NZIC Chemistry
IN NEW ZEALAND

75
2011

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Apology

The editor and staff of Chemistry in New Zealand apologise for the delay in the production and distribution of the October 2010 issue. Not surprisingly, the September Christchurch earthquake and its significant aftershocks impacted on the printer but damage was slight.

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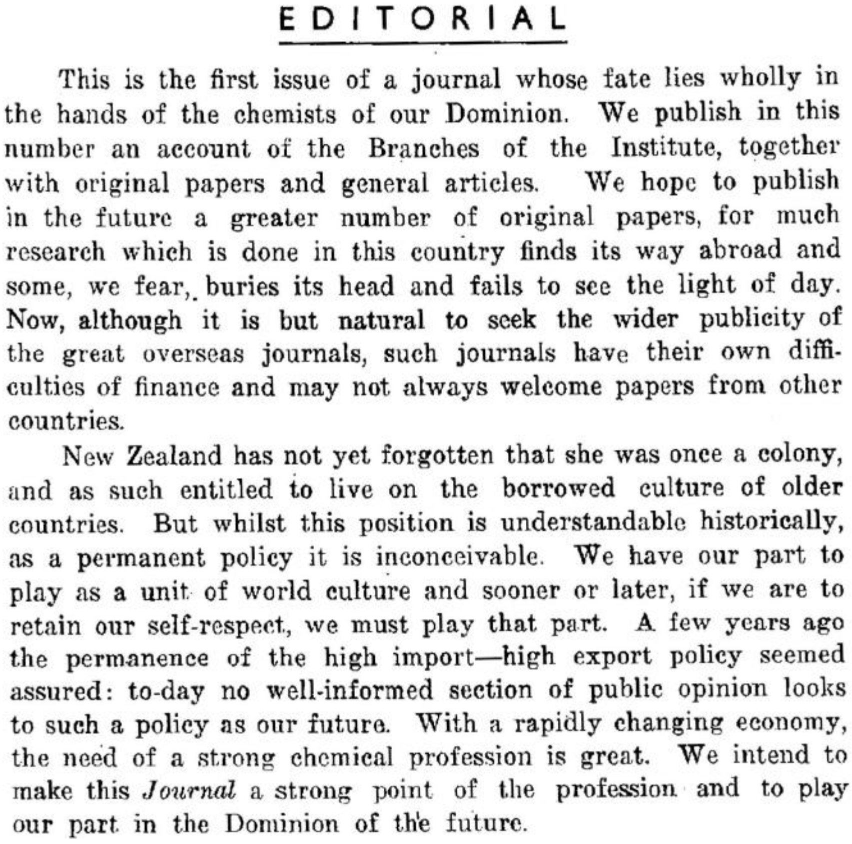

EDITORIAL

This is the first issue of a journal whose fate lies wholly in the hands of the chemists of our Dominion. We publish in this number an account of the Branches of the Institute, together with original papers and general articles. We hope to publish in the future a greater number of original papers, for much research which is done in this country finds its way abroad and some, we fear, buries its head and fails to see the light of day. Now, although it is but natural to seek the wider publicity of the great overseas journals, such journals have their own difficulties of finance and may not always welcome papers from other countries.

New Zealand has not yet forgotten that she was once a colony, and as such entitled to live on the borrowed culture of older countries. But whilst this position is understandable historically, as a permanent policy it is inconceivable. We have our part to play as a unit of world culture and sooner or later, if we are to retain our self-respect, we must play that part. A few years ago the permanence of the high import—high export policy seemed assured: to-day no well-informed section of public opinion looks to such a policy as our future. With a rapidly changing economy, the need of a strong chemical profession is great. We intend to make this *Journal* a strong point of the profession and to play our part in the Dominion of the future.

In was in this way and with these words that *Chemistry in New Zealand* was born in 1936, 75 years ago. As a print medium it continues to publicise the activity of our Branches but it no longer strives for original research reports, as NZ chemists are no less competent or capable than their overseas peers with work that gains international recognition from publication in acclaimed peer-reviewed periodicals. It is possible that these pages play a small part in NZ's contribution to world culture, but it is the Institute itself that does this through its professionalism and its involvement in, for example, Pacifichem and IUPAC. In these international activities the NZIC contribution far exceeds its relative size simply because of the dedication of its members.

As many of you may know, this year will my last as editor of this Journal, a role that I have relished and immersed in, and dealt with a fascinating array of academics, industrialists and students. That the year is the 75th of publication as well as the International Year of Chemistry has demanded that I serve you, the members, to my utmost. In this regard, I have been accommodated by some of this country's most outstanding chemists, some overseas and others in New Zealand with offers to contribute. Not only this, but our great scientists of the day have agreed to adorn our pages during this year. Of course, icing on this 75th anniversary cake is needed and what better way to get this than from Nobel Laureates that have (or have had) involvement with New Zealand chemistry, beginning with the contribution by Sir Harry Kroto in this issue.

The era of print copy publication is rapidly changing and, whilst our forebears may have envisaged a journal set for a centenary, this is looking less and less likely – just think of the electronic changes that have impacted upon us over the last 25 years. It is my sincere hope that *Chemistry in New Zealand* will continue to be distributed in hard copy for a good number of years to come, that it continues through its centenary even if it is an electronic medium, and that the membership of the NZIC continues to be served by editors more capable than I. And it needs an editor to continue the work into 2012, so if you have an interest contact Richard Rendle at the NZIC Office: *rendle@xtra.co.nz*

Brian Halton
Editor

Comment from the President

The arrival of 2011 means that we are now in the International Year of Chemistry, with the official launch to occur at the UNESCO headquarters in Paris on January 27-28, and our own opening event to occur at the Michael Fowler Centre in Wellington on February 9. Many of the details of the NZIC participation in this event have been outlined in the two previous issues of this Journal, along with further information in this issue, so I will not repeat them here. However, I would like to take this opportunity to thank my predecessor Mark Waterland for all of the excellent work he has done in planning for this event.

I would also like to take this opportunity to congratulate our NZIC prize winners for 2010. These were Prof Keith Gordon (Otago University) (**Maurice Wilkins Centre Prize for Chemical Science**), A/Prof David Harding (Massey University, Palmerston North) (**Fonterra Prize for Industrial and Applied Chemistry**), and Dr Jan Giffney (St Cuthbert's College, Auckland) (**ABA Books Denis Hogan Prize for Chemical Education**). Although their names were published in the October issue of this Journal, there was insufficient time to include proper congratulations to the winners, as that issue went to press prior to the official announcement of their success. As this current issue went to press, Keith Gordon was due to be presented with the Maurice Wilkins prize at the Royal Society Honours Dinner in Christchurch on November 10.

This year there will be four NZIC awards, as the joint NZIC–RSC Easterfield Medal, our premier prize for younger chemists that is awarded every second year, will also be included. I would like to encourage all of our members to either consider applying for one of these awards, or nominate a worthy recipient. I would especially like to encourage non-University members to apply. It is perhaps a sad reflection of the way research funding has gone in this country that all winners of the Easterfield Medal since 1990 have been staff members of University Chemistry Departments, yet prior to that date the majority of winners were actually full-time researchers from non-University Chemistry Departments.

While we are on the subject of prizes, I would like to say how pleased I was to see the 2010 Nobel Prize in Chemistry being awarded for an area of chemistry that has great practical application.The award has gone to Richard Heck, Eiichi Negishi and Akira Suzuki for *Palladium-catalyzed cross couplings in organic synthesis* (see the article elsewhere in this issue). I, personally, have used both Heck and Suzuki reactions in my research work, and Suzuki reactions now represent one of the most commonly performed synthetic procedures undertaken by my chemical colleagues in the Auckland Cancer Society Research Centre.

Finally, I look forward to touring all the NZIC Branches this year, and delivering my Presidential Address, which in addition to IYC2011 details, will discuss my recent work on the development of the phosphatidylinositol 3-kinase (PI3K) inhibitor PWT33597 that is targeted to enter human cancer clinical trials with Pathway Therapeutics (*www.pathwaytx.com*) later this year. Parts of the PWT33597 development story are still commercially sensitive, but I will present as much information as I am able. I had a practice run of the talk (minus the synthetic chemistry details) at the Queenstown Molecular Biology Drug Discovery Satellite Meeting in September last, so once the chemistry details are added, I will be ready to go.

Gordon Rewcastle
President

About the President

Gordon Rewcastle obtained his PhD in Organic Chemistry from the University of Auckland in 1978, and after postdoctoral work in the US, joined the Auckland Cancer Society Research Centre (ACSRC) as a medicinal chemist in 1980. Since then he has participated in a number of antibacterial and anticancer drug development projects, and is the author or co-author of over 100 scientific papers and patents in the anticancer area. In all, he has made significant contributions to the development of six of the eight anticancer drugs to have gone to clinical trial from the Auckland Cancer Centre. His initial work concentrated on DNA intercalating anti-cancer agents, and for his contributions to this area he was awarded the NZIC/RSC Easterfield Medal in 1989. The 1990s saw a change in direction to the design and synthesis of tyrosine kinase inhibitors as the main area. This work was performed in close collaboration with the Parke-Davis Division of the Warner-Lambert Co., and culminated in the development of the Epidermal Growth Factor Receptor (EGFR) irreversible inhibitor canertinib (CI-1033) that entered Phase I clinical trial with Pfizer in 1999. Gordon made several important contributions to the design of this drug, including performing its first chemical synthesis in 1997. In 1998 the ACSRC became part of the University of Auckland, and Gordon was promoted to Associate Professor the following year. From 1999 to 2004 he was the Group Leader of a number of Pfizer-funded projects in both the anticancer and antibacterial drug development areas, and in 2005 he became an Associate Investigator with the Maurice Wilkins Centre for Molecular Biodiscovery, where he has been involved in an investigation of isoform-selective phosphoinositide 3-kinase (PI3K) inhibitors as potential anticancer agents. This work recently culminated in the successful development of the PI3K inhibitor PWT33597, which is now in preclinical development with Pathway Therapeutics in the US.

New Zealand Institute of Chemistry

supporting chemical sciences

January News

The Annual General Meeting of NZIC was held in Wellington on November 17, 2010. The newly elected Institute Executive officers are:

President: *Gordon* ***Rewcastle*** (Auckland)

1st Vice-President: *Julian* ***Eaton-Rye*** (Otago)

2nd Vice-President: *Michael* ***Edmonds*** (Canterbury)

Treasurer: *Colin* ***Freeman***

Hon. Gen. Sec: *Richard* ***Rendle***

The President, Mark Waterland presented Fellowship certificates to *Richard* ***Tilley*** and *Peter* ***Tyler***

FNZIC awarded to Richard Tilley (top) and Peter Tyler (bottom)

Peter ***Derrick*** (IFS, Massey) was elected to the Fellowship of the Royal Society of New Zealand on October 6, 2010. He is Professor of Chemical Physics and Physical Chemistry, and Head of the Institute of Fundamental Studies. He was awarded the 2007 Thermo Fisher Scientific Award of the RSC for his research on both fundamental and applied aspects of mass spectrometry, including applications to biochemistry and medicine and, more recently, the 2009 Morrison Medal of the Australian and New Zealand Society for Mass Spectrometry in recognition of significant achievements in an area of mass spectrometry.

The RSNZ Thomson Medal and $15,000 was awarded to Mr *Shaun* ***Coffey*** CRSNZ, chief executive of Industrial Research Limited, for his outstanding leadership in the management of science, and development and application of science and technology to generate wealth for New Zealand.

Prof *Terence* ***Collins****,* a Canterbury Chemistry Alumnus, received the 2010 annual Heinz Award from Heinz Family Foundation for his extraordinary contributions to his field. Each honoree receives $US100,000 for unrestricted use. Terry, an Hon. FRSNZ has worked to reduce the impact of toxic chemicals on the environment.

2011 Subscriptions

Subscription rates have been held at current rates for a number of years. However, with increasing costs and the rise in GST, Council decided (with some reluctance) that it was necessary to raise subscriptions. The new rates with the maximum prompt payment discount in parenthesis are:

FNZIC
$145 ($130)

Member
$125 ($110)

Overseas Member:
$100 ($75)

Retired/Hon Member receiving Journal: $65 ($50)

Student 3 year membership: ($110)

Student 1 year membership: $45 ($40)

NZIC MEMBERSHIP MATTERS

MNZIC

Drs *Rachel* ***Dixon***, *Tim* ***Kemmit***, *David* ***Ackerley***, and Ms *Janelle* ***Sauvageau*** (Wellington)

Miss *Joanne* ***Readman*** (Canterbury)

STUDENT MEMBERS

Mr *Davide* ***Mercadante*** and *Nor Fazliyana* ***Mohtar*** (Auckland)

BRANCH NEWS

AUCKLAND

In recent months NZIC branch seminars in Auckland were given by Prof *Cameron* ***Kepert*** (University of Sydney – September), on *Achieving Advanced Function in Metal-Organic Frameworks*. Also that month A/Prof *Yacine* ***Hemar*** (Auckland Food Science Programme) introduced the topic of *Diffusing-wave spectroscopy: from particle sizing to micro-rheology*, and illustrated how the technique can be applied to particle sizing in micro-rheology of biopolymer solutions and the study of sheared pathological fluids.

University of Auckland

A recent highlight within the Department was the September inaugural lecture of Prof *Penny* ***Brothers*** (Professor of Inorganic Chemistry) on the topic of *Boron and blood: what's the connection?* Penny described how highly coloured porphyrins have been a keen interest of her research career, including the creation of a porphyrin with boron as a non-metal core, even two at a time, leading to novel chemical outcomes. Further research work has included cobalt complexes, corroles and dipyrrins, with applications extending from medicine to materials science; all of which illustrate very aptly how scientists can learn from nature's solutions to chemical problems.

In the last Marsden round, Dr *Jonathan* ***Sperry*** was awarded a Fast-Start grant to investigate the synthesis of natural bis-indoles with potential for use as sunscreens and as the basis for novel anti-cancer agents. Within the University, A/Prof *Yacine* ***Hemar***, and Prof *Conrad* ***Perera*** were successful in gaining a Cross-Faculty Research Initiatives grant to work with A/Prof *Geoff* ***Krissansen*** and Dr *Kevin* ***Sum*** from Medical and Health Sciences. Dr *Viji* ***Sarojini*** was also appointed to a lectureship in the Department.

The general staff in Chemistry have received well-deserved recognition by the University, with Quality Performance Awards in Customer Service to *Janice* ***Choi*** and *Min Young* ***Lee***, and Professional Development Awards to *Raisa* ***Imatdieva*** and *Doreen* ***Ly***.

Departmental publicity has included a lead article in the October 2010 issue of *Auckland Now* featuring Prof *Margaret* ***Brimbl*e** and the University's contribution to Auckland and the international community. Radio broadcasts on a wine chemistry theme have included A/Prof *Paul* ***Kilmartin*** and Dr *Mandy* ***Herbst-Johnstone*** on Australia's ABC network discussing cold storage of Sauvignon Blanc, and wine tutor *Gerard* ***Logan*** on Auckland's bFM talking about his PhD research on the peppery aroma compound *rotundone* in Shiraz wines. Gerard and *Jan* ***Robertson*** also led the highly successful inaugural Upper North Island Wine Challenge awards in early October at the University's Old Government House, hosted by mountaineer and winemaker *Mark* ***Inglis***, with NZ Master of Wine *Bob* ***Campbell*** as Chair of the judging panel.

The Department's food and culinary skills were also to the fore with the food product prototype competition within the Food Science programme. The innovative prizes went to a sausage with a saucy centre, appropriately named as *Saucies*, and chocolate coated Azuki beans took the functional food award. Students and staff also contributed to a highly successful *International Evening* in October, with a global coverage of dishes that showed tremendous variety and flavour.

Recent student achievements include highly placed results in the 2010 Faculty postgraduate poster competition. The winners from Chemistry were *Cosmin* ***Laslau*** (2nd place), *Karthik* ***Kannappan*** (high distinction), and *Raoul* ***Peltier***, *Jennifer* ***Haeger***, *Elizabeth* ***Williams*** and *Danae* ***Larsen*** (merit awards). Cosmin and *Vedran* ***Jovic*** were also Faculty representatives in the University-wide *Exposure* postgraduate research competition, with Cosmin moving into the group of six finalists who gave oral presentations at an evening event and, against high quality competition, he was second; his PhD is being supervised by A/Prof. *Jadranka* ***Travas-Sejdic*** (Polymer Electronic Research Centre). The quality of Cosmin's MSc research has also been recognised through an *International NRW Young Scientist* award for a research paper entitled *Morphological evolution of self-assembled polyaniline nanostructures obtained by pH-stat chemical oxidation* published in *Chemistry of Materials* in 2009. He travelled to receive the € 1,500 prize at a reception in Düsseldorf (Germany) in November.

L-R: Jadranka Travas-Sejdic, Comin Laslau and Jim Metson at the *Exposure* research competition.

Department seminars have included Dr *Leif* ***Lundin*** (CSIRO Food & Nutritional Sciences) on *Food structure-function work in CSIRO; Mike* ***Cooling*** (Auckland Bioengineering Institute) *Making sense of disease with virtual cell chemistry*, and *Peter* ***Nicholas*** (Technical Manager, Tip Top Ice Cream) on *The inside story of NZ's favorite summer treat*. In November, Prof *Vicente* ***Ferreira*** (University of Zaragoza, Spain) spoke on *Chemical systems behind wine aroma perception: overview, genesis and evolution*. He is being hosted in the Chemistry by Dr *Laura* ***Nicolau*** as a Distinguished Visitor, and his visits in 2010 enabled the latest in *aroma reconstitution studies* to be applied to NZ wines. Recently, Prof *Peter* ***Geissinger*** (University of Wisconsin-Milwaukee), a visiting Erskine Fellow at Canterbury University, presented the *Development of methods for measurement of electric fields at protein actives sites and elucidation of their contribution to protein function*.

CANTERBURY

The annual NZIC Trivia and Truffles quiz night was held in mid-October last at the Christchurch Polytechnic Institute of Technology (CPIT). Nineteen teams of three participated in a lively evening of chemistry-oriented questions.

University of Canterbury

The Chemistry Department has acquired a Bruker maXis 3G (Ultra High Resolution Time of Flight) Tandem Mass Spectrometer, a Dionex U3000 HPLC system and a Nitrogen Generator. *Matthais* ***Pelzing*** (Bruker application specialist) gave an informal seminar on September 7th on the full range of capabilities of the new instrument.

On the 5th of August the Department hosted a delegation from the Indonesian Ministry of Education, in NZ to visit Indonesian students studying on their Government Scholarships. The delegation was shown around by *Ian* ***Shaw*** who, conveniently, speaks Indonesian.

Bruce ***Reid*** had worked in the Department for almost 45 years (since February 1966) as a member of the technical staff when he retired on August 10. *Kat* ***Dewey*** left NZ on September 4 to take up a paid intern position at

Foothill Horizons Outdoor Education Center in Sonora, California. Kat enjoyed her time at Canterbury studying and collaborating with the Environmental Chemistry group.

Six Chemistry students, *Yasushi* ***Ishido****, Hiroshi* ***Iwawaki****, Shizu* ***Kibayashi****, Atsuki* ***Matsubara Aki****, Takashi* ***Tamaki*** and *Yuichi* **Yoshimurua** from Osaka University arrived in the last week of September to work in the Department in conjunction with Bridging Programmes. Their stay will see them focusing their English language skills and also working with *Jan* ***Wikaira*** and her students. They presented their work over the previous four weeks in late October. Prof *Cameron J.* ***Kepert****,* (University of Sydney) gave his seminar *Achieving Advanced Function I Metal- Organic Frameworks* detailing the emergence of useful host-guest electronic, magnetic and mechanical phenomena in the design and synthesis of molecular materials and the production of completely new materials phenomena through combination of multiple properties in October as part of his NZ lecture tour.

Other October seminars included: Dr *Anna* ***McConnell*** (Oxford University) who gave a seminar on *Heteroditopic Calix[4]arena Based Receptors for Ion-Pair Recognition and the synthesis of Rotaxames.* She discussed the synthesis and unique ion-pair recognition properties of cyclic calix[4]arena based receptors that can incorporate anion and cation binding sites and the potential applications of these receptors as salt solubilization, membrane transport and extraction agents. Dr *Matthew* ***Addicoat****,* (ANU) presented *Computational Cluster Chemistry and Conformer Chasing*, with two examples of computational investigation into transition metal cluster species showing two different computational methods for searching through all possible conformers of a given species. Dr *Alexander A.* ***Oliferenko*** (Queens University, Belfast) gave a seminar on November 1 entitled *Applications and Molecular Design of Ionic Liquids* that consist of organic cations and anions and have extremely low melting points at or below room temperature. They exhibit unique salvation properties that can be tuned for many stoichiometric and catalytic processes.

Congratulations to *Emily* ***Parker*** for winning a National Tertiary Excellence Award, presented in Wellington in early August last. *Phil* ***Emnet*** was the recipient of the Keith Laugesen PhD Scholarship, which is awarded once every three years to a PhD candidate in science or engineering. *Andrew* ***Gross*** attended the October 2010 Asia Nanotech Camp (Singapore and Malaysia) as a nominee of the MacDiarmid Institute. *Alan* ***Downard*** won the RACI Don Stranks Award for outstanding PhD research at the 39th International Conference of Co-ordination Chemistry. *Clement* ***Roux*** came back from the joint ARNAM/ARCNN 2010 Workshop (advanced materials and nano technology) having won a net book for his talk. *Ian* ***Shaw*** was one of the top three science lecturer nominees for the 2010 UCSA Lecturer of the Year. *Peter* ***Steel*** has been successful in his Marsden application ($885,000 over three years) for his project *New Metallosupramolecular Synthons*.

CPIT

The CPIT science laboratories sustained little damage during the September 4th earthquake and subsequent aftershocks, thanks to a very well designed building and the diligence of the technical staff in their careful storage of equipment.

The Year-11 Chemistry Competition was held on Thursday September 23. Despite initial fears that there might be poor interest due to the earthquake and aftershocks, over twenty teams of three participated from thirteen different schools around the Canterbury region attended. The results were as follows:

1st Hillmorton High School

2nd Rangi Ruru Girls School

3rd Unlimited Paenga Tawhiti.

This event was partially sponsored by the Canterbury Branch of the NZIC.

ESR

Dr *Barbara* ***Thomson*** gave a seminar in October entitled *Chemical contaminants in food: a snapshot of selected events and associated costs* as preparation for presenting at the ACC International Annual meeting in Savannah, USA. Chemical contaminants in food may include pesticides and veterinary drug residues, fungal toxins (mycotoxins), food additives and environmental contaminants such as dioxins, polychlorinated biphenyls (PCB), polycyclic aromatic hydrocarbons (PAHs) and heavy metals. A snapshot of selected events of chemical contamination of food, ranging from mercury in fish in Japan in the 1950s to melamine in Chinese milk powder in 2008, with consideration of the outcomes and associated costs was given.

MANAWATU

Congratulations from the Branch to the following members for their achievements: Prof *Peter* ***Derrick*** who was elected FRSNZ (see above), A/Prof *Dave* ***Harding*** who was awarded the Fonterra Prize for Industrial and Applied Chemistry (as announced in the October issue) and Prof. *Simon* ***Hall*** who has been awarded the 2010 Bayer Innovators Award for Research and Development and has also been elected Fellow of the Royal Society of Chemistry.

In late August, postdoctoral *Sivakumar* ***Balakrishnan*** won first prize in a Nano-Art competition for the best images from nanotechnology research. The judges were impressed by the complexity of the textures in the *Intergrown crystals of a metal-organic framework* image, and commented that it is reminiscent of cubist paintings by Picasso.

The Manawatu and Wellington NZIC Branches were privy to a very interesting inside view of New Zealand Pharmaceuticals in early September last year. The on site tour included the small and (very) large scale facilities currently employed for the manufacture of various products, like pharmaceutical intermediates, carbohydrates and dietary supplements (see also under Wellington).

IFS-Chemistry

Shane ***Telfer*** has been successful in gaining Marsden funding as a PI for his project *Creating nothing out of something – a route to ultraporous metal/organic frameworks*. Dr *Gareth* **Rowlands** has become a Fellow of the New Zealand Institute of Chemistry. A/Prof *Eric* ***Ainscough***, Dr *Paul* ***Plieger***, Dr *Gareth* ***Rowlands***, Dr *Shane* ***Telfer*** and Dr *Mark* ***Waterland*** are congratulated on their success in this year's MURF funding round.

Prof *Richard* ***Haverkamp*** of Massey University returned to NZ last September after spending 3½ months of sabbatical over the northern summer at NTNU (Trondheim, Norway) working on the electronic structure of iridium oxide-based electrocatalysts. *Karl* ***Shaffer*** has submitted his PhD thesis and is eagerly awaiting his oral examination, likely ahead of this appearing in print.

September 2010 saw NZIC President Dr Mark Waterland (Massey University) gave a talk titled *Ramen vs Infrared – The Battle for Vibrational Supremacy*. On September 2 Dr *Osamu* ***Ishitani*** (Tokyo Institute of Technology) spoke on *Architecture of highly efficient photocatalysts for* CO_2 *reduction,* and Prof *Penelope* ***Brothers*** (Auckland University), on *Diboron porphyrins and corroles: unexpected chemistry for both boron and the ligands*. Prof. *Peter* ***Derrick*** acknowledged his award by delivering a lecture *Chemistry: the land of beautiful shapes* at the end of September and then in October Dr *Rob* ***Keyzers*** (Victoria University) gave a talk titled *From vine to wine: the chemistry of grapes and wine*.

OTAGO

The 2010 Branch Interschool Chemistry Quiz was held in late September. Forty-three teams of Year 12 and 13 students, representing twelve schools from around Otago and Southland, competed for the *Bunsen Burner of Wisdom* at the Hutton Theatre in the Otago Museum (numbers were down a bit due to the snow!) The quiz consisted of five rounds of questions, as well as a round of Chemical Bingo, a new addition this year. The annual Chemical Haiku round was also a highlight of the evening. When the dust, and pizza crusts, settled the only team from Kavanagh College, called *Kavanagh*, were declared the winners, with *Free Food*, from Otago Boys High School coming second and *WT Fluorine*, from James Hargest College coming third. As always, our thanks to Poppas Pizzas, the University Book Shop Dunedin, The Otago Museum, the Otago Branch of the NZIC and Otago University for their continuing support of this event, as well as to the students and staff of the Chemistry Department for their work on the evening. And, of course, our thanks to the students and staff who make this such a great event.

The winning Chemical Haiku was:

Your scent of esters
catalyzes our bonding,
lighting my bunsen
Potions Masters

Wanted. Strong acids
kindly donate your protons
to bases in need.
Catalystcaptors

Romeo 'ductant
to Juliet oxidant
says: Lets react now!!
Leo the lion goes Ger

2010 Otago and Southland Interschool Chemistry Quiz winners with the *Bunsen Burner of Wisdom*

The Branch also sponsored a trip to the Ravensdown Fertilizer Plant in September. The tour leader, a previous Otago Chemistry Honours student, gave an excellent presentation about the chemical processes taking place and led a very informative tour. The Branch also held its Annual General Meeting in November following a seminar by the NZIC president, *Mark* ***Waterland***.

University Chemistry Department

The Department co-sponsored the *Ocean Acidification in the South Pacific Workshop* in September. This was the fourth annual workshop with this title and was attended by over 40 scientists and policymakers from NZ and Australia. Visitors to the Department were especially impressed by its measurement capabilities and links with NIWA and the Portobello Marine Laboratory. The Department's ocean acidification research was also highlighted on Radio New Zealand's *Our Changing World* programme, accessible via:

http://www.radionz.co.nz/national/programmes/ourchangingworld/20100902

The polymer and supramolecular gel group (*Lyall* ***Hanton*** and *Stephen* ***Moratti***) was sorry to say farewell to Remi Boissezon who left us after a productive final year project to return to France. *John* ***McAdam*** recently returned from presenting a poster at the 66th International Society of Electrochemistry in Nice, France and three of the group presented at Pacifichem 2010 in December. The new labs are almost complete and will soon be fully operational. Welcome to *Asif* ***Noor*** from Pakistan who is starting a PhD on catenated polymers jointly with *James* ***Crowley***.

Victoria ***Milway*** will depart Brooker's Bunch at Christmas, returning to the UK. *Jamie* ***Lewis*** has completed his Honours year and will start a PhD at University College Dublin with *Martin* ***Albrecht*** early next year. Both *Juan* ***Olguin*** and *Worku* ***Gobeze*** are busy writing their PhD theses and should have submitted by this printing. Worku and his wife Woinshet are proud parents of their first child, Joshua. *Rodolphe* ***Clerac*** and *Corine* ***Mathonière*** visited us in November, thanks to reciprocal Dumont d'Urville funding. They will give Department seminars and tutorials on magnetism and photomagnetism

WAIKATO

University of Waikato

The annual ChemQuest Competition, was held by the Department of Chemistry in October last. A total of 60 teams from the greater Waikato region and Bay of Plenty participated. As usual, this was a fun-filled evening for students studying NCEA level 2 chemistry. The ChemQuest, competition tests the students' knowledge of chemistry in a variety of ways. Alongside traditional general knowledge questions, there are also demonstrations to watch, smells to sniff and identify, and music to listen to - all with a chemistry theme. Spectacles such as balloons exploding in fire and chemical reactions that luminesce kept the students enthralled as they competed for medals and prize money.

Prizes were awarded as per:

1st Place: St Pauls Collegiate ***TEAM*** (Evan Wilson, Andrew McPherson, Chang Zhai,)

2nd Place: St Pauls Collegiate ***CORROSIVE CARNAGE*** (Lucien Nabbs, Mikey Hodge, James Kennedy)

3rd Place: Hamilton Boys High School ***THE PROS*** (Bill Xu, Axton Pitt, Harry Yoon)

4th Place: Waikato Diocesan School ***THE SORCERER'S APPRENTICES*** (Ellen Jung, Julia Ratcliffe, Sarah Wheeler)

5th Place: Hillcrest High School ***MIXED UP*** (Daphene Saw, Winnie Ou, Lisa Liu)

Prizes were generously sponsored by James & Wells Intellectual Property and Hill Laboratories, as well as the Faculty of Science and Engineering, Waikato University. Question masters were *Bill* ***Henderson*** and *Michèle* ***Prinsep***, with *Brian* ***Nicholson*** the chief judge, assisted by numerous other staff and students from the Department.

The winning team, ***TEAM*** (Evan Wilson, Andrew McPherson, Chang Zhai,) St. Paul's Collegiate, Hamilton with (far right) David Macaskill (James & Wells)

Michael ***Mucalo*** attended the 23rd European conference on Biomaterials in Tampere (Finland) in mid-September where he gave an oral presentation on his patented bone replacement material consisting of sintered cancellous bovine bone reinforced by chitosan, known officially as GRAFTOSS. The well run conference gave him ideas for contributing to the organising of the 21st Australasian Society of Biomaterials and Tissue Engineering set for April 27-29, 2011 in Queenstown; he is a member of the organising committee.

Alex ***Burgun***, who is doing a joint PhD with the Universities of Renne and Adelaide, spent a 10-day visit using the MicrOTOF mass spectrometer. PhD student *Toshie* ***Asamizu*** visited Prof *Eva* ***Hey-Hawkins*** in Leipzig during 2010 as part of the joint Marsden grant between the latter and *Bill* ***Henderson***.

Recent Departmental visiting speakers included the RSC Lecture *Achieving Advanced Function in Metal-Organic Frameworks* from Prof *Cameron* **Kepert** (Sydney), *Geothermal Energy in NZ: Silica Management* from *Joe* **Gamman** (Mighty River Power) and *Assembling Mixed-Valence Complexes: a Strategy toward Molecular Quantum Cellular Automata Cells*, from *Alexandre* **Burgun**, (Universities of Adelaide and the Université de Rennes).

NIWA

Bob ***Wilcock*** attended the International Water Association conference on diffuse pollution (DIPCON 2010 – Quebec) during September and gave a talk on geochemical processes affecting *N*, *P* and *E. coli* bacteria in a natural wetland within a dairy farming catchment. He also co-authored a presentation describing diffuse pollution in NZ and visited Prof *Steve* ***Chapra*** at Tufts University (Boston).

WELLINGTON

At the same time as the Council meeting in Christchurch 3 September, the Wellington and Manawatu Branches held a joint meeting that began with a site tour of New Zealand Pharmaceuticals in Linton at 3.30 pm hosted by *Selwyn* ***Yorke*** and *Ghislaine* ***Cousins***. The sixteen visitors, appropriately kitted out in safety clothing, thoroughly enjoyed what they saw and heard. Not surprisingly, the daytime nature of the tour limited the number of Wellingtonians able to travel, but the three Wellington members who registered late missed out as NZP's efficiency had the safety clothing on order. Following the tour the group went into Palmerston North for dinner and a good time was had by all. It was the first joint meeting for a considerable time and the Branches hope to repeat the concept on a semi-regular basis. September 8 Wellington had almost reverted to normal as Prof *Cameron* ***Kepert*** delivered a fascinating description of his work *Achieving Advanced Function in Metal-Organic Frameworks* as the 2009 RSC Australasian Lecture in which he summarized advances in the design and synthesis of molecular materials that encompassed much decidedly new methodologies. The emergence of a range of interesting and potentially useful host-guest, electronic, magnetic and mechanical phenomena were discussed and the considerable versatility of molecular chemistry that offers many opportunities in these areas outlined including:

- *Nanoporosity*. The linkage of molecules with strong binding interactions has generated robust open lattices that are able to act as hosts for molecular guests.
- *Electronic Switching*. The incorporation of spin-crossover centres into nanoporous molecular frameworks has led to the first porous materials that may be switched between multiple electronic states.
- *Negative Thermal Expansion* (NTE, *i.e.*, contraction with heating). These materials are structurally distinct from all existing NTE systems, opening an important new window into this exotic phenomenon.

The October meeting had *David* ***Weller***, a PhD student of NIWA and Otago University tell us about *The Oceanic Methane Paradox; a multidisciplinary approach*. His discussion reminded us that CH_4 is twenty times as potent a greenhouse gas as CO_2 and may affect climatology by creating strong positive feedback processes from the ocean and then accounted for why there is an excess of it in the surface ocean. Methane is produced mostly anerobically and, thus, supersaturation in the surface ocean is counter-intuitive. It is usually attributed to micro-anaerobic zones in sinking particles, but this does not explain observed variations. The phycosphere, the layer surrounding a phytoplankton cell, is an alternative site that has been overlooked despite some evidence of methane production. David showed that the recent research involving chemical, microbiological and molecular techniques found methane production to be associated with particles in sediment traps, in cultures of methanogenic bacteria growing on CO_2, and in incubations of filtered seawater. The increasing incidence of eutrophication and toxic algal blooms, both globally and around NZ, and the predicted warming and stratification of the surface ocean, may lead to increased methane production via bacterial processes in the phycosphere.

The November meeting was timed to host the NZIC AGM in Wellington on the 17th (Officers for 2011 are listed under "News"). After the meeting Dr *Rob* ***Keyzers*** (Victoria, SPCS) spoke on *From Vine to Wine: The Chemistry of Grapes & Wine* in which he described wine as an extremely complex, biotechnologically derived consumer product with huge market appeal. Its production is mainly by the interaction of yeast upon grape-derived nutrients during fermentation, although modifications to the taste, flavour and aroma can be made by suitable ageing in oak barrels or through application of other biochemical sources, *e.g.* secondary fermentation by other microbes; the source of wine flavour and aroma is therefore from multiple biogenic origins. He began with an introduction to grape and wine chemistry and concluded with recent examples of experiments to explore the origins, be it grape or yeast, of a variety of important wine volatiles. The lecture was followed by a festive season tasting.

Victoria University

Promotions in Chemistry in October 2010 were significant with *Joanne* ***Harvey*** and *Mattie* ***Timmer*** joining the ranks of Senior Lecturer, and *Richard* ***Tilley***, NZIC's 2009 Easterfield Medallist, becoming an Associate Professor.

Peter G. K. ***Clark***, an MSc (Hons.) student in chemistry has been awarded one of the 2011 ***Woolf Fisher Scholarships*** in NZ for PhD study at Oxford University. Awarded to up to three outstanding NZ graduate students each year, the Woolf Fisher Scholarship recognises outstanding academic ability and the other qualities which Sir Woolf Fisher most admired, namely integrity, kindness and generosity, leadership, boldness of vision and exceptional zeal, keenness and capacity for work. Peter intends visiting Chemistry Departments before leaving for the UK in October so as to be appropriately informed on this country's chemical research effort. Given that Peter is *Rob* ***Keyzers***' first graduate student and is heading to Oxford, it bodes well for the future of the new VUW research group. PhD students Almas Zayya (Spencer) and Amane Shiohara (Tilley) have successfully completed their PhD degrees. Almas is now a full-time mother while Amane is hoping to gain a postdoctoral post in the northern hemisphere.

Peter Clark - courtesy of VUW Image Services

On 21 September, Prof *Osamu* ***Ishitani*** (Tokyo Institute of Technology) visited the School, met with faculty. He presented a seminar about molecular photocatalysts for the reduction of CO_2 - a problem of increasing global importance. Ishitani's group elucidated the mechanism of photoreduction in rhenium-based photocatalysts, enabling them to design and synthesize the most efficient photocatalysts seen yet for CO_2 reduction. In early October Dr *Nigel* ***Lucas*** (Otago University) met with the VUW/MacDiarmid materials scientists and told us about his work, initially at the Max Planck Institute for Polymer Research (Mainz, Germany) with Prof. *Klaus* ***Müllen***, and most recently at OU on well-defined, soluble synthetic graphenes (a monomolecular layer of graphite) and graphene-metal complexes that are synthesized starting with simple, yet elegant, Diels-Alder chemistry. Early-to-mid-November visitors included Profs *Krister* ***Holmberg*** (Chalmers University, Sweden) who spoke on *lipases at interfaces*, *James K.* ***McCusker*** (Michigan State University) *Spin Effects on the Physical and Photophysical Properties of Molecules* and *Peter* ***Geissinger*** on *Electric field measurements at protein active sites and their contribution to protein function*.

The recent Marsden round saw *Justin* ***Hodgkiss*** receive a fast-start grant of $300,000 for his project *Ultrafast electron dynamics in molecular semiconductors*. *Kerstin* ***Burridge-Lucas*** successfully completed her PhD under *Jim* ***Johnston***'s supervision in September last. Her thesis *Gold and Silver Nanoparticles as High Value Colourants and Multifunctional Entities for Natural Fibres and Minerals* cover her contribution to the technological advance that has allowed for clothing impregnated with the coloured nanoparticles.

A Story About an Almost Extinct Species – Left Field Science

Harold Kroto

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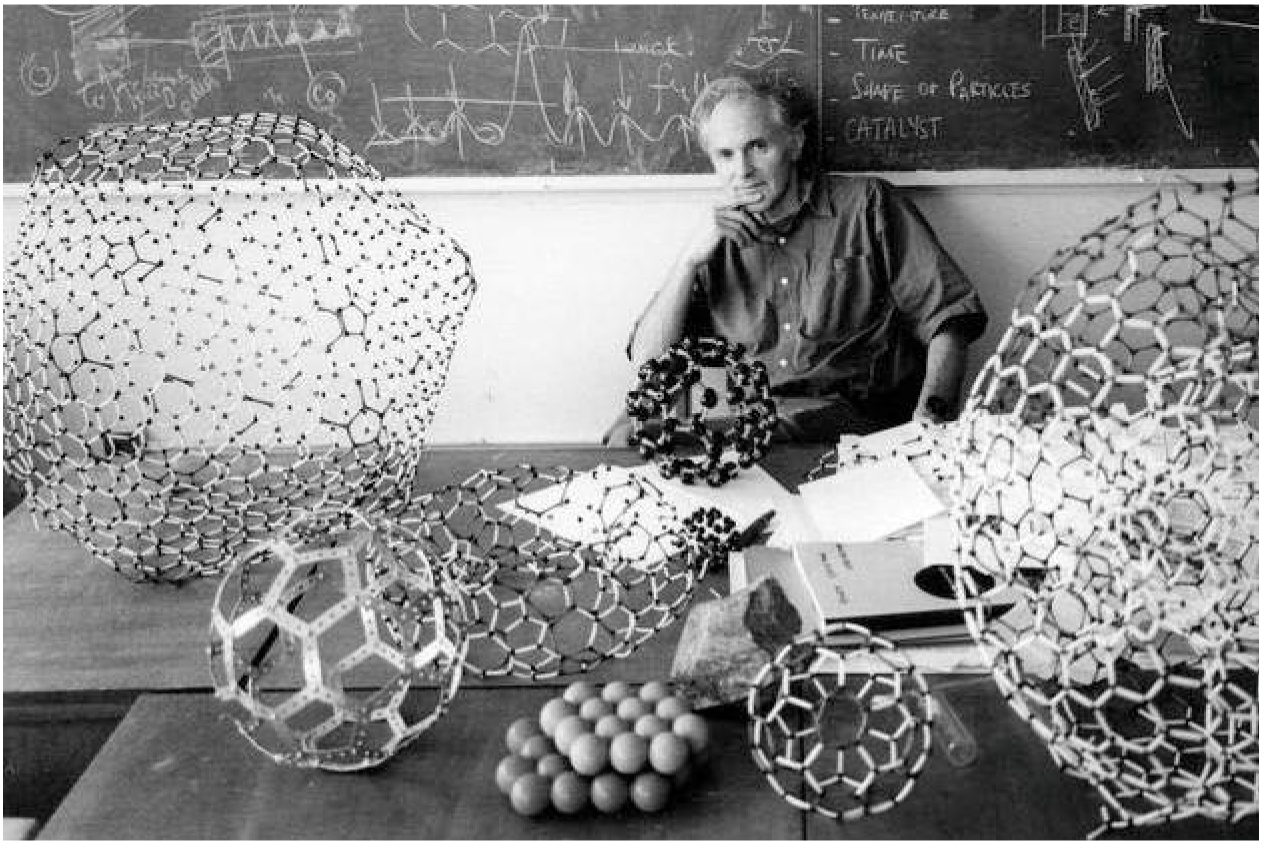

About the Author

Sir Harry Kroto was born in the UK and attended Bolton School, where he was a contemporary of Sir Ian McKellen; his BSc and PhD degrees are from the University of Sheffield. After postdoctoral research at the National Research Council in Canada and Bell Laboratories in the US, he took up a lectureship at the University of Sussex in 1967, becoming full professor in 1985, Fellow of the Royal Society in 1990 and Royal Society Research Professor from 1991–2001. He joined Florida State University in 2004. He was knighted in 1996 and served as RSC President from 2002-2004.

Harry Kroto's doctoral studies included some unpublished research on carbon suboxide (C_3O_2) that led him to have a general interest in molecules containing chains of carbon atoms with numerous multiple bonds. In the 1970s he began to look for molecules such as cyanobutadiyne and cyanohexatriyne spectroscopically, and found them between 1975 and 1978. It was his attempt to explain them that led to the discovery of the C_{60} molecule. He had heard of the laser spectroscopy work being done by Smalley and Curl at Rice University in Texas and suggested that he be allowed to use the Rice apparatus to simulate the carbon chemistry that occurs in the atmosphere of a carbon star. The experiment carried out in September 1985 not only proved that carbon stars could produce the chains but revealed the existence of the C_{60} species. He received (with Curl, and Smalley) the 1996 Nobel Prize in Chemistry for this work.

$H{-}C{\equiv}C{-}C{\equiv}C{-}C{\equiv}N$	$H{-}C{\equiv}C{-}C{\equiv}C{-}C{\equiv}C{-}C{\equiv}N$
cyanobutadiyne	cyanohexatriyne

Sir Harry is a member of the MacDiarmid Institute Board, and a regular visitor to NZ, and expected for the AMN5 conference in Wellington in February.

At the University of Sussex in the early 70s my colleague David Walton had developed an ingenious way to create very long linear carbon chain molecules - the polyynes – consisting of carbon atoms strung together like beads on a string. Indeed, David had succeeded in making a whole series of these molecules, the longest of which had some 32 carbon atoms in a row. I had been fascinated by carbon chains ever since my PhD work (1961-64) and David's polyynes re-awakened this interest and, in particular, initiated ideas about how very long carbon chains might vibrate. The image in my mind was of the way I had seen a wave blip travel along a long slack wire (or rope) and of a travelling wave in a canal or river such as the Severn Bore. I wondered how quantum mechanics would handle these sorts of problems. Could we study the highly excited vibrational levels of such chains and observe quantum properties gradually metamorphose into this sort of classical visually-imaged behaviour as implied by the Bohr Correspondence Principle.

I had tried for several years (in the end *ca*. 6 years – but that is another story!) to obtain my own microwave spectrometer and finally succeeded in Sept 1974. Well these were the (heady!) days of the UK's dual support system in which young researchers like me would receive a modest contribution to their everyday research running costs from the Government *via* a departmental allocation. This was really a rather good scheme as the executive committee of the department – the dean together with senior researchers – are the only people likely to know what was likely to be best for the future of the department. They had an incentive to make sure that the young people (like me – then!) that they had hired could do some research without having to spend inordinate amounts of time begging, cap-in-hand, for funding from essentially faceless committees. These committees are invariably manned by over-worked scientists who by-and-large knew almost nothing about the field and had almost no time to give the applications the attention they really deserved. I later became a member of various SRC or SERC or EPSRC (one never knew what it was called from one day to the next!) committees: Physical Chemistry, the Radio Astronomy, a Synchrotron Beam Line Allocation (chairman!) and the main Chemistry Committee. During this period I realised what a senseless mechanism this was for disbursing funding for fundamental scientific research in universities. Often one relied on one person on a committee who might or might not have sufficient expertise in the particular field to adjudicate on a particular application.

About 1974 the late Colin Eaborn – founding professor of the School of Molecular Sciences - had a stroke of genius. Colin initiated a *BSc by Thesis in Chemistry* course at Sussex in which undergraduates took the Preliminary Course for the first two terms of the first year and then for the next seven terms carried out research and wrote a thesis. They had two supervisors in disparate fields and also had to pass seven of the mainline courses. On average they did better than the students who followed the standard degree tracks. This course was a fantastic success, producing a steady stream of outstanding young researchers and many of the resulting theses were unquestionably of PhD calibre. I put together a project with David for this course to synthesize some polyynes and study them spectroscopically. As luck would have it an exceptional student, Andrew Alexander, decided to work with us. I had been a bit apprehensive at first as Alex did not have a very strong mathematical background and microwave spectroscopy analysis did need Quantum Mechanics and a significant degree of familiarity with mathematics. There was however no need to worry as Alex threw himself into the project with a degree of enthusiasm that comes from embracing one's own project. He synthesised some long(ish) chain species starting with one with five carbon atoms and studied their infrared and NMR and microwave spectra.

During the decade from 1967 onwards a revolution in astrophysical chemistry took place. It had its origins in the brilliant discoveries made by Charles Townes' group using radioastronomy, which detected radio spectra from the interstellar molecules in the dark clouds in the space between stars. Laboratory microwave spectroscopists, like me, followed these fascinating advances with great interest as we were producing the radio data that astronomers could use to tune the receivers of their radio telescopes. At the same time as we were measuring the radio frequency of our polyynes, I received a preprint of a paper by Takeshi Oka, a friend and former colleague at the National Research Council in Canada, which described some of his radioastronomy observations. I wrote to Takeshi to see if he might be interested in a collaboration to detect our carbon chain molecule in space using our laboratory measurements. In the event, together with Canadian astronomers, we detected the first long carbon chain molecule to be found in space. This breakthrough encouraged us to synthesize and study even longer chains and detect them in space. David devised the synthesis and a gifted graduate student, Colin Kirby, took time off from his main project to make it. We ultimately discovered that there were very long carbon chain molecules, in totally unexpected large amounts, in space. These results, between 1975 and 1985, led me to conclude that our carbon species could not be created by the interstellar chemical processes that were being proposed at the time to account for interstellar molecules in general. I wondered if the carbon chains might be a special case, and most likely produced in the atmospheres of red giant carbon stars and subsequently expelled into the regions of the interstellar medium where we had detected them.

During the Easter of 1984 I visited Rice University in Texas at the invitation of my friend and fellow spectroscopist Bob Curl. During this visit Bob suggested that I visit a colleague's laboratory. During this visit to Rick Smalley's laboratory, Rick expounded, excitedly, the way in which his newly created cluster beam machine worked, using a laser to vapourize metals. During his demonstration I began to formulate, in my mind, a project to simulate in the laboratory the conditions I thought might occur in a red giant star and be responsible for the carbon chains we had detected by radioastronomy. I discussed the possibility of a joint project with Bob that evening. Some seventeen months later Bob called me in the UK to say that they were, at last, going to try the experiment and asked whether I was interested in coming to Rice to participate. In the event I did not hesitate, I paid for my own intercontinental air ticket and during the 15 day visit in September 1985 carried out the research with undergraduates Jim Heath, Sean O'Brien and Yuan Liu that resulted in the serendipitous discovery of the C_{60} molecule. This discovery led ultimately to a whole new field of Organic Chemistry – the Fullerenes, the re-discovery of the carbon nanotubes and the award a Nobel Prize in Chemistry in 1996. For what it is worth, Google lists the following - Results: about 588,000 hits for *fullerene* and about 1,440,000 for *nanotube*.

This work of our group showed that, at that time, the general understanding of carbon chemical processes on a nanoscale was totally wrong. Although 25 years on, conjecture has proven to be correct, back then six of the first set of papers published by leading groups in the field of cluster science claimed we were the ones that were wrong! Fortunately, our manuscript went to *Nature (UK)* and did not go to any of these groups to be refereed! One might hypothesize over the possibility that had we had the (essentially impossible) prescience to submit a research proposal to carry out this study it would almost certainly have gone to some of these groups for *peer review* – and presumably would have been turned down.

The discovery of C_{60} had its 25th anniversary last year (2010) and it is only now that applications appear to be on the horizon. One of the most important properties of C_{60} is that it is an outstanding electron trap and the commercialization of organic solar cells doped with fullerenes (which improve the efficiency of electricity production by about an order of magnitude) and printed on inexpensive thin plastic is now imminent. On the medical front, fullerene cages are able to trap biologically toxic atoms inside the cage physically, rather than chemically, and their application as non-toxic MRI imaging and radioactive anti-cancer agents appears also to be imminent. The Mitsubishi Company has invested some $20 M in a plant which produces fullerenes by a combustion process in tens of kilogram quantities. It may be worth pointing out that not only did I try to convince some leading combustion scientists that C_{60} was being produced by combustion but I was vehemently criticised in papers by some of them for suggesting this heresy. In fact, applied combustion scientists, (who do the sort of *strategic* research so beloved of Mrs Thatcher) missed this and should have discovered C_{60} some 60 years ago. The carbon nanotubes which, as mentioned above, were a spin-off re-discovery from the C_{60} breakthrough have already found applications and are the focus of developments that promise paradigm-shifting advances in materials engineering and electronics. It is also worth noting that the apparatus at Rice that we used was originally designed to produce species by laser photofragmentation of gaseous precursors. However, in the initial tests of the system, the laser accidentally hit the aluminium wall of the apparatus producing large aluminium clusters efficiently. The apparatus was immediately modified to laser vapourize refractory materials and a major breakthrough in cluster science was born. This is yet another typical example of the way important scientific advances are made serendipitously.

In summary, none of the three key experiments in this story was part of any research proposal. The initial study was just hatched to understand some fundamental aspects of molecular quantum mechanics and enable an undergraduate to obtain a BSc degree. The second radioastronomy discovery of the large carbon-containing molecules in space was also not part of any research proposal but an idea based on the undergraduate project. It was proposed informally in a letter to a former colleague in Canada who happened to have access to a radio telescope. The Nobel Prizewinning discovery of C_{60} itself was an idea suggested during a chance visit to Rice University and I paid my own air fare to Houston to carry out the experiment myself. It was not in any research proposal either. Furthermore, the apparatus used was built to do quite a different experiment. One further point is that six months after I returned to the UK in 1967, my glorified postdoctoral position at Sussex was converted to a tenured lectureship taking a massive weight off my shoulders. Whatever pressure there was for me to succeed at research was pressure I put on myself. Today in the UK, the young researchers often spend several years on research fellowships worrying about their future and how they will be able to continue to support their families if they do not make the grade. In the US, a similar invidious situation pervades as young scientists with tenure track appointments need to obtain NSF grants or they will be fired. I understand that the success rate is now less than 20%. These really are not conditions conducive to the unfettered mindset necessary for many young people to make the creative advances that are needed for the future of society. Richard Feynman, in Chris Sykes' wonderful BBC interview, speaks about how important such an unpressured mental environment is for creativity.

There may be some lessons here about how some fundamental breakthroughs occur and how strategic or applied science can fail. There may also be lessons to be learned about the peer review process and the impossibility of predicting the major discoveries themselves, let alone the future impact of any discoveries. There may be lessons too about the age-old point that, time-and-again, it is only when discoveries are made that possible applications become obvious and then almost invariably made by scientists in a totally different field from that of the original discoverer. Excellent examples are the applications of lasers to eye surgery and bar-code scanners at supermarket cash desks, which I doubt were in the mind of Charles Townes who developed the microwave amplifier by stimulated emission of radiation. I suspect personally, that in general, the mindset of those who are successful at making fundamental breakthroughs in the sciences is fundamentally very different from those of the entrepreneurs who are successful at applications – perhaps even orthogonal in many cases. Whichever way, those who fund research should ponder these facts and the following: In the 70's a rough notional estimate of the split between overall funding in the UK for fundamental and applied research, respectively, was *ca*. 15%:85%. Halving the 15% to 7.5% by introducing strategic initiatives was a catastrophic cut in fundamental science. It probably took the level down below the threshold of viability for fundamental science at which the UK appears to have been rather good in the past; it was, arguably, a drop in the ocean for applied research, at which it is arguable that the UK has not been that good.

History has shown time-and-again that the basics of the above story are very often the way that important breakthroughs occur. Indeed, it is blindingly obvious that the really unexpected and unpredictable discoveries are invariably more important than those that are the result of targeted initiatives. The discovery of C_{60} was the result of an experiment to understand stellar and interstellar chemistry and, thus, a totally *Left-field* breakthrough. This *Left-field Science* is now almost extinct and one might ponder how well a team will do if it cannot field players in left field – or in cricket rather than baseball parlance on the off-side. However, my experience is that one can point out the above obvious issues until one is blue-in-the-face, and no one with any influence on science funding ever takes a blind bit of notice!

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Raman Microscopy as a Structural, Analytical and Forensic Tool in Art and Archaeology

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About the Author

Robin Clark, CNZM, FRS, is Sir William Ramsay Professor Emeritus of Chemistry at University College, London (UCL). He was born in New Zealand and educated at Christ's College and the University of Canterbury, before moving to the UK and UCL in 1958 for PhD study in chemistry.

He joined the faculty at UCL in 1962, rose to become Dean of Science and then, for 20 years, Sir William Ramsay Professor of Chemistry, now emeritus. He has lectured in many countries (NZ included), acted as visiting professor in numerous universities sharing his expertise in transition metal chemistry, mixed valence chemistry, metal-metal bonding and spectroscopy. He work is recorded in more than 500 publications and he remains remarkably active.

He has made major contributions to most aspects of Raman and resonance Raman spectroscopy, but it is his recent pioneering applications of these and other techniques to the characterization of pigments in artwork and archaeology that has gained him widespread international recognition.

Recent awards include the Czech Spectroscopy Association's Marci medal, the RSNZ Sidey medal and the inaugural Franklin-Lavoisier Prize of the Maison de la Chimie (Paris) and Chemical Heritage Foundation (Philadelphia). He was elected Hon. FRSNZ in 1989, FRS in 1990 and Companion of the New Zealand Order of Merit (CNZM) in 2004, and International Member of the American Philosophical Association in 2010, the third New Zealander since its founding in 1743. He is the 2011 RSNZ Distinguished Speaker and will be opening the touring portrait exhibition ***The Science of Art*** in March in Wellington and then undertaking a national lecture tour.

Introduction

Having left New Zealand in 1958 with research experience in diffusion-controlled reactions (Walter Metcalf, Canterbury University College) and high pressure chemistry (Bill Fyfe, Otago University) to study for a PhD on the chemistry of the early transition metals (Ron Nyholm, UC-London), it would not necessarily be clear to readers as to why I might be in a position to write an article for CiNZ on the seemingly unrelated topic above. In brief, my research at UCL over the past *ca*. 50 years kept evolving from my PhD topic through different aspects of physical inorganic chemistry (ligand-field theory, mixed-valence chemistry, metal-metal-bonded species, linear-chain complexes, *etc*.) to spectroscopy (electronic, infrared, Raman, resonance Raman, electronic Raman) and many other topics. Some of these, notably Raman spectroscopy (along with yet further techniques), I chose to bring together in the last decade or so for a common purpose after recognising the serious lack of scientific study on pigments, dyes, *etc*. used on artwork and archaeological artefacts. Specifically, it was clear that there was a great need to be able, rapidly and unambiguously, to identify such materials at micrometre sizes on artwork of all sorts and to establish artists' palettes in different regions and at different periods. Not only would this contribute in a major way to scholastic knowledge in the area, but it would provide a firm scientific basis for the identification of art forgeries. The following outline illustrates how these studies have developed and the nature of some of the long-standing problems solved.

The Raman Effect, first detected in 1928 in Calcutta by C.V. Raman, has developed into a powerful method for the study of gases, liquids, glasses, solutions and solids, whether organic or inorganic. The changes in frequency of the incident photons scattered inelastically from materials of all sorts are unique to each material and are collectively referred to as its Raman spectrum. This is a unique fingerprint of the material on which the laser beam from the source is incident. Raman spectroscopy was used traditionally, in conjunction with infrared spectroscopy, to obtain the vibrational frequencies of virtually all normal modes of a compound and, by use of group theory, to establish the symmetry and then the force constants of the molecule. Large numbers of studies of these sorts have been published, from the early classic works of Herzberg, Wilson, Decius and Cross, to the compilations of data on inorganic materials by Nakamoto[1] and many others. The theory of the Raman Effect has been well set out by Long.[2]

Many compounds crystallise in more than one polymorph, each having different properties, hence it is vitally important to be able to distinguish these apart. Each crystallises in a different space group, with different point or site groups for each atom, and so the infrared and Raman spectra of each polymorph are distinct. Obvious cases in point are calcite and aragonite (each $CaCO_3$), rutile, anatase and brookite (each TiO_2), *etc*.[3-6] These extensive studies over several decades have led to the realisation that Raman spectroscopy, and especially its newer variant in which the laser beam is focussed onto the sample via a microscope, Raman microscopy (RM), would be an ideal, precise technique with which to probe the identities of pigments and dyes used in art and archaeology.[3-10]

Raman Microscopy as an Analytical Technique

The identification of pigments on manuscripts, paintings, postage stamps, enamels, glasses, ceramics, stuccoes, icons, polychromes, papyri and archaeological artefacts is critically important to understanding the history of an object and in the resolution of problems related to restoration, conservation, dating and attribution of artwork. Many techniques, both molecular and elemental, have been used for such studies, but the former are the more important since they lead to the identification of the pigment, which is usually a molecule rather than an element. Raman microscopy (RM), significantly a molecular technique, has emerged as a consequence of major recent advances in optics and detector technology as probably the most suitable of such techniques on account of its high spatial (*ca*. 1 μm) and high spectral (*ca*. 1 cm^{-1}) resolution, its molecular specificity, its excellent sensitivity by way of charge-coupled device (CCD) detectors, and the fact that most items may be analysed non-destructively and *in situ*. Furthermore, the introduction of small, portable spectrometer systems, albeit of lesser performance (Raman microprobe systems) has been advantageous for the study of immovable or awkward items forming part of our cultural heritage, such as cave paintings and statues in galleries. The identification of pigment degradation products on artwork is also a matter of great interest because studies addressing possible degradation pathways give insight into the nature of the environment in which the artwork or archaeological items have been held. Some geological conversions, such as that of malachite to azurite, are very slow, but many chemical reactions taking place on artwork, such as that of hydrogen sulfide with lead or copper pigments, are very fast. The source of the hydrogen sulfide is atmospheric or *via* bacterial attack on sulfur-containing binders.

The immense literature on pigments is now well documented in substantial articles and reviews[3-10] as well as in libraries of pigments and minerals.[11-13] Most minerals are long established and have well defined structural and spectroscopic properties, such as those relating to colour as a function of particle size, density, physical and chemical stability, *etc*. Obviously, synthetic pigments have known first dates of manufacture, a fact that is key to the possible dating of illuminated manuscripts and paintings. That is, a synthetic pigment cannot appear on a work of art that supposedly predates the year of first manufacture of the pigment. If it does, then either the artwork is a forgery or it has been restored at a later date, a matter made evident by whether or not there is under paint.

It is important to emphasise that it is not possible to authenticate artwork; thus in *The Logic of Scientific Discovery*, originally published in 1934, three years before he emigrated from Vienna to Christchurch, Karl Popper postulated that scientific hypotheses can never finally be confirmed as true, and are acceptable only in so far as they manage to survive numerous attempts to falsify them.[14] The art world and especially auction houses often leave much to be desired in this context, seemingly offering artwork and artefacts for sale without first having carried out perceptive scientific tests for forgery.

Scientific Investigation of Artwork

A few highlights of recent Raman studies at UCL on high profile manuscripts, artwork and artefacts follow. All such studies involve the critically important establishment of palettes, which in some cases lead to resolution of long-standing ambiguities.

*Lindisfarne Gospels (*ca. *715 AD) and Other Early Manuscripts*

The British Library contains one of the world's foremost collections of Anglo–Saxon manuscripts, many of which have been very well studied from a palaeographical standpoint. However, until recently, little had been known as to the materials used in their construction and illumination – their pigments and binders. No Anglo-Saxon recipe books for artists' pigments are known to exist, and later ones – even price lists – were unreliable, being subject to mistranslation; moreover, the terms used were often ambiguous, being used for more than one pigment. A particularly notable codex is the Lindisfarne Gospels, a work of art which, to many, represents the pinnacle of artistic achievement in manuscript illumination (Fig. 1). Considered to have been created around 715 AD by Eadfrith, the then Bishop of Lindisfarne in Northumbria, in honour of St. Cuthbert who was himself Bishop of Lindisfarne from 685–687 AD, the major pages display fantastic complexity of zoomorphic interlace ornament as well as contrastingly simple evangelist portraits. The most significant discovery[15] was that the blue pigment used is indigo ($C_{16}H_{10}N_2O_2$; derived from the woad plant indigenous to

Fig. 1. St. Jerome's prefatory letter to Pope Damasus on his Latin Vulgate translation of 405 AD. Copyright The British Library Board, Cotton Nero iv; reproduced with their permission and that of the John Wiley & Sons, *J. Raman Spectrosc*. – see ref. 15.

England) and not lazurite ($Na_8[Al_6Si_6O_{24}]S_n$) as had until then been believed. Lazurite in 715 AD was known to have been found only in the Badakshan mines in the Hindu–Kush area of Afghanistan and so, to have been used on the Gospels, would have required the existence, improbably, of a trade route at that date between these mines and Northumbria. The correct identification of the blue as indigo rather than lazurite removed the need for such an unlikely proposition. Several other detailed studies of Anglo–Saxon and early English manuscripts have also been carried out successfully by RM. In addition, the semi-precious gemstones used to decorate the plates of embossed silver attached to the oak cover of the Carolingian manuscript, the *Tours Gospel*, *Evangelia Quatuor*, were identified to be silica (SiO_2, white, cat's eye), emerald [$Be_3Al_2(Si_6O_{18})$, beryl, green, coloured with traces of Cr^{3+}], carbuncle [$Fe_3Al_2(SiO_4)_3$, iron garnet, red-brown], and sapphire [Al_2O_3, very pale blue, trace amounts of Cr^{3+}].[16]

Until recently, many unsubstantiated identifications made by purely visual means had become accepted as fact, having been repeatedly quoted uncritically. Thus, the traditionally accepted triptych of the insular palette, red lead (Pb_3O_4), orpiment (As_2S_3) and verdigris [basic copper(II) acetate, $(MeCO_2)_2Cu.Cu(OH)_2$, and a suite of closely related compounds] was by no means always adopted by artists at the time, as shown by RM; thus, the green pigment verdigris was shown to have been substituted in many cases by a mixture of orpiment and indigo, the mixture being known as vergaut.

*Arabic Treatise Containing Early Maps and Celestial Diagrams (*ca. *1200 AD)*

The Arabic treatise *The Book of Curiosities of the Sciences and Marvels for the Eyes* at the Bodleian Library contains a series of early maps and celestial diagrams that are of great importance to the history of medieval cartography. The treatise consists of two books, the first pertaining to celestial (astrological and divinatory) matters and the second to terrestrial (descriptive and historical) matters. Considered to date from *ca*. 1200 AD in Egypt, the work includes: two world maps, one circular and one rectangular; maps of the Indian Ocean, Mediterranean and Caspian Seas; maps of the Mediterranean islands of Sicily and Cyprus and of the cities of al-Mahdiya (now Mahdia, in Tunisia) and Tinnis in the Nile delta; and unique maps of the Nile, Euphrates, Tigris, Oxus (now referred to as the Amu Darya) and Indus rivers. The pigments used for the illustrations were shown by RM[17] to consist of cinnabar (HgS), orpiment, lazurite, indigo, carbon black, white lead [$2PbCO_3.Pb(OH)_2$], and a copper-based blue (possibly a form of verdigris), red ochre (essentially haematite, Fe_2O_3) and gold, additional shades being obtained by way of numerous pigment mixtures. Some pigments had partly degraded. The analysis provides a starting point for building up knowledge about the production at this time in Egypt of secular, illuminated Arabic manuscripts as distinct from Korans. The identification of light-sensitive orpiment and hydrogen sulfide-sensitive white lead may be important for the development of future conservation strategies for such manuscripts. Many other studies of Korans have now been carried out.

*Gutenberg Bibles (*ca. *1455 AD)*

Johann Gutenberg in Mainz (Germany) was responsible in the middle of the 15th century for the invention of European printing using movable metal type, an invention which had a profound impact on Western culture. Of the *ca*. 180 copies of the bibles he produced, about 135 were printed on paper and about 45 on vellum, some 48 copies having survived until the present day. The palettes of eight of these immensely valuable (multimillion pound) Bibles have been established by RM, *viz*. the King George III in the British Library (London) and others held at Eton College (Windsor) and Lambeth Palace (London), the Bibliotheque Mazarine and the Bibliotheque Nationale de France (both in Paris), and the Staatsbibliothek zu Berlin and the Niedersächsische Staats und Universitätsbibliothek, Göttingen.[18] Most of these are brilliantly illuminated codices, the red, yellow, black, blue, green and white pigments on the King George III version, for instance, consisting of vermilion (HgS), lead tin yellow type I (Pb_2SnO_4), carbon black, azurite [$2CuCO_3.Cu(OH)_2$], malachite [$CuCO_3.Cu(OH)_2$], verdigris, chalk ($CaCO_3$), gypsum ($CaSO_4.2H_2O$) and white lead, in agreement with the instruction contained in the accompanying model book. The illuminations in the British Library and Eton College Bibles are similar to one another, consisting of brilliantly interwoven flora and fauna around the columns of printed text. (Fig. 2).

Fig. 2. Illumination on the prologue page of the King George III version of the Gutenberg Bible. Copyright The British Library Board, C.9.d.3 f4v-f5; reproduced with their permission and that of the American Chemical Society,– see ref. 18

*Bourdichon Miniatures (*ca. *1499 AD)*

Studies of miniatures taken from the *Book of Hours of Louis XII* by Jean Bourdichon, painter at the Royal Court of France from 1499 to 1521, by RM and X-ray fluorescence have revealed that the extensive palette includes 13 traditional pigments and dyes, along with the unusual artists' materials specular haematite (Fe_2O_3), iron pyrite (FeS_2) and mosaic gold (SnS_2). Possibly the most interesting feature of Bourdichon's palette is, however, the presence of metallic bismuth, found to have been used for only a few decades round 1500 AD to convey the impression of a soft mid-grey (wismuthmalerei, see Fig. 3). It is characterized by first-order Raman lattice modes at 70 and 97 cm^{-1} and their overtones.[19]

Fig.3. *The Nativity*, Bourdichon, *ca*. 1499 AD; copyright the Victoria and Albert Museum, E.949-2003 and reproduced with their permission - see ref. 19.

*Vermeer Painting: Young Woman Seated at a Virginal (*ca. *1670 AD)*

Until 2004 there were considered to be only about 35 authentic paintings by the famous Delft artist, Johannes Vermeer (1632–1675), but in that year the art world accepted the case for a 36th. The painting *Young Woman seated at a Virginal* had originally been regarded as having been painted by Vermeer, but this attribution became unclear in 1947 when Hans van Meegeren revealed that he had painted a number of 'Vermeers' himself and sold seven to unwitting museums and collectors (including one to Hermann Goering) during the period 1937–1945. However, extensive art historical and scientific research in the late 1990s and early 2000s has led to persuasive evidence consistent with a re-attribution of this particular painting to Vermeer; in consequence of this, when sold at Sotheby's auction house on 6 July 2004, it realised GBP 16.2M.[20]

Many stylistic and other arguments are in favour of this re-attribution, including the discovery that the thread count of the canvas, 12/cm in both the warp and the weft is identical to that on Vermeer's long accepted painting *The Lacemaker* held in the Louvre gallery in Paris. On the scientific side, three pigments were identified by RM (Fig. 4), lead tin yellow (type I), lazurite, and vermilion, all of which were available to Vermeer and known to have been used by him in *ca*. 1670. Lead tin yellow (type I) is a crude date-marker pigment in the sense that it is understood to have been used only in the period *ca*. 1450–1700 AD. Moreover, the finding of the rare and expensive mineral lazurite, rather than the much cheaper synthetic equivalent (ultramarine blue), itself suggests that the painting may predate 1828, the year in which the latter version was first synthesized. The attribution is, however, still subject to the strictures of Popper.[14]

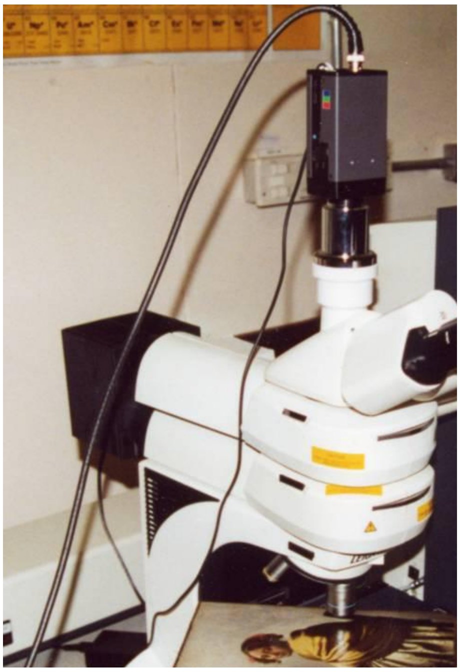


Fig. 4. Painting *Young woman seated at a virginal* under study by Raman microscopy to identify the pigments present. The results provided evidence consistent with the attribution of the painting to Vermeer and none to the contrary. Copyright the American Chemical Society and reproduced with permission – see ref. 20.

Icons

Extensive RM studies have been carried out on, and on cross-sections from, many Russian, Albanian and Greek icons, often in conjunction with laser-induced breakdown spectroscopy (LIBS) and other techniques. These reveal details of the stratigraphy of overpaintings on icons (Fig. 5).[9]

Detection of Forgeries

Many studies have led to, or contributed to, the realisation that a significant proportion of works of art throughout the world are forgeries. These are illustrated with the four examples that follow.

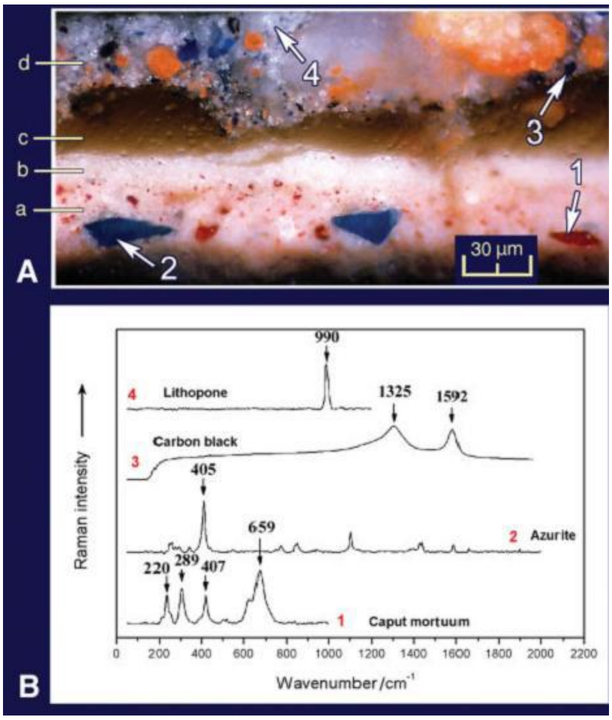


Fig. 5. A. Cross-section of a monastic habit painted on a Greek icon; photography with a microscope in reflected light. B. Spectra of pigments taken with a Raman microscope. Identification: (1) underlayer: caput mortuum, lead white, azurite, red lake and yellow ochre (2) highlight: lead white and grains of caput mortuum; (3) varnish; (4) overpainting: ultramarine blue, minium, lithopone and carbon black. Copyright John Wiley & Son and reproduced with permission – see ref. 9.

Egyptian Papyri (supposedly ca. *1250 BC)*

Six Egyptian papyri, supposedly dating to the time of Ramses(II) and Nefertari (*ca*. 1250 BC) were shown to have palettes which include six modern pigments, *viz*. Prussian blue ($Fe_4[Fe(CN)_6]_3$ $14{-}16H_2O$), ultramarine blue, a Hansa yellow, pure white anatase (TiO_2), phthalocyanine blue [$Cu(C_{32}H_{16}N_8)$], phthalocyanine green [$Cu(C_{32}H_{16-n}Cl_nN_8)$], and two β-naphthol reds; the dates of first manufacture of these modern pigments are 1704, 1828, *ca*. 1910, *ca*. 1920, 1936, 1936, 1939 and possibly *ca*. 1950, respectively. Thus, the papyri studied are clearly 20th century forgeries. Authentic papyri such as those held in the Petrie Museum at UCL were found to have been painted solely with mineral pigments such as Egyptian blue ($CaO.CuO.4SiO_2$ or its mineral equivalent cuprorivaite), orpiment, haematite, malachite, carbon and pararealgar (As_4S_4).[21]

The Vinland Map

The Vinland Map, held at Yale University (New Haven) is a world map on parchment that includes, significantly, representations of Iceland, Greenland and the north-eastern seaboard of North America. On the bases of cartographical, palaeographical and philological analyses the map was originally thought to have been drawn from two different prototypes around 1440 AD, implying that it predates, by some 50 years, the discovery of America by Christopher Columbus in 1492 AD. However, detailed studies by McCrone[22] and others of the black ink defining the lines showed that the yellow-brown material forming the background to the lines contains substantial (up to 50%) anatase (TiO_2). This material was shown to have a particle size (*ca*. 0.15 μm) and particle size distribution (very narrow) that is characteristic of the synthetic post *ca*. 1920 product, and not of natural anatase. The clear indication is that the Vinland Map is a 20th century product.[23] RM confirmed that anatase is present in the ink alone of the Map and that the black component is carbon black, not an iron gallotannate[24] as some had supposed. Despite controversy, much of it perpetuated by the scientific popular press and Nordic protagonists, the situation remains clear that the Vinland Map is a forgery.[25]

Postage Stamp Forgeries: Mauritius 1847, Hawaii 1851

RM offers an effective, rapid and non-destructive way of identifying the pigments and dyes used in the inks, paper, and cancel marks of postage stamps. Thus, the rare and valuable (up to GBP 0.5 M) so-called Hawaiian Missionary stamps (2, 5 and 13 cents, issued in 1851) from the Tapling Collection at the British Library were shown to have been printed using Prussian blue as the blue pigment. In addition, the paper fibres of the stamps were shown in the case of the 13 cent stamp to have been interspersed with ultramarine blue to act as an optical brightener to counteract the effects of the yellowing of paper or cloth fibres with time, *cf*. Reckitt's blue/dolly blue added several decades ago into copper urns during the washing of white clothing for this reason. Distinctions between genuine and forged or reproduction stamps can sometimes be drawn on the basis of the pigments used.[26] Raman microscopy at UCL contributed to the final opinion expressed by the Royal Philatelic Society in 2006 that the rare so-called Grinnell Hawaiian Missionary stamps are forgeries dating from the late 1800s/early 1900s and not *ca*. 1851, thereby closing a matter which has been controversial since 1918 when the *rediscovery* of 72 Grinnell stamps was first reported.

Similar studies of the earliest Mauritian stamps (1847) have been carried out, notably on an extremely rare one penny stamp (1d, orange-red; used), a rare 2d stamp (blue; unused), as well as a reproduction stamp (1905), early forgeries, and Britannia-type stamps (1858–1862). No numerical value is expressly printed on any stamp, the nominal value being designated solely by its colour. The pigments used were identified by RM to be red lead on the 1d stamp, Prussian blue on the 2d stamp, chrome green – a mixture of chrome yellow (PbCrO4 and Prussian blue – on the 4d stamp, and vermilion on the 6d (orange) stamp. The blue 2d stamps were known to have been converted illegally to the much rarer, and thus more valuable, green 4d ones, evidently by painting an aqueous slurry of chrome yellow over the surface of 2d stamps and allowing them to dry. Such forgeries could, however, be detected by RM examination of the stamp edges. The technique of RM has great potential for the expertizing of stamps, *i.e.* distinguishing between genuine and forged or reproduction stamps.[27] The New Zealand Chalon issue stamps of 1855, in particular the *Dwarf* issues, have also been examined recently in London by RM.

Ingles (15th Century Maestro) and the Spanish Forger (mid-20th Century)

Some miniatures believed to be authentic work by the 15th century Spanish maestro Jorge Ingles became suspect forgeries in the mid-20th century on stylistic and compositional grounds. However, no systematic study of the identities of the materials used on these miniatures (now believed to number over 300) had been carried out until 2009, when five were subjected to RM and X-ray fluorescence analyses. These revealed that the pigments used on each of the Spanish forger's miniatures include not only traditional materials of Ingles' period, *e.g.* vermilion, carbon black, red lead, lead white and indigo, but also four much later ones (chrome yellow, Scheele's green, emerald green and ultramarine blue). These results were, obtained easily and provided a firm scientific basis for recognising the modern forgeries.[28]

Scientific Investigations in Archaeology

Pioneering Raman and other scientific studies have opened up many new fields of research in archaeology.[6] Recent examples are discussed according to the supposed dates of each artefact.

*Chinese Sherds (*ca. *4200 BC)*

The white background layer (slip) on painted sherds (Yangshao culture, Henan, China, *ca*. 4200 BC) has been shown by RM to contain anatase, leading to claims that this material had been used as a white pigment for over 5000 years. However, native anatase is relatively rare, impure and expensive and its Raman scattering cross-section is extraordinarily high, perhaps 1000 times that of kaolinite clay, the assumed prefiring host material of the sherds.[29] SEM/EDX analyses of further Yangshao sherds from another site (Yiquanma) indicate that their white slip contains just 1 wt% of TiO_2 (made up of anatase, rutile and other titanium ores). Hence, the anatase component is not present in sufficient proportions to determine the pigmentary properties of the slip, despite the fact that its scattering dominates the Raman spectrum of the sherds.[30] The detection of anatase in Chinese sherds and also in Roman ceramic pots and sherds from the East Midlands in these trace amounts does not imply, as has been suggested, that native anatase had been sourced and used as a white pigment for thousands of years. It is a component at the *ca*. 1 wt% level in kaolinite from many parts of the world, notably Georgia, USA, and it has been detected by RM in countless sherds based upon kaolinite matrices in similarly very low proportions.

Punic Make-up Materials (4th-1st Century BC)

Ten archaeological Punic make-up materials from Tunisia dating from the 4th to the 1st centuries BC have been analysed by RM and synchrotron X-ray diffraction techniques in order to identify the materials used by Carthaginians for cosmetic purposes on the living and for ritual purposes on the dead.[31] Haematite and cinnabar (HgS) were the most commonly found red pigments, in both cases along with quartz and sometimes calcium carbonate, clay and possibly madder. However, no clear distinction could be drawn between living and ritual uses for these materials.

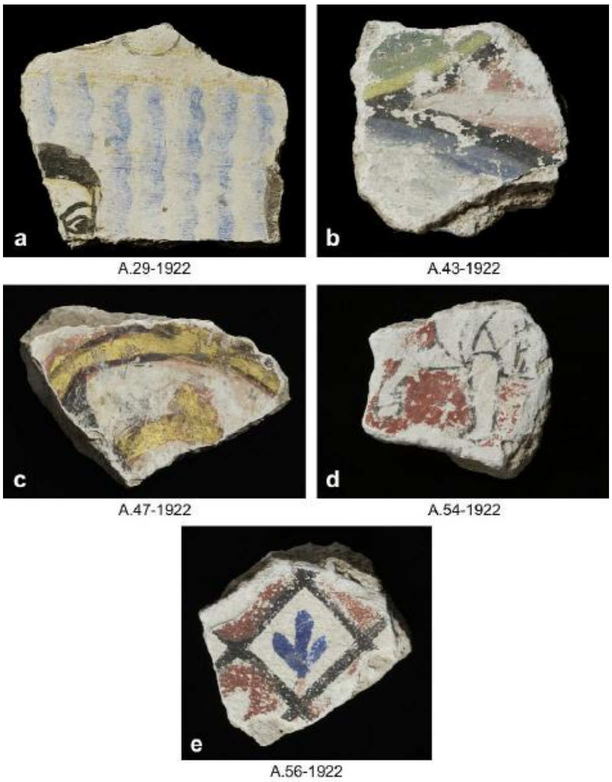
Iraqi Stuccoes (9th Century AD)

The archaeological finds (which numbered over 1100) from Samarra made by Sarre and Herzfeld (1911– 1913) have recently been studied scientifically for the first time. Six 9th century Iraqi stuccoes from Samarra (Fig. 6) have been analysed by RM and the following pigments identified: carbon black, haematite, gypsum, lazurite, lead white, orpiment, pararealgar, red lead, vermilion, and the chi-phase of As_4S_4.[32]

Fig. 6. Stuccoes, Samarra, 9th Century Abbasid art. Copyright Elsevier Limited. and reproduced from *J. Archaeol. Sci.* with permission – see ref. 32.

Puebloan Ceramics from the American Southwest (ca. 1100–1300 AD)

The Ancestral Puebloan (Anasazi) period (*ca*. 900–1300 AD) of the American southwest has yielded much pottery of great interest. Raman and infrared spectroscopy has been used to characterise the black pigments on black-on-white potsherds referred to as *Mesa Verde Whiteware*, which date to *ca*. 1100–1300 AD. This study has led to conclusive evidence for the use of carbon-based paints.[33] Maghaemite (γ–Fe_2O_3) and magnetite (Fe_3O_4), found alternatively or mixed with a carbonaceous pigment, were also found on some sherds. Infrared measurements indicated that little, if any, organic material from biogenic precursors of the black pigment or from pigment binding agents remained in the paints. RM could potentially indicate the nature of the original raw materials, including clays, tempers and pigment phases, as well as the firing temperatures and atmospheres employed in the production of these artefacts.



Identification of Iron Oxide Impurities in Earliest Industrial Processed Platinum (1842)

A detailed investigation of the impurities present in a

19th century Russian platinum coin (3 rouble) reveals the presence of three types of iron oxide, *viz*. magnetite, iron deficient magnetite and haematite.[34] These oxides had been formed during the heating of the impure platinum metal powder as part of the refining process in operation in Russia from 1828 to 1843, and were found by RM to be dispersed in the matrix of metallic platinum containing *ca*. 1 wt% iron. The presence of these inclusions reflects the incomplete refining practice for native platinum at that time. The state of oxidation of the iron in iron oxides with the magnetite structure directly influences the paramagnetic properties of these coins, and may also be related to the wavenumber of the most intense Raman band (650 - 700 cm^{-1}) of the oxide. The study has made it possible to understand the limitations of platinum technology during its first large-scale production in the first half of the 19th century. The refinement and production process was a major industrial and metallurgical achievement at this time, when not all the platinum group metals to be removed from the native platinum ore were actually known, and the melting point of platinum (1769 ºC) could not be reached industrially.

Pigment Degradation to Produce Lead and Copper Sulfides

Galena (PbS) is an important raw material for the lead smelting and photoconductor industries, a model material for quantum dot research, an ingredient in ancient cosmetics and also in modern hair dyes, *e.g. Grecian Formula*,[35] and a visually offensive black degradation product of white lead in artwork. In the last context, PbS has now been identified successfully by RM on partly degraded manuscript illuminations, despite its black colour which is not conducive to efficient light scattering.[36] Much consideration has been given to procedures for reversing the unwanted chemical change of lead pigments. CuS behaves similarly.[37]

Detailed Raman studies have now also been carried out on millimetre-sized crystals of PbS under resonance Raman conditions and the phonon modes identified and assigned. In order to confirm the vibrational nature of the features observed, Raman spectra were obtained on natural crystals (mineral and synthetic with natural isotopic abundances) as well as on crystals highly enriched (99%) with ^{34}S.[38,39]

Conclusion

The artificial separation of the arts and the sciences is now being reduced largely by the efforts of scientists throughout the world: the scientific study of artwork and artefacts being an area which is expanding rapidly. Many exciting new avenues are opening up, especially in the use of surface-enhanced Raman and resonance Raman spectroscopy for the faster and more effective identification of dyes; such materials are frequently very difficult to identify by RM alone on account of their high background fluorescence.[40] Collaboration between the arts and sciences has improved, largely through the initiatives of scientists as now recognised by the *Proceedings of the US National Academy of Sciences*[41] and the entire June 2010 issue of *Accounts of Chemical Research*.[42] The field has also recently attracted the active attention of Richard Ernst, 1991 Nobel Laureate in Chemistry (NMR spectroscopy), who has developed a gantry for the RM study of large paintings, notably central Asian ones.[43] On the wider front, many pigments have been found also to be important in areas outside of colour technology.[44] Thus, anatase is photoactive, leading to its role in smart glass, catalysis, nanotechnology, and the study of the wavenumber dependence of Raman bands on nanoparticle size.[45]

References

1. Nakamoto, K. *Infrared and Raman Spectra of Inorganic and Coordination Compounds*, Wiley: New York, 5th edn.1997.
2. Long, D. A. *The Raman Effect,* Wiley: Chichester, 2002.
3. Best, S. P.; Clark, R. J. H.; Withnall, R. *Endeavour* **1992**, *16*, 66-73.
4. Clark, R. J. H. In *Scientific Examination of Art,* National Academies Press: Washington DC, 2005, pp. 162–185; Burgio, L.; Ciomartan, D. A.; Clark, R. J. H. *J. Mol. Struct.* **1997**, *405*, 1-11.
5. Clark, R. J. H. *J. Mol. Struct*. **1995**, *347*, 417-428.
6. Smith, G. D.; Clark, R. J. H. *J. Archaeol. Sci*. **2004,** *31*, 1137-1160.
7. Best, S. P.; Clark, R. J. H.; Daniels, M. A. M.; Porter, C. A.; Withnall, R. *Stud.Conserv.* **1995**, *40*, 31-40.
8. Burgio, L.; Clark, R. J. H.; Stratoudaki, T.; Doulgeridis, M.; Anglos, D. Appl. Spectrosc. 2000, 54, 463-469; Burgio, L.; Melessanaki, K.; Doulgeridis, M.; Clark, R. J. H.; Anglos, D. *Spectrochim. Acta B* **2001**, *56*, 905-913.
9. Daniilia, S.; Bikiaris, D.; Burgio, L.; Gavala, P., *et al. J. Raman Spectrosc*. **2002**, *33*, 807-814.
10. Clark, R. J. H. *Chem. Soc. Rev*. **1990**, *19*, 107-131; **1995**, *24*, 187-196; *C.R. Chimie* **2002**, *5*, 7-20.
11. Bell, I. M.; Clark, R. J. H.; Gibbs, P. J. *Spectrochim. Acta A* **1997**, *53*, 2159-2179.
12. Burgio, L.; Clark, R. J. H. *Spectrochim. Acta A* **2001**, *57*, 1491-1521.
13. Bouchard, M.; Smith, D. C. *Spectrochim. Acta A* **2003**, *59*, 2247-2266.
14. Popper, K. R. *The Logic of Scientific Discovery*, Hutchinson: London, 1962.
15. Brown, K. L.; Clark, R. J. H. *J. Raman Spectrosc*. **2004**, *35*, 4-12, 181-189; 217-223.
16. Clark, R. J. H.; van der Weerd, J. *J. Raman Spectrosc*. **2004**, *35*, 279-283.
17. Chaplin, T. D.; Clark, R. J. H.; McKay, A.; Pugh, S. *J. Raman Spectrosc*. **2006,** *37*, 865-877.
18. Chaplin, T. D.; Clark, R. J. H.; Jacobs, D.; Jensen, K., *et al*. *Anal. Chem*. **2005**, *77*, 3611-3622.
19. Burgio, L.; Clark, R. J. H.; Hark, R. R.; Rumsey, M. S., *et al*. *Appl. Spectrosc*. **2009**, *63*, 611-620.
20. Burgio, L.; Clark, R. J. H.; Sheldon, L.; Smith, G. D. *Anal. Chem*. **2005**, *77*, 1261-1267.
21. Burgio, L.; Clark, R. J. H. *J. Raman Spectrosc*. **2000**, *31*, 395-401.
22. McCrone, W. C. *Anal. Chem*. **1988**, *60*, 1009-1018.
23. Towe, K. M. *Acc. Chem. Res*. **1990**, *23*, 84-87.
24. Brown, K. L.; Clark, R. J. H. *Anal. Chem*. **2002**, *74*, 3658-3661.
25. Towe, K. M.; Clark, R. J. H.; Seaver, K. A. *Archaeometry* **2008**, *50*, 887-893.
26. Chaplin, T. D.; Clark, R. J. H.; Beech, D. R. *J. Raman Spectrosc*. **2002**, 33, 424-428.

27. Chaplin, T. D.; Jurado-Lopez, A.; Clark, R. J. H.; Beech, D. R. *J. Raman Spectrosc*. **2004**, 35, 600-604.

28. Burgio, L.; Clark, R. J. H.; Hark, R. R. *J. Raman Spectrosc*. **2009**, *40*, 2031-2036.

29. Murad, E.; Koster, H. M. *Clay Minerals* **1999**, *34*, 479-485.

30. Clark, R. J. H.; Wang, Q.; Correia, A. *J. Archaeol. Sci*. **2007**, *34*, 1787-1793.

31. Huq, A.; Stephens, P. W.; Ayed, N.; Binous H., *et al*., *Appl. Phys*. A **2006**, *83*, 253-256.

32. Burgio, L.; Clark, R. J. H.; Rosser-Owen, M. *J. Archaeol. Sci*. **2007**, *37*, 756.

33. van der Weerd, J.; Smith, G. D.; Firth, S.; Clark, R. J. H. *J. Archaeol. Sci*. **2004**, *31*, 1429-1437.

34. van der Weerd, J.; Rehren, T.; Firth, S.; Clark, R. J. H. *Mater. Charact*. **2004**, *53*, 63-70.

35. Walter, P.; Welcomme, E.; Hallegot, P.; Zaluzec, N. J., *et al*. *Nano Lett.* **2006**, *6*, 2215.

36. Smith, G. D.; Derbyshire, A.; Clark, R. J. H. *Stud. Conserv*. **2002**, *47*, 250-256.

37. Smith, G. D.; Clark, R. J. H. *J. Cult. Heritage* **2002**, *3*, 101-105.

38. Smith, G. D.; Firth, S.; Clark, R. J. H.; Cardona, M. *J. Appl. Phys*. **2002**, *92*, 4375-4380.

39. Etchegoin, P. G.; Cardona, M.; Lauck, R.; Clark, R. J. H., *et al*., *Phys. Stat. Sol. (b)* **2008**, *245*, 1125-1132.

40. Leona, M.; Stenger, J.; Ferloni, E. *J. Raman Spectrosc*. **2006**, *37*, 981-992.

41. Burgio, L.; Clark R. J. H.; Hark R. R., *Proc. Nat. Acad. Sci.* **2010**, *107*, 5726-5731.

42. *Acc. Chem. Res.* **2010**, *43*, June issue.

43. Ernst, R. R. *J. Raman Spectrosc*. **2010**, *41*, 275-287.

44. Price, L. S.; Parkin, I. P.; Hardy A. M. E.; Clark. R. J. H. *Chem. Mater*. **1999**, *11*, 1792-1799.

45. Zhang, Z.; Brown, S.; Goodall J. B. M.; Weng, X., *et al*. *J. Alloys Compounds* **2009**, *476*, 451-456.

2011 International Year of Chemistry:

Calendar of Events

January

Marie Curie Lecture Series starts and continues throughout year

February

Advanced Materials and Nanotechnology 5 Conference, Wellington (Feb 7 – 11) including:

- VIP Science Class in Chemistry
- IYC2011 Launch Event and Public Lecture by Sir Richard Friend - 9 Feb
- Special Presentation of Launch Event to Year 12/13 students

The Molecular Anthology Project opens for submissions

March

Opening of Portrait Exhibition at New Zealand Portrait Gallery by Prof Robin Clark. Exhibition continues through March/April in Wellington and then around NZ

RSNZ Distinguished Speaker lectures nationwide: Professor Robin Clark

Molecular Anthology Project continues

Elemental Project begins

April

Molecular Anthology Project continues (submissions end)

May

Chemistry in Fibre Project begins (through the RSNZ)

Molecular Anthology Project (Voting)

July

ChemEd conference in Palmerston North (July 17-20)

Nature of Science Series begins (with the RSNZ)

Molecular Anthology Project Completed – Presentation at ChemEd Conference

August

RadioNZ lecture series

October

Prof Bob Grubbs, 2003 Nobel Laureate, Erskine Fellow in residence at University of Canterbury

November

2011 Research Honours Dinner

Elemental Project concludes

December

NZIC Conference in Hamilton

Exhibition of Elemental Project at NZIC Conference

***Up-to-date information will be posted on the NZ website:* www.yearofchemistry.org.nz**

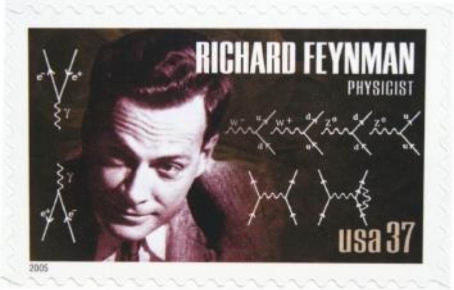
Nanotechnologies – a New Branch of Chemistry?

Alan Smith, Managing Director AZ-TECH, UK (e-mail: *SmithAZT@aol.com*)

About the Author

Alan Smith's career began as a lecturer then he moved into industry and is now the managing director of AZ-TECH. He is the author of numerous papers on nanotechnology (often in IUPAC's *Chemistry International* and reprinted in these pages), and lectures worldwide on the topic to schoolchildren, the general public, international experts, and Heads of State. He is an advisor on nanotechnology for several governments and has facilitated over 50 technology roadmaps for establishments in many countries. His latest publication is a book on roadmapping emergent technologies; and a free booklet on nanotechnology for schools has been prepared for translation into a number of languages for ISESCO. Alan kindly agreed to provide an article for Vol. 75.

In 2005, the US Mail issued a stamp commemorating the contribution to science made by Richard Feynman, the 1965 Nobel Laureate in physics. He had worked on the Manhattan project in World War II, but his legacy was a talk at the California Institute of Technology in 1959 entitled *There's plenty of room at the bottom*.[1] In a nutshell, he was forecasting that if you went down to the nanoscale then you would see some interesting and exciting property changes. At that time it was not possible to work down at that scale, and we had to wait for Heinrich Rohrer and Gerd Binnig, two other Nobel Prize winners in physics (1986), to develop the scanning tunnelling microscope. It was only then that nanotechnology seemed to take off.



For most people it is difficult to appreciate how small a nanometre is, but a few well used examples bring it home. There are a billion (10^9) nanometres (nm) in a metre, which means that a human hair has a diameter of around 80,000 nanometres. If a gull lands on the deck of an aircraft carrier, the battleship sinks one nanometre lower in the water! A red blood cell is 7,000 nm across, a virus 150 nm, and a DNA strand 2 nm.

Size is not the key factor in potential property changes; the massive surface area increase is what provides those changes. To understand this, imagine a one metre cube of a chemical product; the surface area of the six-sided cube would be 6 m^2. If that cube of chemical was ground down into 1 millimetre cubes, there would be a billion of them and the surface area would be 6,000 m^2. If the chemical was ground down to 1 nm cubes, there would be 10^{27} particles and the surface area would be 6,000,000,000 m^2, that is 6,000 km^2. The whole of New Zealand occupies 268,000 km^2, and the Metropolitan area of Wellington is about 1,400 km^2!

For the chemist, benefits are clearly seen with recent work with gold, which is an excellent catalyst at the nanoscale but fairly inert as larger particles. Companies such as Johnson Matthey have realised that car catalysts are much more effective at the nanoscale, because of the massive increase in surface area.

Products

Actually, nanotechnologies are not something new, they have been with us all of our lives. As soon as we pop out the womb we have to rely on our own nanofluid; blood is a nanofluid. The next thing that happens is that we get a drink of milk; milk contains nanoparticulate casein. As we get older we are drinking from a bottle of beer; the plastic PET bottles incorporate nanotechnology to keep the flavour in and prevent UV light from degrading the product. Whisky contains nanoparticles; it may appear as a clear product but the nanoparticles are actually there. If you used a hair drier this morning, you would have produced tungsten nanoparticles, which are given off as the heating element warms up. So some nanotechnology-based products are natural and others have been deliberately engineered, often to enable nanotechnologies to provide beneficial properties.

Lobby groups in some countries appear to be anti-science and against progress. Recently we have seen their attention directed to GM foods; and they predicted that the Hadron Collider at CERN on the Swiss/French border would see us all disappearing into a black hole. Stem cells have also been in the limelight, and nanotechnologies have had more attention than they deserve. Nanotechnologies cut across all market sectors: it is difficult to define what is meant by nanotechnologies since they encompass ultrafine particles, emulsions, and thin films, and are both natural and produced by us. Some of the lobby groups are even asking for a moratorium on anything *nano*. Toxicologists are also making hay while the sun shines with a plethora of studies looking especially at what are being called engineered nanoparticles. However, at an international conference (Nanotoxicology 2010) held in Edinburgh, the main speaker, Prof. Gunter Oberdörster (University of Rochester), argued that most studies are of limited value to a risk assessment as they have been performed at unrealistic exposure doses. Unlike chemists, lobby groups and few toxicologists seem to have an understanding of risk assessment. A chemical as simple as hydrogen peroxide can serve as a mouthwash but also as a rocket fuel!

Major technologies seem to come along in waves, with solid state physics in the fifties leading on to microelectronics that provide the electronic devices we now accept as commonplace. In the seventies, biological science produced biotechnology which has had such an impact on healthcare, but now we are seeing the start of nanoscience and nanotechnology developing new functional materials which are listed as being used in over 1,000 new products in many sectors (Fig. 1).[2] As with most new developments, it is the high profit areas that are the first to accept and promote new products, but already nanotechnology is encroaching into most industry sectors. The potential markets for nanotechnology-based products have been estimated as $US1 trillion by 2015 in a much quoted report from the US National Science Foundation in 2000.

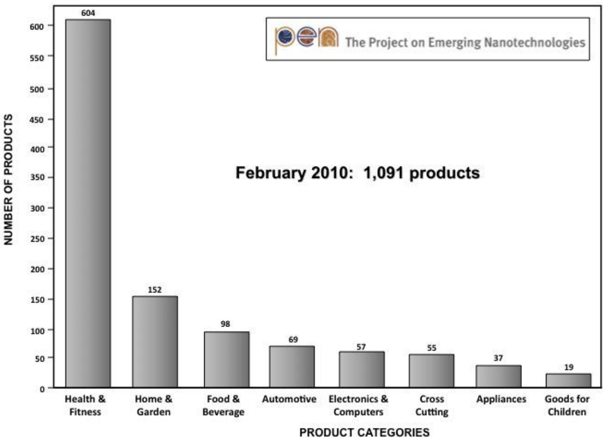
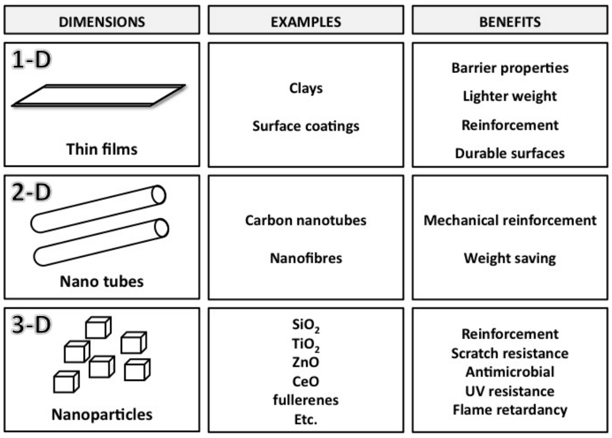


Fig. 1. Nanotechnology-based consumer products inventory

Already it is clear that the benefits provided by nanotechnology-based products far outweigh any potential problems. The nano-components being used come in different forms, thin films, nanotubes, and nano-particles, as illustrated in Fig. 2.



DIMENSIONS	EXAMPLES	BENEFITS
1-D Thin films	Clays Surface coatings	Barrier properties Lighter weight Reinforcement Durable surfaces
2-D Nano tubes	Carbon nanotubes Nanofibres	Mechanical reinforcement Weight saving
3-D Nanoparticles	SiO_2 TiO_2 ZnO CeO fullerenes Etc.	Reinforcement Scratch resistance Antimicrobial UV resistance Flame retardancy

Fig.2. Types of nanotechnologies

Sports and Leisure

The sports and leisure sector often leads with the introduction of new products, because it can cope with higher costs through greater margins. For example, Formula One motor sport pioneers new developments before we see them on our own cars. Plastic panels have replaced metal panels in most cars and today the polymer is *reinforced* with nano-sized platelets, thereby providing reduced weight and improved strength. These platelets come from bentonite clays; the same clays that are used for thickening water-based non-drip paints. Each 8 μm grain of clay contains over a million platelets and, a bit like reinforcing concrete, the platelets strengthen the polymer when incorporated at around 15%. However, the platelets have to be well dispersed to give the increased strength, so the inorganic clay has to be compatibilized using quaternary ammonium salts to encourage it to be mixed into the polymer.

Wilson Sports have used clay platelets in tennis balls. At Wimbledon, the cry of *new balls please* echoes across the courts, because the players strike the ball so hard nowadays, forcing the air out after only a few games. The new Wilson balls have clay platelets dispersed in the butyl rubber, and the millions of tiny platelets provide a very tortuous route for any gas molecules trying to escape. The balls therefore hold their pressure for far longer than conventional balls.

There are even better developments for weight saving on the horizon, by using carbon nanotubes (CNTs) that are minute whiskers with a diameter of about 1 nm. These CNTs have only been identified in the last 20 years but they are formed when just about anything is burned. If you burned your toast this morning, you produced about 10^{-12} kg of CNTs! However, the chemists have come up with a more efficient route to their manufacture, and they are beginning to find application in several sports and leisure applications.

Roger Federer and the Williams ladies use Wilson racquets which contain about 3% CNTs in the plastic material used for the racquets. Rafa Nadal now uses Babolat racquets which have also gone *nano*. Floyd Landis won the Tour de France a few years ago, being the first to use a bike which had a CNT-plastic frame. The SOLO crossover alternative energy car from California-based Velozzi has CNTs for all its body panels, and achieves 100 miles per gallon.

There is an additional property that CNTs provide which is also being seen in new products. This makes use of the ability of CNTs to conduct electricity and also heat. Metal fuel lines in cars are being replaced by CNT-plastic tubes, and the fuel pumps on the Audi A4 and A5 models are no longer metal but are CNT-plastics.

As will be discussed later, there have been suggestions that CNTs could have toxicity issues, but more recent developments are indicating that graphene, single tiny sheets of graphite, have similar properties to CNT; potentially at much reduced cost. The 2010 Nobel Prize for physics was awarded to Andre Geim and Konstantin Novoselov, at the University of Manchester, for their pioneering work on graphene.

Textiles

Some of the earliest applications for nanotechnology have been in the field of textiles, overcoming the problems of coating fabrics by conventional means, which make them feel stiff and uncomfortable. A US-based company, Nano-Tex, is leading in this area, with nanotechnology coatings being used in many leading suppliers' favourite brands. Nano-Tex uses this revolutionary technology to enhance fabrics at a molecular level; producing material that resists spills, repels stains, wicks away moisture, and resists static, without sacrificing comfort. These coatings are now finding application not just in apparel, but in home textiles, and commercial interiors, providing fabrics that retain their natural softness and which are more durable. As well as shirts and trousers, it is now possible to buy curtains, carpets and upholstery that have been treated with nano-scale surface materials.

For stain resistance, the fibres are coated with a thin layer of a super hydrophobic material that mimics the water repellancy of lotus leaves, which have quite a bumpy surface when viewed at close to nano-scale. A drop of water landing on the leaf runs off because of a cushion of air that is under the droplet; a bit like how a hovercraft moves along. As it runs off, it gathers dirt and provides a cleaner surface. Nano-Tex's *Coolest Comfort* provides breakthrough moisture wicking, where, fundamentally, each fibre has been transformed by nanotechnology to give a fabric which balances body temperature, and allows it to breathe. The next development from Nano-Tex is likely to be cotton that is made to permanently feel like silk, again based on very thin nanotechnology coatings.

In addition, it is also possible to purchase socks and under-garments that are odour resistant. For these, the fibres either have had silver nanoparticles incorporated into them, or they have been coated with silver nanoparticles. Silver has a long history of use as an antimicrobial - the Assyrians around 2,500 BC carried their water in silver containers, and even today the Bedouins put a silver coin in their leather water carriers knowing that the water will stay fresh for longer. At nanoparticulate scale, silver is an excellent anti-microbial and, more recently, it has been found that nanoparticulate copper also offers anti-microbial properties.

Marks and Spencer have been carrying out a trial in the UK with pyjamas impregnated with these antimicrobial properties, which are claimed to be clinically proven to reduce the risk of MRSA (Methicillin-resistant *Staphylococcus aureus* that is also called multidrug-resistant *Staphylococcus aureus*), the bacterium responsible for several difficult-to-treat infections in humans. Rohan market silver-impregnated underpants that are antimicrobial, and more recently the US space programme has employed similar technology. Koichi Wakata, a Japanese astronaut has recently returned from a trip on board the shuttle Endeavour having visited the International Space Station. On his return, he admitted that he had been wearing the same pair of underpants for a month. The underpants are part of a trial for when astronauts visit Mars. They are antistatic, flame retardant, odour-eating, antimicrobial, and water absorbent, and appeared to stand up well during the 57 million mile journey. The clothing was designed by the Japanese Space Agency and is known as J-Wear. It is made of cotton and polyester but with what is described as a futuristic silver coating that gives it the special properties. There are also socks, T-shirts, trousers and leggings in the range.

Food and Drink

The Helmut Kaiser Consultancy[3] estimated that worldwide sales of nanotechnology in the food sector would rise to over $US20 billion by 2010, with nanotechnology products for food and beverage packaging having reached $US860 million in 2004.

There are several areas where different nanotechnologies will have a marked impact in the food area:

- Packaging, *e.g.* lighter weight; novel barrier materials; sensor technology for food traceability and shelf-life
- Food safety, *e.g.* antimicrobials; rapid food spoilage detection, analysis of other contaminants
- Functional coatings, *e.g.* antimicrobial surfaces; easy clean surfaces, food processing equipment
- Nutrition, *e.g.* enhanced bioavailablity of nutrients and vitamins; controlled release of fat from products
- Texture, taste and health improvement, *e.g.* lower fat, salt or sugar products; *cleaner* labels by improved ingredient functionality.

Alcoa have been active in promoting lighter weight packaging materials, with clay-based nanocomposite materials, but they also provide barrier properties to retain the flavour of foodstuffs and prevent the ingression of oxygen, water, and unwanted odours that are detrimental to the flavours. Bayer have developed a new plastic film, Durethan® KU 2-2601, based on polyamide and clay platelets that are impervious to gases and provide enhanced gloss to the film.[4] They say that these new films will *make sure that the smell of Swiss cheese will not mix with that of salami in the refrigerator at the grocery store*. There are also major opportunities for nanotechnologies in *track and trace* messaging on packaging which are already under development.

Food safety is a major issue in most countries, and with silver being such an excellent antimicrobial, it is being used in a variety of plastics for refrigerators, food packaging and many other food contact areas. FresherLonger™ food storage containers, infused with silver nanoparticles, give clear examples of how the storage time for foods can be extended[5] with 24 hour growth of bacteria being reduced by over 98% compared with conventional containers.

Not surprisingly, all this new product activity has attracted the attention of lobbying groups, including activists who have demanded that the Environmental Protection Agency in the States stops the sale of over 200 nanosilver products[6] that they say are potentially dangerous. However, FERA (previously known as the Central Science Laboratory) has carried out leaching tests for the UK's Department of Environment, Food and Rural Affairs (DEFRA) to determine whether the clays or silver nanoparticles can escape from the polymers into which they have been dispersed. Even under extreme damage conditions, only background traces of silver were detected and no clay material was extracted, which suggests that that there is no need for concern if the nanomaterials are locked into plastics.

The size of particles hitting the tongue affects the taste and texture, as well as the bioavailability of foodstuffs. By controlling the size in foods these properties can be altered to the benefit of the consumer. There are some who are concerned about the addition of nano particles to foods, but it is not widely recognised that many natural and processed foods are already structured at the nanoscale as well as having a proportion of nano particles present. Salt also has been shown to have a faster taste perception when the size is reduced, and one of the projects of Eminate,[7] a wholly owned subsidiary of the University of Nottingham, is the production of ultrafine salt, which enables certain products to be formulated with less salt because of the greater taste sensation from much smaller salt granules.

Transport

A sugar cube has around one in ten million atoms on its surface whereas a one nanometre cube of sugar has 80% of its atoms on the surface. The huge surface area achievable at the nanoscale is a feature of car catalyst developments. As well as the weight saving and increased modulus provided for plastics by clays and carbon nanotubes, metal engine covers have been replaced by polymeric materials. The Mitsubishi Shogun model was one of the early examples using silica nanoparticle-based plastics to repel the heat which would cause a conventional plastic to melt.

If a moth had not evolved with anti-reflective eyes, a bat or owl would be able to pick it off quite easily. The Audi TT Roadster has copied the moths' eyes anti-reflective nanoscale patterns for its instrument panel so that it can be seen clearly in sunny conditions.

Bowling balls were the first objects to have anti-scratch surfaces achieved through a final lacquer containing alumina nanoparticles. This technology is now used for the final coating on Mercedes cars.

A spin out from Oxford University, Oxonica, has developed cerium oxide nanoparticles which are used at part per million levels in diesel fuel for cars. They catalyze the burn of the fuel, giving around 15% more miles per gallon, and because of a more efficient burn, there are less exhaust fumes. Unfortunately, the company ran into patent problems.

The Audi Le Mans Quattro (R8 model) has shock absorbers based on magnetic nanoparticles suspended in a fluid. Although there are many new applications in the automotive sector, the largest use of nanoparticles has been in tyres in the form of carbon black nanoparticles. This has been used for nearly a hundred years and currently the market size is in excess of 6 million tonnes per annum.

In the aerospace sector, the potential for weight saving is enormous. The new Airbus A380 is made up of around 17% composite materials based on carbon fibres, whereas the Boeing 787 Dreamliner, with composite wings, comprises about 50% composites. CNTs offer even more weight saving, so we can expect the next generation aircraft to be even lighter in weight (Fig. 3). Another feature of the Dreamliner is that it has special silver nanofilters which, in flight, maintain high quality air, killing 99.7% of influenza viruses.

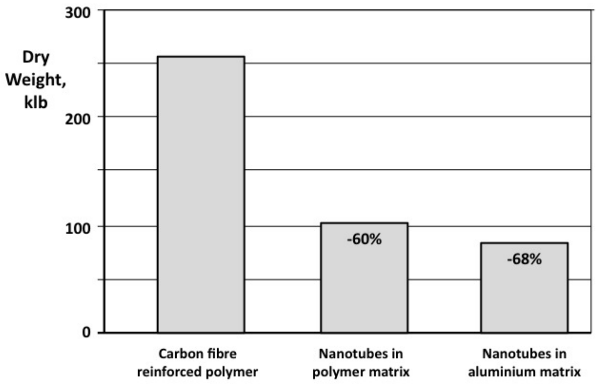


Fig. 3. Weight reduction with carbon nanotubes

Super hydrophobic surfaces, like those used for textiles, have the potential to be used on aircraft to repel moisture that should mean that de-icing planes will become something of the past. Other nano-thick functional coatings have been designed to be much harder wearing ones, and others provide stealth coatings for military aircraft. In the US, the Department of the Air Force are researching biomimetic coatings; trying to copy the pearl layers of an oyster shell which manages to produce these ceramics without the use of very high temperatures.

Construction

The construction sector has not adopted nanotechnology as rapidly as it might, but there are clear opportunities in weight saving and functional surfaces. There is also some work going on to reduce the weight of concrete by forming nanostructured material, and other nanostructured products are being developed to insulate buildings (as well as cars and planes) from noise and heat. However, one application that has seen good growth is the use of a 35 nm thick layer of titanium dioxide on glass. Pilkington Glass has developed this technology over the last 20 years, with the coating going onto the outside of the glass during the float glass process. When photons from the sun hit the glass the titanium dioxide catalyses the breakdown of the dirt on the pane, and the next time it rains the residue is washed off (Fig. 4). Very applicable when it comes to cleaning the windows in a glass skyscraper! Using the same technology, an EU-funded project has developed coatings of nanoparticulate titanium dioxide for buildings so that environmental pollution, in the form of nitrogen and sulfur oxides, is broken down. The first building to apply this technology was the new Jubilee Church in Rome; one is left wondering whether this could help solve the pollution problems in many big cities.

There is considerable progress being made with photovoltaic cells. The conventional use of silicon, which has become increasingly expensive, is also the subject of nanotechnology-based research. Thin nano-films of silicon, and other materials, such as cadmium telluride and copper indium gallium selenide, are being developed, but there is also attention on what nature manages to do. Plants grow, by using chlorophyll catalysts to convert water and carbon dioxide into their energy contributor and oxygen, and solar cells are now being developed that try to copy that process. These have been developed by Prof. Michael Grätzel, (Ecole Polytechnique de Lausanne) and use dye catalysts coated on nanoparticles to provide a large surface area to capture photons. Other work in the field of photovoltaics is examining organic polymers.

Fig. 4. Nano coated glass-fronted building.

Household Products

Although numerous household products have always had nano-features, there is now much more effort being placed in using the properties that nanotechnology brings. Just about anything that has been ground down will have a proportion of nanoparticles in it. Even the miller in the Middle Ages knew that when he was grinding his flour, he would get a varied particle size distribution. The larger lumps would be no good for making decent bread, but he would certainly have been producing some nanoparticulate material!

Hydroxyapatite nanoparticles are being used in many toothpaste applications. Using this natural material builds up minute cracks in the enamel which prevent people eating very cold ice cream. Many of the more expensive sunscreen and anti-ageing products contain nanoparticulate titanium dioxide which is much more effective as a barrier against harmful UV light than the conventional micro particles and does not appear white, like Aussie cricketers' noses, when rubbed on the skin. Despite lobby groups saying that these nanoparticles are harmful, tests have not shown any indication that they are harmful, even on damaged skin, probably because the particles tend to flocculate, but still retain a large, effective surface area. Many emulsion-based products are down at the nanoscale. Some of the hair shampoos that also contain conditioners are designed so that the conditioner is released when the hair is finally rinsed.

Nanotechnology-based products are particularly diverse in the home. There has been an EU project called PolyCond, which has produced a prototype electrical plug that has replaced brass with CNT-plastic for the pins. This gives 82% weight saving at one fifth the cost of a brass pin, and gives an overall saving of 40% for the finished plug. Drill bits are coated with thin nano-layers so that they last longer, and similarly some Wilkinson Sword razors have the cutting blades coated with nano-layers of diamond. There are products for waterproofing stoneware so that it is not eroded; the Firth of Forth Railway Bridge in Scotland, the first steel bridge in the world, was painted in 1890 and since then it has been painted continuously ever since. At last they will not have to paint it again! For the past 25 years the painters have been using nano-based paints that are much more effective at controlling corrosion.

Ten years ago, if you impatiently removed paper from your computer printer, you finished up with ink all over your fingers. This does not happen now, because some of the inks are nanoparticulate and the paper has nanoparticles on it. The increase in surface area means that the solvents evaporate much more rapidly and give instant drying.

Healthcare

Healthcare is where nanotechnology will probably make the most impact, with the development of novel drug delivery systems specifically targeting the location of the problem. At the nanoscale, particles are more soluble, so there are companies looking at using nanoparticulate pharmaceuticals at lower than conventional doses, thereby having fewer side effects. At the nanoscale things happen more rapidly and more sensitively, and already we are beginning to see nanosensors that are aimed at detecting the disease before it has a hold on the body. Some of these sensors are able to detect just a few molecules; not dissimilar to a dog being able to smell a pheasant 100 yards away.

Nanoparticulate imaging products are also being used to give finer definition of where problems might be occurring. Flocculating nanoparticles, which exhibit colour depending on their ability to diffract light, can change colour, and this type of indicator is used in pregnancy test kits for example. The whole healthcare field is likely to see major changes - certainly a sector to watch.

Energy and the Environment

Undoubtedly, the energy sector will benefit from nanotechnologies through developments that have already been discussed in this article. In addition to the nanotechnology research on photovoltaics, there is much research on new batteries to provide longer life, easier recharging, and also storage of energy.[8] Lighter weight blades for wind turbines are being promoted with CNT technology by Bayer. The larger the blade diameter, the more power is generated (Fig. 5), but large heavy blades are either slow to move in the wind or need electricity to get them started, and occasionally break under the strain. Nanotechnology offers stronger and lighter weight blades.

Nanotechnology will surely have a major effect on the environment. More durable materials and surfaces will produce longer life products - and we are currently only seeing the tip of the iceberg in terms of exciting developments.

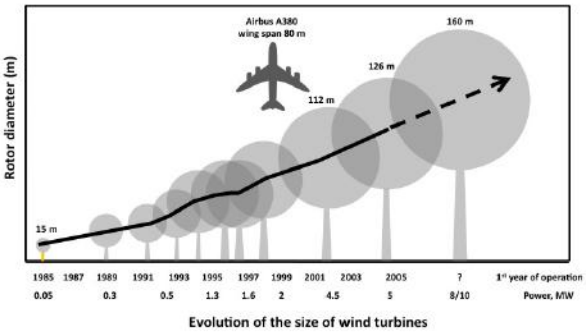


Fig. 5. Relationship between power output and wind turbine diameter

As well as the airborne pollution, previously mentioned, there is also the potential to clean up ground pollution. Work is being carried out with suspended iron nanoparticles being pumped into contaminated ground where they can catalyse the breakdown of a variety of pollutants. They are then sucked out of the ground once they have been effective.

Societal Issues

There has been considerable hype associated with nanotechnology, from industrialists and academics wanting more government funding, from lobby groups needing more membership subscriptions, and from toxicologists who seek more funding for toxicity testing. In reality, we are seeing more anti-science being reported in the press, often nowadays directed at nanotechnology. In a world recession, lobby groups and the media should show more responsibility and base their thoughts more on fact. A report from Cientifica stated: *For policy makers who are not scientific experts (and few are) speculative concerns are given equal weighting with scientific results*. An interesting report from Oxford Economics in the UK said that for every 5 GBP earned in the UK 1 GBP came from chemists, and in a population of 61 million, 5.1 million jobs are dependent on chemists. Clearly, we need more backing for technology developments, starting with politicians; that is what provides growth.

In some countries, however, nanotechnology is not regarded as a problem and *nano* is added to products as a marketing tool to indicate that it is something innovative and exciting. You can purchase Nano-water in China, which has nothing nano about it; in Thailand you can purchase Nano Breast Serum, which if you rub it in the right places stops your breasts sagging. The Nano iPod and the Tata Nano car may have some circuitry down at the nanoscale, but there is nothing really nano about them, other than them being a bit small. However, in the US, many companies that were proud to add *nano* into their name when they were launched are now changing their names just to avoid unwanted hassle.

An issue is that nanotechnologies are particularly broad and cut across all market sectors, and there is no good definition describing what it is or even which parts of it might potentially be a problem. The recent definition of a nanomaterial by the OECD describes it as: *Nanomaterials intentionally produced to have specific properties or specific composition, a size range typically between 1 nm and 100 nm and material which is either a nano-object,* i.e. *that is confined in one, two, or three dimensions at the nanoscale, or is nanostructured,* i.e. *having an internal or surface structure at the nanoscale.*

The very act of boiling an egg means that it is a nanomaterial since boiling it produces a nanostructured material! Furthermore, a report[9] produced by OECD and Allianz, states that in a normal room there are 10,000 nanoparticles in a single square centimetre, and this increases dramatically as one goes into a forest or into a street. This means that with every breath, you are inhaling a cocktail of around 5 million nanoparticles. Much of the work on formulating nanoparticles into products is all about stopping them flocculating, so that might be happening in the atmosphere. However, nanoparticulate atmospheric pollution causes the colours of sunsets, which is mostly the result of volcanic action; after Krakatoa exploded in 1883, there were decades of bright red sunsets.

There is also great potential for nanotechnologies to be having an impact on the developing world, particularly through healthcare, solar energy, and water purification. The latter has not been mentioned previously, but there are now nano-membranes which will remove bacteria and viruses, and other contaminants, from polluted water.

For the chemist, nanotechnologies present opportunities in cleaner processing, improved formulations, and many new product opportunities. As a White House press release said:[10] *Nanotechnology is the next industrial revolution.*

References

1. First published in the Feb. 1960 issue of Caltech's Engineering and Science, but now made available with their permission on the web at http://www.zyvex.com/nanotech/feynman.html.
2. The Project on Emerging Technologies, Woodrow Wilson International Center for Scholars, Consumer Products Inventory at http://www.nanotechproject.org/inventories/consumer.
3. Helmut Kaiser Consultancy, *Nanotechnology in Food and Food Processing Industry Worldwide 2006-2010-2015*, http://www.hkc22.com/Nanofood.html.
4. Bayer presentation: *Securely wrapped – nanoparticles make Durethan® films airtight and glossy*, http://www.research.bayer.com/edition_15/15_polyamides.pdfx.
5. Examples of FreshLonger™ food storage containers, http://mrsec.wisc.edu/Edetc/SlideShow/slides/nanoparticles/silver2006.html.
6. International Center for Technology Assessment, May 2008, http://www.icta.org/detail/news.cfm?news_id=206&id=218.
7. Eminate, http://www.eminate.co.uk/eminate/.
8. Smith, A.; Tolfree, D. *Phys. World*, Oct. **2009**, 40-45.
9. Allianz and OECD, *Opportunities and Risks of Nanotechnologies*, 2004, http://www.oecd.org/dataoecd/32/1/44108334.pdf.
10. White House Office of the Press Secretary, *National Nanotechnology Initiative*, January 2000, http://clinton4.nara.gov/WH/New/html/20000121_4.html.

Seeing Atoms: The Rise and Rise of Crystallography in Chemistry and Biology

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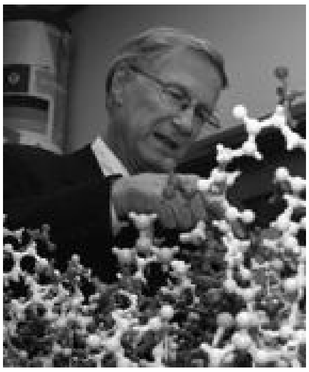
About the Author

It can be said, in all fairness, that Ted Baker established structural biology in New Zealand with his pioneering work at Massey University on the proteins actinidin and lactoferrin. His work was recognized by the award of the 2006 RSNZ Rutherford Medal as well as an International Research Scholar award from the Howard Hughes Medical Institute and election as President of the International Union of Crystallography (1996-99). His research group numbers close to 40 and focuses on the analysis of protein structure and function, X-ray crystallography, structural genomics, molecular biology, bioinformatics and structure-based drug design.



Introduction

The award of the 2009 Nobel Prize for Chemistry to Ada Yonath, Thomas Steitz and Venkatraman Ramakrishnan for their pioneering work in determining the structure of the ribosome in atomic detail[1] was a tribute to the extraordinary personal achievements of the three scientists themselves. It was also a tribute to X-ray crystallography as an approach to understanding the chemistry of life. The ribosome is a huge complex of proteins and nucleic acids, which orchestrates the reading of a code from messenger RNA (mRNA), recruitment of the correct amino acids in the right sequence and synthesis of the polypeptide chain. How was this made possible? The size of the task is staggering when one considers that the smallest and simplest of ribosomes, from bacteria, still have molecular weights in excess of 2.5 million Da (more than 150,000 non-hydrogen atoms). Compare this with my own PhD studies in the 1960s in which solving the structure of a 30-atom copper complex was a year's work!

The past fifteen years have seen no fewer than four Nobel Prizes go to scientists who used X-ray crystallography to unlock the mysteries of biology in terms of their underlying structural chemistry: 1997 John Walker and the ATP synthase; 2003 Roderick MacKinnon and the potassium channel; 2006 Roger Kornberg and the eukaryotic transcription apparatus; and then the ribosome in 2009. How has this come about? Coincidentally, it is almost exactly 100 years since Lawrence Bragg's brilliant insight opened the way to the use of X-ray crystallography as a general method for determining the three-dimensional structures of molecules. With this in mind, the historical development of crystallography will be traced before focusing on its importance in biology today and what the future may hold.

Crystallography: Seeing Atoms

X-ray crystallography grew out of the extraordinary flowering of physics at the opening of the 20th century. The discovery of X-rays in 1895 was followed by the discovery of X-ray diffraction by Max von Laue in 1912 and the almost immediate recognition by 22-year-old Lawrence Bragg, just beginning his PhD, that by looking at the phenomenon in a different way one could use it to determine the atomic structures of crystals. His insight was to think in terms of the reflection of X-ray waves from planes of atoms drawn through a crystal (the famous *Bragg's Law*). The first structures seem very simple to us today (NaCl, CsCl, *etc*.) but in fact they were quite profound; at that time it was not known whether sodium chloride *molecules* existed. Linus Pauling was to develop his extraordinarily influential ideas of chemical bonding from the stereochemistries and interatomic distances he found in such crystal structures. Lawrence Bragg described the excitement and opportunities of this era as being *like looking for gold and finding nuggets lying around everywhere* (he was born in Australia, after all!). His father William Bragg, with whom he shared the Nobel Prize in 1915, wrote a book entitled *On the Nature of Things* in which he said *by this means one can see atoms in crystals*.

This concept of seeing atoms is what has driven generations of crystallographers to explore the natural world. It inspired my postdoctoral mentor, Dorothy Hodgkin, as a teenager; on reading it, she is said to have gone immediately to her mother to say: *Now I know what I want to do in life*. There is, perhaps, no better description of the possibilities that were opened up than that given in her 1964 Nobel Prize address of her time with J. D. Bernal (another of the great figures in crystallography) as a young PhD student in Cambridge:

> *…our scientific world ceased to know any boundaries. ..... we explored the crystallography of a wide range of natural products, the structure of liquids and particularly water, Rochelle salt, isomorphous replacement and phase determination, metal crystals and pepsin crystals, and speculated about muscle contraction.*

In 1934 she and Bernal took the first X-ray diffraction picture from a protein crystal (pepsin) and the wonderful array of spots led them to say in a short report in *Nature*[2] that *It is clear that we [now] have the means of... arriving at far more detailed conclusions about protein structure than previous physical or chemical methods have been able to give*. This prescient statement, more than 20 years before the first protein structure would be solved, and at a time when the chemical make-up of proteins was still not known, opened the way to today's discoveries.

Crystallography in Chemistry

The importance of crystallography for chemistry was immediately obvious although it took many years to be fully realized. Interestingly, key figures such as William Bragg and Bernal were encouraging mentors of women scientists, beginning a long tradition of women crystallographers that continues today. Encouraged by Bragg, Kathleen Lonsdale (née Yardley) was one of the first. Using crystals of hexamethylbenzene given to her by the eminent chemist C. K. Ingold, she provided the first experimental proof that the benzene ring was flat, with all C-C bond lengths and angles equal.[3] Ingold said of her 1929 published account of the benzene structure, *[O]ne paper like this brings more certainty into organic chemistry than generations of activity by us professionals*. In the 1930s, Dorothy Hodgkin began her pioneering studies of natural products, driven by the conviction that chemistry must embrace X-ray crystallography to bring certainty and precision. At that time, the standard approach to determining complex organic structures involved degradation into small fragments, identification of the fragments, and the synthesis of the target molecule in the laboratory. Dorothy's revolutionary analyses of molecules such as cholesterol, penicillin and vitamin B_{12} showed the power of crystallography to reveal entirely novel chemical structures with close to absolute certainty, for example, the β-lactam ring in penicillin[4] (Fig. 1) and the completely unexpected cobalt-carbon bond in the B_{12} coenzyme. This latter discovery, presented quite matter-of-factly in a short paper in *Nature*,[5] could truly be said to have foreshadowed the huge field of organometallic chemistry.

Structural analysis by crystallography involves millions of repetitive calculations carried out on thousands of X-ray reflections (the diffraction data), and the advent of computers truly can be said to have transformed its potential. For her work on B_{12}, by far the most complex structure to have been attempted at that time, Dorothy Hodgkin realized that all the three-dimensional data would have to be used. A fascinating account of her collaboration with UCLA crystallographer Ken Trueblood tells of how electron density maps would be calculated at UCLA, on one of the first computers to become available at an academic institution, the maps interpreted in terms of atomic structure by Dorothy in Oxford, and the new model returned to UCLA for the next round of calculations.[6] The IBM 1620 computers that were the first to be installed in NZ, at Canterbury and Auckland Universities in 1963, were pitifully slow and horrendously expensive; with 20K of memory they were a million times slower than today's PC, and their cost in today's currency equates to more than $1 M. Nevertheless, they began a revolution. With the development in the 1950s of direct methods of phasing X-ray data, which led to Nobel Prizes for Jerome Karle and Herbert Hauptmann in 1985, crystallography soon achieved its potential as an almost-routine tool in chemistry; crystal structures of small- to moderate-sized molecules literally can be determined within minutes of collecting the data. Importantly, however, it also has another role as a key research tool for creative chemists developing areas such as crystal engineering of metal-organic framework structures. There is great potential from these studies for developing entirely novel materials as solutions for such pressing problems as the storage of CO_2 and other gases.

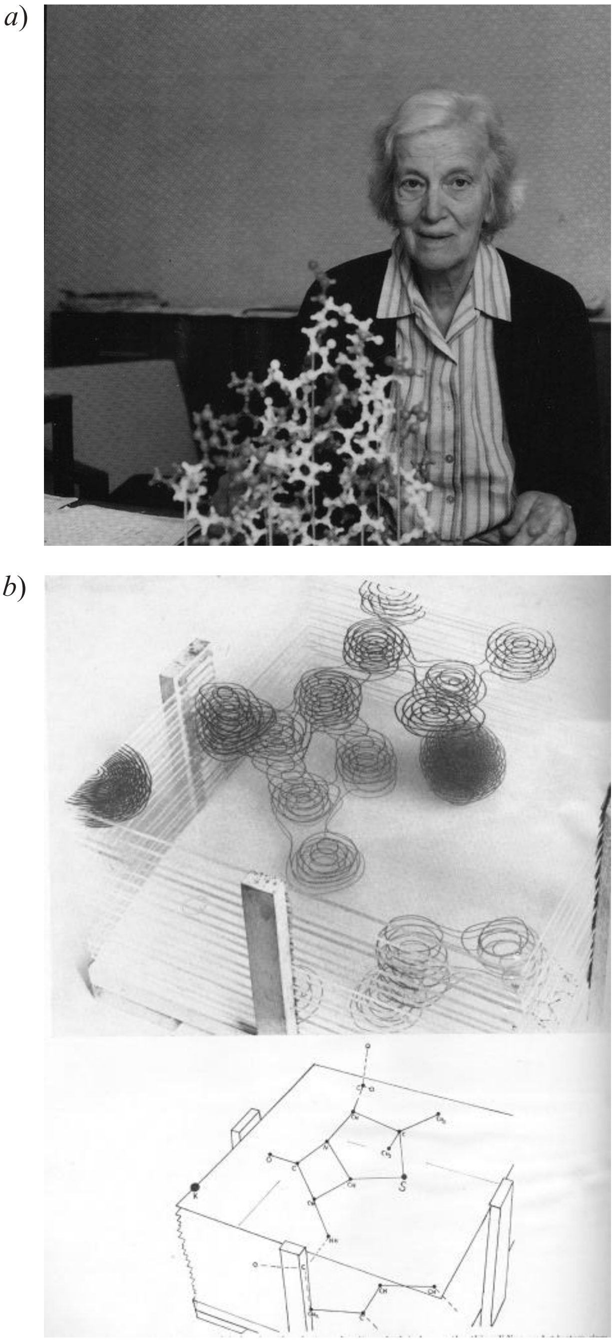


Fig. 1. (a) Dorothy Hodgkin, shown with a model of the protein hormone insulin; (b) the crystallographic solution of the structure of penicillin, showing a portion of the electron density map (upper) and its interpretation in terms of the four-membered β-lactam ring (lower). Reprinted from ref. 4 with permission.

Biological Crystallography: Its Birth and Growth

The full flowering of biological crystallography began in the 1960s, heralded by the 1964 Nobel Prizes in Medicine and Chemistry. The awards to Crick, Watson and Wilkins for the structure of DNA and to Kendrew and Perutz for the first protein structures (myoglobin and haemoglobin) both depended on X-ray diffraction: in the first case, fibre diffraction;[7] and in the second, single-crystal X-ray analysis.[8] It can be said fairly that without crystallography the molecular biology of today could not exist.[9]

The spectacular growth of this field is illustrated by a plot of the numbers of protein structures deposited year by year in the Protein Data Bank (PDB)[10] (Fig. 2). In the 1960s and 1970s, protein crystallography was a heroic undertaking requiring years of X-ray data collection, preparation of heavy-atom derivatives and manual model building into hand-drawn electron density maps. Today, growth is exponential with almost 10,000 new protein structures determined in 2009 and nearly 70,000 now deposited in the PDB. These structures are not only more numerous, but also of higher quality and far more complex – some of them truly mind-boggling – with an ability to illuminate biology in an ever more powerful way.

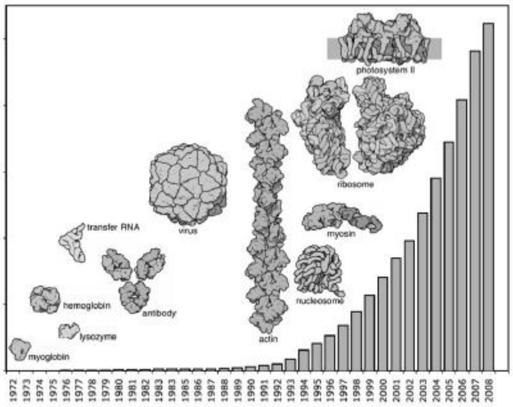


Fig. 2. Growth in the number and complexity of structures in the Protein Data Bank (courtesy of the RCSB Protein Data Bank – see ref 10).

What has driven this growth, and what developments have made it possible? Firstly, it is the understanding of biological mechanisms that 3D structure brings. A living cell is extremely crowded, with thousands of different proteins and other molecules jostling for space (the total protein concentration is estimated at about 30 g/L). In this environment, specificity is everything; a protein must perform its own task, efficiently and without error, and the 3D structure of a protein is critical, defining its chemistry and the spatial constraints on its substrates. Secondly, structural knowledge provides new opportunities for applications, in areas such as structure-based drug design, or in the development of new tools in biotechnology. This is now starting to extend into the design of biologically-based materials as we understand more about the structural make-up of natural fibres such as spider silk and muscle.

Driven by the demand for structural information, a series of technical developments have transformed the field and these include:

- *Advances in molecular biology*. The development of recombinant DNA technologies and the availability of whole genome sequences enables a researcher to take any gene of choice, insert it into a suitable laboratory host cell, *e.g.* the bacterium *E. coli* as a kind of cellular test tube, and then express the protein that is encoded by that gene. This makes rare proteins available in the milligram amounts necessary for structural studies.
- *Synchrotrons*. Providing extremely intense, narrow beams of X-rays, these allow a complete X-ray data set (tens of thousands of reflections) to be obtained in less than an hour, from crystals as small as a few microns in size. Moreover, the wavelength (energy) of the X-rays is tuneable, making it possible to optimize anomalous scattering effects that open the way to powerful methods of phase determination. The X-rays can be tuned to the absorption edge of a metal atom in a protein. Alternatively, using molecular biology, selenomethionine can be substituted for the amino acid methionine in the target protein, and the anomalous scattering properties of the Se atoms used for phase determination.
- *New crystallization methods*. Micro-methods and robotics have drastically decreased the amounts of protein required and at the same time increased success levels. Using nanolitre amounts (typically 100 nL protein droplets) dispensed by a liquid handling robot, as many as 500 crystallization experiments, exploring different pH, buffers, precipitants, can be set up in a couple of hours, using only 0.5 mg of protein in total.
- *Cryo-crystallography*. Protein crystals are soft, fragile and typically contain 40-60% solvent. The ability to freeze them at liquid nitrogen temperatures, with the aid of cryo-protectants, gives protection against radiation damage during X-ray data collection and means that complete data sets can be obtained from a single crystal.
- *Computational power*. Vastly increased computational power and graphics capabilities have facilitated automated structure solution and model building methods. In favourable cases, it is now possible for moderate-sized proteins, to solve the structure and build a complete model into the electron density literally within 24 hours of completing the data collection. Compare this with the laborious model building using wire model components that was typical of protein crystallography in the 1970s (Fig. 3).

Fig. 3. The author building a wire model for actinidin, the first protein structure to be determined in New Zealand (*ca.* 1977) – see ref 11.

Revealing Biological Function: The Big, the Bold and the Beautiful

There may perhaps be no better example of the ability of biological structures to transform understanding than the so-called MHC molecules that are expressed on the surface of human cells. MHC stands for *Major Histocompatibility Complex*; these molecules were first brought to light by their involvement in tissue rejection when organ transplants began to be performed, but what they actually did was a mystery. The first MHC crystal structure, the class 1 MHC molecule HLA-A2, solved by Pamela Bjorkman in Don Wiley's Harvard laboratory in 1987, fundamentally changed immunology. It showed, at the top of the molecule, a groove between two α-helices (Fig. 4a). Strikingly, this groove contained *extra density*, attributed to peptides bound in the groove.[12] This immediately led to the hypothesis, now a central paradigm in immunology, that when a cell is infected, the MHC molecules display peptides taken from the infectious agent and display them at the cell surface as a signal to other immune cells (*helper* and *killer* T cells) that an immune response is needed. One structure changed immunology forever!

The size and complexity of biological structures is a major factor in their ability to catalyze reactions that would not normally occur under physiological conditions (aqueous solution, near-neutral pH), and to do so with great specificity and control. This is true of the ribosome, the huge RNA-protein complex (more than 50 proteins and three large RNA molecules) that synthesizes polypeptides (Fig. 4b). If amino acids are mixed in solution they do not spontaneously form polypeptides because peptide bond formation requires that the amino group be unprotonated in order to attack the carboxyl carbon. This is orchestrated within the large (50S) ribosome subunit where a perfectly-placed 2'-OH from an adenine residue of RNA shuttles a proton from the attacking amino group to the leaving group as the peptide bond is formed.[13] Selection of the correct transfer-RNA (tRNA), which carries the next amino acid to be added to the growing polypeptide chain, is the job of the smaller (30S) ribosome subunit, which decodes the messenger RNA, selects the correct tRNA and passes it to the peptide synthesis site.[14] The process is highly dynamic, and the complete ribosome assembly is a perfect example of a tightly-orchestrated machine.[15]

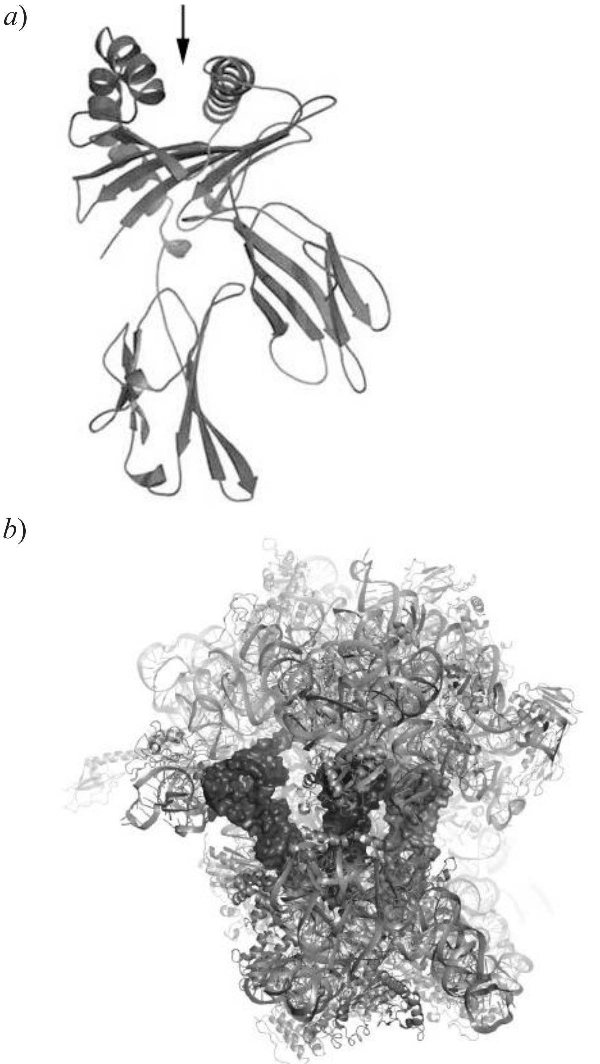


Fig. 4. (a) Structure of an MHC class I molecule, showing the groove (arrowed) between two α-helices, where peptides from foreign antigens are displayed for immune surveillance; (b) structure of a complete (70S) bacterial ribosome - at the centre (in space-filling representation) are three tRNA molecules that flit in and out carrying amino acids to the polypeptide synthesis centre (courtesy of Dr Venki Ramakrishnan).

As the ribosome aptly demonstrates, one of the great strengths of X-ray crystallography is that the size of the target is essentially irrelevant; if it can be crystallized, its structure can be solved. Remarkably, the first virus structure, that of tomato bushy stunt virus (TBSV), was solved as long ago as 1978,[16] facilitated by the high symmetry that characterizes the protein coats of many of the smaller viruses. The protein shell of TBSV is formed by 180 protein subunits arranged with icosahedral symmetry. It is fascinating to see how nature exploits the assembly principles of the icosahedron in structures as complex as viruses and as simple as the C_{60} allotrope of carbon, not to mention the architectural creations of Buckminster Fuller. Detailed atomic structures have now been determined for the capsids of many icosahedral animal viruses, such as poliovirus, rhinovirus (the common cold virus) and foot-and-mouth disease virus. Even larger viruses are now falling prey to crystallography, some spectacular examples being blue-tongue virus, which infects cattle, rotavirus, the cause of diarrhoea in children, and dengue virus.[17] For these more complex viruses, crystallography is increasingly being used in tandem with cryo-electron microscopy, with atomic structures of individual protein components of the virus being docked into the cryo-EM density to create composite pictures of the whole assembly.[17]

Paralleling the work on viruses are other recent crystallographic studies that focus on biological *containers*. Todd Yeates, at UCLA, has investigated micro-compartments that can be found in many bacteria (Fig 5a). These have beautiful protein shells formed from exquisitely-packed protein subunits (Fig. 5b), rather like viral shells, but instead of enclosing DNA or RNA as viral shells do, these micro-compartments enclose small reaction chambers. They contain enzymes that carry out biotransformations, with the protein shell having holes that allow reagents in but keep toxic intermediates inside.[18] A quite different and highly intriguing example concerns naturally-occurring protein crystals, being investigated by Peter Metcalf at Auckland University. Instead of using a standard protein shell like TBSV, poliovirus and most other viruses, some insect viruses form their protective shell from a crystal lattice, formed from a protein that spontaneously crystallizes round the virus. These crystals are exceptionally stable, resisting 1 M HCl. They are also very tiny, typically 1-5 μm (Fig 6), and thus pose severe experimental problems. Solution of their structure was a technical tour-de-force, and revealed a remarkably dense packing of protein molecules through the crystal that no doubt plays a major part in their stability.[19]

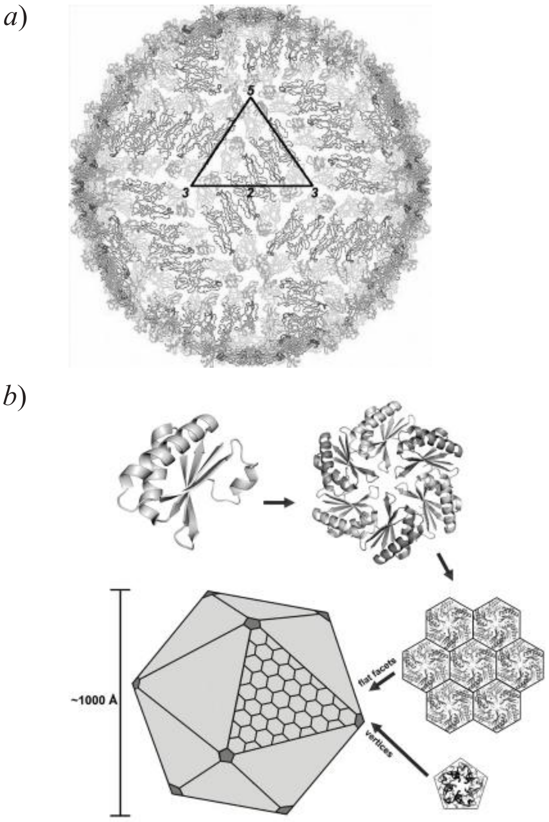


Fig. 5. (a) Protein shell of dengue virus; the icosahedral asymmetric unit is enclosed by the triangle and contains three protein subunits (courtesy of Dr. Michael Rossmann); (b) assembly of the protein shell of a bacterial micro-compartment, the carboxysome (see ref 18), which encloses two enzymes that carry out CO_2 fixation *in situ*. The icosahedral protein shell is formed by two structural proteins, one that forms hexamers that provide the flat facets, and another that forms the pentameric vertices (courtesy of Dr. Todd Yeates).

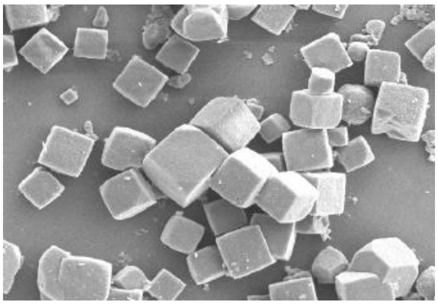


Fig. 6. Polyhedrin crystals - these tiny crystals, <5 μm in their largest dimension, are formed naturally from the viral protein polyhedrin in an infected insect, and enclose viral particles as a protective crystal shell for propagation of the virus (courtesy of Dr Peter Metcalf).

Towards New Medicines

Historically, the discovery of drugs has largely been a process of trial-and-error. The targets of these medicines were unknown and side effects were discovered the hard way. As more has been learned about the molecular basis of disease, it has become possible to develop drugs specifically against deliberately-chosen targets. Crystallography, and knowledge of protein 3D structure, is now playing an ever-increasing role in this approach to new medicines, as is illustrated by drugs developed against two viral diseases, HIV-AIDS and influenza.

The near-panic that came with the AIDS epidemic of the 1980s led to the first triumph for crystallography and structure-based drug design. The goal in this approach is to find a protein that is critical to the survival or spread of the infectious agent, solve its structure and design specific inhibitors against it. In the fight against AIDS, two key targets, the HIV protease and the HIV reverse transcriptase, were quickly crystallized and their structures solved. The HIV protease proved to be *druggable* and within seven years the first drugs were in the clinic. Although not a cure, the drugs continue to be improved, and the disease is now manageable. The beauty of the structure-based approach is that knowledge of exactly how a molecule binds to its target enables a medicinal chemist to see exactly where a substituent might be added, or where it cannot be, during the difficult process of optimization.

Influenza is a rather different target but the process is similar. There are two key proteins on the surface of the virus: the haemagglutinin (H) that enables it to bind and get into cells, and the neuraminidase (N) that helps it spread. Crystal structures have been determined for both, but so far only the neuraminidase has proved druggable. Nevertheless, by seeing exactly how the natural substrate binds in the active site and identifying an unused pocket (Fig. 7), a small group of researchers in Melbourne were able to develop a drug that binds 10^5 times more strongly to the enzyme than the natural substrate does, leading to the first successful anti-influenza drug.[20]

More recently, the vastly-increased speed of X-ray crystallographic analysis has been exploited in a new approach to obtaining the initial lead compounds that can be developed subsequently into drugs. Called fragment screening,[21] it uses small libraries comprising 500-1000 *fragments*; small (M_r < 250 Da) and chemically-tractable chemical species. These bind only weakly, but the idea is that by starting small one can elaborate on those that do bind, or stitch them together into larger, stronger-binding compounds. The screening to find the initial *hits* is done with mixtures of *ca*. five compounds at a time, either by NMR or by crystallography, but crystallography is used to find exactly where they bind to guide their elaboration. In a typical operation, everything is automated: a robot mounts the crystal, data are collected and processed automatically, and the software scans the resulting electron density maps to see if and where fragments have bound. This is indeed high-throughput crystallography.

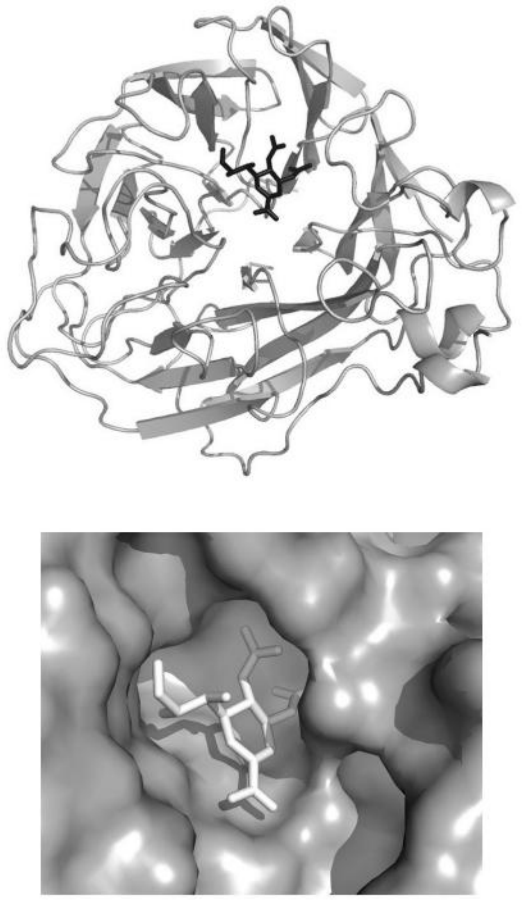


***Fig.** 7*. Upper: Influenza virus neuraminidase, the target of anti-influenza drugs such as Relenza and Tamiflu - the protein structure is depicted with the drug binding site shown. Lower: The active site cavity that binds the drug; pockets in the active site that were not filled by the natural substrate were exploited in the drug design (images courtesy of Dr Peter Colman).

Discovery and Surprise

Finally, one of the fascinations of biology is in the seemingly infinite capacity for surprise. This is just as true of protein structures as it is of animal behaviour. Crystallography plays its part here, too, in the discovery of some very surprising reactions with intriguing chemistry. One such example is Green Fluorescent Protein (GFP), a protein from jellyfish that displays vivid green fluorescence. The amino acid sequence of GFP gave no clue to the colour and there appeared to be no associated cofactor. It turned out that the colour came from an intrinsic cofactor that was generated from an intramolecular reaction; the extended polypeptide was unremarkable but, as it folded up into its functional β-barrel form, a spontaneous reaction occurred that generated the fluorescent cofactor. The crystal structure[22] shows this cofactor with beautiful resolution (Fig. 8a), and has been used to help design fluorescent molecules with quite different colours. GFP and its derivatives have proved to be remarkably powerful as imaging agents and the original discoverers received the Nobel Prize in 2008.[23]

An example from our own laboratory graphically illustrates the potential for discovery. A PhD student of mine, HaeJoo Kang, expressed, purified and crystallized a protein from *Streptococcus pyogenes*, the cause of *strep throat*. We knew from its amino acid sequence that it would be on the surface of the bacterium, anchored to the cell wall. The first surprise came from the discovery (by other researchers) that this protein, unromantically called Spy0128, forms pili. The pili are long, hair-like, covalent polymers in which hundreds of Spy0128 molecules are joined end-to-end like beads on a string, with an adhesin molecule at the tip. These pili enable the bacterium to attach to and colonize human cells, yet are so thin that they had never before been seen, despite more than 100 years of study of this bacterium! A second surprise came from the crystal structure. In two places, we found continuous electron density linking the side chains of pairs of amino acids, lysine and asparagine (Fig. 8b), and interpreted it as an amide linkage, referred to as an isopeptide bond because of its similarity to peptide bonds. Analysis by mass spectrometry confirmed this, and further work showed that the bond forms spontaneously when the protein folds and the amino acids are brought together in a specific environment.[24] These bonds, which give extraordinary resistance to mechanical stress, are critical for maintaining the integrity of the long, thin polymers (Fig. 8b). Textbooks describe disulfide bonds as the only covalent cross-links between side chains within proteins, but clearly this is not so. The structure contained enough information to predict that they might actually be quite common in certain types of proteins, and interestingly they are increasingly turning up in protein structures. Their potential for materials design is obvious.

Finally, for weirdness, it is hard to go past a protein that is used by a tropical frog to build *foam nests*, nests of a protein-based foam that is used to make a bed for the frog's eggs. Coloured blue and whimsically named *Ranasmurfin*, this protein was crystallized and analyzed by X-ray crystallography. It turned out to have an extraordinary series of cross-links, apparently generated by an intramolecular reaction that joined four amino acid side chains into a Lys-Tyr-Tyr-Lys unit that bound zinc.[25] One wonders how many more strange reactions there are out there in the natural world, waiting to be discovered.

Concluding Comments

The complexity of biological systems demands exquisite control of specificity and a crucial role for three-dimensional structure. Structural biology thus provides a natural bridge between chemistry and biology by its ability to define biological systems and mechanisms at an atomic level. Remarkable technological advances in X-ray crystallography over the past 20 years, coupled with developments in NMR and cryo-electron microscopy (not discussed in this article, but highly complementary) now make biological structural information highly accessible. Many of the steps in structure determination are beginning to be automated. The frontier has shifted to the more challenging systems – membrane proteins, protein-protein complexes, biological machines and assemblies – for which the key requirements are to find tractable forms for analysis. Behind these frontier targets, however, the structures of simpler proteins will provide the knowledge that fuels many applications in biomedicine, biotechnology and nano-science. Above all, this is still *discovery science*, with many more of Lawrence Bragg's *gold nuggets* yet to be found.

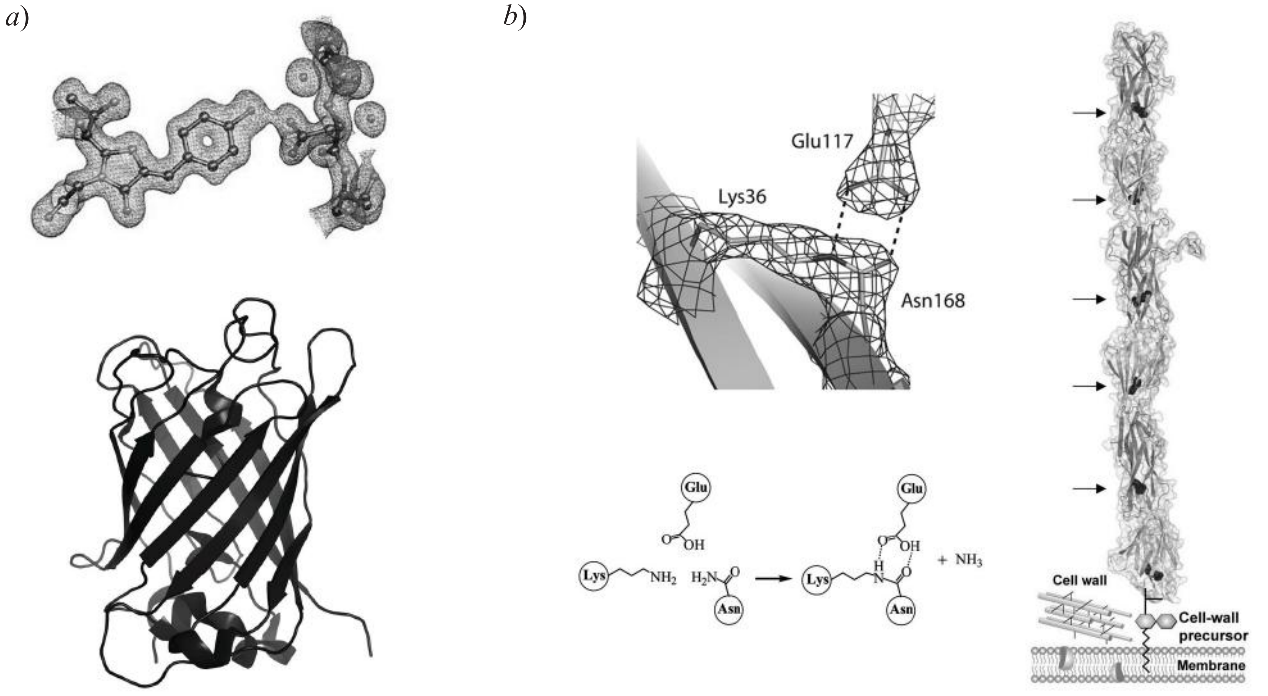
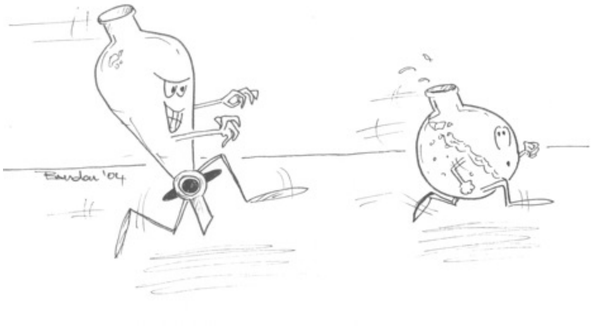


Fig. 8. Examples of spontaneous intramolecular reactions in proteins: (a) Green fluorescent protein; upper image shows the electron density for the chromophore, formed by a spontaneous reaction involving residues 65-67 when the protein folds; the phenolic ring is derived from Tyr66, while lower image shows the folded GFP molecule. (b) Example of an intramolecular isopeptide bond formed spontaneously on protein folding; at left is the electron density for a Lys-Asn isopeptide bond found in a protein that forms polymeric pili on Streptococci, with the bond-forming reaction shown below. In the assembled pilus (right) these repeated bonds (arrows) give great mechanical strength (courtesy of HaeJoo Kang).

References

1. See: *Chem. in NZ* **2010**, *74*, 32-38.
2. Bernal, J. D.; Crowfoot, D. *Nature* **1934**, *133*, 794-795.
3. Lonsdale, K. *Proc. Roy. Soc. Lond*. **1929**, *A123*, 494-515.
4. Crowfoot, D.; Bunn, C. W.; Rogers-Low, B. W.; Turner-Jones, A. in *The Chemistry of Penicillin* 1949, pp. 310-367; Princeton University Press, Princeton, NJ.
5. Lenhert, P. G.; Hodgkin, D. C. *Nature* **1961**, *192*, 937-938.
6. Trueblood, K. N. in *Structural Studies on Molecules of Biological Interest: A Volume in Honour of Dorothy Hodgkin* (Eds. Dodson, G.; Glusker, J. P.; Sayre, D.) 1981, pp 87-105; Oxford University Press, 1981.
7. Watson, J. D.; Crick, F. H. C. *Nature* **1953**, *171*, 737-738; Wilkins, M. H. F.; Stokes, A. R.; Wilson, H. R. *Nature* **1953**, 171, 738-739; Franklin, R. E.; Gosling, R. G. *Nature* **1953**, *171*, 740-741.
8. Kendrew, J. C.; Bodo, G.; Dintzis, H. M.; Parrish, R. G., *et al. Nature* **1958**, *181*, 662-666.
9. Dickerson, R. E. *Present at the Flood: How Structural Molecular Biology Came About* 2005, Sinauer Associates, Sunderland MA.
10. See: http://www.pdb.org/pdb/home.
11. Baker, E. N. *J. Mol. Biol*. **1977**, *115*, 263-267; **1980**, *141*, 441-484.
12. Bjorkman, P. J.; Saper, M. A.; Samraoui, B.: Bennett, W. S., *et al. Nature* **1987**, *329*, 506-511; 512-518.
13. Schmeing, T. M.; Huang, K. S.; Kitchen, D. E.; Strobel, S. A.; Steitz, T. A. *Mol. Cell* **2005**, *20*, 437-448, *Nature* **2005**, *438*, 520-524.
14. Schmeing, T. M.; Voorhees, R. M.; Kelley, A. C.; Gao, Y.-G. *et al. Science* **2009**, *326*, 688-694; Gao, Y.-G.; Selmer, M.; Dunham, C. M.;Weixlbaumer,A. *et al*. *Science* **2009**, *326*, 694-699.
15. Schmeing, T. M.; Ramakrishnan, V. *Nature* **2009**, *461*, 1234-1242.
16. Harrison, S. C.; Olson, A. J.; Schutt, C. E.; Winkler, F. K.; Bricogne, G. *Nature* **1978**, *276*, 368-373.
17. Kuhn, R. J.; Zhang, W.; Rossmann, M. G.; Pletnev, S. V. *et al. Cell* **2002**, *108*, 717-725.
18. Tanaka, S.; Kerfeld, C. A.; Sawaya, M. R.; Cai, F. *et al. Science* **2008**, *319*, 1083-1086; Tanaka, S.; Sawaya, M. R.; Yeates, T. O. *Science* **2010**, *327*, 81-84; Yeates, T. O.; Crowley, C. S.; Tanaka, S. *Annu. Rev. Biophys*. **2010**, *39*, 185-205.
19. Coulibaly, F.; Chiu, E.; Ikeda, K.; Gutmann, S. *et al. Nature* **2007**, *446*, 97-101.
20. von Itzstein, M.; Wu, W.-Y.; Kok, G. B.; Pegg, M. S. *et al. Nature* **1993**, *363*, 418-423.
21. Murray, C. W.; Blundell, T. L. *Curr. Opin. Struct. Biol*. **2010**, *20*, 497-507.
22. Ormo, M.; Cubitt, A.; Kallio, K.; Gross, L.; *et al. Science* **1996**, *273*, 1392-1395; Yang, F.; Moss, L.; Phillips, G. *Nature Biotechnol*. **1996**, *14*, 1246-1251.
23. See: *Chem. in NZ* **2009**, *73*, 39-41.
24. Kang, H. J.; Coulibaly, F.; Clow, F.; Proft, T.; Baker, E. N. *Science* **2007**, *318*, 1625-1628.
25. Oke, M.; Ching, R. T.; Carter, L. G.; Johnson, K. A. *et al. Angew. Chem. Int. Ed.* **2008**, *47*, 7853-7856.

ChemScrapes



After a few failed reactions and no sign of improvement, Jimmy simply didn't need to be worked up like this.

Brendan Burkett

Structural Chemistry & the Design of High-T_c Superconductors

Jeffery L. Tallon

Industrial Research Ltd, and The MacDiarmid Institute for Advanced Materials & Nanotechnology, PO Box 31310, Lower Hutt (e-mail: *J.Tallon@irl.cri.nz*)

About the Author

Jeff Tallon is a Distinguished Scientist and senior research scientist with the High-Temperature Superconductors (HTS) devices group of Industrial Research Ltd. He was named a Companion of the New Zealand Order of Merit in the 2009 Queen's Birthday Honour's List and, in recognition of his work enabling the creation of a new, high-value HTS industry for NZ, was awarded (with Dr Bob Buckley), the inaugural Prime Minister's Science Prize for outstanding achievement in science. Jeff is most well known for his research, beginning in the 1980s, into the highly unusual properties of high-temperature superconductors. He and his colleagues have discovered and patented many novel HTS materials, including the only material currently being developed for cables, magnets, motors and transformers.

Jeff served as Deputy Chair of the Marsden Fund in 1999-2001, introducing the Fast Start programmes for young and emerging researchers, received the Rutherford Medal in 2002 and is currently a member of the National Science Panel that promoted the establishment of the Chief Science Advisor to the Prime Minister.

The essential elements of the structural chemistry of high-T_c superconductors are reviewed and trends and correlations are highlighted, focussing largely but not exclusively on the author's work. Most significant is the contradictory effects of altering ion size and applying external pressure. Increasing ion size stretches the Cu-O bond length and universally increases $T_{c,max}$, while application of pressure increases $T_{c,max}$ and compresses the Cu-O bond. Understanding these contrary observations gets to the heart of the science of high temperature superconductors and enables the design of the optimal superconductor.

Introduction

The International Year of Chemistry is also the centennial of the discovery of superconductivity by Heike Kammerlingh-Onnes at the University of Leiden and it is also 25 years since the discovery of high-temperature superconductors (HTS) by Bednorz and Mueller.[1] Though superconductivity is generally regarded as the domain of physics it is, in fact, intimately associated with synthetic and structural chemistry, and this theme will be developed in the present paper. Kammerlingh-Onnes received the 1913 Nobel Prize, not for the discovery of superconductivity but for the liquefaction of helium, and for about a decade he had a global monopoly on liquid-helium-based cryogenic research. For their part Bednorz and Mueller received the 1987 Nobel Prize – the shortest interval between discovery and award in the history of the Nobels.

It took some 46 years before a theory of conventional low-temperature superconductivity (LTS) was developed. In 1957, Bardeen, Cooper and Schrieffer[2] recognized that interactions between electrons and phonons induce pairs of electrons with opposite momentum to bind into so-called *Cooper pairs*. These singlet pairs, with zero spin, act as bosons and they undergo Bose-Einstein condensation into a ground-state superfluid. In view of this long gap between discovery and developing a successful theory for LTS, perhaps it is not too surprising that we are awaiting still a satisfactory microscopic theory for HTS. Be that as it may, there is still a great deal that we do understand about HTS based on thermodynamics, symmetry, and correlations of physical properties with structure. It is possible, on the basis of these considerations, to design the ideal HTS material and a number of approaches to this central chemical challenge – the optimal structural design of high-temperature superconductors – are outlined.

Structural Chemistry

HTS Cuprates: Defect-Perovskites

The cuprates form structurally-rich families of defect-perovskites with perhaps the only common feature within the families being the square-planar corner-shared sheets of CuO_2 in which the superconductivity originates. These sheets lie in the *ab* plane and are only weakly coupled along the *c*-axis. Such a structure provides what is generally regarded as an essential element in HTS, namely quasi-two-dimensional electron dynamics, which is key to the very high T_c values found in these materials. As a result of this two-dimensionality, it is essential to line up the grains of an HTS conductor in order to make practical wires which will support a large electrical current.

To illustrate both this commonality and diversity in HTS cuprates the structure of three related compounds $YBa_2Cu_3O_{7-\delta}$ (T_c = 93 K), $Y_2Ba_4Cu_7O_{15-\delta}$ (T_c = 97 K) and $YBa_2Cu_4O_8$ (T_c = 80 K) are shown in Fig. 1. These are referred to in shorthand as Y-123, Y-247 and Y-124, respectively. The square-planar CuO_2 sheets lie at the bases of the square pyramids shown in the figure. These planar sheets straddle a bare Y^{3+} ion (small pale grey circles) per unit cell (and in other HTS compounds, a bare Ca^{2+} ion – see Fig. 2 below). These opposing pairs of square pyramids sandwiching Ca or a rare-earth element are a common motif for so-called *bilayer* HTS compounds where each Cu atom is five-coordinated to oxygen. The

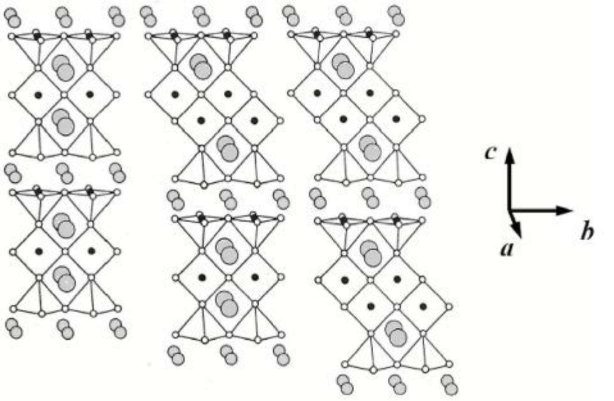


Fig. 1. The structure of Y-123, Y-247 and Y-124, respectively, showing square pyramid oxygen coordination about the planar Cu atoms (small black circles) and linear CuO chains in the *b*-direction; Y-123 has single chains, Y-124 double chains and in Y-247 single and double chains alternate. Large light grey atoms: Ba; small grey: yttrium.

two-sheets within the bilayer are quite strongly coupled while the coupling between successive bilayers is weak.

The ideal perovskite of formula, ABO_3, is cubic with the smaller A^{3+} cation located at the cube corners octahedrally coordinated to six oxygens, while the larger B^{3+} cation is located at the cube centre and is twelve-coordinated to oxygen, four in-plane, four above and four below. In the structures of Fig. 1, Cu adopts the perovskite A position while Y adopts the B position but lacks the four in-plane coordinated oxygens. The cuprates are thus oxygen-deficient perovskites, and they *must* be oxygen deficient since Cu is not trivalent.

Between successive CuO_2 bilayers in the three compounds of Fig. 1 lie one dimensional Cu-O chains extending in the *b*-direction straddled on either side by BaO layers with Ba^{2+} occupying the perovskite B site. Such intermediate layers between the CuO_2 layers are referred to generally as *block layers*. For Y-123 the chains are single CuO chains, for Y-124 they are double Cu_2O_2 chains, and for Y-247 single and double chains alternate. These chain layers can be thought of as square-planar, corner-shared CuO_2 planes with every second row of oxygen atoms absent, again emphasizing that these are oxygen-deficient perovskites. These chains, whether double or single, prove to be very important as they are metallically conducting and they contribute to the superconducting state by what is known as *proximity-induced superconductivity*. They are not intrinsically superconducting but they are induced to be so by their proximity to the naturally superconducting CuO_2 layers.[3]

The double chains of Y-124 (and Y-247) are very stable and remain stoichiometric at all temperatures to compound decomposition (see below). On the other hand, the single chains are not so stable, and when the temperature is raised oxygen diffuses out. When Y-123 and Y-247 are synthesized at high temperature these chains are almost emptied of oxygen, *i.e.* the composition of the chains is $CuO_{1-\delta}$, where δ is close to 1. Under these conditions, Cu in the (empty) chains is monovalent while the Cu in the CuO_2 planes is divalent. Both Y-123 and Y-247 must be slow cooled in oxygen in order to load up these vacant oxygen sites and to allow the oxygens there to order into the extended linear Cu-O chains shown in the figure. Only when δ is reduced to zero, and these chains are well ordered, are these compounds optimized for superconductivity. We secured US, European and Japanese patents for this intermediate compound of formula $Y_2Ba_4Cu_7O_{15-\delta}$ and it has the best intrinsic properties of all HTS cuprates.[4] Unfortunately, no one has succeeded in making a practical conductor out of this material yet – perhaps a task for the future.

The apical oxygen at the apex of the square pyramid is displaced away from the Cu at the base by the Jahn-Teller effect. This lifts the degeneracy of the orbitals, leaving a half filled $d_{x^2-y^2}$ band which is split by the Mott-Hubbard interaction to result in an antiferromagnetic insulator in the undoped state. Doping initiates an insulator-to-metal transition and the onset of superconductivity. It is generally observed that as the Jahn-Teller displacement of the apical oxygen is increased so the maximum observed T_c is also increased.

Homologous Series

A further structural feature of the HTS cuprate families is the tendency to form homologous series with the same *block layer* in each member, but with different numbers of CuO_2 sheets residing between the block layers. Fig. 2 illustrates this for the n = 1, 2 and 3 members of the *BSCCO family* of general formula $Bi_2Sr_2Ca_{n-1}Cu_nO_{2n+4+\delta}$, which we were first to describe.[5] These have single-layer, bilayer and trilayer CuO_2 stacks and, as n is increased by 1, an additional Ca layer and CuO_2 layer are inserted into the structure. The core superconducting $Sr_2Ca_{n-1}Cu_nO_{2n+2}$ sub-stack is a defect perovskite, while the double Bi_2O_2 layer (the two flats sheets of Fig. 2) forms a defect rock salt structure with the in-plane oxygens residing off-centre, closer to the square-planar Bi atoms. Significantly, T_c rises across this series with $T_c = 18$ K for $n = 1$, $T_c = 95$ K for $n = 2$ and $T_c = 110$ K for $n = 3$. It is possible, though very difficult, to make higher homologous members, n = 4, 5, *etc*., but here T_c is found to progressively fall again. Understanding this overall progression is a key challenge in the science of HTS and we will return to the question later.

These compounds are also defect perovskites with a disconcerting array of co-existing defect structures. Typically about 5% of Bi resides on the Sr site; in the $n = 2$ member Ca and Sr can intersubstitute, though they cannot in the $n = 3$ member. Excess oxygen (denoted by δ in the formula) resides in interstitial sites between the BiO layer and the SrO layer. Remarkably, they can be located, one by one, using high-resolution scanning tunnelling microscopy.[6] Excess oxygen also resides in the BiO layer,[7] forming an incommensurate structural wave extending in the *b*-direction with periodic bands of Bi^{5+} in perovskite stripes forming a washboard structure with the background rock salt structure comprising Bi^{3+}. So, these materials are structurally and electronically complex, and the unusual defect structures that they exhibit reflect their proximity to several structural and electronic instabilities.

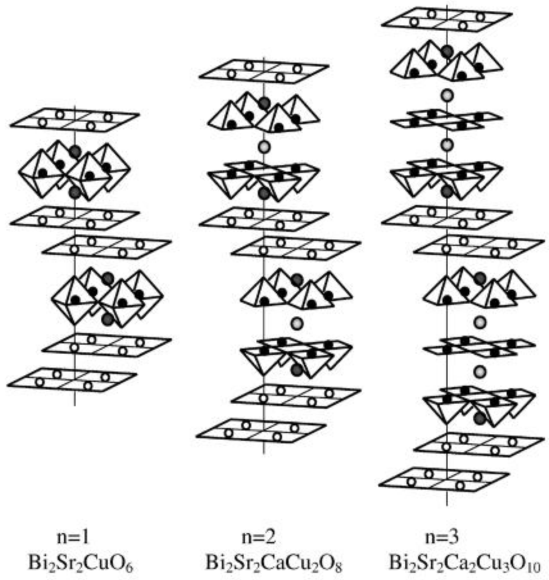


Fig. 2. The homologous structures of $Bi_2Sr_2CuO_{6+\delta}$, $Bi_2Sr_2CaCu_2O_{8+\delta}$ and $Bi_2Sr_2Ca_2Cu_3O_{10+\delta}$, the $n = 1$, 2 and 3 members of general formula $Bi_2Sr_2Ca_{n-1}Cu_nO_{2n+4+\delta}$ in common shorthand notation, they are referred to as Bi-2201, Bi2212 and Bi-2223 and exhibit T_c values of 18 K, 95 K and 110 K, respectively.

The $n = 3$ member $Bi_2Sr_2Ca_2Cu_3O_{10+\delta}$ was first identified by our group[5] and was the subject of protracted patent disputes in the USA and Europe over more than a dozen years. Bi-2223 is very slow forming and it takes several weeks to fully react, though synthesis can be accelerated by partial substitution of Pb for Bi.[8] It was this material that was used to make the first generation of HTS wires and we licensed the composition to American Superconductor Corporation. The double Bi_2O_2 layer is weakly bound and, as a consequence, all these BSCCO compounds exhibit a flaky microstructure similar to mica or graphite. Under shear deformation the BiO layers slide over each other such that a simple rolling deformation will align the grains into long extended sheets sharing the same *ab*-plane orientation. Of the approximately 70 known HTS cuprates,[9] BSCCO is the only one in which the grains can be aligned by a rolling deformation, as is needed for a high-current conductor. It is for this reason (combined with its exceptionally high T_c value) that Bi-2223 was quickly established as the only practical HTS conductor for nearly 20 years.

Other homologous cuprate families also exist.[9] The thallium family,[10] of general formula $Tl_2Ba_2Ca_{n-1}Cu_nO_{2n+4+\delta}$, is isostructural with the BSCCO family with Tl-2201 having $T_c = 90$ K, Tl-2212 having $T_c = 118$ K and Tl-2223 having $T_c = 128$ K. Another thallium family has the Tl_2O_2 double layer replaced by a single layer $Tl_{0.5}Pb_{0.5}O$ with members naturally referred to as Tl-1201, Tl-1212 and Tl-1223, *etc*. Their general formula is $Tl_{0.5}Pb_{0.5}Sr_2Ca_{n-1}Cu_nO_{2n+3+\delta}$. Another very important Hg-based family[11] is isostructural with this latter family where $Tl_{0.5}Pb_{0.5}O$ is replaced by a bare Hg, *i.e.* the oxygen in the layer is removed. This has the general formula $HgBa_2Ca_{n-1}Cu_nO_{2n+2+\delta}$, and the $n = 3$ member, $HgBa_2Ca_2Cu_3O_{8+\delta}$, exhibits the highest T_c known amongst the cuprates (135 K under ambient pressure and 165 K under high pressure). Again, the Hg family exhibits a rise then fall in T_c as n increases ($T_c = 95$ K, 125 K, 135 K and 128 K for $n = 1$, 2, 3 and 4, respectively).

Phase Diagrams

Electronic Phase Diagram

The cuprates exhibit a universal phase diagram with doping and, to illustrate, the single-layer compound $La_{2-x}Sr_xCuO_4$ is considered. When $x = 0$ the parent compound La_2CuO_4 is an undoped antiferromagnetic (AF) insulator, as noted above. Substitution of Sr^{2+} for La^{3+} removes electrons from the hybridized Cu-O orbitals, and thus dopes in holes. The doped hole concentration, p, is just $p = x$. In other cuprates, subject to thermodynamic and chemical constraints, hole doping can be achieved by similar altervalent cation substitutions or by increasing the oxygen content. Importantly, the cuprates seem to display a common phase diagram when T_c is scaled by its maximum value in the phase curve, $T_{c,max}$. A schematic representation of the generic phase diagram is shown in Fig. 3.[12,13]

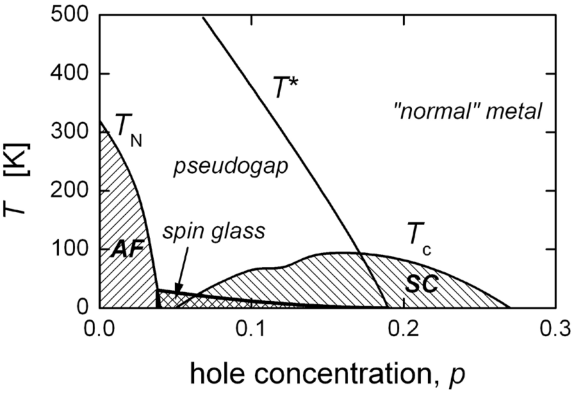


Fig. 3. The universal phase diagram for hole-doped HTS superconductors showing a region of AF ordering at low p and superconductivity (SC) at higher doping. Optimal doping, where $T_c = T_{c,max}$, occurs at $p = 0.16$ holes/Cu. The *overdoped region* corresponds to $p > 0.16$ while the *underdoped region* corresponds to $p < 0.16$. Short-range AF correlations occur in a region below T^*, known as the *pseudogap* state, and these compete with SC below T_c. The pseudogap energy scale $T^* = E_g/k_B$ falls to zero at critical doping $p_{crit} = 0.19$, which may be a quantum critical point. There is a spin-glass state at intermediate doping and the system progresses towards a *normal* metal at high doping.

Long ago we showed that the generic T_c(p) phase curve followed the universal parabola:[14]

$$T_c = T_{c,max}\,[1 - 82.6\,(p\text{-}0.16)^2] \qquad \text{(Eq. 1)}$$

although this ignores the small plateau shown in Fig. 3 that occurs near $p = 1/8$ (= 0.125) and which is common to a number of HTS cuprates and possibly to all. Certainly it is present in $La_{2-x}Sr_xCuO_4$, $YBa_2Cu_3O_{7-\delta}$, $Y_{0.8}Ca_{0.2}Ba_2Cu_3O_{7-\delta}$ and $HgBa_2CuO_{4+\delta}$, and in some variants of $La_{2-x}Sr_xCuO_4$ such as $La_{1.6-x}Nd_{0.4}Sr_xCuO_4$; T_c is fully suppressed there to zero. This is due to a competing AF *stripe phase*, where the parent spins and doped charges spatially separate into 1D or 2D stripes.[15] It has long been known that HTS tend to form such stripes but it is still not clear whether this is coincidental or crucial for SC.

The phase diagram shows the progression from long-range AF at low doping; through a region of short-range

AF order (the so-called pseudogap region below T^*); the onset of superconductivity at $p = 0.05$ rising to a maximum at optimum doping, $p = 0.16$, and the eventual decline in T_c in the *overdoped region*. In the heavily overdoped region, the cuprates progressively become more or less conventional metallic conductors, exhibiting many characteristics of the so-called Fermi liquid. Thus, there is a progressive crossover from strong correlations (magnetism) at low doping to weak or negligible correlations at high doping and an associated transition from insulating to metallic behaviour. A key question is whether there is a quantum phase transition at the point where T^* falls to zero at the critical doping $p_{crit} = 0.19$.[16] If so, then the occurrence of superconductivity and the dome-shaped $T_c(p)$ phase curve is due to strong quantum fluctuations above and near p_{crit}. There should be an insulator to metal transition at this point also (as observed[17]). Theory predicts that in this case the resistivity is linear-in-T above p_{crit} (as also observed) and the normal-state specific heat diverges logarithmically (not yet observed because SC conceals the normal state).[18] Despite dramatic improvements in the resolution of the many spectroscopies brought to bear on these questions the answers remain frustratingly elusive.

The above brief discussion outlines the electronic phase behaviour of the *hole-doped* cuprates. It is possible to dope *electrons* into some cuprates and thus explore the mirror image of the phase diagram shown in Fig. 3. Examples include $Nd_{1-x}Ce_xCuO_4$ and $Pr_{1-x}Ce_xCuO_4$, where Ce^{4+} is substituted on to a Nd^{3+} or Pr^{3+} site. Clearly, this is the converse of Sr^{2+} substitution on a La^{3+} site. However, the phase diagram for electron-doped cuprates is not quite the mirror image of that for hole-doped cuprates. Firstly, the AF domain is broader. This makes sense because the electrons dope on to Cu orbitals resulting in spin vacancies. This simply weakens the AF correlations. In the hole-doped cuprates, the holes are doped onto the O orbitals adding an extra spin and, thus, actually frustrating the AF correlations. Secondly, the SC dome in the electron-doped cuprates is more narrow, but there does appear to be a similar T^* line and putative quantum critical point lying at the centre of the dome[19] suggesting that the essential physics of the electron- and hole-doped cuprates is basically the same. A structural difference is that the hole-doped cuprates always possess somewhere in their structure an apical oxygen which is Jahn-Teller displaced away from the CuO_2 plane, whereas the electron-doped cuprates are restricted to structures with no apical oxygen. This surely means that the apical oxygen does not play a central role in the mechanism of electron pairing. However, the electron-doped systems all have relatively low T_c values and do not discount a secondary role for the apical oxygen through one of its associated phonon modes. Isotope substitution effects provide more light on this question, as discussed below.

Compositional Phase Diagrams

Compositional and structural phase diagrams play a key role in defining the synthesis conditions and doping prospects for perovskites in general and the cuprates are no exception. As noted, these materials are complex and often the observed structures reflect a compromise between the natural bond lengths in the block layer and those in the CuO_2 layers. This is the origin of the already-noted off-centre location of O atoms in the BiO layers of BSCCO.[7] Fig. 4 shows the domains of stability[20,21] of $YBa_2Cu_3O_{7-\delta}$, $Y_2Ba_4Cu_7O_{15-\delta}$, and $YBa_2Cu_4O_8$. The last compound is the low-temperature stable phase but the phase boundary is at sufficiently low temperature under ambient PO_2 that $YBa_2Cu_3O_{7-\delta}$ generally remains metastable as it is cooled. This is the case even if it is slow cooled, and this is fortunate as it is necessary to load in oxygen (reducing $\delta \rightarrow 0$) in order to achieve optimal SC properties. When $YBa_2Cu_3O_{7-\delta}$ is cooled to the dashed curve (marked O/T in Fig. 4) the $CuO_{1-\delta}$ chains have loaded to about 50% occupancy, *i.e.* $\delta \approx 0.5$, and the symmetry changes from tetragonal to orthorhombic in a 2nd order phase transition.[22,23] To the left of this line oxygen sites in the chain layer are randomly occupied and the structure is tetragonal, while to the right of the line oxygen atoms preferentially occupy the sites that form linear chain segments along the b-axis. This yields the orthorhombic phase. The tendency to form chains leads, in a well annealed sample, with $\delta \approx 0.5$, to alternating full and empty chains. It is also possible to achieve other ordered structures with an alternation of two full chains followed by one empty chain when $\delta \approx 0.33$, and alternation of one full chain followed by two empty chains when $\delta \approx 0.67$.

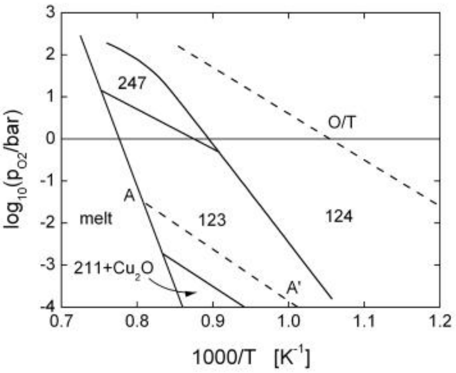


Fig. 4. The oxygen phase diagram for the Y/Ba/Cu/O system with Y-247 composition. The line O/T marks the orthorhombic/tetragonal transition in Y-123, the line A-A′ marks the phase boundary between Cu_2O and CuO and the line below this shows where Y-123 decomposes to $Cu_2O + Y_2BaCuO_5$ (referred to as 211).

Generally, elevated oxygen pressure (typically 60 bar O_2 pressure) is used to synthesize Y-124 or Y-247 in order to achieve temperatures sufficiently high to enable solid-state synthesis of these high-pressure phases. The horizontal solid line marks 1 bar of O_2 pressure and it cuts the Y-247 domain just above where it pinches off. In 1989, we discovered how to synthesize Y-247 in 1 bar of oxygen within this narrow domain (855-870 °C) by using $NaNO_3$ or KNO_3 as a reaction-rate enhancer. In the absence of some form of catalyst, the synthesis is just too sluggish (synthesis of Y-124 is harder still). Conveniently, the alkali evaporates during synthesis leaving pristine Y-247. We were surprised to discover the resultant material, $Y_2Ba_4Cu_7O_{15-\delta}$, was a 95 K superconductor (which we later improved to 97 K). What was particularly satisfying was that we were able to predict this narrow domain beforehand and our first attempt at 865 °C was successful.[22,23] We subsequently found that the addition of Ag powder also acted as a suitable catalyst while remaining inert to the superconductor itself.

Phase diagrams like this are immensely useful. Of course, the melt line is important for the growth of single crystals by slow cooling across the melt boundary. We traversed samples of Y-124 from the stable region low down on the phase diagram ($PO_2 = 2 \times 10^{-4}$ bar) briefly into the Y-123 stability region to the left of the A-A′ line for a few seconds to a few minutes before returning to the stable Y-124 domain. The result was that Y-124 rapidly decomposed to Y-123 leaving precipitates of CuO within the structure. These precipitates are effective in pinning magnetic flux lines and the result was a 50-fold increase in critical current density.[23]

Fig. 5 shows the phase diagram for the stability of Bi-2212 and Bi-2223 where the overall composition is Bi-2223. Most importantly, this shows that the region of stability of Bi-2223 is very narrow and like Y-247 it pinches off, but in this case at higher pressure. The vertical line shows 1 bar O_2 pressure and here Bi-2223 is unstable. Any attempt to synthesize this in oxygen would have proved fruitless. Even in air (short solid vertical line) there is just a slender stability domain of about 5 °C where Bi-2223 can be synthesized. In early 1988, we discovered this narrow window and synthesized bulk Bi-2223, identified its composition and structure, and determined its behaviour as a function of oxygen content and doping. Bi-2223 became the material of choice for first generation HTS wires. Importantly, we recognised in our patents that Bi could be partially substituted by Pb because that subsequently proved to accelerate the reaction to the Bi-2223 phase sufficiently to make it a practical manufacturable process.[8] Moreover, reference to Fig. 5 shows that the synthesis range is much broader at low PO_2 and manufacturing is now typically carried out at $PO_2 = 0.077$ bar, indicated by the short vertical dashed line.

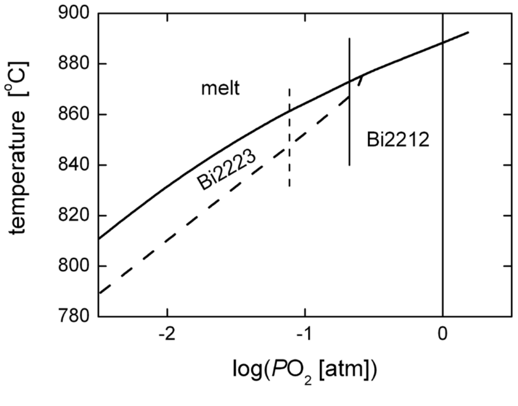


Fig. 5. The temperature/oxygen partial pressure phase diagram for the B/Sr/Ca/Cu/O system with Bi-2223 composition. The bold curve is the melting line while the short vertical solid line denotes ambient air where the stability range for $Bi_2Sr_2Ca_2Cu_3O_{10+\delta}$ is just 5 °C wide; the short vertical dashed line shows typical current manufacturing PO_2.

Systematics

The above basic ideas lay the foundation for exploring a number of systematic relationships that in principle allow the rational design of optimal high-T_c superconductors. The ensuing discussion does not just focus on maximising the value of T_c but, perhaps more importantly, addresses the practical issue of maximising the critical current density especially in an applied magnetic field.

Role of Multiple CuO_2 Layers

We have noted that the T_c value in an homologous series rises with the number of CuO_2 layers per unit cell up to n = 3 or 4 then falls again. To understand the role of multiple CuO_2 layers in controlling the value of T_c, it is useful to consider the standard BCS formula[2] for T_c, *viz.*:

$$T_c = 1.13h\nu_B \exp[-1/(N_0V)] \qquad \text{(Eq. 2)}$$

Here h is Plank's constant, N_0 the density of states (DOS), V the electron pairing interaction mediated by, *e.g.* phonons or magnons, and ν_B the characteristic frequency of the phonon or magnon. In conventional low-T_c superconductors the pairing is mediated by phonons so typically ν_B is the Debye frequency. The key point here is that T_c is governed exponentially by the DOS and, thus, the presence of a van Hove singularity (vHs) associated with the two-dimensionality can have a dominant effect since N_0 diverges at the vHs. This probably plays a central role in causing the very high T_c values in the layered cuprates.

Let us consider what happens when the doping (the hole concentration, p) is increased. In the cuprates, the pairing is almost certainly mediated by magnetic interactions and, as noted, these diminish as p increases. Thus, both ν_B and V decrease with increasing doping.[24] This would suggest that the highest T_c values might be achieved at low doping. However, in single-layer cuprates the vHs is located right at the far edge of the SC domain shown in Fig. 3 around $p \approx 0.27$. This is where the magnetic interactions are weakest and it is not surprising that $T_{c,max}$ is low for these. On the other hand, a bilayer system has two degenerate orbitals that are split by the (weak) coupling between them into a lower bonding (B) and a higher antibonding (AB) orbital. This splits the vHs with the AB vHs moving to lower doping,[25] where the magnetic interactions are stronger, and so T_c rises, and quite dramatically so. A trilayer system splits the three-fold degenerate orbitals into three levels which push one of the vHs to even lower doping and hence still higher T_c.

This cannot continue indefinitely because the block layer transfers a fixed quantity of doped charge into the CuO_2 layers. As the number of CuO_2 layers is increased the doped charge becomes increasingly diluted.[14] If we think of each layer as having its own phase diagram as shown in Fig. 3 then, eventually, all the layers become underdoped and T_c declines. Worse still, once there are more than two CuO_2 layers they are no longer structurally and electronically equivalent. A three-layer cuprate has two identical outer layers and a different inner layer. This inner layer tends to be less doped than the outer layers.[26,27] Ideally, one would like to achieve equal doping in all layers so that all could simultaneously be optimized. In principle, this could be done by judicious site substitution or some form of structural distortion, but these might prove difficult to achieve and no-one has yet explored this as a computational chemistry problem. Interestingly, the application of pressure squeezes further charge transfer from the block layers to the CuO_2 planes – it is an indirect means of systematically increasing the doping. By applying pressure to three-layer cuprates such as $Bi_2Sr_2Ca_2Cu_3O_{10+\delta}$[28] and $Tl_2Ba_2Ca_2Cu_3O_{10+\delta}$,[29] one finds that T_c rises to a maximum as the outer layers reach their optimum doping, and then it falls for an interval where the inner layer is underdoped and the outer layer is overdoped. Then T_c rises again as the inner layer approaches optimum doping, and it rises much higher than the first maximum. One expects that at high enough pressure both inner and outer layers are overdoped. Clearly, (i) the inner layer (lacking apical oxygens) has a significantly higher intrinsic T_c value than the outer layers[28,30,31] (see T_c *Correlations*) and (ii) if the doping were uniform across all three layers then higher T_c could be obtained. By no means have we found the best HTS superconductors yet.

Role of Block-Layers

As noted, between the bilayers and trilayers in Figs. 1 and 2 lies an essentially inert layer, referred to as the *block layer*. This acts firstly as a charge reservoir that provides the source of the doped charge in the CuO_2 layers, either through oxygen non-stoichiometry or altervalent cation substitution. The block layer provides charge compensation for the doped electrons or holes such that the overall charge is neutral, as it must be. Secondly, the block layer provides a substrate that determines the Cu-O bond-length. This bond length plays an important role in controlling the thermodynamic stability (see *Thermodynamic Stability*) and also the maximum T_c value (see T_c *Correlations*). Adjacent multilayers are weakly coupled by quantum mechanical *inter*layer tunnelling of electron pairs across the block layer, while the multilayer itself is quite strongly coupled *intra*layer. These couplings can be probed by, for example, infrared spectroscopy and they play an important role in determining the strength of the superconducting state.

Other high-T_c compounds discovered after the cuprates also possess this weakly-coupled layered structure, including MgB_2 and, more recently, the iron pnictides (layered iron arsenic compounds). Therefore, it seems a general conclusion that this quasi-two-dimensionality is important – it imposes the van Hove singularity, which introduces a very large DOS when the doping level is close to the vHs. But, there is a trade-off here because a purely 2D electronic system cannot be a superconductor. Indeed, it is clear that most cuprate superconductors are too two-dimensional and some coupling along the *c*-axis is definitely desirable, both to increase T_c and to increase the critical current in a magnetic field. This can be quantified through the so-called *irreversibility field*. In the presence of a magnetic field, flux will concentrate into discrete tubes of exactly one flux quantum, given by $h/2e$, where e is the electronic charge. The field outside these tubes of flux is suppressed to zero by circulating supercurrents and the composite object is referred to as a *vortex*. When a current passes through the superconductor there is a lateral force on the vortex (the Lorentz force) which is normal to the field and the current flow. If the vortex should move under this force the process is dissipative and, though we have a superconductor, it does not display zero resistance. Great efforts are expended, therefore, to control the microstructure to pin these vortices through various precipitates and defects.[21] In a 3D system, a vortex is continuous along its length and more or less rigid. However, in a layered quasi-2D system the vortex is a stack of current loops within each CuO_2 plane. These are referred to as *pancake vortices* and they can decouple from each other if the field is too high. You may pin one section of the vortex but adjacent sections can decouple and slide under the Lorentz force. Therefore, pinning is a much greater challenge in layered high-T_c superconductors. This decoupling occurs at a critical field known as the irreversibility field, H^*. If $H < H^*$ then the pancakes are strongly coupled and zero DC resistance is accomplished, but if $H > H^*$ then decoupling occurs and the superconductor becomes resistive. Clearly, one wants to increase the coupling across the block layer to ensure that H^* is as high as possible.

This coupling is governed by quantum mechanical tunnelling and, therefore, varies exponentially with the thickness, t_b, of the block layer. A simple calculation shows that $H^* \propto \exp(-t_b/\xi)$, where ξ is a fixed characteristic length. Fig. 6 shows $\ln(H^*)$ plotted against t_b for many different cuprates[32] and the expected relationship is well satisfied. There are a number of subtleties present in this plot. Firstly, H^* varies strongly with doping, so that all values are compared at the same doping state, namely optimal doping where $p = 0.16$ and T_c maximizes. Secondly, the true block layer spacing for Y-123 and Y-247 is shown by the open symbols that definitely do not fit the correlation. But, as noted, the chain layers in both of these compounds are metallic and superconducting by proximity effect, so the block-layer spacing, over which the coupling must extend, is the plane-to-chain distance not the plane-to-plane distance. The former is exactly half the latter and it is these coupling lengths that are used in plotting the solid data points.

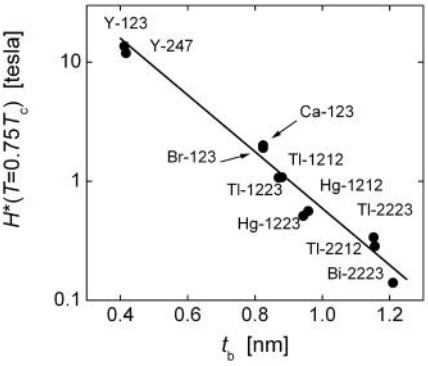


Fig. 6. The irreversibility field H^* at 0.75 T_c for optimal doped cuprates as a function of block-layer spacing, t_b. Ca-123 denotes $Y_{0.8}Ca_{0.2}Ba_2Cu_3O_{6.61}$ and Br-123 denotes $YBa_2Cu_3O_{6.2}Br_{0.8}$; for Y-123, t_b is taken to be 0.42 nm, the chain-to-plane distance.

This not only confirms the basic correlation shown in Fig. 6 but provides indirect evidence for proximity-induced SC on the chains. More rigorous studies using muon spin relaxation to probe the superfluid density in these materials confirms this picture.[33] As a test of this interpretation, the figure also shows H^* for Ca-doped Y-123 and for Br-doped Y-123 where the chains have been fully disrupted while retaining the same optimal doping state. Here, the effective block-layer distance is now the plane-to-plane distance and the value of H^* is reduced accordingly, in keeping with the overall correlation. What is notable in this figure is the fact that Bi-2223, which forms the first generation HTS wire technology, has the poorest irreversibility field of all the cuprates, while Y-123 which forms basis of second generation HTS wire technology has the best. This is a primary motivation for implementing this material – its critical current in a magnetic field is superior to all other HTS except Y-247.

Bond-Valence Sums

As noted, there are several HTS cuprates where the doping value, p, is directly calculable from the composition. Two examples will suffice. In the case of $La_{2-x}Sr_xCuO_4$ it is simple to see that $p = x$. For $Y_{1-x}Ca_xBa_2Cu_3O_6$,where the chain layer has been fully deoxygenated and the chain coppers are Cu^{1+}, then $p = x/2$, since the doped charge x is distributed over two CuO_2 layers. However, for most other systems the doping state is not directly calculable because of oxygen and cation non-stoichiometry. A simple example is $YBa_2Cu_3O_{7-\delta}$, where the doped charge 2(1-δ) is uncertainly distributed over the separate chain and plane coppers. In this case, the use of bond valence sums has proved useful in fairly accurately determining p. The bond valence sum (BVS) about a Cu atom within a structure is given by:[34]

$$V_{Cu} = \Sigma_j \exp [- (r_j-r_0)/0.37] \qquad \text{(Eq. 3)}$$

where the sum is over the nearest-neighbour oxygens, r_j is the bond length for each neighbour and r_0 is a characteristic length for the Cu-O pair. The value of r_0 for many cation-anion pairs has been tabulated by Brown.[34,35] Such BVS values have been used to estimate the doping state as $p = V_{Cu} - 2$ or, indeed, the valence of any of the relevant cations is given by its BVS. However, in view of the fact that the doped holes reside dominantly on the oxygen orbitals, it seemed to the author that one needs also to include oxygen BVS to determine the overall doped charge which can be distributed over both Cu and O orbitals. An expression similar to Eq. 3 is used for the oxygen BVS, V_O, except that the sum now includes all nearest-neighbour Cu-O pairs as well as Ba-O and Y-O pairs. The total doping state was estimated as:[36]

$$p \approx V\_ = 2 + V_{Cu} - V_{O2} - V_{O3} \qquad \text{(Eq. 4)}$$

where O2 is the oxygen residing between two coppers aligned in the *a*-direction and O3 is the oxygen residing between two coppers aligned in the *b*-direction. This also allows the definition of another composite BVS, which is a nominal measure of the relative distribution of doped charge between the oxygen and copper orbitals, namely:[36]

$$V_+ = 6 - V_{Cu} - V_{O2} - V_{O3} \qquad \text{(Eq. 5)}$$

This second parameter is extremely useful and also acts as a measure of stress in the plane – negative values indicate a compressive stress, while positive values indicate a tensile stress.

Polycrystalline samples of $Y_{1-x}Ca_xBa_2Cu_3O_{7-\delta}$ were synthesized and structural refinements were performed on neutron diffraction data collected at the Argonne National Laboratory.[37] From the bond-lengths, BVS values were calculated and values of V_ calculated from Eq. 4 are plotted in Fig. 7 as a function of δ for calcium contents of x = 0, 0.1 and 0.2. These show an initial linear region followed by a plateau as δ → 1. The plateau can be understood from the fact that when δ = 1 all the chain coppers are Cu^{1+}. When δ is reduced fractionally below unity the oxygens in the chain layer are dilute and isolated such that each incorporated oxygen merely changes the valence of the two adjacent coppers to Cu^{2+}. As long as no chain segments are formed, there is full charge balance in this process and no charge is transferred to the CuO_2 planes. Here p is independent of δ. Only when chain segments form at higher oxygen concentration is there residual charge. This is transferred to the planes and p starts to rise. As noted, when δ is exactly 1 the value of p is exactly x/2. In Fig. 7 this is very nearly satisfied by $V\_$ and we believe that all estimates of p in Fig. 7 should be rigidly shifted by just +0.01.

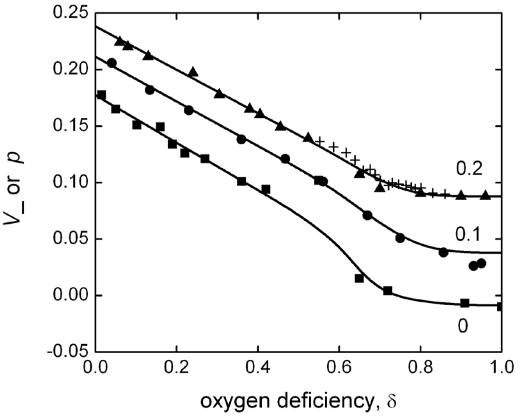


Fig. 7. The variation of p, estimated from the BVS parameter $V\_$, with oxygen deficiency in $Y_{1-x}Ca_xBa_2Cu_3O_{7-\delta}$. Values of x are shown for each curve; near full oxygenation the curves are linear with slope 0.21 holes/oxygen while as δ → 1 the hole density is independent of δ; actual values of p are probably 0.01 larger in all cases.

T_c Correlations

This BVS procedure allows an estimate of the doping state of the rather complex $Y_{1-x}Ca_xBa_2Cu_3O_{7-\delta}$ system that has become a standard in the field. When we consider the value of V_+ as a function of δ, it turns out to be constant across the entire doping range. This is useful because it means that $V\_$ and V_+ are orthogonal with respect to oxygen doping. On the other hand, it is a very different story when we consider V_+ across a range of different HTS cuprates. Fig. 8 shows $T_{c,max}$ plotted against V_+ for 33 different cuprates. There is a remarkable correlation that shows $T_{c,max}$ trending steadily upwards as the CuO_2 planes are brought under increasing tensile stress and the doped charge is displaced increasingly onto the O_{2p} orbitals. The uppermost four data points are for trilayer cuprates where we have the option of calculating V_+ for the inner plane or for the outer planes. The data plotted are for the inner plane and if V_+ is calculated for the outer planes the data points lie deep on the compressive side, completely uncorrelated with the other cuprates.[32] It is clear, therefore, that it is the inner planes that determine the magnitude of $T_{c,max}$ even though, as noted, the inner plane is well short of optimal doping.[28]

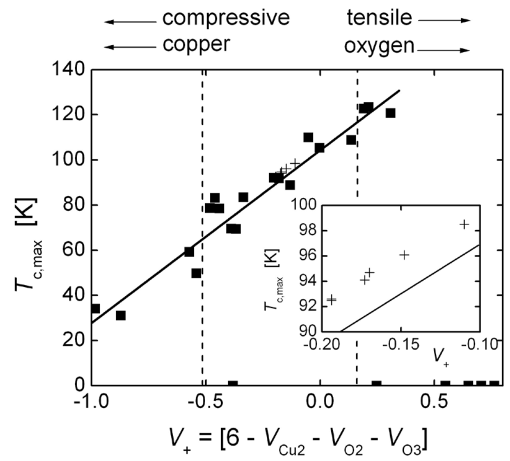


Fig. 8. The correlation of $T_{c,max}$ with the bond valence sum parameter V_+. Negative values of V_+ correspond to a compressive in-plane stress and holes tending to reside more on Cu 3d orbitals while positive values correspond to a tensile in-plane stress and holes tending to reside more on oxygen 2p orbitals.

The clear implication of this correlation is that a strategy to increase T_c would include stretching the Cu-O bond by, for example, substituting larger cations. However, V_+ is a more complex measure than merely that of Cu-O bond length – it may, *e.g.* be increased by moving the apical oxygen further away. Consistent with this, the inner layer in trilayer systems has no apical oxygen at all and this displays a higher intrinsic T_c value than do the outer layers which have an apical oxygen. Nonetheless, the simple approach of substituting larger equivalent cations seems to be well borne out. Fig. 8 also shows data (crosses) for six different $RBa_2Cu_3O_7$ where R is a lanthanide rare-earth element ranging from La to Yb;[38] the inset enlarges this region. On progressing across the lanthanide series the ion size progressively contracts. At the same time $T_{c,max}$ is progressively diminished. In the figure, this progression can be seen to follow the broader correlation with essentially the same slope. In similar fashion, $T_{c,max}$ in $Bi_2Sr_{1.6}R_{0.4}CuO_6$ is found to systematically decrease as R decreases. Based on these considerations, given that the highest T_c thus far observed is found in $HgBa_2Ca_2Cu_3O_8$ ($T_{c,max}$ = 134 K), it is to be expected that this record would be further raised in the material $HgRa_2Ca_2Cu_3O_8$ where barium is replaced by the larger radium. The complications of radioactivity have prevented any attempts to synthesize this material!

Thermodynamic Stability

There is an unexpected link between the above ideas and the thermodynamic stability of the HTS cuprates at different temperatures and oxygen partial pressures, PO_2. We found that all those cuprates with a good lattice match between the block layer and the CuO_2 layer, such that the CuO_2 layer was under neither tension nor compression, decomposed on the stability boundary between CuO and Cu_2O. This is the line A-A′ shown in Fig. 4, where $\log_{10}(PO_2)$ is plotted *vs* 1000/*T* (K^{-1}), and it is the limit of stability of Cu^{2+} relative to Cu^{1+}. For these unstressed cuprates it is the CuO_2 layer that determines the stability. This includes all the cuprates found between the two vertical dashed lines of Fig. 8. On the other hand, those compounds where there is a mismatch between the block layer and the CuO_2 plane, either in tension or compression, remain stable to much higher temperatures than the A-A′ boundary. For these, it is the block layer that determines the thermodynamic stability and this includes all cuprates which lie outside the two vertical dashed lines of Fig. 8. These limitations are important for determining the upper limits for annealing the cuprates. They can also be used as a guide to annealing conditions suitable for causing partial decomposition as is often needed to control the microstructure for enhanced flux pinning.

The Contrary Effects of Pressure

We close this section by noting the anomalous effects of pressure on T_c. The correlation summarised in Fig. 8 would suggest that any means by which the lattice can be expanded will increase T_c and, conversely, any means by which it is compressed will decrease T_c. Hence one would expect the application of external pressure to reduce T_c. In fact it does the opposite.

We have measured the pressure dependence of T_c in $YBa_2Cu_4O_8$ using a *home-built* beryllium-copper clamp cell in a SQUID magnetometer.[39] Additionally, the sample was oxygen isotope exchanged by extended annealing at 750 °C in ^{18}O and then, after measurements, back exchanged again in ^{16}O. Fig. 9 shows T_c *vs P* for the two isotope-exchanged samples. In both cases T_c rises very rapidly – at a rate of +5.24 K/GPa for ^{18}O and +5.4 K/GPa for ^{16}O. A slight negative curvature is also evident and it is known that $T_c(P)$ reaches a maximum of 106 K at about 10 GPa before falling at higher pressure. As noted, this behaviour is puzzling because Fig. 8 suggests that such a compressive stress should *decrease* T_c. Indeed, given the typical compressibility of the cuprates, converting the ion-size effects noted in Section 4.4 into an effective internal (or chemical) pressure, one would expect T_c to *fall* at 5 or 6 K/GPa. The magnitude is right but the sign is wrong.

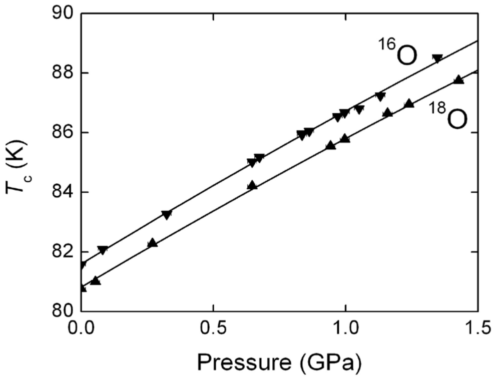


Fig. 9. The pressure dependence of T_c for $YBa_2Cu_4O_8$ where all oxygens in the compound are exchanged for either ^{16}O or ^{18}O isotopes. In both cases T_c rises very rapidly – at +5.24 K/GPa for ^{18}O and +5.4 K/GPa for ^{16}O; reproduced from ref. 39.

This contradiction is a crucial observation and it is the author's view that its resolution will lead to a major advance in our understanding of HTS. The underlying issues and possible solutions are beyond the scope of the present discussion. Nonetheless, it is likely that pressure suppresses fluctuations and thereby increases T_c, while decreasing ion-size probably distorts the Fermi surface, shifting the location of the vHs to higher doping – this would decrease the DOS and thereby reduce T_c. Again, quantum chemistry calculations could shed much light on this hypothesis. The impact of pressure and ion size on other physical properties, such as the magnetic correlations and pairing interactions, will also play a significant role and research efforts should be directed towards disentangling all these competing behaviours.

Substitution Chemistry

The versatility of the cuprates lies in their diversity of structural families and their propensity for forming homologous series. It also lies in their ability to accommodate a wide range of atomic substituents into the parent compounds. These may be of various sorts generally separable into (i) substitutions in the block layer and (ii) substitutions in the CuO_2 layer. The former may be of the same valence and, therefore, impact only through ion-size effects or they may be altervalent and change the doping state (as well as impose ion-size effects). In either case their impact is incremental. The substitutions into the CuO_2 layers are generally strongly deleterious towards superconductivity.

Doping

There are two main reasons for altering the doping state of HTS cuprates: firstly, in order to optimise the intrinsic superconducting properties and, secondly, to explore the physical and chemical properties as a function of doping across the entire phase diagram in order to probe the fundamental mechanisms underlying their normal and superconducting state. The easiest route is to change the oxygen content. Thus, $YBa_2Cu_3O_{7-\delta}$ may be shifted from the undoped insulating state ($p = 0$, $\delta = 1$) to the onset of superconductivity ($p = 0.05$, $\delta \approx 0.6$), to optimal doping ($p = 0.16$, $\delta \approx 0.13$), to critical doping where the pseudo-gap vanishes ($p = 0.19$, $\delta \approx 0$) simply by varying the oxygen content. Typically, we anneal the sample to equilibrium in a flow of $O_2 + N_2$ gas at fixed temperature in a vertical furnace; then, using a magnetic release mechanism, quench directly into liquid nitrogen in order to freeze in the desired oxygen stoichiometry. The physical properties may then be explored and the process repeated to progress across the phase diagram. The so-called *critical doping state* is the desired target for applications because this is where the superfluid density and critical current density is maximized. As noted, the sample is a little overdoped relative to optimal doping where T_c is maximized, but this is a small sacrifice in relation to the very substantial improvement in practical properties, especially performance in a magnetic field, that is achieved by this rather small increase in doping. We have patents to cover this process of fine tuning.

Often one may wish to extend the doping in $YBa_2Cu_3O_{7-\delta}$ to higher levels in order to explore the more deeply overdoped region. This cannot be done by further increases in oxygen content. Instead, one typically has to resort to altervalent substitution where Ca^{2+} is substituted for Y^{3+} in the composition $Y_{1-x}Ca_xBa_2Cu_3O_{7-\delta}$. The solubility limit is around $x = 0.2$ and, even here, the synthesis is tricky, requiring reactions close to the melting point, leaving a window of just a few degrees C. In this way, a maximal doping of $p \approx 0.24$ can be achieved with T_c reduced to about 45 K in the overdoped region. It is somewhat frustrating that most substitutions in HTS cuprates cannot shift far away from optimal doping. There are a few exceptions, such as $La_{2-x}Sr_xCuO_4$ where the doping level can be changed from $p = x = 0$ to $p = x = 0.3$. But this tendency for as-synthesized HTS to sit somewhere generally near optimal doping and to resist doping far away from this is rather thought-provoking and suggests a close relationship between structural stability and the occurrence of superconductivity. In particular, it may be that T_c is optimized close to a structural instability and, indeed, there is a strong tendency in these systems to phase separate or to exhibit various forms of electronic and structural inhomogeneity. Avoidance of a vHs is likely to play a role here.

The above substitution of Ca^{2+} for Y^{3+} is a hole-doping substitution, which in general can be promoted by using a low oxygen partial pressure in the synthesis atmosphere. Electron-doping substitutions, *e.g.* La^{3+} for Ba^{2+}, are generally promoted using a high oxygen partial pressure. It is also possible to co-dope Ca^{2+} for Y^{3+} and La^{3+} for Ba^{2+}, resulting in the compound $Y_{1-x}Ca_xBa_{2-x}La_xCu_3O_7$. As may be expected, the doping does not alter but disorder is progressively increased with increasing x. Surprisingly, disorder has little effect – even the superfluid density, which is very sensitive to pair-breaking, is barely diminished.[40]

These types of altervalent substitutions can be used across the wide variety of HTS cuprates to increase or decrease the doping state, although one often encounters narrow solubility limits, as discussed. Just one further example is needed to establish the pattern. The compound $Bi_2Sr_2CaCu_2O_{8+\delta}$ is limited to a narrow range around optimal doping by varying the oxygen content as described by the value of δ. The doping state may be reduced (electron doping) by substituting Y^{3+} for Ca^{2+} or increased by substituting Pb^{2+} for Bi^{3+}. Furthermore, there is a tendency for some Bi^{3+} to substitute on the Sr^{2+} site as noted, even in the pure compound; this is an electron doping substitution. Using the above guidelines this can be suppressed by synthesizing under low oxygen partial pressure.

Ion-Size Effects

It is the author's view that ion-size effects provide an important (but as yet relatively unused) key to unravelling the physics of HTS. Therefore they deserve considerable discussion. A productive approach would be to explore non-doping homovalent substitutions such as Ca^{2+} for Sr^{2+} (smaller) or Ba^{2+} for Sr^{2+} (larger), or substitution across the lanthanide series for Y^{3+}. The questions to be asked are: (i) What is the effect on key superconducting parameters? (ii) What is the effect on the pseudo-gap temperature, T^*, and energy, E_g? (iii) If pairing originates in the magnetic correlations, what is the effect on the magnetic exchange energy J? (iv) Do these substitutions shift the van Hove singularity to lower or higher doping? (v) How do these shifts correlate with the effects of external pressure? (v) How do they correlate with the strain effects of lattice mismatch in epitaxial thin films on single-crystal substrates? and (vi) How do all these correlate with T_c? This offers a rich arena of on-going studies on HTS utilising such techniques as Raman scattering, specific heat, NMR, electron tunnelling and electron transport – magnetoresistance, Hall effect and thermoelectric power.

Isotope Exchange

Conventional superconductors derive their Cooper pairing from the interaction of electrons and phonons. This was first evidenced by the observed reduction in T_c when an element was replaced by a heavier isotope. Eq. (2) shows that T_c is proportional to the characteristic frequency, ν_B, of the pairing correlation and in conventional superconductors the pairing is mediated by phonons. So ν_B is the Debye frequency that varies inversely as the square root of the elemental mass. Thus, we have the isotope effect coefficient:

$$\alpha \equiv -(\Delta T_c/T_c)/(\Delta M/M) = 0.5 \qquad \text{(Eq. 6)}$$

Here, α is the ratio of the fractional change in T_c to the fractional change in isotopic mass, and it takes the value 0.5 because of the square root dependence of the Debye frequency on mass. In 1950, precisely this relationship was found in the case of the isotopes of Sn[41] and this was the crucial guide that ultimately established the BCS theory of SC.

It is widely believed that the HTS cuprates derive their pairing interaction from magnetic correlations, and here the large value of T_c would be partly established by the very large magnetic energy scale given by $J = 1390$ K (expressed in temperature units), *cf.* the Debye temperature of about 270 K. This being the case, one would not expect an isotope effect. However, Fig. 9 shows that there is an oxygen isotope effect indeed, albeit small – α is about 0.075, rather less than the value of ½ given in Eq. 6. Moreover, α grows dramatically with underdoping and possibly diverges at $p = 0.05$ where SC disappears.[42] We understand this divergence as arising from the pseudo-gap which competes with SC.[42] Thus, we conclude that there is a residual underlying isotope effect but it is small, suggesting that perhaps both phonons and magnetism play a role in forming Cooper pairs, though phonons are (probably) the junior partner. Site selective isotope exchange shows that it is only the oxygens in the CuO_2 plane that contribute an isotope effect.[43] Apical oxygens thus play little or no role in SC pairing.

Summary: The Ideal TS Superconductor

Drawing all the above thoughts together we can say, in conclusion, that there are a number of clear guidelines to establish the ideal cuprate superconductor. Firstly, $T_{c,\max}$ will be maximized by stretching the lattice as much as possible through appropriate atomic substitutions and/or lattice mismatch in epitaxial thin films. This is opposite to the effect of applying an external pressure, probably because the latter primarily works towards suppressing fluctuations. In order to suppress fluctuations under ambient conditions, it is beneficial to enhance the interlayer coupling, probably best achieved through metallizing one of the interlayers in the block layer. The Y-123 and Y-247 class of superconductor achieve this naturally via the chain layer(s) that are metallic and in which superconductivity seems to be induced by the well-known proximity effect. To achieve the highest critical current density, it is necessary to tune to critical doping ($p_{crit} = 0.19$) rather than optimal doping ($p = 0.16$). However, if the material is to be operated at low temperature, and because the irreversibility field, H^*, continues to steepen with overdoping, it could be beneficial to overdope a little beyond p_{crit}. Again, H^* is increased by increasing the interlayer coupling either by metallizing an interlayer or by reducing the block-layer spacing t_b. This can be achieved by removing one or more layers within the block layer, or by reducing ion sizes within the block layer. The latter would have the effect of *reducing* $T_{c,\max}$ so one is left with a compromise between T_c and critical current density. Of these, current density is probably the most important. It is possible to remove layers from the block layer and, indeed, this is the cause of the increased value of H^* seen in Fig. 6 in progressing from Tl-2212 to Tl-1212 and from Tl-2223 to Tl-1223, where one of the TlO layers has been removed.

By means of judicious site substitution one ought to be able to secure a more even distribution of charge in trilayer HTS so that both inner and outer layers can be optimized simultaneously. This could result in very large increases in $T_{c,\max}$. We also have much to learn about how to shift the vHs to lower doping in order to capture a larger DOS. But the ideal HTS would be the so-called infinite-layer compound where every second layer is a CuO_2 layer. Such a system would be very strongly coupled. The intervening divalent alkali earth should be as large as possible and, therefore, should be Ba^{2+} (if we abandon Ra^{2+}). Then it needs to be doped, preferably with a large monovalent ion such as K^+. This leads us to $Ba_{1-x}K_xCuO_2$ or even $Ba_{1-x}Rb_xCuO_2$ where $x = 0.19$. This cannot be synthesized under ambient pressure but possibly under high-pressure/high-temperature synthesis, or preferably through physical deposition of thin films. We shall see.

References

1. Bednorz J. G.; Muller, K. A. *Z. Phys.* **1986**, *B 64*, 189.
2. Bardeen, J.; Cooper, L. N.; Schrieffer, J. R. *Phys. Rev.* **1957**, *106*, 162, *108*, 1175.
3. Tallon, J. L.; Bernhard, C.; Binninger, U.; Hofer, A. *et al.* *Phys. Rev. Lett.* **1995**, *74*, 1008.
4. Tallon, J. L.; Pooke, D. M.; Buckley, R. G.; Presland, M. R.; Blunt, J. *Phys. Rev. B.* **1990**, *41*, 7220.
5. Tallon, J. L. Buckley, R. G.; Gilberd, P. W.; Presland, M. R.; *et al.* *Nature* **1988**, *333*, 153.
6. McElroy, K.; Lee, J.; Slezak, J. A.; Lee, D.-H. *et al.* *Science* **2005**, *309*, 1048.
7. Stoto, T.; Pooke, D.; Forro, L.; Kishio K. *Phys. Rev.* **1996**, *B54*, 16147.
8. Tallon, J. L. Buckley, R. G.; Gilberd, P. W.; Presland, M. R. *Physica* **1989, *C 58***, 247.
9. Eisaki, H.; Kaneko, N.; Feng, D. L.; Damascelli, A. *et al.* *Phys. Rev.* **2004**, *B 69*, 064512.
10. Sheng, Z. Z.; Hermann**,** A. M. *Nature* **1988**, *332*, 55, *60*, 937.

11. Putilin, S. N.; Antipov, E. V.; Chmaissem, O.; Marezio, M. *Nature* **1993**, *362*, 226.
12. Tallon, J. L. Williams, G. V. M.; Flower, N. E.; Bernhard, C. *Physica* **1997**, *C282-287*, 236.
13. Niedermayer, Ch.; Bernhard, C.; Blasius, T.; Golnik, A. *et al*. *Phys. Rev. Lett*. **1998**, *80*, 3843.
14. Presland, M. R., Tallon, J. L. Buckley, R. G.; Liu, R. S.; Flower, N. E. *Physica* **1991**, *C176*, 95.
15. Tranquada, J. M.; Sternlieb, B. J.; Axe, J. D.; Nakamura, Y.; Uchida, S. *et al*., *Nature* **1995**, *375*, 561.
16. Tallon, J. L.; Loram, J. W.; Williams, G. V. M.; Cooper, J. R., *et al. Phys. Stat. Solidi* **1999**, *(b)215*, 531.
17. Boebinger, G. S.; Ando, Y.; Passner, A.; Kimura, T. *et al. Phys. Rev. Lett.* **1996**, *77*, 5417.
18. Trovarelli, O.; Geibel, C.; Mederle, S.; Langhammer, C. *et al. Phys. Rev. Lett.* **2000**, *85*, 626.
19. Alff, L.; Krockenberger, Y.; Welter, B.; Schonecke, M. *et al. Nature* **2003**. *442*, 698.
20. Pooke, D. M.; Buckley, R. G.; Presland, M. R.; Tallon, J. L. *Phys. Rev.* **1990**, *B41*, 6616.
21. Tallon, J. L.; Pooke, D. M.; Buckley, R. G.; Presland, M. R. *et al. Appl. Phys. Lett.* **1991**, *59*, 1239.
22. Tallon, J. L. *Phys. Rev.* **1989**, *B39*, 2784.
23. Tallon, J. L.; Schuitema, A. H.; Tapp, N. J. *Appl. Phys. Lett.* **1998**, *52*, 507.
24. Storey, J. G.; Tallon, J. L.; Williams, G. V. M. *Phys. Rev.* **2007**, *B6*, 174522.
25. Kaminski, A.; Rosenkranz, S.; Fretwell, H. M.; Norman, M. R. *et al*. *Phys. Rev.* **2006**, *B73*, 174511.
26. Trokiner, A.; Le Noc, L.; Schneck, J.; Pougnet, A. M. *et al. Phys. Rev.* **1991**, *B44*, 2426.
27. Statt; B. W.; Song, L.M. *Phys. Rev*. **1993**, *B48*, 3536.
28. Chen X.-J.; Struzhkin, V. V.; Yu, Y.; Goncharov, A. F. *et al. Nature* **2010**, *466*, 950.
29. Jover, D. T.; Wijngaarden, R. J.; Griessen, R.; Haines, E. M. *et al. Phys. Rev.* **1996**, *B* 54, 10175.
30. Haines, E. M.; Tallon, J. L. *Phys. Rev*. **1992**, *B45,* 3172.
31. Ideta S; Takashima K; Hashimoto M; Yoshida T. *et al. Phys. Rev. Lett.* **2010**, *104*, 227001.
32. Tallon, J. L. Williams, G. V. M.; Bernhard, C.; Pooke, D. M., *et al. Phys. Rev.* **1996**, *B53*, R11618.
33. Tallon, J. L.; Bernhard, C.; Binninger, U.; Hofer, A. *et al. Phys. Rev. Lett.* **1995**, *74*, 1008.
34. Brown, I. D. *J. Sol. State Chem*. **1989**, *82*, 122.
35. Brown, I. D.; Altermatt, D. *Acta Cryst*. **1985**, *B41*, 244.
36. Tallon, J. L. *Physica* **1990**, *C168*, 85.
37. Tallon, J. L. Bernhard, C.; Shaked, H.; Hitterman; R. L.; Jorgensen, J. D. *Phys. Rev.* **1995**, *B51*, R12911.
38. Williams; G. V. M.; Tallon, J. L. *Physica* **1996**, *C258*, 41.
39. Suresh, N.; Storey, J. G.; Williams, G. V. M.; Tallon, J. L. *Phys. Rev.* **2008**, *B78*, R100503.
40. Tallon, J. L.; Bernhard, C.; Niedermayer, Ch. *Supercon. Sci. Tech.* **1997**, *10*, A38.
41. Allen, W. D.; Dawton, R. H.; Lock, J. M.; Pippard, A. B.; Shoenberg, D. *Nature* **1950**, *166*, 1071.
42. Williams; G. V. M.; Tallon, J. L.; Quilty, J.; Trodahl, H. J.; Flower, N. E. *Phys. Rev. Lett.* **1998**, *80*, 377.
43. Khasanov, R.; Shengelaya, A.; Morenzoni, E.; Angst, M. *et al. Phys. Rev.* **2003**, *B68*, 220506.

Chemistry in the Waikato: Developments Since 1985

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In the minds of most New Zealanders, the Waikato has a bucolic image of green pastures where one might expect the practice of chemistry to be confined to educational establishments and routine testing laboratories in dairy factories. In fact, within the area encompassed by the Waikato Branch of the NZIC (which includes the Coromandel Peninsula, the Bay of Plenty, Rotorua, Taupo, and the King Country), sulfuric acid, superphosphate fertilizer and hydrogen peroxide are all manufactured on a large scale; the region also includes two pulp and paper mills, a gold mine and 17 power stations, all of which employ chemists and carry out research and development as well as routine analysis and monitoring. Hamilton city alone is the home of more than 1000 professional research scientists, one of the highest per capita figures in the world. In the King Country, the name McDonalds is associated with limestone, rather than with hamburgers; customers of this company, the country's largest producer of lime products, are as diverse as the NZ Steel mill at Glenbrook, agricultural enterprises, road construction and repair, and overseas gold mines.

Energy is one of the Waikato's most important products, and energy issues are being actively addressed in many laboratories, large and small, throughout the region. About 40% of NZ's coal is mined around Huntly. The Waikato River hosts eight hydroelectric power stations, while the Tongariro Project, to the south of Lake Taupo, has two. The eight geothermal plants between Taupo and Rotorua now provide about 10% of the country's total electric power generation. From an environmental perspective, geothermal power is renewable, subject to the need to regenerate plants after some years of drawing steam; the downside is that the exploitation of geothermal bores has, in the past, polluted the Waikato River and some of its tributaries with toxic elements such as arsenic and thallium. The first geothermal power station was established at Wairakei in 1958; four were commissioned between 1989 and 1998, and three more since 2008. The uncharacteristically smooth progress of meeting resource management requirements for the completion of the most recent projects has been facilitated by the remarkable spirit of cooperation and partnership that has been nurtured between Mighty River Power Ltd., and local iwi. Much of the chemistry associated with the efficient operation of these stations involves the prevention of amorphous silica deposition in the pipelines. The hot water accompanying the steam from the bores is rich in colloidal silica, whose conversion into particulate amorphous silica is catalyzed by hydroxide ion. Thus pH control, by addition of sulfuric acid, is essential. The great thermal power station at Huntly (furnishing 17% of the country's power) was designed to use either natural gas (piped from Taranaki) or locally mined coal, or a combination of both. The supply of fuel to Huntly has been problematic from time to time, on account of dwindling reserves of natural gas and periodic deficiencies in coal supplies, although the latest indications are that natural gas from the Maui field may last for another 10-20 years. Since about the year 2000, around half of the plant's coal needs have been supplied from Indonesia, via the Port of Tauranga (and often – controversially – transported to Huntly by road instead of the much more economical rail link through the Kaimai Tunnel).

The other major customer for Huntly coal is the aforementioned NZ Steel mill at Glenbrook, which also uses calcium carbonate from McDonald's quarry near Te Kuiti for flux formation. The iron comes from the ilmenite ironsand deposits at Waikato North Head. The titanium content of these ironsands – long regarded as a nuisance in the iron smelting process – is now seen as an important resource. In 2010, the Titanium Development Association, in partnership with the Government, established an Applied Powder Metallurgy Centre in Tauranga. This evolved from Titanox Development Ltd., which was established in 1997 to exploit the development of titanium products along lines suggested by the work of Deliang Zhang at Waikato University. The power station at Meremere, north of Huntly, which was fuelled by coal from a mine at Maramarua, was decommissioned in 1991. At the same time, the Maramarua mine was abandoned but its reopening has been mooted recently. Several smaller coal mines operate around the region. Aerial prospecting for coal seam methane is under way over the North Waikato, and electric power generation from this new source may begin in late 2011 or early 2012. NZ's most northerly wind farm, at Te Uku, west of Hamilton, is expected to contribute about 6 MW to the national grid when it is commissioned in March 2011. Overall, the Greater Waikato region generates nearly half of this country's electricity supply.

Hamilton is the service centre for the region, but the rapid development of the Port of Tauranga since the opening of the Kaimai tunnel rail link in 1978 has transformed Tauranga and Mount Maunganui into important industrial centres. Superphosphate fertilizer is produced at Mount Maunganui from imported raw materials. The heaviest concentration of chemistry-based research in the Waikato region is to be found on the adjacent campuses of the University of Waikato and what used to be known as the Ruakura Research Station on the northeastern boundary of Hamilton. The Waikato can claim at least two historical distinctions having international repercussions for chemistry and its applications. In 1889, the MacArthur-Forrest cyanide process for the extraction of gold from relatively low-grade mineral sources – a splendid example of applied co-ordination chemistry, developed in Glasgow in 1887 – was successfully tested for the first time at the Crown Battery in Karangahake (between Paeroa and Waihi), and soon became almost universally employed in gold mining. Ruakura's interest since the 1920s in the agricultural consequences of cobalt deficiency in pumice soils played a part in the history of Vitamin B_{12} and led to important developments in atomic absorption spectroscopy by J.E. Allan in the 1950s. His work is commemorated by NZIC Waikato Branch *J.E. Allan Memorial Prize*, awarded annually since 1973 to the best second year chemistry student at the University of Waikato.

The University of Waikato enrolled its first chemistry students in 1970, with Alex Wilson (the diversity of whose talents defied any classification) at the helm assisted by Malcolm Carr (organic chemistry), Ken Mackay (inorganic chemistry) and Peter Morris (physical chemistry). They had been supplemented by the end of 1972 by Chris Hendy (geochemistry/analytical chemistry), Alan Langdon (physical chemistry), Lyndsay Main (organic chemistry) and Derek Smith (inorganic/theoretical chemistry). By the beginning of 1976, they had been joined by Brian Nicholson (inorganic/organometallic chemistry) and Alistair Wilkins (organic natural products/analytical chemistry). Waikato had sought to develop an academic structure based on Schools of Study, within which departmental entities were only loosely delineated. Thus, within the School of Science, the Department of Chemistry worked closely with Biological Sciences and Earth Sciences in the same building, with common facilities such as a workshop, store and tearoom. Alex Wilson combined the duties of Dean of the School with Headship of the Chemistry Department. These arrangements were intended to facilitate interdisciplinary activities and to discourage interdepartmental rivalries. Thus, for example, geochemistry papers were taught jointly by Chris Hendry in Chemistry and Peter Hodder in Earth Sciences, and two biochemists (Peter Molan and Roy Daniel) were jointly responsible to the Heads of Chemistry and Biological Sciences. Staff routinely cited their affiliation as *School of Science* rather than *Department of Chemistry* in their publications and conference presentations. But by the mid-1980s, the departmental structure was becoming entrenched. With the demise of the quinquennial grant system and the implementation of the 1989 Education Amendment Act, by the 1990s the pursuit of the all-important EFTS (effective full-time student) count had become the major academic preoccupation. Chemistry's student numbers fluctuated throughout this period of bewildering change. After a dip in the mid-1980s, the Department grew steadily until the mid-1990s, and additional full-time staff members were appointed between 1988 and 1995. Rick Ede, who had taken MSc and PhD degrees at Waikato in the 1980s, was needed to fill the gap in organic chemistry following Malcolm Carr's retreat into science education (as discussed further below). Organic chemistry was further strengthened by the appointment (1991) of Michèle Prinsep, who specializes in the characterization of marine natural products having medicinal potential. In 1994, Rick moved to NZ Forest Research in Rotorua to pursue his interests in wood pulp technology; he is currently CEO of Unitec. Rick was replaced by Merilyn Manley-Harris, whose expertise in carbohydrate chemistry sustained the Department's links with the forestry industry; Merilyn is presently Chairperson of the Department. Student demand for research opportunities in analytical and environmental chemistry led to the appointment of Nick Kim, who later defected to the Waikato Regional Council (now Environment Waikato). By this time (early 1990s), the rapid growth of the BSc(Tech) programme (see below) necessitated the appointment of staff who combined an industrial background with academic excellence; Bill Henderson (formerly at Albright & Wilson, Birmingham, UK) fitted the bill admirably. Michael Mucalo, a physical chemist with a background mainly in electrochemistry, extended his interests and expertise into areas appropriate for the development of external collaboration, for example, the use of animal bones in biomedical materials.

As befitted a brand new Chemistry Department, from the earliest days staff members were encouraged to develop initiatives in teaching. Malcolm Carr became Director of CSMER (Centre for Science and Mathematics Education Research), which is now the Centre for Science and Technology Education. CSMER's work attracted international interest and regular visitors from overseas; by about 1985 Malcolm's involvement had become almost a full-time job, and Geoff Mills was appointed to a four-year Junior Lectureship in 1986 to assist with the teaching of organic chemistry. He was joined soon afterwards by Chris Kirk, who combined the roles of teaching organic chemistry with the coordination of BSc(Tech) industrial placements. The BSc(Tech) programme was developed in the 1980s as a four-year degree with the same academic content as a normal BSc. It was supplemented by papers in Management and had two spells of work in an industrial environment that totalled about nine months. Alan Langdon played an important part in the planning of this initiative. The BSc(Tech) degree proved to be very popular; students correctly surmised that this qualification would enhance their employability, and there was the added attraction of earning a decent wage during part of the course. But the programme involved a great deal of work for the academic staff of Chemistry, who had to find industrial placements for a growing number of students as well as providing for their pastoral care, liaising with their external supervisors, assessing their reports and so on. Chris Kirk, who had joined the Department from the Taranaki Polytechnic, had the responsibility to coordinate the BSc(Tech) programme across the School; this soon became a full-time job. When Chris moved on to Massey University in 1995 (he is currently Deputy Vice-Chancellor at Lincoln University), he was replaced by Richard Coll, an inorganic chemist who is now Director of Cooperative Education.

From time to time, other staff members have been seconded to University positions outside the Chemistry. Tony Cartner, appointed as Lecturer in Physical Chemistry in 1980, went half-time in 1995 to become Associate Dean of the School, and later joined the Pathways College which deals with university preparation, continuing education and student learning. To add to the diversification of the Chemistry Department staff's activities, Ken Mackay did a stint as Dean in the nearly 1990s; he was succeeded by the earth scientist Richard Price, the first full-time Dean of what was by then termed the School of Science and Technology. In the late 1980s, papers in Materials Science and Process Technology were introduced by Professor Nigel Sammes, who is now at the Colorado School of Mines. A Bachelor of Technology degree was offered, and Alan Langdon became closely involved. When in the 1990s ambitious proposals were put forward for a Bachelor of Engineering degree, Alan played an important part in the arduous process of placing Engineering courses on the University's books and securing their recognition by the Institute of Professional Engineers of New Zealand (IPENZ). The Chemistry Department is now part of the Faculty of Science and Engineering, the *School* concept having been finally abandoned. Much of the research carried out in the Department of Engineering (for example on fuel cells, the chemical stability of composite materials, and metal-ceramics composites) is chemistry-based.

The research developments in the Waikato Chemistry Department since the mid-1980s are notable. By 1985, the Department was especially noted for coordination and organometallic chemistry, analytical and environmental chemistry, and chemical education, as well as general inorganic, organic and physical chemistry. Waikato was then particularly well equipped, by national standards, for multinuclear NMR, far infra-red spectroscopy, gas chromatography, X-ray fluorescence and atomic absorption spectroscopy. A Raman spectrometer was on the way, as was a 400 MHz Brücker NMR spectrometer. From the 1990s, all of these have been significantly upgraded. In 1985, mass spectrometry facilities were relatively rudimentary and the University was heavily reliant on Pat Holland at Ruakura for MS work. The University's MS equipment has been greatly improved, although Ruakura still has superior instrumentation for high resolution GCMS work. Waikato was the first NZ University to acquire an electrospray mass spectrometer in 1995. This was exploited especially by Bill Henderson and his graduate students, often in collaboration with Brian Nicholson. Bill, and a former student (Scott McIndoe - now at the University of Victoria, British Columbia) published the highly acclaimed 2005 Wiley monograph *Mass Spectrometry of Inorganic and Organometallic Compounds*. In the first NZ Performance Based Research Funding (PBR) exercise in 2003, the Waikato Chemistry Department was ranked first equal; in 2006, it achieved the straight first position. At the end of the first decade of the present century, the Department faces serious challenges. Apart from the scarcity of resource, there are uncertainties with regard to staffing. People appointed in the 1970s have reached, or are about to reach, the point of retirement. In 2008-9, Peter Morris, Derek Smith and Lyndsay Main, with a total of 111 years of service behind them, all retired. Only two replacements have been appointed, Graham Saunders (inorganic chemistry) and Joseph Lane (computational/physical chemistry). Further retirements are inevitable over the next few years and replacement is problematic.

In 1974, Alex Wilson established the group now known as the *Waikato Radiocarbon Dating Laboratory*. A major focus of interest in recent years has been the application of carbon dating to NZ and Pacific archaeology. Also affiliated to the Faculty of Science and Engineering is the *International Global Change Institute*, an interdisciplinary group focusing on the human dimension in environmental change. In 1992, the National Institute for Water and Atmospheric Research (NIWA) was formed as a Crown

Research Institute (CRI) and by the late 1990s it had established a laboratory on the Waikato campus. Activities of general interest to chemists include water quality testing, control of biofouling on boat hulls, extraction of biofuel from wastewater, and studies of climate change.

In 1992, what was formerly known as the Ruakura Agricultural Research Station underwent major restructuring with the establishment of Crown Research Institutes. Ruakura had been the home of a number of semi-autonomous institutes including the Meat Industry Research Institute of New Zealand (MIRINZ) that was a self-contained operation having, for example, its own library, separate from the Ruakura library. MIRINZ contributed to the Waikato's output of chemistry through such work as studies of the physicochemical changes accompanying the freezing and thawing of meat, and the identification of odiferous substances that make sheep meat disagreeable to many Asian people. Ruakura became the home of two CRIs in 1992: AgResearch and HortResearch. Both embraced several research institutes around the country, but Ruakura today houses the national headquarters of AgResearch, the country's largest CRI with about 900 workers employed on its Ruakura campus. Prior to the restructuring of 1992, the various Ruakura institutes were largely devoted to ongoing, long term Ministry-funded projects. Since its incorporation as a CRI, AgResearch has become increasingly reliant on short-term, contestable project-based funding that, naturally, leads to a roller coaster ride of financial ups and downs, with periodic redundancies. Among the continuing AgResearch activities of interest to chemists since 1992 are:

- Studies of rumen ecology with emphasis on the abatement of greenhouse gas emissions;
- Bio-based products, especially textiles;
- Development of endophytes for enhancing the production and persistence of ryegrass.

In 2009, AgResearch established a Dairy Research Farm at Tokanui, in South Waikato, to study environmental and genetic influences on milk production. Other important AgResearch work in the Greater Waikato includes studies of water quality in Lake Taupo, for example, it has been established that the leaching of nitrogen into the lake comes largely from cow urine patches and not from applied fertilizer.

The aforementioned MIRINZ was established in 1955 as a partnership between NZ Government and meat producers/processors, with Government and industry providing about equal contributions. In the late 1980s, the Meat Producers Board appointed a Meat Research and Development Council to oversee its interest in MIRINZ while, in the early 1990s, the Government grant was replaced by a competitive bidding regime. Thus, MIRINZ became a *stand-alone* commercial research institute. Financial uncertainties and shortfalls led to the merger of MIRINZ with AgResearch in 1999. Recent work by MIRINZ of most interest to chemists would be its studies of meat tenderness, especially the use of electrical stimulation to prevent toughness.

In 2008 HortResearch merged with Crop & Food Research to form a new CRI, Plant and Food Research. The Ruakura branch includes the Biological Chemistry and Bioactives Group, which investigates the biochemistry of plant flavour and texture development, and the metabolism of foods. From the mid-1980s, a Science Park in Hamilton, with links to the University and Ruakura, was mooted and this became a reality in 2001, with the University, AgResearch and Wintec (formerly the Waikato Technical Institute) as strategic partners. It is intended as a hub of biotechnological research and currently has more than 50 tenants.

Outside the University/Ruakura complex, Hill Laboratories is the major centre of chemical activity in Hamilton. Hill, NZ's largest analytical testing company began in Hamilton with a small laboratory in the city centre in 1984. It later moved into the same building as the Waikato Regional Council and eventually took over all four stories. Hill also has a separate Air Quality Laboratory, as well as a unit in the Hamilton Innovation Park dedicated to Food and Bioanalytical Testing. Hill Laboratories recently merged with Analytica, taking over the latter's Hamilton premises. Smaller chemical manufacturers in Hamilton include Mortech Industries, who supply their own brand of biodegradable, formaldehyde-free embalming fluid.

The Enovik Degussa plant near Morrinsville is NZ's largest manufacturer of hydrogen peroxide (*ca.* 19,000 tonnes p.a.). Established in 1990, about 60% of its output is supplied to the pulp and paper mills at Kinleith (Tokoroa) and Kawerau for the bleaching of paper. Until around 1980, chlorine was used for bleaching paper and generated *in situ* by the electrolysis of brine using mercury electrodes. However, the leakage of mercury into waterways became recognized as being environmentally offensive and alternative electrodes were substituted. For some years chlorine was superseded by electrochemically-generated chlorine dioxide but, since the 1990s, the use of peroxide has enabled totally chlorine free bleaching. Rick Ede (mentioned above) did postdoctoral research on peroxide bleaching of paper in Finland before his appointment as a lecturer at Waikato. Enovic Degussa also supplies hydrogen peroxide to the gold mining industry both in NZ and Australia for the oxidation of cyanide in wastewater to the much less toxic cyanate. The site at Morrinsville was chosen on account of the proximity of rail links to both pulp mills, as well as to the Port of Tauranga and Hamilton.

The fortunes of the two pulp mills – both owned by Carter Holt Harvey – have declined since the mid-1980s. The world market for newsprint faces an uncertain future and the demand for telephone directories - a major end product of NZ-produced paper – is falling. Of particular interest to chemists is the management and monitoring of effluents from the pulp mills. The discharge of chlorinated organic compounds has been largely eliminated since the adoption of chlorine-free bleaching methods. Since the mid-1980s biological oxygen demand has been drastically reduced by secondary biological treatment of the effluent, decomposing organic compounds by forced aeration. The pulp mills are heavy users of electricity and each has its own power station. At Kinleith, a co-generating plant burns waste

The University of Waikato campus *ca*. 2005; chemistry is housed within the semicircular buildings (middle left); courtesy Central Communications, Waikato University.

wood to generate about 40 MW that is mostly used on-site. Kawerau has a geothermal plant (100 MW) and this provides much of the area's residential power requirements as well as those of the pulp mill, which is the country's second biggest industrial user of electricity (after the aluminium smelter at Tiwai Point).

In 1992, the Forest Research Institute in Rotorua became a CRI, renamed Scion in 2005. Much of Scion's research is devoted to Energy and Materials. Prospects for bioenergy include liquid biofuels, woody biomass resources, and energy modeling techniques to evaluate the thermodynamic efficiency of bioenergy systems. Scion's industrial biotechnology group is also interested in the possibilities for use of lignin in green chemistry and the development of biopolymers as adhesives, coatings and fibre-composites, thus providing naturally-occurring and renewable sources as alternatives to petrochemical-based products.

Looking to the future – or going forward, in management speak – it is difficult to predict the likely directions of chemistry research at Waikato University and Ruakura. Both campuses are dependent on the lottery of contestable funding from various sources, while the University is also at the mercy of the vagaries of student demand and Government policy. In both institutions, staff numbers are presently under threat. On the positive side, we may expect much expansion of research into geothermal power. Mighty River Power Limited, which owns most of the present geothermal stations, expects to increase their generation from the present 400 MW to 1000 MW by 2020. The future of the Waikato coal mining industry is uncertain, given the environmental objections and the country's obligations towards control of carbon emissions. As already noted, the Huntly coal mines have sometimes been unable to meet the demands of the local thermal power station on top of their other contractual obligations. But the imminent exploitation of coal seam methane, without necessarily digging for new coal deposits, may prolong the viability of the field. If Gerry Brownlee has his way, we can expect a great deal of mineral exploration in the Kaimai Range and its northern extension into the Coromandel peninsula. The present price of gold (which has almost trebled in the last five years) may encourage the reopening of old mines closed in 1998 in the Thames/Coromandel area - such as the Golden Cross mine - and perhaps prospecting for new ones. The Tui mine on the western slopes of Mount Te Aroha furnished sulfides of lead, copper and zinc until its abandonment in 1973. The tailings, which also contain cadmium, have been a source of environmental concern ever since and the Government set aside $10 M in 2007 to complete the cleanup of the site. The full exploitation of NZ's mineral resources, according to Mr. Brownlee's prescription, would provide many opportunities and challenges for chemistry in the Waikato.

The 2010 Nobel Prize in Chemistry

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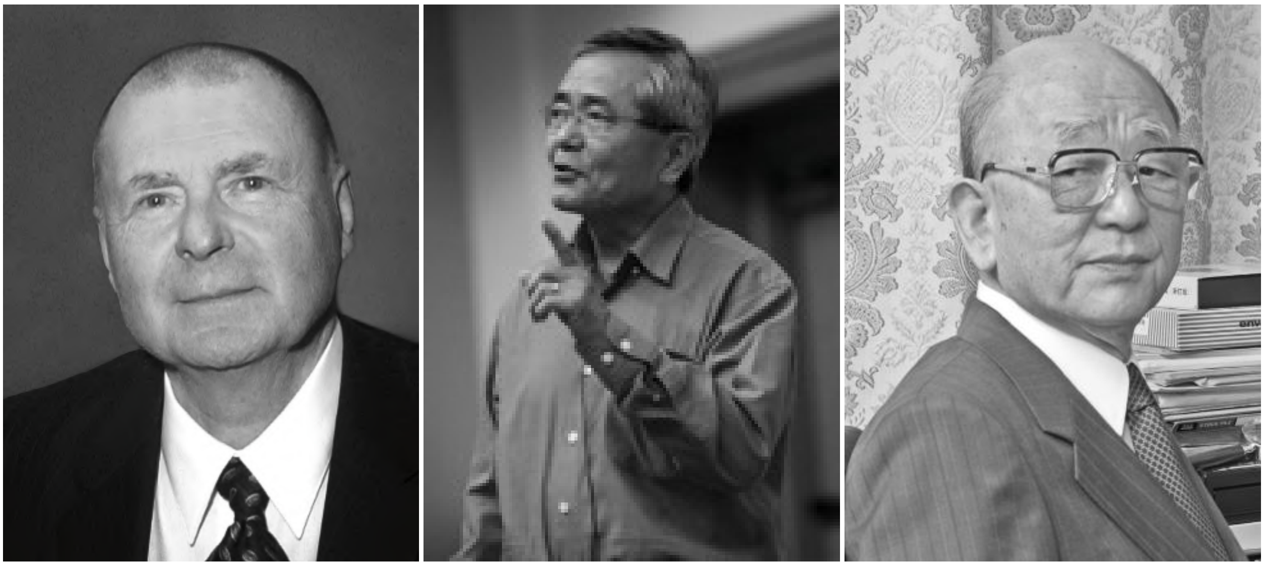


L-R: Richard Heck (courtesy Delaware University/Kathy Atkinson), Ei-ichi Negishi (courtesy Purdue University/Mark Simons) and Akira Suzuki (courtesy International Relations/Hokkaidō University)

The 2010 Nobel Prize in Chemistry was awarded jointly to three stalwarts of organic chemistry: **Richard F. Heck** (University of Delaware, USA)**, Ei-ichi Negishi** (Purdue University, USA) and **Akira Suzuki** (Hokkaidō University, Japan), by the Swedish Academy of Sciences *for palladium-catalyzed cross couplings in organic synthesis*.

The prize recognises the work of these three chemists, who have developed reactions that enable more efficient ways of linking carbon atoms together to build the complex molecules that are improving our everyday lives. The Heck, Suzuki and Negishi reactions, examples of palladium-catalyzed cross coupling reactions, stem from separate work in the 1960s and 1970s that developed reactions using palladium to construct whole molecules at lower temperatures and with less waste than before. They provide a marvellous example of great work carried out in parallel. The painkiller naproxen, a generic sold in the US under the brand name Aleve, Merck & Co.'s allergy treatment Singulair, and Boscalid, a fungicide made by BASF SE, are among the chemicals made possible by their work.

Introduction

The 2010 Nobel Laureates have received the customary medals minted in gold, but it is their work with another noble metal—palladium—that earned Heck, Negishi, and Suzuki their 2010 award. Palladium-catalyzed cross coupling reactions, in which palladium is used to catalyze the formation of carbon-carbon bonds, are widely used to make complex molecular structures. It is a well deserved and long overdue honour, and it is hard to overstate the importance of their processes in modern day synthetic chemistry; they have been employed to make materials, pharmaceuticals, and other biologically active compounds. Although chemistry bookmakers had been expecting that Pd-catalyzed cross-coupling chemistry would earn the Nobel Prize for many years, Heck, who is now 79 and living in the Philippines, told *Chemistry & Engineering News* that his win was *totally unexpected*.

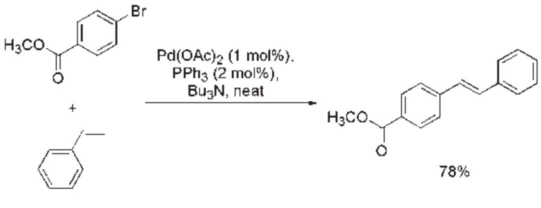
The pioneering chemistry discovered by Heck in 1968 uses Pd to wed an aryl halide with an olefin; it has been, and continues to be, of great use. Negishi, who is now 75 and the H. C. Brown Distinguished Professor of Organic Chemistry at Purdue University, used Pd to catalyze couplings of organozinc reagents with organohalides in 1977. Negishi likened the Pd-catalyzed cross-couplings to the Grignard reaction, which earned 31 year old Viktor Grignard the 1912 Nobel Prize. He told reporters that the cross coupling methods not only complement but surpass the versatility of the Grignard. Akira Suzuki was born in 1930 in Hokkaidō, studied at the university there, gaining his PhD, and then became assistant professor. For two years he was a postdoctoral fellow (1963–65) with H. C. Brown at Purdue and after returning to the University of Hokkaidō he became a full professor there. It was a little while after Negishi that Suzuki began developing a Pd-catalyzed coupling of organoboron compounds with organohalides. With his retirement from the University of Hokkaidō in 1994, he took several positions in other Universities: 1994–1995 at Okayama University of Science and 1995–2002 in Kurashiki University of Science and the Arts, but is now back at his *alma mater*.

The Chemistry of Palladium-Catalyzed Cross-Coupling Reactions

The formation of carbon–carbon bonds is the Holy Grail of organic chemistry because it enables the construction of complex organic molecules from simpler precursors. Palladium-catalyzed cross couplings, as honoured by the 2010 Nobel Prize, provide the cornerstone of this effort by allowing the connection, at carbon, of two compounds with virtually any hybridization. These reactions involve coupling of an organic halide (often a haloalkene or aromatic halide) with either an alkene (the Heck reaction), an organozinc reagent (the Negishi reaction), or an organoboron reagent (the Suzuki reaction).

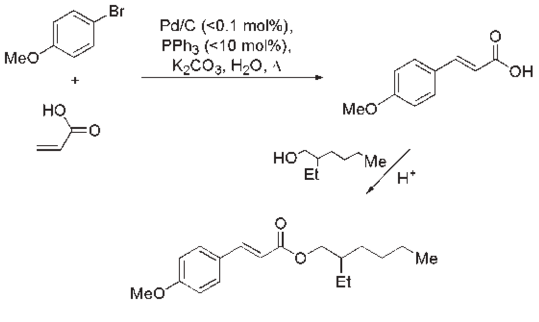
The Heck Reaction

In 1968, Heck began studying the palladium-catalyzed alkylation and arylation of unsaturated molecules using organomercury reagents as the source of the transferred alkyl or aryl group.[1,2] At that time, the addition of metal alkyls and aryls to alkenes was known, but very few examples involved the transition metals other than for polymerization. The original Heck procedure was soon improved by Mizoroki (1971) and Heck (1972) through the use of organic halides in place of the toxic mercury reagents.[3,4] The 1974 modification by Heck to involve palladium in truly catalytic amounts was achieved by use of an amine base [which reduces the spent catalyst to the active Pd(0) species] and a phosphine ligand, representing the Heck reaction as we know it today (Scheme 1).[5] The preferred stereoisomer tends to be the *trans*-olefin, for steric reasons, and the transferred organic group ends up attached to the less electron-rich terminus of the alkene.



Scheme 1

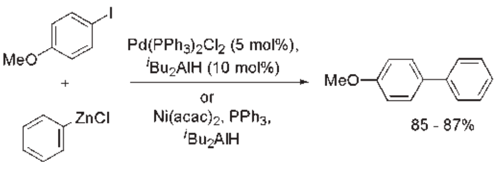
The Heck reaction has been widely used industrially, including in the synthesis of octyl methoxycinnamate, the active component of most sunscreens. Scheme 2 shows an example of this reaction in water, at very low catalyst loadings, demonstrating the convenience and power of this reaction.[6]



Scheme 2

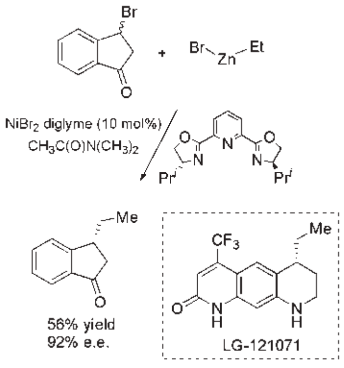
The Negishi Reaction

The 1977 report, by Negishi and co-workers, of the cross coupling between organic halides and organozinc reagents heralded the advent of a very mild procedure for reliably constructing C–C bonds.[7] Catalysis with either nickel(0) or palladium(0) effects the transformation as illustrated by Scheme 3.



Scheme 3

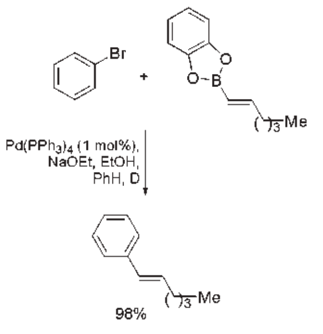
The mildness of the reaction conditions renders them suitable for use with many substrates, including sp^3-hybridized organic halides with β-hydrogens – often a challenge in cross-coupling reactions. Extension of the Negishi cross coupling into the arena of asymmetric synthesis is elegantly demonstrated by Fu's enantioselective preparation of a key intermediate *en route* to the first orally active, non-steroidal androgen receptor agonist, LG-121071 (Scheme 4).[8] A chiral ligand for the metal catalyst produces the observed stereoselectivity. It is noteworthy that the reaction can be performed in air and that both enantiomers of the racemic starting material are transformed into the highly enantiomerically enriched product.



Scheme 4

The Suzuki Reaction

The Suzuki cross coupling, also known as the Suzuki-Miyaura reaction, was first reported in 1979. The two seminal papers[9,10] describe the reactions of alkenylboron reagents with alkenyl and aryl halides (Scheme 5). The low toxicity and cost of boron reagents and the fact they may be readily accessible by hydroboration of an alkyne has led to increasing applications.[11] It is now possible to perform Suzuki reactions with boranes ($R–BR'_2$), boronic acids [$R–B(OH)_2$], boronates [$R–B(OR')_2$] or organotrifluoroborates [$(R–BF_3)^+$] as the boron reagent. The transfer of the organic fragment R from boron to palladium as part of the mechanism (*vide infra*) is greatly facilitated by base, through formation of a four-coordinate 'ate'-complex. The versatility of the Suzuki reaction has recently been extended to encompass alkyl halide and alkyl boron partners,[12] and aqueous reaction conditions.[13]



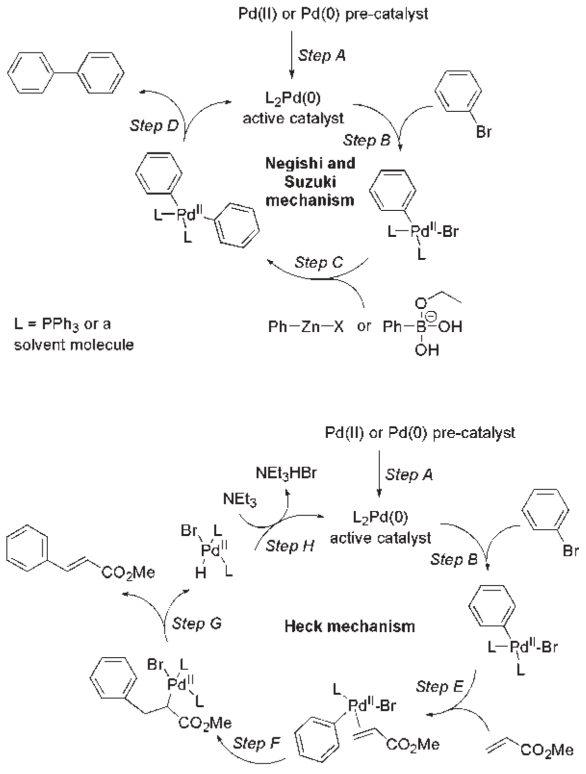
Scheme 5

Mechanistic and Experimental Details

The cross-coupling mechanism (Scheme 6) involves, initially, *in situ* generation of the active Pd(0) catalyst from a less reactive, storable and often commercially available precursor, a *pre-catalyst*, through either reduction or ligand substitution (Step A). The first step of the catalytic cycle is oxidative addition (Step B), wherein the Pd(0) catalyst inserts into the C–X bond of the organic halide and is oxidized in the process. The mechanism then proceeds through transmetallation (Step C), in which an organic group is transferred from the organometallic precursor (a zinc or boron species for Negishi and Suzuki, respectively) to the Pd(II) complex. The resultant bis-organopalladium complex then undergoes reductive elimination (Step D) to produce the new C–C bond of the product and regenerate the catalyst. Technically, the Heck reaction is not a cross coupling, as it follows a different mechanistic pathway beyond the oxidative addition (Step B). Specifically, alkene complexation to the oxidized palladium (Step E) is followed by migratory insertion of the alkene π-bond into the Pd–C bond (Step F). The ensuing process is β-hydride elimination (Step G), producing the substituted alkene product and a palladium hydride. Because the migratory insertion produces a *syn*-relationship between the Pd and the organic substituent, and the β-hydride elimination requires a *syn*-relationship between the Pd and the removed hydrogen, there are stereochemical (and sometimes regiochemical) consequences of this sequence. However, in acyclic cases with two geminal β-hydrogen atoms, the *trans*-alkene is favoured. The active catalyst is regenerated by reduction of the palladium hydride by way of a base-promoted elimination of hydrogen halide, *e.g.* HBr (Step H).

Together with the Nobel Prize winning methods, the Stille reaction (using an organostannane), the Hiyama coupling (using an organosilicon) and the Sonogashira reaction (using an alkyne) represent the main (named) metal-catalyzed cross couplings. The versatility and reliability of the Stille reaction has made it one of the most heavily used couplings, despite its involvement of highly toxic organotin reagents. It seems likely that, if John Stille was still alive, he would have shared in the 2010 Nobel Prize. Tragically, he was killed in the crash landing of United Airlines Flight 232 in 1989 at Sioux City, Iowa.

It will come as no surprise to those working in the field of synthetic organic chemistry that three of the past ten Nobel Prizes (2010, 2005, 2001) have been awarded for transition metal-catalyzed reactions. The very nature of transition metals lends their ability to wed organic chemical functionalities that would otherwise be unreactive. Heck, Negishi and Suzuki together pioneered some of the most industrially useful, reliable and mechanistically interesting reactions of all time, so this Nobel Prize award is entirely appropriate and timely. No doubt, the future will bring further improvements and new procedures.



Scheme 6

References

1. Heck, R. F. *J. Am. Chem. Soc.* **1968**, *90*, 5518–26.
2. Heck, R. F. *J. Am. Chem. Soc.* **1968**, *90*, 5535–8.
3. Mizoroki, T.;Mori, K.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581.
4. Heck, R. F.; Nolley Jr, J. P. *J. Org. Chem.* **1972**, *37*, 2320–2.
5. Dieck, H. A.; Heck, R. F. *J. Am. Chem. Soc.* **1974**, *96*, 1133–6.
6. Ewenson, A.; Croitoru, B.; Shushan, A. US Pat. 5728865, 1998.
7. Negishi, E-i.; King, A. O.; Okukado, N. *J. Org. Chem.* **1977**, *42*, 1821–3.
8. Arp, F. O.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 10482–3.
9. Miyaura, N.; Suzuki, A. *J. Chem. Soc., Chem. Commun.* **1979**, 866–7.
10. Miyaura, N.; Yamada, K.; Suzuki, A. *Tetrahedron Lett.* **1979**, *20*, 3437–40.
11. Miyaura, N.; Suzuki, A. *Chem. Rev.*, **1995**, *95*, 2457–83.
12. Kirchhoff, J. H.; Netherton, M. R.; Hill, I. D.; Fu, G. C. *J. Am. Chem. Soc.* **2002**, *124*, 13662–3.
13. Liu, L.; Zhang, Y.; Wang, Y. *J. Org. Chem.* **2005**, *70*, 6122–5.

Dates of Note

Robert **Hare** was born on Jan 17, 230 years ago, in 1781. He was the American chemist who devised the first oxy-hydrogen blowpipe for the purpose of producing great heat and melted sizeable quantities of platinum with it. *Hans* **Goldschmidt** was born 150 years ago on Jan 18, 1861. Apart from inventing the thermite process (adopted worldwide for welding railroad and streetcar rails), he also co-invented sodium amalgam. His father, Theodor, founded Chemische Fabrik. As we noted in the last issue, Jan 23, 1911 marks the French Academy's rejection of *Marie* **Curie** to a vacant seat for a physicist. It is also the 82nd birthday of *John* **Polanyi**, who shared the 1986 Nobel Prize for Chemistry. *Polykarp* **Kusc**, the German-American physicist who shared the Nobel Prize for Physics in 1955 for his accurate determination that the magnetic moment of the electron is greater than its theoretical value, was born 100 years ago on Jan 26.

In 1911 on Jan 26, *Glenn* **Curtiss** piloted the first hydroplane flight at North Island, San Diego, with a successful take-off from water and landing on water, and in 1986, 25 years ago this same day, the *Voyager II* space probe made closest approach to Uranus approaching to within 81,500 km (50,600 m) of Uranus's cloud tops. On Jan 27 in 1921, ***Einstein*** suggested the possibility of measuring the universe, which startled the audience in his address *Geometry and Expansion* to the Prussian Academy of Sciences in Berlin.

Jan 30, 1901 marks 110 years since the world's tallest geyser was discovered by Dr *Humphrey* **Haines**. It was, of course, NZ's ***Waimangu*** (black water) ***Geyser*** near Rotorua that erupted on a 36 hour cycle for four years, hurling black mud and rocks in the air. Its natural eruptions stopped in 1904 when a landslide changed the local water table. Eruptions typically reached 600 feet. Some super bursts are known to have reached 1,600 feet (10 times as high as Yellowstone's famous Old Faithful), higher even than the Empire State Building. *John* **Bardeen**, the American physicist who was co-winner of the Nobel Prize for Physics in both 1956 and 1972 died 20 years ago on Jan 30 in 1991. He was involved with the invention of the transistor and then in the theory of superconductors. *Ferdinand* **Prosche** died 60 years ago on this day in 1951.

On Feb 2, 15 years ago died *Ray* **McIntyre** – he invented Styrofoam while employed by Dow. Feb 3 marks 75 years since radon E was discovered in the Berkeley laboratories. *Alan* **MacDiarmid** died just four years ago – Feb. 7, 2007 – and had a new science building at Victoria University named after him last July. Element 112, ununbium, was generated on Feb 9, 1996; it loses an alpha particle to give the 110 nucleus. *Julius* **Thomsen** was born 185 years ago on 16 Feb, 1826. He was a Danish chemist and tabulated the amount of heat released or absorbed in 3,500 chemical reactions as well as preparing the first table of the relative strengths of acids.

100 years ago on Feb 17 General Motors made the first car with a self starter, a Cadillac. Biochemist *Robert* **Huber** was born on Feb 20, 1937; he shared the 1988 Nobel Prize for chemistry with Deisenhofer and Michel, for the determination of the 3D structure of a protein complex essential to photosynthesis in bacteria. *Otto* **Wallach** died on Feb 26, 1931 He was the German chemist who gained the 1910 Nobel Prize for Chemistry for identifying terpene compounds. *Linus* **Pauling** was born on Feb 28, 1901. He applied quantum mechanics to the study of molecular structures, particularly in connection with chemical bonding. Pauling received the Nobel Prize for Chemistry in 1954 and the Nobel Prize for Peace in 1962.

Mar 1, 2011 is the 100th anniversary of ***van't Hoff***'s death. It is also the day in 1813 that Michael Faraday was appointed as assistant to Humphry Davy at the Royal Institution; he succeeded him as Professor of Chemistry in 1820. Perhaps more importantly, *John* **Pell**, the English mathematician who introduced the division sign (obelus, ÷) into England was born 400 years ago on Mar 1, 1611. Born 180 years ago on Mar 3 was *George M.* **Pullman** the American industrialist who invented the Pullman sleeping car used on railways. Mar 6 marks 350 years since the election of the first president of the Royal Society in 1661 – Sir *Robert* **Moray**, and a day later 100 years ago the first coin operated locker was patented. On Feb 17, 75 years ago, *Niels* **Bohr** gave his *bowl of balls* explanation of the effect of bombarding particles at a nucleus.

On Mar 9, 1611, the Dutch astronomer *Johannes* **Fabricius**, observed the rising sun through his telescope, and saw several dark spots on it - perhaps the first ever observation of sunspots. The same day 70 years ago has significance for the editor. *Irène* ***Joliot-Curie*** died on 17 Mar 1956. With her husband Frédéric Joliot-Curie, she was jointly awarded the 1935 Nobel Prize for Chemistry for their discovery of new radioactive isotopes prepared artificially. Mar 22 marks one year since the death of Sir *James Whyte* **Black**, the Scottish pharmacologist who developed the drugs, propranolol and cimetidine, propranolol being the first clinically useful beta blocker. *Hermann* **Staudinger**, the German chemist who received the 1953 Nobel Prize for Chemistry for discovering that polymers are long-chain molecules, was born Mar 23, 1881. The day also marks 75 years since a leukemia patient was the first ever to be injected with a radioactive isotope; it is also the day 150 years ago that tramcars began operating in London. Mar 29 marks 125 years since the first batch of Coca Cola was brewed over a fire in a backyard in Atlanta, Georgia. *Robert Wilhelm* **Bunsen** was born 200 years ago on Mar 31; where would we be without the Bunsen burner!

Noted crystallographer Dame *Kathleen* **Lonsdale** died 40 years ago on Apr 1, 1971 and *François-Marie* **Raoult** (of Raoult's law fame) the same day in 1901. *Feodor* **Lynen**, the German biochemist who shared (with Konrad Bloch) the 1964 Nobel Prize for Physiology or Medicine for his research concerning the mechanism and regulation of the cholesterol and fatty acid metabolism, was born on Apr 6, 100 years ago. *Melvin* **Calvin** was also born 100 years ago, on Apr 6. He was the American biochemist who elucidated the mechanism by which carbon dioxide is incorporated into green plants, receiving the 1961 Nobel Prize for Chemistry. In the Calvin Cycle, he described the *dark reactions* of photosynthesis occurring during the night to turn carbon dioxide into sugar. *Benjamin* **Eisenstadt**, the American inventor of Sweet 'n Low artificial sweetener in 1957, died on April 8, 1996 and *Elisha Graves* **Otis**, the American inventor of the automatic safety brake for elevators, died 150 years ago this day. However, in 1886, on this day 125 years ago, the first *dry* cell, which used zinc as its primary ingredient and was encased in a sealed zinc container, was patented by German scientist, *Carl* **Gassner**, His battery was much like the carbon-zinc, general-purpose batteries on the market today. Apr 12 marks 50 years since *Yuri* **Gagarin** became the first man to orbit the Earth, while the 14th is 50 years to the day since Lawrencium (Lw, 103) was produced in the US.

Chemistry success stories from the Marsden Fund 2010

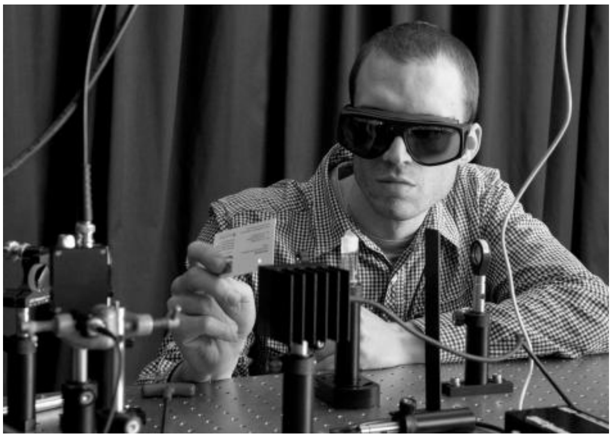
The Marsden Fund supports research excellence in science, technology, engineering and maths, social sciences and the humanities.

A total of 1089 preliminary proposals were submitted to the Marsden Fund 2010 and of these 252 were called to submit full proposals. From this 102 proposals were funded. Almost one-third of the awards this year (34) are Marsden Fast-Starts, designed to support outstanding researchers early in their careers. This data is published on the Marsden website at *http://marsden.rsnz.org/*

Some of the successful Chemistry projects funded this year are summarised below.

Dr. Justin Hodgkiss, Victoria University Wellington

Project title: *Ultrafast electron dynamics in molecular semiconductors*



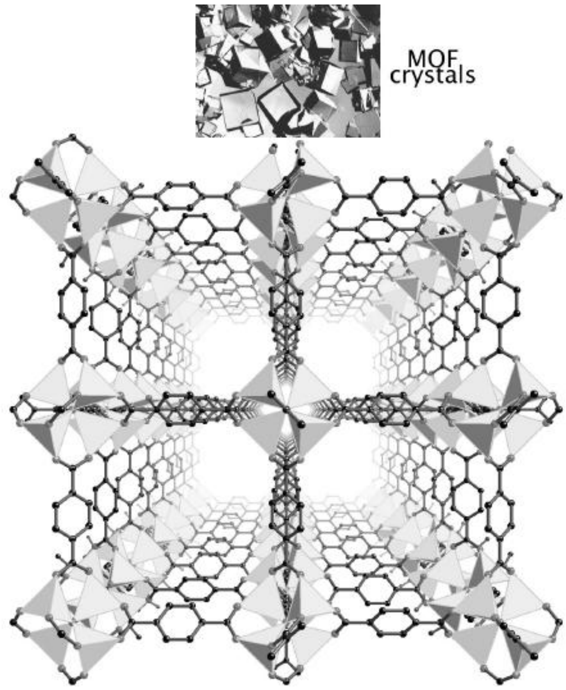
This study is dependent upon exceptionally short laser pulses in order to study ultrafast electron dynamics in organic solar cells. Many organic molecules and polymers have an electronic structure similar to inorganic semiconductors such as silicon – the material most widely used in today's solar cells. But the propensity of electrons to be shared and transferred between individual molecular components varies widely and is poorly understood. Understanding the pathways by which light absorption triggers the release of tightly bound electrons holds the key to the widespread deployment of organic semiconductors in printable solar cells.

This work will tackle the problem by zooming in to femtosecond timescales (millionths of a billionth of a second) to directly explore the transfer of electrons. We will measure the interaction of timed sequences of laser pulses with electrons on ultrafast timescales. In doing so, we will capture snapshots of the dynamically changing electronic landscape in molecular semiconductors. Our aim is to determine whether photocurrent generation in organic solar cells can be explained by ultrafast bursts of electronic dynamics.

Website: *http://www.victoria.ac.nz/scps/staff/justin-hodgkiss.aspx*

Dr. Shane Telfer, Massey University

Project title: *Creating nothing out of something: A route to ultraporous metal-organic frameworks*



Research on metal-organic frameworks (MOFs) is one of the most exciting and dynamic areas of modern chemical science. A key feature of these materials is their porosity, which allows small molecules to freely diffuse in and out via the voids and channels. Real-world applications in gas sorption, separations, catalysis, and drug delivery are rapidly emerging. We plan to pioneer a general method for the synthesis of open, ultraporous MOFs with unique attributes by creating large pockets of empty space in preformed frameworks. We will use a recent breakthrough made in our laboratory as a springboard for this research project. This breakthrough came in the form of a successful strategy for combating the natural tendency for frameworks to interpenetrate. Bulky units are appended to the ligand struts, which are specifically designed to "self-destruct" upon heating to produce small, volatile molecules that escape from the material. Thus 'nothing' is created out of 'something' to enhance the porosity of these materials. We will capitalise on this for the development of catalysts that facilitate 'greener' industrial processes and materials that are able to sieve carbon dioxide from streams of gas.

Website: *http://ifs.massey.ac.nz/people/staff.php?personID=28*

Professor P. J. Steel
University of Canterbury

Professor F. R. Keene
James Cook University, Australia

Project title: *New metallosupramolecular synthons*

Modern material science and nanotechnology routinely exploit the properties of materials that contain metal atoms linked by organic molecules (ligands). We intend to dispel the current dogma that the best such bridging ligands use nitrogen heterocycles and carboxylic acids to bind the metal. Indeed, we contend that many hitherto overlooked interactions of organic functional groups with metal atoms can be harnessed to provide new building blocks for preparing both discrete and polymeric supramolecular assemblies. In this context, we will synthesise a diverse range of new bridging ligands that will be combined with various metals to assemble nanoscale species with defined architectures. By strategic design of these ligands and the appropriate choice of metal atoms we expect to prepare many new compounds that will have useful applications as functional materials, such as catalysts, sensors and multiple electron transfer agents. Examples will include 1D-coordination polymers, 2D-networks, 3D-frameworks (MOFs) and discrete assemblies such as molecular cages and helicates. Novel chiral and mixed-metal assemblies will also be studied and applications of these assemblies in organic synthesis will be investigated.

Website: *http://www.chem.canterbury.ac.nz/people/steel.shtml*

Website: *http://www.jcu.edu.au/phms/staff/JCUPRD_031314.html*

Dr. Jonathon Sperry
The University of Auckland

Project title: *Synthesis of natural bis-indoles – prevention and chemotherapy of cancer*

Substituted indoles are among the most common and important heterocycles in nature – the indole nucleus is represented in a vast range of pharmaceuticals and materials, and is one of the most important structural subunits for the discovery of new drug candidates. It is therefore unsurprising that a plethora of indole syntheses exist in the literature. In recent years, the synthesis of indoles using the palladium-catalysed coupling of 2-iodoanilines with alkynes (Larock indole synthesis or heteroannulation) has gained widespread use in academic and pharmaceutical environments owing to the wide range of readily available precursors, its functional group tolerance and the general ease of execution. However despite the popularity of this reaction, it is surprising that its application to the construction of bis-indoles remains entirely unexplored. This presents a clear opportunity not only to dramatically extend the scope of this important reaction and the fundamental chemistry of the indole nucleus, but also to discover a novel route to a bis-indole - a medicinally important heterocyclic motif that often requires lengthy preparations that are not amenable to chiral or delicate substrates.

Website: *http://web.chemistry.auckland.ac.nz/staff-profile-jahia.aspx?staffid=247*

We would also wish to congratulate Prof. Jeff Talon and Prof. Sir Paul Callaghan who were also successful in obtaining Marsden funding in Chemistry but who were unfortunately unable to contribute to this article.

Submissions to the 2011 Marsden preliminary funding round are now open with a closing date of Thursday 3rd February 2011.

Laboratory Intellectual Property

Tim Stirrup and Katherine Hebditch

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A common question that comes up in our meetings with inventors around New Zealand is what exactly can be protected using intellectual property (IP) rights. Finding the appropriate mix of IP assets is an important strategic decision that will depend on the nature of the IP, the market conditions, expected return on investment and a host of other factors. However, of most relevance to laboratory-based scientists will be patents. In this article we provide an outline of what constitutes an invention and how it can be protected using a patent.

A patent grants the owner an exclusive monopoly to make, use, license and sell the invention for a period of twenty years from the application date of the patent. In return for this state-sanctioned monopoly, the inventor must disclose how to work the invention to the public. Knowledge of the invention can then be built upon for the greater good and any person can make, use or sell the invention after the monopoly period expires. Importantly, this monopoly is limited by territory; an NZ-granted patent cannot be used to take legal action against someone who makes, uses or sells the patented invention in, for example, Australia.

In order to be granted a valid patent, the invention must be novel and involve an inventive step in light of what has previously been published or used. An inventive step is defined as a step that a person with skill in the field of the invention would not consider to be an obvious extension of what is already known.

The subject matter of the invention must also not be excluded from patentability. The following exclusions from patentability exist in New Zealand and some other countries:

- Substances in the form as they are found in nature. This exclusion means that genes or proteins themselves are not patentable although an isolated gene, *i.e*. a recombinant nucleic acid sequence, or an isolated protein is potentially patentable
- Inventions or discoveries of a purely theoretical nature. For example discovery of a theory to describe the polymerisation of a compound would not be patentable. However, a method of producing a polymer using the theory, or the polymer itself when made by the method would potentially be patentable
- Methods of medical treatment of humans. In New Zealand and Europe (although not in Australia and the USA) medical methods are excluded on the grounds it would be inconvenient to the state to allow the possibility of legal action being taken against medical practitioners for treating their patients
- Inventions deemed to be contrary to morality. In New Zealand this includes methods involving the use of human embryos and methods of cloning humans

There are checks and balances that ensure consistency in application of patent law over time. However, the subject matter excluded from patentability does evolve in response to government policy - enacted by the Intellectual Property Office of New Zealand (IPONZ), legislative reform and patent cases that come before the Commissioner of Patents or the Court. This evolution is an inevitable part of patent law as science and technology will always push the boundaries of the legislation and what we are morally willing to accept. As an example, there has been recent debate about whether software should be excluded from patentability. The new Patents Act due to be introduced in the latter half of 2011 will likely exclude some software from patentability, although deliberations regarding the definition of *software* and the effects of this exclusion are ongoing.

The patent specification

The patent specification is a legal document that describes the invention and sets out the limits of the monopoly claimed. All specifications are published by IPONZ after the application has been examined and accepted. A specification must contain a detailed description of the invention and how it is put into practice. In the chemistry and biotech fields this will typically include examples of research that demonstrates the invention. The specification must also include a set of claims – a series of numbered statements that set out the limits of the monopoly covering the invention. Specifications also typically include a description of the background to the invention (termed the prior art).

A patent specification should be drafted, or at least reviewed, by a patent attorney to ensure that it covers the potential commercial uses of the invention and provides a strong position to take action against any party that makes, uses, sells or imports the invention without the patentee's permission. If such infringement proceedings ever need to be taken, the potentially infringing party is likely to analyse the patent for weaknesses that may raise questions about the validity of the patent. Accordingly, the skill of drafting a patent specification is not only in enabling the patentee to enforce their rights to the invention but also in potentially avoiding a legal battle by limiting the possibility that a question of invalidity can even be raised.

What can be claimed?

The claims define particular aspects of the invention that can be protected and may include claims to the following:

- a product/compound/polymer, *etc*. – for example, a novel compound to treat a disease or a novel catalyst to enhance the efficiency of a reaction
- a composition/formulation – often a composition/formulation will include the raw compound of the invention in combination with suitable additives typically required for use. Alternatively it may be that the active ingredient is not novel but the formulation is new.
- an apparatus/device – for example, a novel analytical machine
- a method of production – for example, a novel synthesis
- a method of treatment of a disease – as noted above, in New Zealand and Europe this form of claim will need to be limited to methods of treating non-human animals or in vitro methods to treat cells
- a use of a compound – for example, the use of a novel compound to produce a pharmaceutical
- a system – a combination of one or more novel components that forms a system
- a kit – at least one part of the kit must be novel or the kit is constructed so that when used, it achieves a novel result
- isomers/enantiomers – often one isomer or enantiomer is more active or has a different biological effect to the other isomers or enantiomer. If this was not expected or predicted it may be possible to get a patent for the single isomer or enantiomer even if the mixture of isomers or the racemic mixture is already known.
- an isolated or recombinant nucleic acid/protein – for example an isolated gene that when expressed in a plant confers resistance to a herbicide.
- a non-naturally occurring microorganism – for example a novel microorganism that has undergone selective breeding so that it breaks down crop silage at a faster rate.

The claims of a patent are drafted so that they target parties that are likely to infringe the patent by producing or selling the invention. For example, the production of a new agrochemical could result in several parties infringing the claims. The chemical manufacturers may infringe method of manufacture and compound claims. The agrochemical producers or distributors may infringe compound, composition and kit claims. The end-user may infringe compound, composition, kit and possibly method of use claims. In this way, the patent owner protects their position in the market and is in a position to make the best use of their competitive advantage through licensing or selling the invention.

Selection inventions

In chemistry, the situation often arises that a general class of compounds is known but researchers have identified a subset of compounds with a specific desirable and unexpected property. This type of invention is often referred to as a *selection* invention and a patent may be granted for the subset of compounds provided that:

- all compounds of the subset have the particular unexpected property
- the unexpected property is restricted to the subset of compounds
- the compounds in the subset have not been specifically described or made
- the unexpected property is not obvious in light of the prior art.

This type of patent rewards research into areas where there is existing knowledge but where further research unearths useful properties.

Patents are recognised as essential parts of the knowledge ecosystem that sustains our competitiveness on the world stage. Recognising which aspects of our research are potential IP assets and taking steps to protect them in the most effective way possible is an important step in developing and commercialising the fruits of our labour in New Zealand.

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

katherine.hebditch@baldwins.com or
tim.stirrup@baldwins.com

Patent Proze, Baldwins Intellectual Property, PO Box 5999,
Wellesley Street, Auckland

Katherine Hebditch and Tim Stirrup of Baldwins Intellectual Property in Auckland specialise 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. Tim obtained his PhD in molecular biology from the University of Southampton in the UK in 2007. He is also working towards registration as a patent attorney.

Conferences

Fifth International Conference on Advanced Materials and Nanotechnology (AMN-5)

7-11 February 2011, Wellington Convention Centre, Wellington, New Zealand

See: *www.macdiarmid.ac.nz/amn-5*

Science Communication Conference: Listening to the Other Side

21-22 February 2011 - Auckland

See: *www.scanz.co.nz*

23rd International Congress of Heterocyclic Chemistry

31 July – 4 August 2011, Glasgow, Scotland, UK

See: *http://www.ichc2011.com/*

22nd International Symposium: Synthesis in Organic Chemistry

11-14 July 2011, Cambridge, United Kingdom

Poster abstract deadline: 14 March 2011

See: *www.rsc.org/ConferencesAndEvents/RSCConferences/OrganicSynthesis2011/index.asp*

6th International Symposium on Macrocyclic and Supramolecular Chemistry (ISMSC)

3 - 7 July 2011, Brighton, United Kingdom

See: *www.rsc.org/ConferencesAndEvents/RSCConferences/RSCConferences/6-ISMSC/index.asp*

Tenth International Conference on Materials Chemistry (MC10)

4 - 7 July 2011 at University of Manchester, U.K.

See: *www.rsc.org/ConferencesAndEvents/RSCConferences/MC10/index.asp*

15th International Conference on Biological Inorganic Chemistry (ICBIC 15)

7-12 August 2011, Vancouver, Canada

See: *http://icbic15.ubcconferences.com/*

6th International Symposium on Advancing the Chemical Sciences — Challenges in Organic Materials & Supramolecular Chemistry

2 - 5 September 2011, Beijing, China.

See: *www.rsc.org/ConferencesAndEvents/ISACS/Organic-MaterialsAndSupramolecularChemistry/Home.asp*

NZIC Conference 2011

Sunday 27 November - Thursday 1 December 2011, The University of Waikato, Hamilton, New Zealand

See: *www.nzic2011.co.nz/*

2012 International Symposium on Macrocyclic and Supramolecular Chemistry (ISMSC-2012)

Sunday 29 January — Thursday 2 February 2012, The University of Otago, Dunedin, New Zealand

Please register interest via: *www.otago.ac.nz/ismsc2012/*