1805-1821 period.[16-20]

It was towards the end of the 18th century that the gaseous products from coal were beginning to receive attention. William Henry analysed the constituents of the gases produced and distinguished between some of them by chemical methods, and he studied their suitability for lighting. Thus, he showed that the gas mixtures comprised carbonic acid (CO), carburetted hydrogen (CH_4), hydrogen, olefiant gas (CH_2=CH_2) together with some carbonic acid gas (CO_2) and sulfureted hydrogen (H_2S). He was in disagreement with other authors of the day in that he correctly showed the composition of the gases from coals, oils and other organic substances such as wood and peat. They comprised mixtures of a few simple compounds, predominantly hydrogen, methane and the oxides of carbon. Henry's last important paper on hydrocarbons[20] contained speculation on the way methane is formed "in natural operations". Although we know that water and charcoal yield hydrogen and the oxides of carbon (water gas), and that the formation of methane in stagnant pools is a microbial process, Henry's speculation provides one of the very early attempts to give a mechanism in terms of the atomic theory. One needs to remember that water was thought to be 'OH' and methane (carburetted hydrogen) 'CH_2' in reading that section of the original paper which appears below.[20] Not only does he account for the products as he saw them, he also proposes a metathetical way in which the 'OH' and 'C' approach and separate, a concept some 150 years ahead of olefin metathesis.

> The process, by which carburetted hydrogen gas is evolved in natural operations, is no doubt the decomposition of water, and admits of being explained on the atomic theory of Mr. Dalton, by supposing two atoms of charcoal to act at once on two atoms of water. One atom of charcoal attracts the two atoms of hydrogen, forming carburetted hydrogen gas, and the other atom of charcoal unites with two atoms of oxygen, constituting carbonic acid. This is illustrated by the annexed figure, in which two atoms of charcoal C.C. are represented as interposed between two atoms of water, each consisting of an atom of hydrogen and an atom of oxygen. Dividing the diagram vertically into three parts, we have the original substances; and separating it horizontally, we obtain the two new compounds. This theoretical view of the subject is confirmed by the fact, that the carburetted hydrogen, formed at the bottom of stagnant pools, is never accompanied by carbonic oxide, but always by carbonic acid, the full quantity of which is prevented from appearing, in consequence of the absorption of a great part of it by the mass of water, under which the changes are taking place.
>
> 
>

Beyond these insights, it was a result of William Henry's 1808 paper[17] that ethylene became easily identifiable. He showed that it forms an oily liquid (1,2-dichlorethane) on mixing with chlorine and it was from this and the 1795 work of Dutch chemists (Deimann, van Troostwyck, Lauwerenburgh and Bondt) that it became known as *olefiant gas*. This organic reaction was also well ahead of the understanding of halogen addition to multiple carbon-carbon bonds and some 20 years before Wohler's urea synthesis.

Henry's involvement with the gas lighting industry included experiments which showed that sulfureted hydrogen (H_2S) was the main contaminant of raw coal gas and that the best coals for illumination purposes unfortunately gave the greatest quantity of H_2S.[15] He suggested that the most effective way of removing the contaminant would be by agitation with quicklime and water. Thus, raw coal gas could be used for lighting only in well ventilated areas unless the hydrogen sulfide was removed. Samuel Clegg tried to put this into practise in a mill in Coventry in 1809 but it was unsuccessful because of the short time that the gas and lime were in contact. It seems that Clegg and Henry then collaborated in the installation of gas lighting at Stonyhurst College, the Jesuit College in Lancashire. This was the first non-industrial building to be so illuminated. For this they constructed a vessel containing lime-water through which the raw gas was bubbled prior to passing

to the gas holder. Henry showed that the purified gas was perfectly free of the contaminant and the installation was a complete success. Lime was then used as a "sweetener" for the gas over the next fifty years.[15]

William Henry's reputation was significant and he was invited to let his name be advanced for the inaugural Regius Chair in Chemistry at Glasgow University. He declined on the grounds of his family business, his health, and his growing family; he had nine children of whom six lived to maturity. The position went to Henry's friend from Edinburgh days, Thomas Thomson, who held it from 1818 until his death. William became a man of considerable wealth with homes to match. By the late 1820s his health was deteriorating and he took no further part in experimental chemistry, becoming an elder statesman whose opinions and views were sought and valued by many. He was elected a Fellow of the Royal Society in February 1809, having been awarded their prestigious Copley Medal in 1808. He held the position of Vice-Chairman of both the Literary and Philosophical Society and the Natural History Society of Manchester and was one of the founding members and life member of the British Association for the Advancement of Science. His 1799 textbook *An Epitome of Chemistry: In Three Parts* was renamed *Elements of Experimental Chemistry* and enjoyed considerable success, going through eleven editions over some 30 years.[21]

After the marriage of his son Charles in 1834, William and the rest of his family moved to Pendlebury, some four miles out of Manchester. He died there some two years later on September 2, 1836. His neurological pains had increased to the extent that during the night he went to his private chapel and ended his life with a bullet through the mouth. His son, William Charles (who had qualified in medicine at Edinburgh in 1827, was an Honorary Physician at the Manchester Infirmary from 1828 and elected FRS in 1834), like his father before him, had been assisting with the magnesia factory and the family business increasingly as his father's health deteriorated. After his father's death he took over the company keeping the name and running it until his own death in 1892. However, after his father's death he retreated more and more from active participation, taking up the life of a country gentleman at Hatfield near Ledbury in Herefordshire. He also withdrew from practical science but kept many scientific friendships, notably one with Liebig who he had met in Germany and hosted on his first visit to Britain in 1837.

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Dates of Note

Georg Rushd Brandt, the Swedish chemist who discovered cobalt in 1730, was born on July 21, 1694. Sir ***James Chadwick***, the English physicist who received the 1935 Nobel Prize for Physics for his discovery of the neutron, died on July 24, 1974. ***Sergey Vasilyevich Lebedev***, the Russian chemist who developed a method for industrial production of synthetic rubber from his 1910 discovery of the polymerization of butadiene, was born on July 25, 1874. ***Raoul Pierre Pictet***, the Swiss chemist who pioneered cryogenics from his interest in the artificial production of ice for refrigeration, died on July 27, 1929. ***John Dalton*** also died on the same date but in 1844, 170 years ago. ***Francis Crick*** of DNA fame died on July 28, 2004 and noted crystallographer ***Dorothy Hodgkin***, on July 29, 1994. ***Primo Levi***, the Italian novelist, short-story writer and poet who was a chemist most of his professional life and is known for his, *The Periodic Table*, was born on July 31, 1919. In 1874, the Centennial of Chemistry in the US was celebrated by chemists meeting at Northumberland, Pennsylvania, where Joseph Priestley is buried. The chemists commemorated the 100th anniversary of Priestley's discovery of the element oxygen on August 1, 1774.

August 1 is the date in 1890 that ***George Thomas Beilby***, the Scottish industrial chemist who developed the process of manufacturing potassium cyanide, died. Barron ***Carl Auer Freiherr*** von Welsbach, the Austrian chemist, physicist and engineer whose invention of the gas mantle greatly improved the brightness of light that could be obtained from gas lamps, died on August 4, 1929. ***Feodor Lynen***, the German biochemist who shared (with Bloch) the 1964 Nobel Prize for Physiology or Medicine for his research concerning the mechanism and regulation of cholesterol and fatty acid metabolism, died on August 8, 1979. ***Benjamin Silliman***, the American geologist and chemist who founded the *American Journal of Science*, and was Yale's first professor of chemistry and natural history (1802), was born on August 8, 1779. Sir ***Edward Frankland***, the English chemist and father of valency who was one of the first investigators in the field of structural chemistry popularising the concept of the chemical bond, died on August 9, 1899. Sir ***Ernst Boris Chain***, the German-born British biochemist who shared the 1945 Nobel Prize for Physiology or Medicine (with Fleming and Florey) for the work on penicillin, died on August 12, 1979. ***Anders Angstrom***, the Swedish physicist whose pioneering use of spectroscopy is recognised in the name of the angstrom unit (10^{-10} metre) was born on August 13, 200 years ago. ***Johann Friedrich Miescher***, the Swiss biochemist who studied cell metabolism and discovered nucleic acids, was also born on August 13, but in 1844. ***Sune K. Bergstrom***, the Swedish biochemist who shared the 1982 Nobel Prize for Physiology or Medicine, (with Samuelsson and Vane) for the isolation, identification, and analysis of prostaglandins, died ten years ago on August 15, the day the Panama Canal was officially opened 100 years ago.

Robert Bunsen, the German chemist who, with Kirchhoff, showed that each element emits a light of characteristic wavelength but is more recognised for his gas burner, died on August 16, 1899. ***Wendell Meredith Stanley***, the American biochemist who received the in 1946 Nobel Prize for Chemistry (with Northrop and Sumner) for his work on the purification and crystallization of viruses, was born on August 16, 1904. ***Richard Synge***, the British biochemist who shared the 1952 Nobel Prize for Chemistry (with Martin) for the development of partition chromatography, died 20 years ago on August 18. ***Franz Carl Schmelkes***, the chemist known for his discovery of azochloramid or chlorazodin [1-(amino-chloroiminomethyl)-imino-2-chloroguanidine] that is used to sterilize wounds and burns, was born on August 19, 1899. ***Linus Pauling***, the double Nobel laureate who charted the chemical underpinnings of life itself, worked for nuclear peace, and touted the benefits of vitamin C, died 20 years ago on August 19. On this same date in 1839, 175 years ago, ***Louis Daguerre*** announced the daguerreotype photographic process that allowed an image to be chemically fixed as a permanent picture. ***Jöns Jacob Berzelius***, the noted Swedish scientist and a founder of modern chemistry, was born on August 20, 1779. On August 26, 1959, the Morris Mini-Minor was introduced by the British Motor Corporation. ***Carl Bosch***, the German industrial chemist who at BASF directed development of the industrial scale process for production of ammonia, was born on August 27, 1874. The Haber-Bosch process stemmed from the 1908 suggestion by Fritz Haber that nitrogen and hydrogen gases could be combined using high temperatures, high pressure and with catalysts. ***Theodor H.E. Svedberg***, the 1926 Swedish Nobel Laureate who studied the chemistry of colloids and invented an ultracentrifuge, was born on August 30, 1884. ***André-Louis Debierne***, the French chemist considered the discoverer of the element actinium, died on August 31, 65 years ago.

Paul Vieille, the French scientist who, in 1886, invented smokeless powder called Poudre B that revolutionised the effectiveness of small guns and rifles, was born on September 2, 1854. ***Fritz Pregl***, the Austrian 1923 Chemistry Nobel Laureate who developed the microanalytical technique for organic compounds, was born on September 3, 1869. ***Julian W. Hill***, the US research chemist who discovered cold drawing, a technique of strengthening polymer fibres by stretching, was born on September 4, 1904. Together with Wallace Carothers, they had been synthesising polymer chains and removing a sample of the resultant product from the still. Hill observed that the molten polymer could be drawn into fibres, which after cooling could be stretched or "cold drawn" to give remarkably strong fibres with molecular weights over 12,000. ***August Kekulé***, the German chemist who devised the ring structure of carbon atoms and provided the cyclic structure for benzene was born on September 7, 1829. ***Hermann von Helmholtz***, the German physiologist and physicist who developed thermodynamics and introduced the concept of free energy, died on September 8, 120 years ago. ***Thomas Graham***, the Scottish chemist often referred to as the father of colloid chemistry who studied the diffusion of gases and in 1833 proposed the law named after him, died on September 16, 1869. That day in 1884 saw cocaine

first used as a local anaesthetic by Carl Koller to immobilize a patient's eye for surgery; he initiated the modern era of local anaesthesia. ***Karl Raimund Popper***, the noted Austrian-British philosopher of science, died on September 17, 1994. It is 60 years on September 20 since the first successful test compilation and execution of a computer program using what became FORTRAN was run by IBM. ***Richard Zsigmondy***, the Austrian awarded the Nobel Prize for Chemistry in 1925 for his demonstration of the heterogenous nature of colloid solutions and for his methods that have since become fundamental in modern colloid chemistry, died on September 23, 1929. This same date 75 years ago saw the death of ***Sigmund Freud***. ***Robert John Kane***, the Irish chemist who is remembered for his book, *The Industrial Resources of Ireland* (1944), was born on September 24, 1809. ***Paul Scherrer***, the Swiss physicist who collaborated with Peter Debye in the development of X-ray diffraction analysis, died on September 25, 1969. ***Joseph-Louis Proust***, the French chemist who proved that the constituent elements of any pure chemical compound remain invariant regardless of the compound's source and, thus, strongly supported Dalton's law of definite proportions, was born on September 26, 1754. ***Karl Friedrich Mohr***, the German analytical chemist and geologist who invented or improved a number of titration procedures, died on September 28, 1879. The date marks 125 years since the third legal definition of the metre was adopted at the Paris General Conference. ***Friedrich Mohs***, the German mineralogist who devised the Mohs scale to compare mineral harness, died 175 years ago on September 29. ***Jean-Marie Lehn***, the French chemist who (with Pedersen and Cram) was awarded the 1987 Nobel Prize for Chemistry for his contribution to the laboratory synthesis of molecules that mimic molecules in living organisms, has his 75th birthday on September 30; Jean-Marie has been a frequent visitor to NZ of late.

Charles J. Pedersen, the Korean-American who with Lehn and Cram was awarded the 1987 Nobel Prize for Chemistry for his synthesis of the crown ethers, was born on October 3, 1904. ***Maurice Wilkins***, New Zealand-born British biophysicist known for his X-ray diffraction studies of DNA, died on October 5, 10 years ago. Sir ***Harry W. Kroto***, the English chemist who (with Smalley and Curl) received the 1996 Nobel Prize for the discovery of the fullerenes (and another visitor to NZ), has his 75th birthday on October 7. ***Clemens Alexander Winkler***, the German chemist who discovered the element germanium, died on October 4, 1904. ***Max Von Laue***, the noted X-ray crystallographer, was born on October 9, 1879. Sir ***Henry Tizard***, the English chemist, inventor and administrator, who devised the octane rating system for petroleum fuels, died on October 9, 1959. ***Friedrich Bergius***, the German chemist who converted coal dust and hydrogen directly into gasoline and lubricating oils without isolating intermediate products, was born on October 11, 1884. ***James Prescott Joule***, the English physicist and inventor who has the unit of energy named after him, died on October 11, 125 years ago. October 13 marks the day in 1884 when Greenwich, London was adopted as the universal meridian and is the day 100 years ago that ***Garrett Morgan*** invented and patented the first gas mask. Sir ***William Jackson Pope***, the English chemist who produced an optically active compound that contained a chiral nitrogen atom, but no chiral carbon, died on October 17, 75 years ago. ***Christian Friedrich Schönbein***, the German-Swiss chemist who discovered and named ozone in 1840 and was the first to describe guncotton (nitrocellulose), was born on October 18, 1799. ***Marguerite Perey***, the French chemist who identified francium, the last naturally occurring element to be discovered (January 7, 1939), and was the personal assistant of Marie Curie, was born on October 19, 1909. ***Lewis Urry***, the Canadian-American chemical engineer who invented the ubiquitous alkaline battery and, later, the lithium battery, died on October 19, 2004. ***Paul A.M. Dirac***, the English physicist and mathematician who originated quantum mechanics and the spinning electron theory, died on October 20, 1984, as did ***Carl Cori***, the American biochemist who, with his wife Gerty, discovered a phosphate-containing form of glucose and its universal importance to carbohydrate metabolism. On October 21, 1824, ***Joseph Aspdin***, a stone mason, patented Portland cement.

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One country at a time

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You sometimes see "Worldwide Patent Protected" or "Patented Worldwide" on a product, but what does this mean? There is no such thing as a worldwide patent. Patents are granted on a country-by-country basis, with only a few exceptions.

Presently you can file a regional patent application at the European Patent Office which will be examined centrally. However, once the European Patent Office has confirmed the application is allowable, you still have to go through validation in each one of the European countries that you want a patent. The result is a separate patent in each European country each having the same claims. Due to the cost of validating and maintaining patents in a lot of countries most European patent applications are only validated in three to five countries out of a possible 27.

Change in the works

Attempts to set up a unitary European patent to cover the whole of Europe date all the way back to the 1970s. However, it is looking more and more likely that this will become a reality.

On 11 December 2012 the European Parliament voted positively on the latest proposals for a unitary patent and on 20 January 2013 the regulations came into force.

However, the regulations will only apply once agreement can be reached on a Unified Patent Court. The flip side of a unitary patent is that enforcement of the patent, i.e. suing parties which infringe the patent, or validity of the patent must also be considered centrally. An agreement on the structure of the new court was signed by 25 European Union States on 19 February 2013, but it will need to be ratified by at least 13 states, including France, Germany and the United Kingdom before it can enter into force.

At the time of writing this article, it had only been ratified by three states.[1] You will appreciate the pace of law reform in each country can vary dramatically, particularly with elections in some countries. When the agreement will pass the finishing line is anyone's guess.

There is one other thing that may yet upset the unitary patent proposal. Spain has brought two last minute actions before the Court of Justice against the regulations for the unitary patent.[2] The objections are largely technical in nature and include an objection that the European Patent Office will have the power to grant the unitary patent but will not be subject to judicial review. Whether or not these are ultimately successful there will at least be a delay while they are considered.

Pros and Cons

When (or maybe if) the European unity patent becomes available there will be a transition period where applicants can opt out of the unitary patent and stick with the existing system of having separate patents in each country.

Why might you want to do this?

The fees associated with the unitary patent have not yet been confirmed, but it is predicted that the unitary patent will be more expensive to maintain than patents in three or four countries. So if you only wanted patent protection in a limited number of European countries, it may be cheaper to opt out of the unitary patent.

The major disadvantage of the unitary patent will be its "all or nothing" effect. It will give patent protection across Europe, but the patent could also be found invalid across the whole of Europe. This will lead to very high stakes litigation at the new Unified Patent Court. Not only will the court decisions have huge ramifications, the court and the law itself will initially be new and untried. No-one will want to have the first case taken to the new court.

Despite these potential drawbacks a recent survey of individuals responsible for their company's European patent portfolio completed by British firm Allen & Overy has shown 74% expect it to be positive for their company.[3] Maybe people just like the idea of having a patent in as many places as possible. It still seems unlikely there will ever be a "Worldwide patent".

If you have any queries regarding intellectual property related matters (including patents, trademarks, copyright or licensing), please contact:

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1. Austria ratified the agreement on 6 August 2013, France ratified on 14 March 2014 and Sweden ratified on 5 June 2014.
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Katherine Hebditch of Baldwins Intellectual Property in Auckland specialises in chemistry and biotechnology patents. Katherine obtained her PhD in organic chemistry from the University of Manchester in the UK in 2004. She is currently working towards registration as a patent attorney.

Conference Calendar

Pacific Rim Symposium on Surfaces, Coatings and Interfaces (PacSurf 2014)

7-11 December 2014, Hapuna Beach Prince Hotel, Kohala Coast, Hawaii

This new conference is being organised by the American Vacuum Society (AVS) with a ssteering committee composed of representatives from Australia, Canada, Chile, China, Japan, Korea, Mexico, New Zealand, Singapore and Taiwan. Symposium attendees will interact during morning and evening sessions that will include plenary, invited and contributed presentations. The main topics for PacSurf 2014 will be focused on the latest advances in biomaterial interfaces, energy harvesting and storage, nanomaterials and thin films. There will be morning and evening technical sessions with the afternoons free for other activities and discussions.

Submit your abstract by 6 August 2014

See: *www2.avs.org/conferences/PACSURF/index.html*

International Conference on Materials Science and Engineering (ICMSE 2015)

23-24 January 2015, Paris, France

ICMSE 2015 aims to bring together leading academic scientists, researchers and research scholars to exchange and share experience and research results about all aspects of materials science and engineering. It also provides the premier interdisciplinary forum for researchers, practitioners and educators to present and discuss the most recent innovations, trends, concerns and practical challenges encountered, and the solutions adopted.

Paper submissions deadline: 23 July 2014

See: *www.waset.org/conference/2015/01/paris/ICMSE*

Advanced materials and nanotechnology (AMN 7)

8-12 February 2015, Nelson, New Zealand

AMN-7 is the seventh in our biennial series of meetings that focus on the latest research on advanced materials and nanotechnology. This event will continue the best traditions of previous events, which include a range of high-impact plenary presentations, cutting-edge invited and contributed talks, interactive poster presentations and convivial social events. The intimate scale of AMN conferences and the broad interests of fellow delegates offer many opportunities for networking and interdisciplinary discussions.

Parallel session presentations will be clustered around the following central themes: Biological Interface, Engineered Nanosystems, Molecular Materials, Nanoscale Structures and Physical Phenomena

In addition, the programme will feature sessions which will focus on the following topics: Organic Electronics, Graphene, Metal-organic Frameworks and Spintronics.

Abstract deadline: 31 July 2014

See: *www.amn-7.com/page.php?7*

Supramolecular Photochemistry: Faraday Discussion

15-17 September 2015, Downing College, Cambridge, UK

Natural and artificial photosynthesis
New information derived from the study of natural systems will be discussed and used to aid design of artificial photosynthetic systems. Attention will be given to both synthetic light-harvesting antennae and molecular devices capable of efficacious charge-separation.

Light-activated molecular machines and logic gates
The study of multi-component systems where illumination induces controlled mechanical movements (machines) and/or where light can be exploited as input/output information. The relevance to protein folding should not be missed.

Self-organization of photo-active nanostructures
Identifying new and improved ways to assemble supramolecular entities with a photo-active unit, such as liquid crystals, organo-gels, dendrimers, etc. Although synthesis plays a crucial role in the development of such species, the discussion will deal with the synergistic features of the actual assembly.

Luminescence sensing and imaging
The in-situ detection of changes in the local topology and in the concentration of selected substrates, including biologically relevant species.

Oral abstracts deadline: 8 December 2014

See: *www.rsc.org/ConferencesAndEvents/RSCConferences/FD/Photochemistry-FD2015/index.asp*

Pacifichem 2015

14-16 December 2015, Honolulu, USA, North America

The theme of Pacifichem 2015 is Chemical Networking: Building Bridges Across the Pacific, emphasisng the collaborative nature of chemistry as a multidisciplinary science and the opportunities to network with Pan-Pacific research groups at the Pacifichem meetings. Topic areas:

i. The core areas of chemistry
   1. Analytical
   2. Inorganic
   3. Macromolecular
   4. Organic
   5. Physical, theoretical and computational

ii. Multidisciplinary or cross-disciplinary areas of chemistry
   6. Agrochemistry, environmental and geochemistry
   7. Biological
   8. Materials and nanoscience

iii. Chemistry solutions to global challenges
   9. Chemistry of clean energy conversion, storage and production
   10. Bench to bedside: chemistry of health care
   11. Connecting chemistry to society

See: *www.pacifichem.org*

Grants and awards

Prime Minister's Science prizes

Entries are open for the 2014 Prime Minister's Science Prizes. The five awards have a combined value of $1 million.

This scheme has been running for five years and the categories are:

a. Science Prize — $500,000

To an individual or team which has made a transformative discovery or achievement in science that has had a significant impact on New Zealand or internationally

b. MacDiarmid Emerging Scientist Prize, $200,000

To an outstanding emerging scientist undertaking research for a PhD or within five years of the date of the award of a PhD

c. Science Teacher Prize — $150,000

To a science teacher for outstanding achievement in teaching science

d. Science Media Communication Prize — $100,000

To a practising scientist who is an effective communicator, to provide them with an opportunity to further develop their knowledge and capability in science media communication

Deadline for these four awards: 5pm Monday 4 August 2014. The Future Scientist Prize will be awarded to the Supreme Award recipient from the Royal Society of New Zealand's 'Realise the Dream' competition.

See: *www.pmscienceprizes.org.nz/about*

Bayer Primary School Science Fund

The Bayer Primary School Science Fund is sponsored by Bayer and administered by the Royal Society of New Zealand. This fund is to give primary schools the opportunity to apply for funding to support and enhance an existing, or to kick-start a new, environmental science education and 'Nature of Science' teaching and learning programme. (A one page outline of this programme must be submitted with the application form).

A primary school can request a maximum sum of up to $2,000 (GST exclusive) to help fund activities.

Applications close: 12 September 2014

See: *www.royalsociety.org.nz/programmes/funds/bayer-primary-school-science-fund/*

The MacDiarmid Institute for Advanced Materials and Nanotechnology: Discovery Awards 2015

The Discovery Awards is a programme designed for year 12 or 13 Māori and Pasifika secondary pupils, who have demonstrated their interest in science. It gives them the opportunity to work with one of six partners of the MacDiarmid institute in research laboratories with scientists and their post graduate students who will act as day-to-day mentors.

The aim of the programme is to spark the pupils' interest in science, expose them to possible career options and encourage them to enrol in a science degree programme at tertiary level. While academic achievement is an important selection criteria so too are their goals, personal and financial circumstances.

The award of $1000 each is open to Year 12 and Year 13 Māori & Pasifika students successful applicants will get two week lab experience (on 5-16 January 2015) at either: University of Auckland, Victoria University of Wellington, GNS Science or the University of Canterbury Applications close: Friday 12 September 2014

See: *http://macdiarmid.ac.nz/newsroom/events/hub/2014/discovery-awards*

Dumont d'Urville New Zealand-France Science and Technology Support Programme

Funding for New Zealand researchers to travel to France and for researchers in France to travel to New Zealand to work on collaborative projects

The aim of the programme is to promote and support scientific and technological cooperation between New Zealand and French researchers in the public, non-government and private sectors in the following fields: Food, agriculture and fisheries, and biotechnology; Renewable energy and energy efficiency; Biodiversity; and Nanosciences.

Costs of up to $6,000 (GST exclusive) per researcher trip may be sought for the proposed collaborative project.

Applications close: 18 September 2014

See: *www.royalsociety.org.nz/programmes/funds/international-relationships/durville/*