NZIC Chemistry IN NEW ZEALAND

Volume 72, No.2, April 2008

Articles and Features

42 Comment from the President

47 Developing Site-Specific Guidelines for Orchard Soils Based on Bioaccessibility – Can It Be Done?
Sally Gaw, Nick Kim, Grant Northcott, Alistair Wilkins, and Gavin Robinson

51 Medical Applications of SIFT-MS in New Zealand
Wan-Ping Hu and Malina Storer

55 The Quantitation of Ochratoxin A in Foodstuffs Sold in New Zealand
Darren A. Saunders, Shirley Jones, and Rudolf Schmitt

57 From Small Rings to Big Things: Xerography, Sensors, and the Squaraines
Brian Halton

63 BestChoice: Interactive Web-Based Learning
Sheila Woodgate and David Titheridge

67 Obituary: Ken Seal (1923-2007)

68 MALDI-TOF Mass spectrometry of Cyanobacteria: a Global Approach to the Discovery of Novel Secondary Metabolites*
Jonathan Puddick and Michèle R. Prinsep

72 The 2007 Royal Society of Chemistry Australasian Lectureship Tour - Report
Prof. Peter Schwerdtfeger

75 Protecting Cultural Heritage: Reflections on the Position of Science in Multidisciplinary Approaches
Jan Wouters

Other Columns

Inside Cover ChemScrapes - Brendan Burkett
43 NZIC January News
71 Dates of Note
74 New Zealand Science Scene
78 Patent Proze
79 Conference Calendar

Advertisers Index

60-61 Merck
80 Pacifichem 2010
Inside Back IC08

Comment from the President

It is with great pleasure that I assumed the 2008 Presidency of the Institute from Jan Wikaira, and on behalf of the Institute, I would like to thank Jan for all her efforts. I am delighted to report to members that the Institute is in good financial shape, due to the excellent work carried out by preceding Councils, and in particular the prudent financial practices carried out by the Institute's Treasurer, Colin Freeman. This is also an opportune time to express the Institute's gratitude to a number of people who make things run smoothly, through much behind-the-scenes work; Richard Rendle, the Honorary General Secretary; Brian Halton, for his editorial expertise on the Journal, and Fiona Summerfield and Rebecca Hurrell for Journal production. It is also a great pleasure to welcome Peter Hodder to the editorial group. Of course, there are many others who also contribute willingly of their time, especially at the Branch level, and the Institute could not operate without the contributions of many chemists across the country.

Council has recently embarked on a project to electronically archive back issues of *Chemistry in New Zealand*, which will appear on the website in the near future. My thanks go to Mark Waterland for efficient expedition of this project. The Chemical Education Specialist Group continues to develop, thanks to the efforts of Suzanne Boniface and her colleagues, and there are current discussions regarding setting up an ***Environmental, Green and Industrial Chemistry*** specialist group.

Personally, I feel that it is an exciting time to be a chemist. One has to look only at some of the fantastic research being carried out to appreciate that chemists are, slowly but surely, becoming *masters of the molecule*, able to design materials with a wide range of functions. Of course, we still have a long way to go before we can match the marvels of Mother Nature. However, it is rewarding that NZ is able to contribute to the top echelons of international research. Recently, I served on the Marsden *Physical Sciences & Engineering* panel, where the quality of applications was, with very, very few exceptions, of an extremely high standard, from researchers with excellent track records. It is disheartening though, not to be able to fund all but a tiny handful of these proposals. The Marsden Fund is a good fund, but it desperately needs more money in order to support a greater percentage of our researchers.

I am also heartened by the significant number of recent appointments in the chemical sciences in this country. These new researchers are already producing some great work, and the future looks good, as long as they can be financially supported properly. Indeed, the panel who recently assessed the nominations for the Institute's *Easterfield Medal* commented on the number and quality of the applicants. I am very much looking forward to meeting NZIC members, new and old, during my visits to the Branches later in the year, and at the Institute's conference, to be held in Dunedin in December.

And now time for some food for thought. One matter which causes me some concern - and may well have crossed the minds of many other chemists, not just in our country but internationally - is the disparity in standards applied to professional chemists and the general public, when it comes to the handling of chemicals. The public have access to a wide range of rather hazardous substances – concentrated hydrochloric acid in hardware stores, bleach and organophosphorus pesticides in supermarkets, and petrol, to name but a few. These can be purchased *over the counter, no questions asked*, and if you don't bother to read the safety instructions, there is no-one watching over you. Doubtless, the Government puts this issue in the *too hard* basket. Could you imagine a scenario where every person who filled up their car at a petrol station was required to have attended a training course in order to gain a suitable certificate as an *approved handler*? While health and safety standards have – quite rightly – come a long way since the days of characterising your products by tasting them, trends suggest that things will only become even more highly regulated for practising scientists, while the public are likely to remain to do more or less as they wish. Perhaps if the public were forced to attend multiple training courses, and pay significantly more for consumer products as a result, they just might have more appreciation for the long list of dividends that chemists have brought.

Raising the public perception of chemistry has been debated, for many years, by chemical societies far larger than us, and I am not certain that there are concrete solutions. What I am sure of though, is that we must endeavour to convince young people that chemistry is a worthwhile subject. The sense of awe and wonder experienced by children during a *chemistry magic show* indicates that the seed can easily be sown, but in most cases never grows to its full potential. This remains one of our major challenges.

I look forward to discussing some of these issues with you, and I wish you all a successful and productive year.

Bill Henderson

About the President

Prof Bill Henderson is in the Department of Chemistry at the University of Waikato, Hamilton. He has research interests in the chemistry of the platinum group metals and gold, and applications of mass spectrometry to inorganic syntheses. A more extensive biography was published in *This Journal* **2006**, *70*, 61.

New Zealand Institute of Chemistry

supporting chemical sciences

April News

The 2008 International Year of Planet Earth paper in this issue is that by Sally Gaw and co-workers – see page 47

New Year Honours

Dr ***Richard Garland***, Managing Director New Zealand Pharmaceuticals, was appointed as an Officer of the Order of New Zealand Merit for his services to chemistry and pharmaceuticals.

Alan MacDiarmid – Super Plastics Man

An excellent forty minute documentary celebrating the life and work of Prof Alan MacDiarmid is available for download free of charge from the Macdiarmid Institute – www.macdiarmid.ac.nz/superplasticsman.php

NZIC Awards

NZIC is pleased to announce two new sponsors of our awards, Fonterra and The Maurice Wilkins Centre for Molecular Biodiscovery. Nominations for the annual Fonterra Applied and Industrial Chemistry Award ($1000 + plaque), The Maurice Wilkins Centre Prize for Research in the Chemical Sciences ($1500 + plaque), and the Denis Hogan ($500) Award close with the Honorary General Secretary on June 30. For details and conditions see: www.nzic.org.nz

Council News

The 2008 NZIC President is Prof ***Bill Henderson*** (Waikato); 1st-VP is Prof ***John Spencer*** (Wellington) and 2nd-VP Dr ***Mark Waterland*** (Manawatu).

Subscription rates for 2008 remain unchanged and at their 2007 levels.

2011 is the United Nations International Year of Chemistry and Council is investigating various projects as a way of celebrating this.

New Fellow

At its February meeting Council elected ***Richard Tapper*** (Otago – now overseas) to the Fellowship.

Chemistry in NZ

The back issues of *Chemistry in New Zealand* have now been archived and are held on CD/DVD and held by the Hon. Gen. Secretary and the editors. Access via the NZIC web site is to be activated as soon as practicable – see: www.nzic.org.nz

CHEM NZ

Dr ***Alan Happer***, Editor of CHEM NZ, has announced his retirement from the position from the end of 2008. Council is actively seeking a replacement.

Physical Chemistry - Chemical Physics

This journal is owned by a series of chemical societies worldwide and published by the RSC in the UK. NZIC has accepted an invitation to become a co-owner for which it will receive a payment for each article published by NZ resident authors.

Contracts

The contracts for hosting the NZIC Office and the NZIC Journal Managing Editors expire mid-year. Council is to offer renewals to all parties under improved conditions.

Specialist Groups

An ***Environmental Chemistry Specialist Group*** is being established by Dr ***Sally Gaw***. If interested in joining or helping, please contact her via the NZIC Office.

Conferences

The ***2008 NZIC Conference*** is to be held in Dunedin from November 30 to December 4. Appropriate details will appear in the July issue, but a 75th jubilee celebration is planned. Mark your diaries now.

The inorganic chemistry meeting, **IC08**, will follow later: from December 14-18 at the University of Canterbury.

BRANCH NEWS

AUCKLAND

In November, the Auckland Branch of NZIC had a lively talk entitled *Left or Right in Nature? That is the Question* from Prof ***Peter Schwerdtfeger***, the NZIC RSC Australasian lecturer for 2007. His talk brought out the excitement and challenge of trying to predict and measure minute differences between chiral molecules.

University of Auckland

Dr ***Cather Simpson*** hosted an *open house* in the new laser laboratory early last November. The new laser facility is a Science Faculty initiative in partnership with Physics and Chemistry. When fully operational it will boast both nanosecond and sub-picosecond lasers. In November the Department also hosted a mini-symposium involving four academics from the University of Tokushima on topics ranging from biosensors to hydrogen production.

The second annual 2nd year PhD poster competition run late last year, had a very high standard of submissions. The judges - ***David Williams, Graham Bowmaker, Gordon Miskelly*** and ***Kevin Palfreyman*** (Fonterra) – decided to award joint 1st prize to ***Tanja Kjallman*** and ***Amy Tong*** and joint 3rd prize to ***Rhys Finlayson, Stephanie Gueret***, and ***Philip McGill***. Prizes were donated by the Polymer Electronics Research Centre.

David Salter, ***Katrina Graaf*** and a team of technicians and students ran a BASF Kids Lab, a successful initiative which BASF have run internationally. A large number of budding young scientists came to the Department and experimented with a range of polymers.

Dr ***Siew-Young Quek*** has been awarded both a Faculty Teaching Excellence Award and a University of Auckland Teaching Excellence Award. Siew-Young has received consistently outstanding evaluations of her teaching of third-year Food Science students.

Dr ***Duncan McGillivray*** has joined the Department as Australian Institute of Nuclear Science and Engineering Research Fellow. Duncan's expertise lies in the area of neutron scattering, most recently applied to biological systems.

CANTERBURY

There was a very large turnout for the last Branch event for 2007, a combined Canterbury Branch and National NZIC AGM. This took the form of a Christmas afternoon tea and student poster competition. The top award went to ***David Garrett*** for his high-visual-impact poster *Microcontact Printing of Carbon Surfaces Utilizing Spontaneous Reduction of Diazonium Salts*; ***Victoria Peddie*** was runner-up with her poster, presenting not only interesting chemistry but also the natural beauty of New Zealand.

University of Canterbury

Profs ***Murray Munro*** and ***John Blunt*** were the joint recipients of the 2007 *University of Canterbury Research Medal*. They were in the USA in February to receive the prestigious biennial 2008 *Paul J Scheuer Award*, made since 1992 for contributions that have had a major impact on the field of marine natural products or associated fields. As with the UC Medal, this is the first time that there has been a joint award. John and Murray gave a joint talk at the presentation of the award at the Marine Natural Products Gordon Research Conference in Ventura, CA, in February. Their research work, over nearly 40 years at UC has resulted in over 20 patents and more than 100 scientific papers. They have achieved not only scientific recognition, but also significant engagement with industry in the development of pharmaceuticals.

Emily Parker was promoted to Assoc Prof on January 1. ***Sally Gaw***, recently appointed as Lecturer in Environmental Chemistry, has been awarded the *NZ Society of Soil Science's Morice Fieldes Memorial Award* for a PhD thesis of exceptional merit. The thesis, on the *Persistence and Availability of Agrichemical Residues in NZ Soils*, was submitted in 2006 to Waikato University.

The winners of 2007 Chemistry Department awards were: NZIC Prize (200 level) - ***Caleb Allpress***; The Haydon Prize in Chemistry (300 level) - ***Thomas Lechte***; The Jack Fergusson Prize (300-level labs) - ***Solomon Wasseyehun Kelemu*** and ***Lita Leeb***; The C E Fenwick Prize (400-level demonstrator) - ***Paul Thornley***; C E Fenwick Prizes in Chemistry (400 level) - ***Wanting Jiao***; Cuth J Wilkins Prize (MSc thesis) - ***Georgina Biggs***; Dr Gregory S.C. Hii Prize (Organic PhD) - ***Jennifer Burgess***; Ralph H. Earle Jnr Seminar Prize (PhD) - ***David Tra***.

David Garrett was joint winner of the prize for best oral presentation at the MacDiarmid Student Postdoctoral Symposium in Palmerston North last November shared with ***Geoff Wilmer*** from IRL, Wellington. Dave intended to give a presentation on *Covalent Assembly of Vertically Aligned Single Walled Carbon Nanotubes on Graphitic Carbon Substrates* with ***Alison Downard*** and ***Keith Baronian*** as non-presenting coauthors. But in a very interesting twist, the presenters were paired up and told they had to give the others person's talk! That meant the two people had to explain their work to each other and then help each other through the presentations. So the nanotube seminar was presented by Geoff while Dave gave Geoff's talk on *Slides and Roundabouts: the History of the Slip Boundary Condition.*

There have been a significant number of PhD completions and our congratulations go to all: ***Kelly Anderson*** (*Conformationally Constrained Amino Acids* – supervised by Andrew Abell and Alison Downard); ***Janna Mehrtens'*** work on the *Design, synthesis and biological assay of cystein protease specific inhibitors* was supervised by Andrew Abell and Jim Coxon. ***Jennifer Zampese***'s *Molecular Cages of Controlled Size and Shape* was conducted under Peter Steel). ***Sarah Hickford***'s thesis, entitled *Studies in the Chemistry of Marine Natural Products*, was supervised by John Blunt and Murray Munro. ***Brett Davis'*** *Volatile Organic Compounds and Antioxidants in Olive Oil* was conducted under the supervision of Murray McEwan and Colin Freeman. Greg Smith's project, under Greg Russell's supervision, concerned *Investigations into the Effects of Chain-length Dependent Termination and Propagation on the Kinetics of Radical Polymerisation*. ***Jared Panther***'s *Diffusive Gradients in Thin Films for Inorganic Arsenic Speciation* was conducted under the supervision of Alison Downard and Kip Powell. ***Nor Ainy Mahyudin***'s thesis on *Actinomycetes and Fungi Associated with Marine Invertebrates* was in microbiology, but was co-supervised by Tony Cole in Biology and Murray Munro.

Students who received their degrees at the December graduation ceremony were: Drs ***Sarah Lundy*** and ***Sarah Hickford***, ***Matthew Paulik*** (MSc), ***Jeff Mercer***, ***Malcolm Rowney***, ***Thomas Sheehan***, ***Jessica Riley***, ***Jared Steven*** and ***King Sun*** (BSc). ***Wanting Jiao***, ***Daniel Packwood*** and ***Amy Zhang*** won Canterbury Scholarships and ***Penelope Cross*** and ***Michael Hunter*** have Doctoral Scholarships.

Jan Wikaira (on behalf of the 100-Level Development Committee) was granted a UC Teaching Development Grant to *Create Diverse Modes of Delivery in First Year Chemistry*; ***Tim Allison*** has spent the summer working on this project.

Congratulations to ex-students and now staff members of the Department, ***Marie Squire*** and ***Chris Fitchett*** on their January wedding. Marie runs both the mass spectrometer and the NMR and lectures in the Department; Chris returns to lecture at the end of April. Marie has recently joined the NZIC Branch committee.

Editorial Board appointments include: ***John Blunt*** to the *Journal of Natural Products*. ***Peter Steel*** to the *Open Organic Chemistry Journal*, and ***Paul Kruger*** to *Polyhedron*.

Marie Squire and Chris Fitchett on their wedding day

Alexis Pietak (Kingston, Ontario), a new postdoctoral fellow with ***Alison Downard*** and ***Keith Baronian*** is working on a Marsden-funded project that involves interfacing carbon nanotubes to the metabolic and electrically active centres of living yeast and mammalian cells.

The Department welcomes ***Mick Sherburn*** (ANU) as an Erskine visitor. Mick has wide-ranging research interests in the general area of synthetic organic chemistry, particularly in the study of unusual molecules such as dendralenes, cavitands and superbowls. Also joining the Department is ***John Carver*** (University of Adelaide), a Biochemistry Erskine Fellow, and his interests are in protein structure, function and interactions.

Richard Keene (James Cook University in Townsville) has had his Adjunct Professorial status extended to 2011. Em Prof ***Ward Robinson*** has taken up a position as Visiting Professor at the University of Malaya in Kuala Lumpur, with whom he has had a very long and successful collaboration.

Two members of ***Peter Steel***'s research group have departed for jobs in Europe. ***Jennifer Zampese*** is taking up a postdoctoral position with Ed Constable (Basel, Switzerland) and, in a remarkable coincidence, ***William Lewis*** was offered two jobs in the UK on the same day. He has taken a position in Nottingham, running the Chemistry X-ray service. ***Paula Brooksby***, who has been part of the Department for more than 5 years, has now left. Sabbatical visitor ***Marc Cretin***, (with Alison Downard) has returned to France and ***Justin Gooding*** has returned to Sydney.

MANAWATU

Crop & Food Research

Dr ***Julian Lee*** has been appointed to the newly-created position of chief scientist. Announcing the appointment, CEO ***Mark Ward*** said the role of chief scientist was of critical importance to the science-based organisation and Dr Lee would play a key role in ensuring the Institute's science developed to its full potential. *Crop & Food Research's strength is in the area of food innovation across food value chains – particularly the arable, vegetable and seafood value chains. Dr Lee has a wealth of experience in science leadership that spans food production and I am very pleased to announce his appointment.*

Dr Lee has been with the organization for three years as Science Group Manager - Nutrition and Health. In that position he led the Institute's research effort in developing added value food products with health benefits. He had formerly worked at AgResearch (and its predecessors) for 25 years. His research background is chemistry, with specialist research interests including trace element and amino acid metabolism and nutrition, especially related to added value food products from primary production, and attributes for human health.

Julian has managed and governed key science programmes and strategic partnerships in NZ and internationally, building lasting and beneficial relationships between the participants. He was involved in the establishment of both the Pastoral Greenhouse Gases Research Consortium, and the Nutrigenomics collaborative programme which involves the Auckland University, Crop & Food Research, AgResearch, and HortResearch.

NZP

As noted earlier Dr ***Richard Garland***, NZP's Managing Director, received Government recognition in the New Year honours list as an Officer of the Order of New Zealand Merit for his services to chemistry and pharmaceuticals. Richard studied for his PhD at the University of Canterbury with Profs ***Jim Coxon*** and ***Michael Hartshorn*** and has worked at NZP since its inception in 1971. He has held technical, operational, and commercial management positions before becoming General Manager in 1987. His first task was to develop the bile acid purification process, a process, which is still used today and remains the core technology at NZP. Richard has received the NZIC Nufarm Prize for Excellence in Industrial and Applied Chemistry while the Company received the University Business Link Award from Massey University in 2006. Under Richard's leadership, NZP has become a high tech supplier to the global market and is ranked in the top 50 technology companies in NZ. *I am fortunate to have had a great team at NZP which has enabled us to make a useful contribution to the NZ economy over the years* he says.

Massey University

Dr ***Hakan Dal*** (Anadolu University, Eskişehir, Turkey) is spending three 3 months with ***Eric Ainscough*** and ***Andrew Brodie*** on their phosphazene project while ***Carl Otter*** has left the group after a very productive five years; he is now working with ***Shane Telfer*** and ***Mark Waterland***.

WAIKATO

We welcome our own ***Bill Henderson*** as this year's NZIC President.

University of Waikato

Hawke's Bay native, but resident in Britain for 30 years, ***Neil Ward*** (University of Surrey, U.K.) gave a fascinating but also somewhat depressing seminar to the Chemistry Department entitled *A Kiwi Chemist in Argentina in Search of Boron, Arsenic and Water Quality*, which recounted his travels around isolated areas of Argentina sampling water with extraordinarily high natural levels of boron and arsenic. This water was usually the only drinking water available and subsequently the people are suffering many major health problems. Neil was in Hamilton primarily as a plenary

speaker at the New Zealand Trace Elements Group conference *tracenz* which was held at the university in association with the Waikato Branch of the Institute. The conference ran over three days, with other plenary speakers being Profs ***Brian Alloway*** (Reading), ***Bill Maher***, (Canberra), and ***Dave Craw*** (Otago).

In January, doctoral students ***Kelly Kilpin*** and ***Bevan Jarman*** attended OZOM4, the 4th Australasian Conference on Organometallic Chemistry, at ANU in Canberra. A wide range of current research was presented and the conference was dedicated to the retirement of Prof Bruce Wild. Kelly gave a talk entitled *Synthesis & Reactivity of Metallacyclic Gold(III) Iminophosphoranes* and Bevan presented a poster on *Asymmetric Ligands Derived from Carbohydrates*.

Colin Milne, a senior chemistry teacher from Hillcrest High School is in the department this year on a Royal Society Teacher Fellowship. He will predominantly work with ***Michèle Prinsep*** on marine bryozoan natural products chemistry, but is also working with staff at the university's Centre for Science and Technology Education Research (CSTER) on the nature of science.

Richard Coll recently received the James Wilson Award for international research into co-operative education, awarded by the USA-based Cooperative Education and Internship Association. This is the premier award from the CEIA, and means Richard has now received all three major awards for research into cooperative education.

NIWA

Kay Vopel left NIWA in late February to take up a Senior Lecturer position at AUT University's Earth and Oceanic Sciences Research Institute (EOSRI) and School of Applied Sciences. He will keep working on what he is most interested in, namely, the ecology of aquatic interfaces (including animal-sediment interactions, mass transport processes, and biogeochemical transformations) and new technologies for environmental assessment. ***Ines Hotopp***, a German student, has joined the NIWA Aquatic Chemistry group for two months to work with ***Hilke Giles*** investigating effects of fish farm waste on sediment biogeochemistry with a combination of laboratory measurements and numerical modeling.

WELLINGTON

It was announced on December 11 that Dr ***Gordon Leary***, the last of a distinguished line of Directors of the former Chemistry Division of DSIR, had passed away. He is survived by his wife Sheelagh and three adult children.

The inaugural 2008 Branch meeting saw Dr ***Selwyn Yorke*** (NZP) speak to a group of 35 people on *New Zealand Pharmaceuticals in the 21st Century*. He gave a fascinating overview of the recent significant developments at the Palmerston North campus intertwined with enough chemistry to keep the enthusiasts happy.

Industrial Research Ltd.

Dr ***Peter Tyler*** and Prof ***Vern Schramm*** (Albert Einstein College of Medicine) presented their research proposal to the annual Medicines for Malaria Venture (MMV) funding round, held in Geneva, December 6, 2007. Subsequently, Dr ***Tim Wells***, the new CSO of MMV, confirmed by letter that funding of US$750,000 will be made available for the first year of work, starting on July 1. MMV's primary interest is in the design/synthesis of inhibitors [especially against malarial HGX-PRT (phosphoribosyltransferase)] and testing in the *Aotus* monkey / *P. falciparum* model of malaria.

A paper describing inhibitors of the enzyme methylthioadenosine nucleosidase, featuring several authors from the Carbohydrate Chemistry team was selected for the cover of the mid-November 2007 issue of ACS *Chemical Biology* with the descriptor: *Enzyme inhibitors are extraordinarily useful biological tools and potential drug leads as well. Stable transition state analogs are often promising starting points in the design of potent and effective inhibitors. However, probing enzymatic transition states can be difficult due to their short lifetimes and complicated structural and kinetic properties. Gutierrez* et al. *describe a new method for predicting the nature of enzymatic transition states using transition state analogs. Shown on the cover are alternating transition states and associated transition state analogs for methylthioadenosine nucleosidases (MTAN) enzymes.*

A patent has been submitted for the protection of a series of 3rd generation acyclic immucillins which are more potent against human PNP and with a lower cost of goods than our current clinical candidates – Forodesine HCl (cutaneous T-cell lymphoma, chronic lymphocytic leukemia) and R3421 (psoriasis).

Dr ***Richard Fröhlich*** has completed his stay in Graz with ***Arnold Stütz***'s Glycogroup, during which he has synthesized two novel glucosidase inhibitors featuring lipophilic and fluorescent properties. The compounds are currently being screened for their general glucosidase inhibition activity as well as their activity as molecular chaperones for glucocerebrosidase in Gaucher cell-lines and as potential inhibitors of the GM3-endo-glucosidase (anti-cancer).

Dr ***Ruth Falshaw*** was presented in late February with a Professional Development Scholarship worth $4,500 by Sally Hasell of the NZ Federation of Graduate Women Inc.

Victoria University

Andy McFarlane defended his PhD thesis on December 20, but remains as a research assistant in the School with ***Jim Johnston***. ***Rhys Batchelor*** has submitted his PhD thesis and now left the role of School Organic Chemistry Technician that he held since 1992. He is now employed in Nelson by Aquaflow Bionomic Corporation that has ***Ian Miller***'s Carina Chemicals involved in a consultancy role. Dr ***Emma Turner*** is now with the carbohydrate group at IRL.

Recent visitors to the School have included Profs ***Armin de Meijere*** (Göttingen) and ***Koichi Komatsu*** (Kyoto). In separate seminars they described how to go *from simple cyclopropane derivatives to potent biologically active compounds* and *chemistry of cyclic conjugated π-conjugated systems having σ-π interactions*, respectively.

Developing Site-Specific Guidelines for Orchard Soils Based on Bioaccessibility – Can It Be Done?*

Sally Gaw,[a,†] Nick Kim,[b] Grant Northcott,[c] Alistair Wilkins,[a] and Gavin Robinson.[d]

[a]University of Waikato, [b]Environment Waikato, [c]HortResearch, and [d]Hill Laboratories, Hamilton
(e-mail: *sally.gaw@canterbury.ac.nz*)

*This paper is an updated version of that presented at the 2006 WasteMINZ conference. It is reproduced with permission and is the NZIC ***Planet Earth*** designated paper for this issue of *Chemistry in New Zealand*.

[†]Current address Chemistry Department, University of Canterbury, Private Bag 4800, Christchurch.

Introduction

Horticultural land within the periurban fringe of NZ towns and cities increasingly is being developed for residential subdivision. Recent surveys have shown that concentrations of As, Cd, Cu, Pb, and ΣDDT (sum of DDT and its degradation products DDE and DDD) in such soils can exceed criteria protective of human health.[1] Soil ingestion is a key exposure pathway for non-volatile contaminants in soil. Currently in NZ, site-specific risk assessments and the derivation of soil guidelines protective of human health assume that all of the contaminant present in the soil is available for uptake and absorption by the human gastrointestinal tract. This assumption can overestimate health risks and has implications for the remediation of contaminated sites.[2] In comparison, the bioavailability of contaminants is considered when estimating exposure *via* dermal absorption and by ingestion of home-grown produce.[3] Dermal absorption factors and plant uptake factors are included in the calculations for estimating exposures via these routes.

Provided there are tools available to produce robust data on the bioavailability of contaminants in soil, it may be possible to derive site-specific guidelines that incorporate scientifically validated and refined risk scenarios. Site-specific guidelines could reduce the scope and costs of remediation on former horticultural land. A range of *in vivo* and *in vitro* methods have been developed to assess bioavailability of contaminants in soil and these are gaining increasing regulatory acceptance overseas.[4] Little is known about the oral bioavailability of contaminants from NZ soils, and differences in soil properties may mean that overseas data may not be directly applicable to NZ conditions. Herein, we provide an overview of methods to assess bioavailability of contaminants in soil via the oral route, and outline current barriers to using bioavailability in risk assessments for human exposure in NZ. In addition, the results of a preliminary investigation using the Solubility/Bioavailability Research Consortium (SBRC) *Stomach-Phase Extraction* in vitro *method* to estimate[5] the bioaccessible fraction of arsenic, cadmium, and lead in orchard soils are presented.

For human health risk assessments and the derivation of generic and site-specific soil guidelines, daily intakes from the relevant exposure pathways are estimated and compared with toxicological intakes. Intakes of carcinogenic substances are assessed against index doses derived from dose-response relationships, and intakes of threshold contaminants (non carcinogens and non-genotoxic carcinogens) are assessed against tolerable weekly (or daily) intakes.[6] Such toxicological intakes can be derived either from animal dosing trials with appropriate safety factors, or from epidemiological data from populations exposed to the contaminant of interest.[7] Toxicity parameters including tolerable daily intakes and index doses are generally calculated based on the *intake dose*.[5,6]

Definitions

The following definitions, adapted from Paustenbach,[8] are used herein:

> ***Oral Bioaccessibility*** of a substance is the fraction of that substance that is soluble in the gastrointestinal environment and is available for absorption through the gastrointestinal tract and into the bloodstream.
>
> ***Oral Bioavailability*** of a substance is defined as the fraction of an administered dose that reaches the bloodstream by absorption through the gastrointestinal tract.
>
> ***Relative Bioavailability*** - The relative bioavailability of a substance refers to comparative bioavailabilities of different forms of that substance or for different exposure media containing the substance.

Currently, the approach adopted in risk assessments for contaminated soil is to assume that the bioavailability of the contaminant in soil is equivalent to the bioavailability of the contaminant in the matrix used to derive the toxicity parameter.[9] Generally, in the studies used to derive toxicological intakes, the contaminant of interest was ingested with water or food rather than soil.[10] Often, in animal trials, trace elements have been reported as less bioavailable from soil than from other matrices such as food and drinking water[8,11-13] because contaminants can remain adsorbed to soil in the human gastrointestinal tract.[10] Factors that can reduce the oral bioavailability of contaminants in soil include the physicochemical properties, aging, chemical speciation, soil properties, particle size, and soil mineralogy.[5,14]

The following criteria have been proposed to identify when a site-specific bioavailability assessment can be undertaken:[5,11,15]

- Concentrations of contaminants only slightly exceed soil quality criteria.

- A limited number of contaminants exceed soil quality criteria.
- Soil ingestion is a key exposure pathway.
- The form of the contaminant is likely to have low relative bioavailability.
- The key contaminants are well aged in the soil.
- Remediation is costly or suitable techniques are unavailable.
- A large amount of land is involved.
- There is a risk of environmental degradation during soil remediation.

In vivo methods

In the absence of human studies or the availability of suitable epidemiological data, in vivo animal trials,[16] using rabbits, rats, primates and pigs,[5,17] have been used to measure the bioavailability of contaminants. Juvenile swine are commonly used to estimate the oral bioavailability of contaminants in soil for children, and to validate *in vitro* methods,[5,10,13] because they are comparable in size and have similar gastrointestinal physiology.[2,5] Testing protocols vary depending upon the contaminant of interest and the animal species involved.[5]

In animal studies, one group of animals in the trial is fed contaminated soil and the other given the contaminant of interest in a (usually more soluble) form that is comparable to the one used in studies to derive toxicity values. Concentrations of the contaminant of interest present in body tissues and/or excreta are measured at intervals after dosing, and the data are used to calculate a relative bioavailability factor.[5] However, animal trials are time consuming, expensive, and raise ethical concerns.[18] Additionally, concerns regarding the appropriateness of animal models as a surrogate measure for bioavailability in humans stem from differences in physiology and behaviour.[17]

In vitro methods

In vitro tests for measuring the bioavailability of contaminants have been developed to overcome the critical issues associated with animal testing.[4,18] One further advantage of *in vitro* testing is that the tests can be designed to simulate the processes and conditions occurring in the human gastrointestinal tract.[18] *In vitro* methods measure the bioaccessible fraction of contaminants in soil, *i.e*. that proportion of the contaminant that is desorbed from the soil in the human gastrointestinal tract and is potentially available for absorption. *In vitro* methods are suitable only for estimating the bioavailability of contaminants in soil if dissolution of the contaminant of interest is the rate-limiting step for absorption.[4]

In vitro methods are generally based on the paediatric gastrointestinal tract.[5] Soil is extracted at body temperature (37°C) with a simulated gastric fluid prepared from HCl and containing selected enzymes and amino acids. Summaries of the various simulated gastric extraction techniques are presented by Wragg and Cave,[19] Oomen *et al*.,[20] and Grøn and Anderson.[11] Points of difference between simulated gastric extraction methods include solid to solution ratios, the inclusion of food to simulate fed or fasting conditions (dough or dairy products), and the inclusion of a second extraction stage to simulate processes occurring in the intestines.

The bioaccessibility factors determined for some trace elements correlate with relative bioavailability factors obtained from animal feeding trials.[2,5] It should be noted that the correlation between the results from the *in vitro* and the *in vivo* methods may not be a one-to-one relationship.[8] However, not all *in vitro* methods have been validated against animal trials[18] and the bioaccessible fraction does not always correlate with the relative bioavailability measured in an *in vivo* trial.[17] While *in vitro* methods have been developed also for organic contaminants including polycyclic aromatic hydrocarbons (PAHs) and polychlorinated biphenyls (PCBs), validation data for these contaminants have not been published.[16] *In vitro* methods for organic contaminants will prove more difficult to validate using animal trials as the organic compounds also can be metabolised and/or degraded by microorganisms in the intestine.[21]

To date, *in vitro* methods have not been used routinely to estimate the bioaccessibility of trace elements in NZ soils, nor have they been validated against animal trials. However, under the Toxic Substances Amendment Regulations (1999), a comparable simulated gastric acid extraction method is used to screen children's graphic materials, *i.e*. paints and crayons, for toxic levels of selected trace elements.

Examples where *in vitro* testing methods have been used overseas include assessment of the bioaccessibility of naturally high concentrations of trace elements in soil, measurement of the bioaccessibility of arsenic in soil, derivation of site-specific soil criteria for arsenic, and in monitoring the effectiveness of *in situ* stabilization techniques.[22] *In vitro* testing methods also have been used to measure the bioaccessibility of contaminants in matrices other than soil including dust, children's toys, and food.[23]

Case Study: Bioaccessibility of Arsenic, Cadmium and Lead in New Zealand orchard soils

Lead arsenate ($PbHAsO_4$) was widely used as a pesticide in NZ orchards until the 1960s and Cd is a contaminant in fertilisers.[24] Several investigations have shown that NZ orchard soils can contain As, Cd and Pb in concentrations that exceed the levels protective of human health (Table 1).[1,25] These elevated concentrations are of concern when former orchards are converted into residential subdivisions. Contaminated orchard soils meet the criteria detailed above for bioavailability assessments due to the large amount of land potentially involved, the limited remediation options for these elements in soils, and the potential for the remediation activities to have an adverse effect on the environment.

Table 1. Range of selected trace element concentrations (mg/kg) from NZ orchard soils.

Region	As	Cd	Pb	Ref.
Auckland	2-34	0.1-1.1	11-178	1
Tasman	3-48	0.3-1.0	15-243	1
Waikato	4-58	0.8-1.5	14-251	1
Hawkes Bay	4-43	0.05-0.5	16-341	25

Methodology

A modified version of the SBRC's *Standard Operating Procedure for Stomach-Phase Extraction*[5] was used to determine the bioaccessibility of As, Cd and Pb from ten orchard soils. For gastric extractions, the soils were sieved to <250 μm to represent the fraction of soil likely to adhere to children's hands and be ingested.[5] Briefly, for the gastric extraction, 1 g of <250 μm soil was extracted using 100 mL of simulated gastric fluid composed of 0.4 M glycine adjusted to pH 1.5 with c.HCl. The resulting slurries were shaken on an orbital mixing incubator for 1 h at 37ºC, filtered, and analysed for trace elements by ICP-MS.

Results

The percentage of bioaccessible fractions for As, Cd and Pb ranged from 12–45%, 64–100% and 56–83%, respectively. The mean percentage bioaccessible fraction followed the order: Cd > Pb > As and was consistent with order of extraction of metals from soils using the comparable *Simple Bioaccessibility Extraction Test* method developed by the UK Geological Survey.[20] The range of %bioaccessible fraction for metals obtained indicates that the bioaccessibility of these contaminants in orchard soils varies on a site-specific basis. For As and Pb there was a significant correlation (Fig. 1) between the [Fe] and the %bioaccessible fraction, indicating that soil characteristics are a controlling factor for the bioaccessibility of As and Pb. This also suggests that significant portions of these contaminants are present in a chemically speciated form associated with the iron content of the soil - specifically the amorphous iron-hydroxide phase.

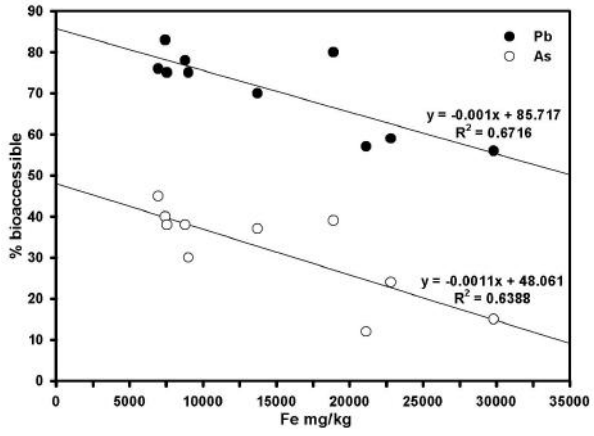


Fig. 1. Relationships between the bioaccessible fraction (%) of As and Pb and the [Fe] (mg/kg) of the <250 μm soil fraction.

Barriers to Using Bioaccessibility Data in Risk Assessments

While the preliminary results presented in Fig. 1 indicate that bioaccessibility of trace elements is likely to vary between orchard sites, there are several barriers to introducing *in vitro* testing as part of risk assessments in NZ in the short term.[2,10,19,26] These barriers include:

1. Lack of international consensus on the appropriate test method(s) to determine bioaccessibility due to:
   - variability of results between test methods, soil types, and test laboratories;
   - concerns of the relevance of *in vitro* tests to human exposures to contaminants in soil, and the scientific validity of the tests;
   - limited method validation including human data and few reference materials to support inter-laboratory validation of methods.
2. Lack of policy to support the use of bioaccessibility adjustments including:
   - guidance on how to incorporate bioaccessibility/bioavailability adjustments into risk assessment.
3. Lack of information on the bioaccessibility of contaminants in food.
4. Questions regarding the appropriateness of adjusting the currently available toxicological intakes.
5. Limited information on the long-term stability of bioaccessibility measurements.
6. Lack of awareness of some end users of the limitations of *in vitro* test methods.
7. Regulatory acceptance.

It is possible that bioaccessibility could be incorporated into risk assessments in the future provided that the issues identified above can be resolved, and international consensus reached. Bioaccessibility of contaminants in soil is an active area of research. There are several international collaborations underway aimed to improve understanding of the scientific validity of *in vitro* bioaccessibility testing, and to identify standard test methods. These include Bioavailability Research Canada (BARC), the Bioavailability Research Group Europe (BARGE), and the Solubility/Bioavailability Research Consortium (US). In addition, the International Standards Organisation (ISO) has recently published a standard for bioaccessibility - *Soil Quality: Assessment of human exposure from ingestion of soil and soil material; guidance on the application and selection of physiologically-based extraction methods for the estimation of the human bioaccessibility/bioavailability of metals in soil* (ISO/TS 17294:2007).

The validity and acceptability of bioaccessibility testing in NZ has yet to be subjected to governmental evaluation. Moreover, NZ has not participated in the international collaborative projects for validating and standardizing *in vitro* test methods for contaminants in soil. The Ministry for the Environment is currently developing *a nationally consistent NZ risk-based methodology for deriving soil*

contaminants for human health.[27] The question of whether or not bioaccessibility-based adjustments are able to be readily accommodated within this methodology will need to be considered by the Ministry's Technical Reference Group as part of this work.

Summary

Internationally, *in vitro* methods are being used to estimate the bioaccessible fraction of contaminants in soil. These chemical extraction methods simulate conditions and processes occurring in the human gastrointestinal tract and provide a surrogate measure of bioavailability. An *in vitro* method was used to estimate the bioaccessible fraction of arsenic, cadmium, and lead in orchard soils and gave values that ranged from 12–45% for As, 64–100% for Cd, and 56–83% for Pb. These results indicate that the oral bioaccessibility of these metals can vary on a site-specific basis and that it may be feasible, under some circumstances, to derive site-specific guidelines to protect human health. However, there are significant barriers to using bioaccessibility data in risk assessments, including questions regarding the relevance of the *in vitro* testing, and a lack of guidance on how to incorporate bioaccessibility values into risk assessments.

Acknowledgements

We are grateful to Environment Waikato for funding the sample analyses, landowners for providing access for sampling, and Hill Laboratories for the gastric extractions and trace element analyses. Drs. Jo-Anne Cavanagh (Landcare Research), Graeme Proffitt (Pattle Delamore Partners) and Lou Gallagher (ESR) are thanked for useful discussions and Peter Cressey (ESR) provided helpful comments on the draft; ESR funded manuscript preparation. Financial assistance to SKG (Waikato University) is acknowledged.

References

1. Gaw, S. K.; Wilkins, A. L.; Kim, N. D.; Palmer, G. T. *et al*. *Sci. Tot. Environ.* **2006**, *355*, 31–47.
2. Juhasz, A.; Smith, E.; Naidu, R.; *Estimation of human availability of arsenic in contaminated soils*. In *Proceedings of the 5thFifth National Workshop on the Assessment of Site Contamination* Langley, A.; Gilbey, M.; Kennedy, B. (Eds.), Adelaide, May 2002. NEPC: Adelaide 2003, 183–194.
3. Ministries of Health & the Environment *Health and Environmental Guidelines for Selected Timber Treatment Chemicals. MfE report ME240*: Ministry for the Environment: Wellington 1997.
4. Grøn, C. *Test for bioaccessibility of metals and PAH from soil. Test selection, validation and application*. See:http://www.bgs.ac.uk/barge/docs/DH_bioaccess_report_v03.pdf (accessed 6 Oct. 2006).
5. Kelley, M. E.; Brauning, S. E.; Schoof, R. A.; Ruby, M. V. *Assessing Oral Bioavailability of Metals in Soil*. Battelle Press: Columbus, Ohio 2002.
6. *Contaminants in Soil: Collation of Toxicological Data and Intake values for Humans*. See: http://www.environment-agency.gov.uk/commondata/acrobat/clr9_675402.pdf (accessed 6 Oct. 2006).
7. WHO *Assessing Human Health Risks of Chemicals: Derivation of Guidance values for health-Based Exposure Limits. Environmental Health Criteria 170*, Geneva 1994.
8. Paustenbach, D. J. *J. Toxicol. Environ. Health B,* **2000**, *3*, 179–291.
9. Oomen, A. G.; Rompelberg, C. J. M.; Bruil, M. A.; Dobbe, C. J. G. *et al*. *Arch. Environ. Contam. Toxicol.* **2003**, *44*, 281–287.
10. Oomen, A. G.; Brandon, E . F. A.; Swartjes, F. A.; Sips, A. J. A. M. *How can information on oral bioavailability improve human health risk assessment for lead-contaminated soils? Implementation and Scientific Basis.* See: http://www.bgs.ac.uk/barge/docs/RIVM_report_711701042.pdf (accessed 6 Oct. 2006).
11. Grøn, C.; Andersen, L. *Human Bioaccessibility of Heavy Metals and PAH From Soil*. Environmental Project No 840. See:http://www.mst.dk/homepage/default.asp?Sub=http://www.mst.dk/udgiv/publications/ 2003/87-7972-877-4/html/default_eng.htm (accessed 6 Oct. 2006).
12. Sarkar, D.; Datta, R. *Environ. Pollut*. **2003**, *126*, 363–366.
13. Schroder, J. L.; Basta, N. T.; Si, J.; Casteel, S. W. *et al*. *Environ Sc.i Technol*. **2003**, *37*, 1365–1370.
14. Sips, A. J. A. M.; van Eijkeren, J. C. H. *Oral bioavailability of heavy metals and organic compounds from soil: too complicated to absorb? An inventarisation of factors affecting bioavailability of environmental contaminants from soil* 1996. See: www.rivm.nl/bibliotheek/rapporten/711701002.pdf (accessed 6 Oct. 2006).
15. Battelle and Exponent *Guide for Incorporating Bioavailability Adjustments into Human Health and Ecological Risk Assessments at U.S. Navy and Marine Corps Facilities. Pt. 2: Technical Background Document for Assessing metals Bioavailability* 2000. See: www.cprm.gov.br/pgagem/usnavy2.pdf (accessed 6 Oct. 2006).
16. National Research Council *Bioavailability of Contaminants in Soils and Sediments. Processes, Tools, and Applications* National Academies Press: Washington, 2003.
17. Drexler, J.; Fisher, N.; Hennington, G.; Lanno, R. *et al. Issue Paper on the Bioavailability and Bioaccumulation of Metals*. Submitted to US Environmental Protection Agency Risk Assessment Forum. ERG, Lexington, USA, 2003.
18. Ruby, M. V. *Hum. Ecol. Risk Assess*. **2004**, *10*, 647-656.
19. Wragg, J.; Cave, M. R. *In-vitro Methods for the Measurement of the Oral Bioaccessibility of Selected Metals and Metalloids in Soils: A Critical Review. R&D Technical Report P5-062/TR/01* 2002. See: http://www.environment-agency.gov.uk/commondata/acrobat/p506201tr_760458.pdf (accessed 6 Oct. 2006).
20. Oomen, A. G.;, Hack, A.; Minekus, M.; Zeijdner, E. *et al*. *Environ. Sci. Technol*. **2002**, *36*, 3326–3334.
21. Schoof, R. A. *Hum. Eco.l Risk Assess* **2004**, *10*, 627-646; Dean, J. R.; Ma, R. *Chemosphere* **2007**, *68***,** 1399-1407.
22. Smith, B.; Rawlins, B. G.; Cordeiro, M .J. A. R; Hutchins, M.G. *et al*. *J. Geol. Soc. Lond*. **2000**, *157*, 885-891; Cave, M. R.; Wragg, J.; Palumbo, B.; Klinck, B. A. *Measurement of the Bioaccessibility of Arsenic in UK Soils: A Critical Review.* R&D Technical Report P5-062/TR02 2002. See: http://www.environment-agency.gov.uk/commondata/acrobat/p506202tr_760444.pdf (accessed 6 Oct. 2006); Juhasz, A. L.; Smith, E.; Weber, J.; Rees, M. *et al. Chemosphere* **2007**, *69,* 69-78; Nathanail, P.; McCaffrey, C.; Ogden, R.; Foster, N. *et al*. *Land Contam. Reclam.* **2004**, *12*, 219-238; Geebelen, W.; Adriano, D. C.; Van der Lelie D.; Mench, M. *et al*. *Plant Soil*. **2003**, *249*, 217–228.
23. Yu, C.H.; Yiin, L.M.; Lioy, P.J.B. *Risk Anal*. **2006**, *26*, 125-134; European Committee for Standardisation *Standard EN 71-3 Safety of Toys – Part 3: Migration of Certain Elements*, 1994; Intawongse, M.; Dean, J. R.. *Food Addit. Contam.* **2006**, *23*, 36-48; Versantvoort, C. H. M.; van de Kamp, E.; Rompelberg, C. J. M. *Development and applicability of an in vitro digestion model in assessing the bioaccessibility of contaminants from food RIVM report 320102002/2004* 2004. See: www.rivm.nl/bibliotheek/rapporten/320102002.pdf (accessed 6 Oct. 2006).
24.. Atkinson, J. D.; Chamberlain, E. E.: Dingley, J. M.; Reid, W. H. *et al. Plant Protection in NZ*, Technical Correspondence School, Department of Education: Wellington 1956; Taylor, M. D.; Percival, H. J. *Environ Pollut*. **2001**, *113*, 35–40.
25. Macaskill, D. MSc Thesis, Waikato University 2004.
26. *Environment Agency workshop on the Potential Use of Bioaccessibility Testing in Risk Assessment of Land Contamination.* Science Report SCO40054. Environment Agency: Bristol, UK 2005; *In-vitro Bioaccessibility Testing: Current Science and Way Forward (Environment Agency Science Update 2)* Environment Agency: Bristol, UK 2007.
27. *Working Towards a Comprehensive Policy Framework for Managing Contaminated Land in NZ - Position Paper*. Ministry for the Environment: Wellington, 2007.

Medical Applications of SIFT-MS in New Zealand

Wan-Ping Hu[a] and Malina Storer[b]

[a]Chemistry Department, University of Canterbury, Christchurch and [b]Syft Technologies Ltd., 3 Craft Place, Christchurch (e-mail: *sunny.hu@canterbury.ac.nz*)

Introduction

Selected ion flow tube mass spectrometry (SIFT-MS) is a relatively new analytical technique which offers real time identification and quantification of trace gases. It has the ability to detect and quantify the volatile organic compounds (VOCs) in various media such as liquid headspace and breath, thus opening up many new opportunities in medical research. NZ was a recipient of one of the world's first miniaturized SIFT-MS instruments that has been situated at the Christchurch Hospital since 2005. Herein we report on progress in the medical applications of SIFT-MS in this country.

The selected ion flow tube technique was developed initially in England in 1976 from modifications to a flowing afterglow system for studying gas phase kinetics. SIFT methodology was applied to investigate reactions between ions and neutral molecules in the gas phase.[1] A swarm of mass-selected reagent ions are carried by fast flowing helium into a flow tube where reactant neutral molecules are introduced at a controlled flow rate into the carrier gas. An ion-neutral reaction takes place and product ions are formed with all ions detected and counted via a second analytical mass spectrometer located downstream from the sample inlet. Under tightly controlled conditions, the rate coefficients for the reaction can be calculated from the decay of the reagent ion and the growth of the product ions.[2] This technique superseded flowing afterglow to become a standard method to study ion-neutral reactions at thermal interaction energies that are applicable in naturally occurring ionized media such as interstellar clouds and our ionosphere. Several laboratories around the world, including ones in NZ have established a large kinetics database and a better understanding of ion-neutral reactions using SIFT technique.[3]

The potential for adapting SIFT methodology to the trace gas analysis of air and breath (now known as SIFT-MS) was realised in 1996 by combining the use of NO^+, O_2^+ as well as H_3O^+ ions as the chemical ionization agents.[4] These three ionic species can be created simultaneously by microwave discharge using humid air as the ion source gas. They do not combine with major ambient gases, but react rapidly with most VOCs within milliseconds. This allows for the detection of rapid changes in test sample analyte concentrations in real time. Since then, the relevant kinetic parameters obtained from measurements of the reactions of these reagent ions with a number of organic molecules have been obtained. These results provide a database for SIFT-MS trace gas analysis in a large variety of applications.[5] Therefore, accurate identifications, and absolute concentrations can be detected using SIFT-MS under well-defined experimental conditions and with calculations utilizing the database of reaction rate coefficients.[6]

Herein we report the development of SIFT-MS in New Zealand, with special focus on medical applications. The first reported physiological study using SIFT-MS in this country[7] measured breath trace gases during exercise in 2000. However, the expansion of SIFT-MS applications here had a much earlier beginning.

After attending an enlightening lecture by David Smith (University of Keele) on the new SIFT-MS technique for breath analysis at the Christchurch School of Medicine, Randall Allardyce of Christchurch School of Medicine (Otago University) began cooperative studies in 1998 with Murray McEwan of this Department in the medical applications of SIFT-MS. They began studying the plume gas of bowel cancer patients using SIFT-MS with Big Bertha (the version of the SIFT instrument at Canterbury University) which took up an entire five meter long laboratory. In 2000, David Smith, Patrik Španěl, and Murray McEwan cooperated in constructing a smaller version of a SIFT-MS and in 2002 *Canterprise* (the technology transfer office of the University), founded Syft Technologies Ltd. to commercialize the technology and develop SIFT-MS applications. The first commercial VOICE100™ version of the instrument (about the size of a photocopier) was launched in March 2005. One of the major applications of this instrument has been to detect and measure fumigant levels within transport containers shipped into seaports. Other applications include the analysis of soil and seabed hydrocarbons in oil and gas exploration,[8] environmental monitoring,[9] occupational hazards,[10] food and flavour analysis,[11] detection of explosives,[12] chemical weapons, narcotics,[13] and bio-security risks.

Since receiving a FRST *Research for Industry* (RFI) grant to develop medical application products, SIFT-MS has made significant contributions to the real time detection of biomarkers in the clinical areas and it is these applications that form the focus of this article. In July 2007, a new generation of the SIFT-MS instrument, the VOICE200®, was released, which is lighter, more sensitive, and more portable than its predecessor. It has been fitted in a van and driven to local primary schools to survey the breath profiles of 230 school children. Additional cooperative studies are currently being carried out between Syft Technologies and renal, respiratory, intensive care, and surgical clinical research groups at the Christchurch School of Medicine.

Selected Ion-Flow Tube Mass Spectrometry (SIFT-MS)

The technique, principles, and theories of SIFT-MS have been detailed in other papers and in several reviews.[2,14] A brief description of the technique is presented here and a schematic diagram of the SIFT-MS device is shown in Fig. 1. The reagent ions H_3O^+, NO^+ and O_2^+ are produced by a microwave discharge of humid air and then focused by

ion lenses into a quadrupole mass spectrometer and mass selected. The mass-selected reagent ions are then injected into a fast-flowing stream of carrier gas through a Venturi orifice. The gas containing the analyte or VOC is introduced through a heated sample inlet into the flow tube at a known flow rate via a calibrated capillary. The precursor ion then undergoes a chemical reaction with the sample forming new product ions. At the downstream end of the flow tube, both the precursor and product ions are focused via electrostatic lenses into a second quadrupole mass spectrometer for mass analysis, and subsequently counted for identification and quantification. The analyte in the sample can be identified by comparing the observed product masses with the database of precursor ion-VOC reaction products. The concentration of the analyte in the sample can be calculated from the ratio of the number densities of ion products to precursor ions and the known experimental parameters and reaction rate coefficients. An example of breath profiles measured in the SIM mode comparing the concentrations of acetonitrile, acetone, hexanal, and isoprene in exhalations of a smoker versus a non-smoker is shown in Fig. 2.

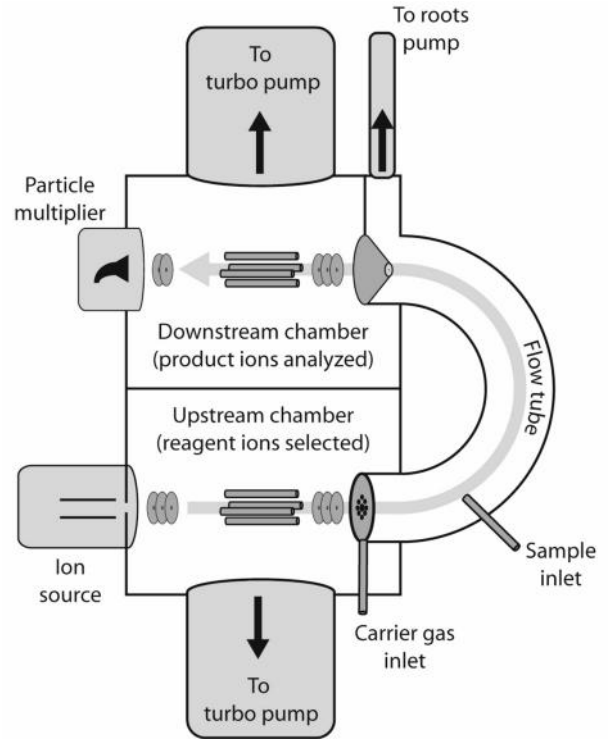


Fig. 1. Schematic diagram of SIFT-MS (reproduced with the permission of Syft Technologies Ltd.).

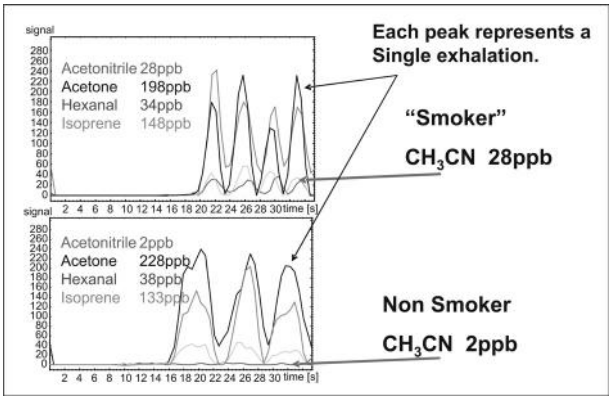


Fig. 2. Breath profile of smoker verse non-smoker (reproduced with the permission of Syft Technologies Ltd.).

For medical applications, SIFT-MS has several major advantages over other analytical techniques, such as GC-MS, ion-mobility spectrometry (IMS) and proton transfer reaction mass spectrometry (PTR-MS).[15] It offers real time detection and quantification of test samples regardless of humidity, and without any requirement for pre-concentration or sample preparation. It can detect several target compounds simultaneously or record full profiles over a selected mass range. The combination of three precursor ions, which react differently with the sample molecules, provides internal verification for accurate compound identification and the ability to distinguish between some isobaric and isomeric compounds.[16] For example, acetone and propanal (C_3H_6O) both result in product ions at *m/z* 59 $(M+H)^+$ by proton transfer from the H_3O^+ ion. However, NO^+ reacts with acetone via addition to form *m/z* 88 $(M+NO^+)$, but reacts with propanal via hydride ion transfer to form $(M-H)^+$ at *m/z* 57. O_2^+ offers further verification because acetone undergoes a charge transfer reaction with partial dissociation resulting in $MeCOMe^+$ (*m/z* 58) and $MeCO^+$ (*m/z* 43). The O_2^+ precursor characteristically undergoes charge transfer reactions with some compounds which do not react with either H_3O^+ or NO^+, *e.g.* NO, NO_2 and some smaller hydrocarbons.[17] Moreover, it reacts with NH_3 in a range of humid samples such as urine, blood headspace, and breath to provide verification for ammonia quantification using the H_3O^+ precursor. With H_3O^+ precursor ions, hydrated ions like $[H_3O^+.(H_2O)_n]$ (*n* = 1-3) and $(MH^+.H_2O)$ are also formed in a sample of air. These provide extra assistance in compound identification and establishing the humidity of the sample.[18]

The SIFT-MS instrument usually operates in one of two modes. The first is the selected ion monitoring mode (SIM), where only count rates of selected precursor ions and product ions are monitored simultaneously. The concentration of the target compound is calculated each time all the precursor and product ions are counted, resulting in a real time response to any changes in the target concentration. The sampling time between each data point depends largely on the collective monitoring time of the precursor ions (typically 25 ms each) and the product ions (typically 100 ms each). It is possible to quantify a large selection of target compounds; however, the more ions that are included per cycle, the longer the sampling time required between each cycle. This SIM mode is ideal for monitoring specific biomarkers in breath, such as ammonia, acetone, and isoprene.

When a large number of product ions are required to be monitored, or potential biomarkers are unknown, it can be more practical to operate under the second mode, which is the full mass-scan mode (MS). In the MS mode, a complete mass spectrum is obtained by sweeping the downstream quadrupole over a selected mass-to-charge (*m/z*) range for a chosen time with a chosen precursor ion. In this mode, the electronic settling time for the quadrupole to switch between difference masses is minimized. As the full mass spectrum of the sample gas is collected, it is possible to compare the *mass profile* of different samples using classifying algorithms.[19] A study on the use of VOC profiles obtained from breath samples analysed by GC-MS has

been reported for the diagnosis of lung cancer.[20] Studies are currently underway utilizing a classifying algorithm to compare mass profiles of control groups of breath samples in order to establish possible *mass profile* classifications and identify potential biomarkers for clinical conditions.

Applications to Medical Diagnosis

As discussed, the high sensitivity (detection range: 50 pptb to 40 ppmv), and real-time non invasive monitoring of breath samples by SIFT-MS make the methodology particularly applicable to medical testing.[21] Since the establishment of SIFT-MS testing capabilities in NZ, there have been several studies carried out which highlight the advantages of this technique.

Identification of infection

SIFT-MS can be used to quantify a number of VOCs in a single assay; this trait can be used to identify organisms or diseases by characterizing a specific VOC fingerprint. For example, Scotter *et al*.[22] found that it was possible to distinguish between several medically important fungi because the presence and quantity of the VOCs produced during culture varied. Although the presence of ethanol, methanol, acetone, acetaldehyde, methanethiol, and crotonaldehyde was dependant on the culture medium, there is potential for species specific identification which would enable targeted treatments.

Similarly SIFT-MS has been used to detect VOCs produced by bacteria. The high sensitivity of SIFT-MS compared to conventional blood culture systems, *e.g*. BacT/ALERT, makes earlier diagnosis of bacteremia (the presence of viable bacteria in the circulating blood) and identification of bacteria from the metabolic VOC fingerprints possible, if several VOC are analysed.[23] The early detection and identification of aerobic and anaerobic blood infections based on SIFT-MS technology provides clinical advantages over conventional methods. It may also be possible to extend this application to predict antibiotic susceptibility by monitoring changes to the bacterial VOC profile in the presence of antibiotics.[24] Potentially, SIFT-MS breath testing of patients could also be used to diagnose the presence of bacterial or fungal infection.

Monitoring exposure

The measurement of exposure to solvents in the workplace is receiving increasing attention by occupational health and safety regulators. SIFT-MS provides a rapid, accurate, and inexpensive method to monitor biological levels of solvents in the headspace of urine, saline, whole blood, red cells in saline, and plasma.[25] The instrument has sufficient sensitivity so that no pre-concentration of the samples are required, and several solvents can be monitored simultaneously if required. This leads to results being reported much more rapidly than by existing GC-MS methods.[26]

We have used SIFT-MS to quantify the amount of methanol, methyl ethyl ketone (MEK), and acetone in the headspace above urine that had known amounts of the solvents added. As expected, there is a linear relationship between the concentration in the urine and the amount measured in the headspace.[26] Similarly, Wilson *et al*.[27] measured the ethanol present in the headspace of blood and aqueous samples that contained known amounts of ethanol and found a linear correlation.

Real time analysis by SIFT-MS allowed this last group[28] to follow the decay of solvent levels after controlled exposure. The decay of xylene and mesitylene quantified in breath samples was fitted to a two compartment model. Concurrent blood samples were taken and it was shown that the amounts measured in the blood headspace and breath samples correlated. The amounts measured in the breath samples were about two-fold higher, which probably reflects the low solubility of the chemicals in blood.[28]

Commercially available Tedlar bags have been used to collect then transport samples to the SIFT-MS instrument when direct analysis is not possible. This technique was used to determine the VOC present in surgical plumes. Mass scans were used to determine VOC of interest, followed by SIM scans to accurately quantify the concentrations present of these and previously determined compounds. The VOCs produced included cardio-toxic HCN and carcinogenic buta-1,3-diene. However, the concentrations of these compounds within the surgical plume were less than those produced by a cigarette.[10]

Breath Analysis

Respiratory inflammation

Volatile halo-amines have been proposed as markers of eosinophil and neutrophil inflammation, however, their low concentration and reactivity in breath had previously made detection difficult. SIFT-MS has been used to measure several highly reactive, rapidly decomposing VOCs of interest. In addition, it has been shown that SIFT-MS has the sensitivity to quantify monobromamine (NH_2Br), monochloramine (NH_2Cl) and dichloramine ($NHCl_2$) in breath.[29]

Dialysis efficacy

As discussed previously, two modes of operation are possible with SIFT-MS: a screening mode, which uses a full mass scan, or the selected ion monitoring (SIM), which targets VOCs. The mass scan mode of SIFT-MS lends itself to the identification of volatile biomarkers, often present in trace amounts that are not detectable by other methods. Comparison of mass scans collected at different stages of a disease, or before and after interventions, can result in the identification of biomarkers for these conditions. The development of a classification algorithm has simplified this process.[19]

The mass scan algorithm has been used to determine which VOCs are most affected by dialysis. Change analysis of density profiles of mass scan VOCs pre- and post-haemodialysis showed that, in breath samples, ammonia was the marker exhibiting the greatest change. Breath ammonia was then monitored by SIM scan prior to and after the completion of dialysis. Traditionally dialysis efficacy is monitored by measuring the urea reduction ratio which requires measurement of plasma urea concentrations pre- and post-dialysis. Laboratory turn-around times for this test means that results are not available until the following dialysis session, and the invasive nature of the blood samples makes moni-

toring dialysis during the session difficult. SIFT-MS analysis of breath ammonia occurs in real time during the dialysis session, and is non-invasive so can be used to optimize the length of dialysis treatments.[30]

The mass scan mode has also been used to determine potential sources of interference in breath analysis. Epton *et al*.[31] investigated the *m/z* values most likely to appear after the use of CFC inhalers after noticing new masses present in the mass scan from a volunteer who had recently used the medication. The ions present were consistent with the predicted spectra of several freons present in the inhalers. The measurement of VOCs with similar masses would be affected by the presence of these compounds, and without the mass scan ability of SIFT-MS this interference may have gone undetected.[31]

Biological processes

The rapid analysis achieved by SIFT-MS is beneficial for monitoring the changes in biological processes. Changes to isoprene, ethanol, and acetone were quantified after cigarette smoking, and the effects of exercise on breath VOC have also been investigated.[13]

Ammonia, acetone, and isoprene vary with time during exercise, in particular breath acetone increased for most subjects and isoprene concentrations decreased.[7]

Conclusion

Real time analysis of breath samples, and rapid analysis, without sample preparation, of the headspace of blood or urine by SIFT-MS are proving to be valuable tools for medical diagnosis and the monitoring of disease. The SIM mode is ideal for quantifying known biomarkers, and the mass scan mode has made it possible to identify previously unknown markers. Bedside testing will become a reality when the instrument is further reduced in size thereby increasing the possible applications of SIFT-MS by allowing breath analysis of immobile patients. Since its establishment in NZ, SIFT-MS has proved to be a useful technique in medical applications, and future work will expand upon these to build the capabilities of SIFT-MS in the medical field.

Acknowledgements

The authors are grateful to Murray McEwan and Randall Allardyce for their helpful input into the preparation of this paper. Syft Technologies Ltd. medical application research is funded by a RFI grant from FRST.

References

1. Adams, N.G.; Smith, D. *Int. J. Mass spect. Ion Phys.* **1976**, *21*, 349-359.
2. Smith, D.; Spanel, P. *Mass Spectrom. Rev* **2005**, *24*, 661-700.
3. McEwan M.J. In *Adv. Gas Phase Ion Chem.* Vol. 1, Adams N.G. and Babcock L.M. (Eds.), JAI Press, Greenwich, CN, 1992, 1-42; Knight, J.S.; Freeman, C.G.; McEwan, M.J.; Adams, N.G.; Smith, D. *Int. J. Mass Spectrom. Ion Proc.* **1985**, *67*, 317-330; MacKay, G.I.; Vlachos, G.D.; Bohme, D.K.; Schiff, H.I. *Int. J. Mass Spectrom. Ion Proc,* **1980,** *36*, 259-270; Copp, N.W.; Hamdan, M.; Jones, J.D.C.; Birkinshaw, K. *et al*. *Chem. Phys. Lett.* **1982**, *88*, 508-511; Glosik, J.; Twiddy, N.D.; Javahery, G.; Ferguson, E.E. *Int. J. Mass Spectrom. Ion Proc.* **1991**, *109*, 75-81; Squires, R.R. *Int. J. Mass Spectrom. Ion Proc.* **1992**, *118*, 503-518; Tsuji, M.; Aizawa, M.; Nishimura, Y. *J. Phys. Chem.* **1995**, *99*, 3195-3200.
4. Spanel, P.; Smith, D. *J. Chem. Phys.* **1996**, *104*, 1893-1899; Smith, D.; Spanel, P. *Rapid Comm. Mass Spectrom.* **1996**, *10*, 1183-1198.
5. Fairley, D.A.; Scott, G.B.I.; Freeman, C.G.; Maclagan, R.G.A.R. *et al*. *J. Chem. Soc. Faraday Trans.* **1996**, *92*, 1305-1309; Matthews, K.K.; Adams, N.G.; Fisher, N.D. *J. Phys. Chem. A* **1997**, *101*, 2841-2847; Spanel, P.; Ji, Y.F.; Smith, D. *Int. J. Mass Spectrom,* **1997**, *165*, 25-37; Wang, T.S., *Spectrosc. Spectr. Anal*., **2006**, *26*, 747-752; Schoon, N; Amelynck, C; Debie, E; Bultinck, P; Arijs, E. *Int. J. Mass Spectrom*. **2007**, *263*, 127-136; Francis, G.J.; Milligan, D.B.; McEwan, M.J. *J. Phys. Chem. A* **2007**, *111*, 9670-9679.
6. Spanel, P.; Dryahina, K.; Smith, D. *Int. J. Mass Spectrom.* **2006**, *249*, 230-239.
7. Senthilmohan, S.T.; Milligan, D.B.; McEwan, M.J.; Freeman, C.G. *et al*. *Redox Rep.* **2000**, *5*, 151-153.
8. Milligan, D.B.; Wilson, P.F.; Mautner, M.N.; Freeman, C.G. *et al*. *J. Environ. Qual.* **2002**, *31*, 515-524; Clough, T.J.; Sherlock, R.R.; Mautner, M.N.; Milligan, D.B. *et al*. *Aust. J. Soil Res.* **2003**, *41*, 421-438.
9. Wilson, P.F.; Freeman, C.G.; McEwan, M.J. *Int. J. Mass spectrum.* **2003**, *229*, 143-149.
10. Moot, A.R.; Ledingham, K.M.; Wilson, P.F.; Senthilmohan, S.T. *et al*. *ANZ J. Surg.* **2007**, *77*, 20-23.
11. Davis, B.M.; Senthilmohan, S.T.; Wilson, P.F.; McEwan, M.J. *Rapid Comm. Mass Spectrom.* **2005**, *19*, 2272-2278; Davis, B.M.; McEwan, M.J. *J. Agric. Food Chem.* **2007**, *55*, 3334-3338.
12. Wilson, P.F.; Prince, B.J.; McEwan, M.J. *Anal. Chem.* **2006**, *78*, 575-579.
13. Senthilmohan, S.T.; McEwan, M.J.; Wilson, P.F.; Milligan, D.B. *et al*. *Redox Rep.* **2001**, *6*, 185-187
14. Smith, D.; Spanel, P. *Int. Rev. Phys. Chem.* **1996**, *15*, 231-271.
15. Critchley, A.; Elliott, T.S.; Harrison, G.; Mayhew, C.A. *et al*. *Int. J. Mass Spectrom.* **2004**, *239*, 235-241. Wilson, H.K.; Monster, A.C. *Occup. Environ. Med.* **1999**, *56*, 753-757.
16. Spanel, P.; Smith, D. *Int. J. Mass Spectrom.* **1999**, *187*, 139-147; Midey, A.J.; Williams, S.; Viggiano, A.A. *J. Phys. Chem. A* **2001**, *105*, 1574-1578.
17. Spanel, P.; Smith, D. *Rapid Comm. Mass Spectrom.* **2000**, *14*, 646-651.
18. Spanel, P.; Smith, D. *Rapid Comm. Mass Spectrom.* **2000**, *14*, 1898-1906.
19. Moorhead, K.T.; Lee, D.; Chase, J.G.; Moot, A.R. *et al*. *Comput. Methods Prog. Biomed* **2008**, Jan 8, E-public. ahead of print.
20. Phillips, M.; Gleeson, K.; Hughes, J.M.B.; Greenberg, J. *et al*. *Lancet* **1999**, *353*, 1930-1933.
21. Freeman, C.G.; McEwan, M.J. *Aust. J. Chem.* **2002**, *55*, 491-494.
22. Scotter, J.M.; Langford, V.S.; Wilson, P.F.; McEwan, M.J. *et al*. *J. Microbiol. Methods* **2005**, *63*, 127-134.
23. Allardyce, R.A.; Langford, V.S.; Hill, A.L.; Murdoch, D.R. *J. Microbiol. Methods* **2006**, *65*, 361-365; Scotter, J.M.; Allardyce, R.A.; Langford, V.S.; Hill, A.L. *et al*. *J. Microbiol. Methods* **2006**, *65*, 628-631.
24. Allardyce, R.A.; Hill, A.L.; Murdoch, D.R. *Diagn. Microbiol. Infect. Dis.* **2006**, *55*, 255-261.
25. Wilson, P.F.; Freeman, C.G.; McEwan, M.J.; Allardyce, R.A. *et al*. *Appl. Occup. Environ. Hyg.* **2003**, *18*, 759-763.
26. Storer, M.; Senthilmohan, S.; George, P. In *Harnessing New Technology for Clinical Diagnostics*, Hyatt Regency: Union Station, St. Louis, Missouri, 2007.
27. Wilson, P.F.; Freeman, C.G.; McEwan, M.J.; Milligan, D.B. *et al*. *Rapid Comm. Mass Spectro.* **2001**, *15*, 413-417.
28. Wilson, P.F.; Freeman, C.G.; McEwan, M.J.; Milligan, D.B. *et al*. *Rapid Comm. Mass Spectrom.* **2002**, *16*, 427-432.
29. Senthilmohan, S.; Kettle, A.; McEwan M.J.; Dummer, J. *et al*. *Rapid Comm. Mass Spec* **2008**, *22*, 677-681.
30. Scotter, J.; Moorehead, K.; Allardyce, R.A; Storer, M. *et al*. Int. Assoc. Breath Research *Breath Analysis Summit 2007: Clinical Applications of Breath Testing* Cleveland, Ohio, 2007.
31. Epton, M.J.; Ledingham, K.; Dummer, J.; Rhodes, B. *et al*. Int. Assoc. Breath Research *Breath Analysis Summit 2007: Clinical Applications of Breath Testing: 2007*, Cleveland, Ohio, 2007.

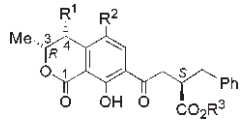
The Quantitation of Ochratoxin A in Foodstuffs Sold in New Zealand

Darren A. Saunders,[a] Shirley Jones,[a] and Rudolf Schmitt[b]

[a]Institute of Environmental Science and Research (ESR) Ltd, 27 Creyke Road, Ilam, Christchurch and [b]University of Zurich, Switzerland (e-mail: *darren.saunders@esr.cri.nz*)

Introduction

Ochratoxins are naturally occurring mycotoxins produced primarily by *Aspergillus ochraceus* and *Penicillium verrucosum*.[1] Ochratoxin A (OA; **1**) is the most abundant and the most toxic of the mycotoxin group that also includes ochratoxins B (**2**) and C (**3**), **4**, the 4-hydroxy derivative of **1**, and methyl esters of ochratoxins A, B, and C where R^3 = Me.[2] Ochratoxin A occurs in plants such as cereals (mainly wheat, oats and barley), beans, nuts, coffee and cocoa beans, dried fruits, spices, and wine. It has also been found in the kidney's of pigs fed with contaminated feed;[3,4] it is nephrotoxic, hepatotoxic, carcinogenic, teratogenic, genotoxic, and immunotoxic.[4,5]



1, ochratoxin A: $R^1 = R^3 = H$; $R^2 = Cl$
2, ochratoxin B: $R^1 = R^2 = R^3 = H$
3, ochratoxin C: $R^1 = H$; $R^2 = Cl$; $R^3 = Et$
4, $R^1 = OH$; $R^2 = Cl$; $R^3 = H$

The Joint UN Food and Agriculture Organization and World Health Organization Expert Committee on Food Additives (JECFA) has proposed a provisional maximum tolerable weekly intake of 0.1 µg/kg body weight for **1**; the European Union recently adopted a limit of 2.0 µg/kg for it in red and white wines.[5] Of the spices, paprika and chilli are particularly prone to contamination. In general, the limit adopted by the international spice trade for **1** is in the range 10-20 µg/kg.[2] The European Union has proposed tolerance levels for **1** of 1 µg/kg for infant foods and 5 µg/kg for other foods. Other countries with legislation applying to 1 have regulatory limits ranging from 1 to 50 µg/kg.[4,6] Little information is available regarding the presence of **1** in NZ foodstuffs, although ESR undertook a survey of 160 selected foods and wines including coffee, cereals, grains, dried fruit, and pate in 2000.[7]

During 2007 we extended this study to examine a range of NZ foodstuffs employing an improved detection method for **1** that is based upon HPLC analysis. Hereafter this is referred to as the 2007 survey.

Experimental

The amount of ochratoxin A (**1**) in a variety of foodstuffs including cereals, dried fruits, spices, and wines was determined using an High-Performance Liquid Chromatographic (HPLC) method that was adapted primarily from that of Lobeau *et al*.[8] After establishing the validity of the analytical procedure, a small survey of the levels of **1** in foodstuffs known to be prone to OA contamination, and available locally (except for wines that were purchased in Auckland), was conducted (see Table 2).

Method - sample extraction

A sample of the foodstuff (15 g) was blended with 150 mL of 4:1 MeOH/aqueous $NaHCO_3$ (3% w/v). The mixture was then filtered through Whatman No 4 filter paper and a 10 mL aliquot of the filtrate was removed and diluted to 50 mL with 0.01 M phosphate buffered saline (pH 7.4) containing casein (0.1% w/v). This solution was then passed through an OchraTest immunoaffinity column (Vicam USA; #G1034) under gravity. The column was subsequently washed with two 5 mL aliquots of deionised water.

Ochratoxin A (**1**) was eluted from the immunoaffinity column with methanol (4 mL) which was concentrated to dryness at 50°C (reduced pressure) and the residue made up to 1 mL with the HPLC mobile phase.

HPLC analysis

Column: 220 x 4.6 mm i.d. Applied Biosystems RP-18, 5 µm bead diam. with a 15 x 3.2 mm i.d column. RP-18, 7 µm bead diam. guard column; mobile phase: MeCN (47%), aq.AcOH (53%; 1% v/v); flow rate: 1.5 mL/min; detection: fluorescence λ_{ex} = 333 nm, λ_{em} = 460 nm; injection volume: 50 µL

Linearity and reproducibility

The ochratoxin standard curve was linear over the range 0.1–50 µg/L, all $r^2 > 0.99$. The limit of detection (LOD) in samples was <0.1 µg/kg (chromatographic peak to baseline noise ratio: 3:1). The limit of quantification (LOQ) in samples was <0.5 µg/kg (ratio chromatographic peak to baseline noise 10:1); spiked recoveries were > 80% over the range 0.1 – 50 µg/L ochratoxin regardless of matrix investigated.

Table 1. Repeatability

Matrix	OA spike Conc (µg/kg)	No repeats	[OA] found (µg/kg)	CV[a] (%)
Wine	5	5	4.6	4.3
Bread	2	5	2	10.5
Bread	10	5	10	8.4
Paprika (authentic)	43.2	5	43.2	7.6

[a]Coefficient of variation

Results

Table 2. Ochratoxin A (1) in local and imported foodstuffs purchased in Christchurch.

Food Matrix	Total samples	+ve samples	% +ve	Range OA (1)/µg/kg
Cereals	**23**	**7**	**30**	**0.11-2.85**
Extruded	13	3		0.20-1.12
Muesli	9	4		0.11-2.85
Weetbix	1	0		
Coffee	**8**	**7**	**88**	**<0.1-1.02**
Dried Fruits	**10**	**3**	**30**	**0.28-1.02**
Apricots	2			
Dates	2	1		1.02
Figs	2			
Prunes	1			
Raisins	3	2		0.28-0.74
Spices	**10**	**10**	**100**	**0.23-50.60**
Chilli	4	4		0.23-39.91
Nutmeg	2	2		4.26-23.52
Paprika	4	4		13.28-50.6
Wines[a]	**21**	**1**	**5**	**1.25**

[a]Red and white wines both foreign and domestic

Discussion

The levels of ochratoxin A (**1**) in the majority of foodstuffs, *i.e.* bread, cereals, dried fruit, and coffee were below 5 0 µg/kg, while all the wines (foreign and domestic) had levels below the European Union 2 0 µg//L regulatory limit.

As with the 2000 survey, the 2007 investigation found the highest percentage of positive samples to be from coffee. In 2000 this comprised all samples (n = 21; 100%) with the amount falling in the range 0.2-2.7 µg/kg. The 2007 survey showed seven of eight samples to be positive (88%) but with a lower content range of 0.05-1.02 µg/kg. In 2000 the highest levels of **1** occurred in dried fruit (0.1 to 22 µg/kg; n = 10) whereas in 2007 the range was 0.28-1.02. The presence of **1** in cereals differed little from those found in 2000 (0.1-0.77 µg/kg; n = 22; 38% positive). However, the levels in some of the spice samples in this 2007 survey exceeded the recommended allowable concentrations used by the spice industry, especially for chilli and paprika. In addition, baby foods that tend to have lower regulatory limits set for **1** were not investigated. The relatively high levels of **1** in some cereals suggest further work in this area to be prudent.

It is known, at least in regard to paprika, that low moisture content (<11%) and water activity (<0.75) are crucial in preventing mould growth.[2] Water activity (a_w) is a measurement of the energy status of the water in a system. It indicates how tightly water is bound within a substance and is measured on a scale from 0 to 1.0. Pure water has an a_w value of 1.0 and saturated aqueous sodium chloride 0.76. Water activity is a useful parameter in determining food quality and safety as most moulds, yeasts, and bacteria cannot grow in products with an a_w of < 0.7. Water activity of foodstuffs can be determined easily and quickly using a water activity meter.[9] Further investigation of the relationship between water activity, moisture content, and the levels of **1** in spices may result in a simple and inexpensive means of ensuring that these levels are kept within acceptable limits.

Acknowledgements

The authors thank both Valerie Orchard and Dr Stephen On (ESR) for their support and encouragement. This study was funded from MoRST (Ministry of Research, Science & Technology) capability funding.

References

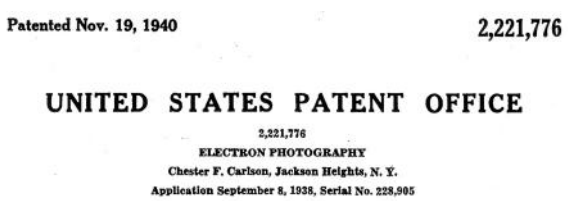
1. Sibinda, L.; De Saeger, S.; Van Peteghem, C. *J. Chrom. A* **2002**, *959*, 327-330; Ringot, R.; Cango, A.; Schneider, Y. and Larondelle, Y. *Chemico-Biol. Interactions* **2006,** *156*, 18-46.
2. Almela, L.; Rabe, V.; Sanchez, B.; Torella, F. *et al*. *Food Microbiol.* **2007**, *24*, 319-327.
3. Joosten, H.; Goetz, J.; Pittet, A.; Schellenberg, M and Bucheli, P. *Int. J. Food Microbiol.* **2001**, *65*, 39-44.
4. Solfrizzo, M.; Avantaggigiato, G. and Visconti, A. *J. Chrom. A* **1998**, *815*, 67-73.
5. Ratola, N.; Barros, P.; Simoes, T.; Cerdeira, A. *et al. Talanta* **2006**, *70*, 720-731.
6. Medina, A.; Valle-Algarra, F.; Gimeno-Adelantado, J.; Mateo, R. *et al. J. Chrom. A* **2006**, *121*, 178-183.
7. Shaw, I.; Stanton, D. and Mitchell, J. *Survey of susceptible foods for ochratoxin A*. A report to the NZ Ministry of Health, June 2000.
8. Lobeau, M.; Saeger, S.; Sibanda, L.; Barna-Vetro, I. And Peteghem, C. *Food Additives Contam.* **2007**, *24*, 398-405.
9. AquaLab Operators Manual - Water Activity Meter: Decagon Devices, Inc.; see. *www.decagon.com/aw*.

From Small Rings to Big Things: Xerography, Sensors, and the Squaraines

Brian Halton

School of Chemical & Physical Sciences, Victoria University, PO Box 600, Wellington
(e-mail: *brian.halton@vuw.ac.nz*)

The process that has become the modern miracle of photocopying was discovered in 1938 by patent attorney Chester Carlson who had studied chemistry in college, but gained a BSc in physics. His patent was granted in November 1940 under the title *Electron Photography* (Fig. 1).[1] The term ***xerography*** (*xeros*: dry, *graphos*: writing) was coined subsequently because there were no liquids involved in the chemical process.[2,3] Without the *Xerox* life would be almost impossible, especially as it extends to laser (and LED) printers and copiers. It took Carlson years to stimulate interest in developing the potential of what he had found: it was only through the non-profit *Battelle Memorial Institute* of Ohio and an agreement in 1947 with the small Rochester photopaper company *Haloid*, that the invention progressed to the first commercial office copier. The 914 copier, as it was known, appeared in 1959 and copied sheets 9 x 14 inches in size; Haloid has evolved into what we now know as the *Xerox Corporation*.



Patented Nov. 19, 1940 2,221,776

UNITED STATES PATENT OFFICE

2,221,776

ELECTRON PHOTOGRAPHY

Chester F. Carlson, Jackson Heights, N. Y.

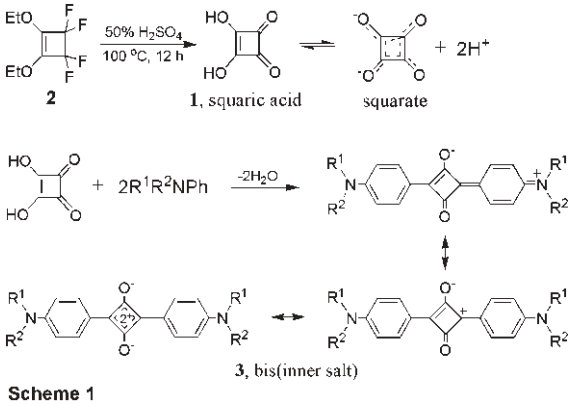
Application September 8, 1938, Serial No. 228,905

Fig. 1. Frontispiece of Carlson's patent (from http://www.freepatentsonline.com).

The basic principles of xerography are simple enough. First, a positive charge is applied to a photoconductive surface (the photoreceptor) and then the image of a document is exposed on this surface, which causes the charge to drain away from the surface in all but the dark image areas (these remain unexposed and thus charged). Next, a negatively charged powder (a dry ink or toner) is cascaded over the surface so that it adheres to the positively charged parts and creates a visible image. By placing a sheet of positively charged plain paper over the image, the negatively charged powder is attracted to the paper electrostatically, transferring the image. Finally, the powder image is fused to the paper by heat and the photoconductive surface cleaned ready for subsequent use.

Laser printing was also introduced by Xerox in the mid-1970s, but its true potential has been realised only with the advent of the personal computer, the internet and data transfer. In the modern machine the document is moved automatically from the document handler to a platen that is housed under it, scanned, and the data stored in the raster memory (a raster is a horizontal strip of dots across the page). From here the digitized image of a page is projected by the laser onto the charged photoreceptor belt to give the latent image as described above. More than >90% of the photoreceptors currently used are organic photoconducting materials.[3] Magnetic rollers brush the belt with oppositely charged dry ink and create the visible image by adhering to the latent image. As the copy paper moves from its storage tray towards the belt, it is charged to the same polarity as the belt and thus attracts the dry ink from it, so creating the image that is heated and pressed between two rollers to fuse the dry ink to the paper. The process is repeated until the entire document is printed. The original single layer device evolved to a bilayer system, where the charge generation and charge transport functions are separated into two discrete layers. It is the availability of the organic photoreceptor that impacts most on xerographic copying. Various classes of organic photoconductive pigments have been developed and successfully used in the bilayer device. These need to be insulators (or have low conductivity) in the dark but become conductors upon exposure to light.[3]

This is where small ring chemistry, inextricably linked to W. H. Perkin Jr. and the 1880s,[4] and all too often dispelled as mere chemical curiosity, comes into play. In 1959 (when the 914 copier was released) Cohen, Lacher and Park[5] reported a new cyclobutadienoacid derivative, the diketocyclobutenediol **1**, that was subsequently given the trivial name of *squaric acid*.[6] It is best prepared by complete hydrolysis of the tetrafluorodiether **2**. Because each carbon centre of **1** is sp^2 in nature, the molecule is exceptionally acidic (pK_a *ca.* 3.0) and exists entirely in the symmetrical dianionic *squarate* form $(C_4O_4)^{2-}$.



Scheme 1

Some three years later, the condensation of squaric acid with reactive pyrroles was recorded[7] prior to tertiary aromatic amines being employed in the reaction (Scheme 1).[8] The reaction products, illustrated by **3**, are highly conjugated and intensely coloured betaine (di-ionic) dyes with high melting points, as expected for polar molecules. They differ from earlier dyes because the salts are intramolecular (inner) rather than ion-paired with a dye base; they were named *squaraines*.[7] These derivatives absorb at long wavelength (620-670 nm in solution; 700-850 nm in the solid state) and fluoresce with reasonable quantum yield. Their excited state lifetimes mean that their photostabilities are good and photosensitivity over the visible-near IR region is excellent. The

ground and excited singlet states (S_0 and S_1) of **3** are intermolecular donor-acceptor-donor (D-A-D) charge-transfer in nature, with the nitrogen atoms the donors and the central four-membered ring the acceptor. In the solid state the layers are *ca*. 35 nm apart (Fig. 2). Intramolecular charge-transfer occurs during $S_0 \rightarrow S_1$ excitation, but this is largely (~80%) confined to the central C_2O_4 moiety.[9] The absorption characteristics and *intermolecular* charge-transfer of the squaraines form the basis of their use in diode laser printers, copiers, and multifunctional copier-printers. Initially, they were used as sensitizers for ZnO photoconductors,[10] but were recognised as bilayer photoconductors in 1974.[11] Because their absorption matches well to the diode laser, there was rapid development in the 1980s of their syntheses, and patents appeared for their composition and uses.[12] Fluorinated derivatives were patented for photoconducting imaging,[13] and studies on the structural and electronic properties[9] continue even now.[14] In 1993, the unsymmetrical fluorodiether **4** was recorded as the most outstanding squaraine known.[3]

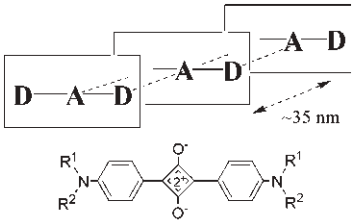
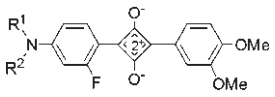
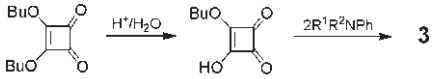


Fig. 2. Schematic of squaraine stacking



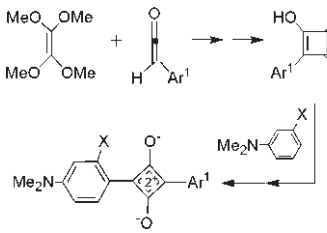
4

Despite these advances, it was found that residues from the squaric acid synthesis were carried through to the squaraines and that these reduced the efficiency of xerography by imposing low charge-acceptance and a high *dark-conductivity*. In 1986 Law and Bailey[15] removed these obstacles by providing derivatives from a route that avoided squaric acid itself (Scheme 2). The squaraines from this so-called *ester route* have a smaller particle size with different crystallographic orientation that gives rise to improved xerographic properties. Further development came from the same authors in 1990 from their use of the [2 + 2] addition of a ketene to an alkene (Scheme 3) that allowed for easy synthesis of unsymmetrical derivatives.[16]



3

Scheme 2

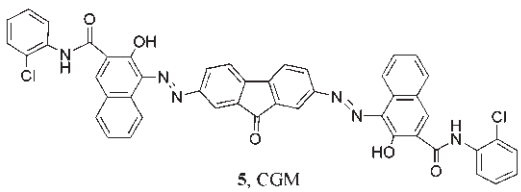


Ar^1 = 4-$MeOC_6H_4$- or 3,4-$(MeO)_2C_6H_3$-,
X = H, OH, Me, or F

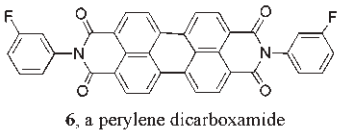
Scheme 3

Of course, it is not just squaraines that are used as photoreceptors for xerography. Chart 1 depicts the important classes of compounds that are in use,[3] which include azo pigments such as **5** (known as CGM), perylenes (exemplified by bisamide **6**), and phthalocyanines **7** which may or may not have a co-ordinated metal.

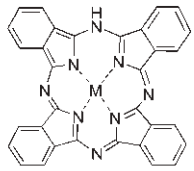
Chart 1



5, CGM



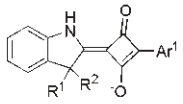
6, a perylene dicarboxamide



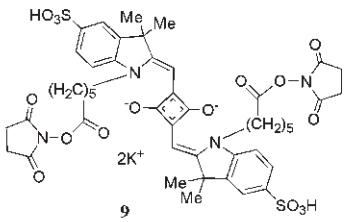
7, a phthalocyanine,
M = metal or 2H

Since the squaraines are long wavelength-absorbing fluorescent materials with acceptable quantum yields, reasonably long excited state lifetimes, and good photostabilities, they have also found use in fluorescence-based assays.[17] The most suitable compounds for biological applications carry an indolenine derivative, *e.g.* **8** (Chart 2), as these have the highest photostabilities. Importantly, their use is further enhanced because quantum yields and lifetimes increase significantly upon covalent and noncovalent binding to proteins [bovine serum albumin (BSA), antibodies]. The absorption range allows use with the commercially available 635- and 650-nm diode lasers, and the detection limit for *e.g.* **9**, in blood was shown to be half that of an alternative commonly used fluorophore.[18] Even the simple phenolic squaraine **10** binds to BSA with a profound colour change in solution and in gel - pink to deep purple - and it is some five times more sensitive than dyes in common use.[19]

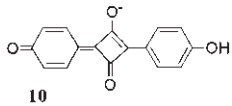
Chart 2



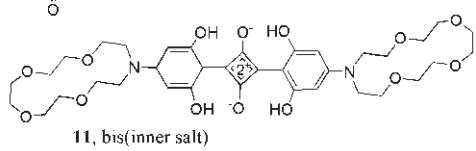
8, an indolininyl
squaraine



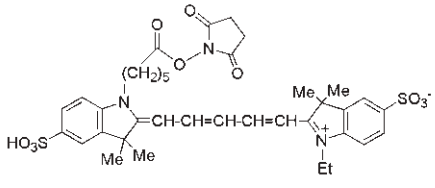
9



10



11, bis(inner salt)



12, Cy5

Fluoroionophores containing azacrown-substituted squaraines, *e.g.* **11**, have been used for Na^+ and K^+ sensing in plasticized PVC matrices and provide an alternative to use of flame emission spectroscopy.[20] A fluorescent squaraine-

containing chemosensor that signals change in the pH 7-10 range works in wholly aqueous solutions.[21] The electrophilic squaraine four-membered ring also has been used in aqueous solution for a highly selective colorimetric chemo-dosimeter for thiol-containing compounds; derivatives have been used successfully in the determination of low molecular mass aminothiols in human plasma.[22] Ring-substituted squaraines are at least as effective as the indolium dye Cy5 **12** that is a commonly used fluorescent label. As the squaraines are excited with both red and blue diode lasers or light emitting diodes, they can be used as fluorescent probes and labels for intensity- and fluorescence lifetime-based biomedical applications.[23] However, such uses for squaraines have been significantly limited by their chemical sensitivity to attack by strong biological nucleophiles and their ability to form non-fluorescent self-aggregates. The most recent advances have had a marked impact on both of these problems: specifically, encapsulation of the thread-like squaraine dye inside an interlocked pseudorotaxane structure adds very significant stability.[24] As an example, the molecular cage **13** complexes squaraine **14** and, in the presence of Na^+, gives the rotaxane **13⊂14⊃**Na_2 as its perchlorate salt (Scheme 4). The Na^+ ions provide ion-specific binding to the encapsulated thread-like squaraine dye and the pseudorotaxane structure protects it from attack. Analogues with Zn(II)-dipicolylamine coordination centres, *e.g.* **15⊂16,** are formed from macrocycle **15** and **16** (Scheme 4).[25] Such pseudorataxanes are cell-targeting ligands with **15⊂16** having a photobleaching half-life 10 times greater than that of the Cy-5 analogue **17** (Chart 3). The rotaxane **15⊂16** $4NO_3^-$ is some 20 times more stable than Cy-5 and provides an extremely bright, highly stable near infrared (NIR) fluorescent probe for *in vitro* and *in vivo* optical imaging of live and fixed cells. Such derivatives seem set to be superior substitutes for Cy-5 in many biological applications.[25] Such stabilization has an analogy with amphiphilic squaraines (derivatives of **3** with ether, alcohol and carboxyl substituents) that interact efficiently with micelles with little change in their absorption characteristics.[26] Again, the squaraine is encapsulated and the fluorescence lifetime is more than doubled in Triton X-100, **18**. The encapsulated squaraine appears to sit close to the micelle surface near the polar head groups and, because micelles mimic biological media, applications are likely.

Pharmacologically acceptable derivatives of bromo- and iodo-derived squaraines **19** (Chart 3) find use as sensitizers in photodynamic therapy (PDT), an emerging procedure for diagnosis and treatment of cancer as it involves the inactivation of living cells.[27] After intravenous injection, the tumor tissues selectively retain the photoactive sensitizer (the squaraine) that liberates the highly reactive species upon exposure to specific NIR radiation. Cellular constituents are then damaged and eventually die. PDT is a safer treatment than conventional chemotherapy and radiotherapy, since the induction of cytotoxicity ceases when the light is switched off. The quinaldine-based squaraines, *e.g.* **20**, appear to have much potential here.[28]

By the mid-1990s the ability of squaraines such as the bis(trihydroxybenzene) derivative **21** to provide nanocrystalline semiconductor films with TiO_2, ZnO and SnO_2 colloids was recognised, and their possible use in sensitizing large bandgap semiconductors continues to be explored.[29]

Scheme 4

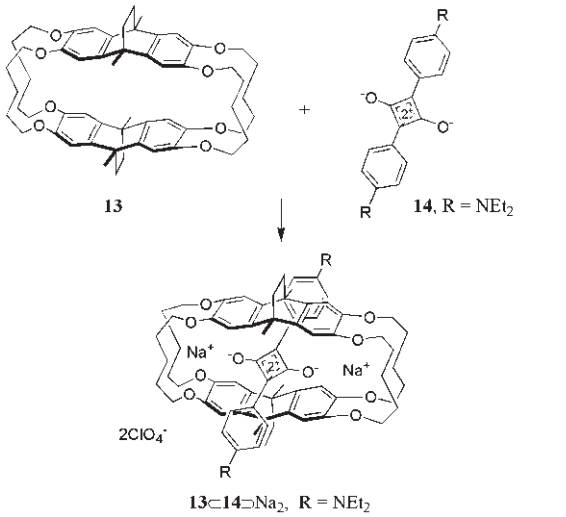
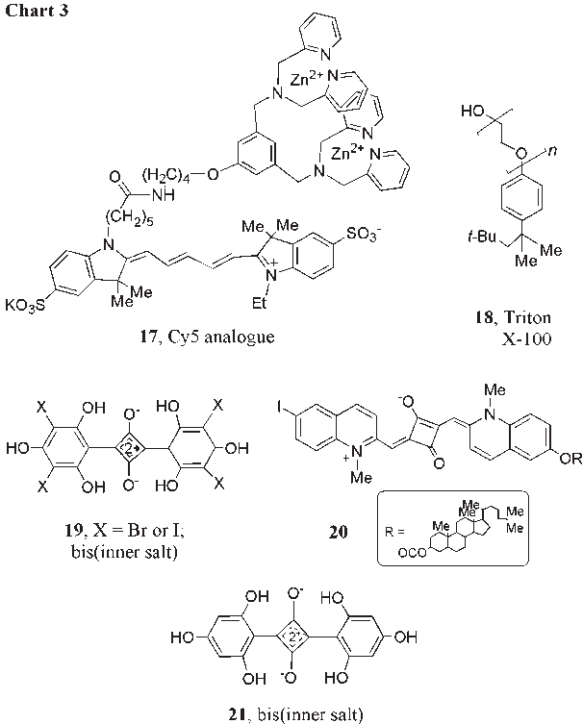


Chart 3



Squaraine-containing non-linear optical (NLO) devices were patented over a decade ago[30] and NLO properties continue to receive attention. Derivatives with peripheral arylethene moieties, *e.g.* **22** (Chart 4), provide compounds whose independent components are separately represented in functional

Merck Ltd.
P.O. Box 1246
Palmerston North, 4440. New Zealand
Phone: (06) 356 7328 Fax: (06) 356 7311
Email: info@merck.co.nz

IS.19823 NZIC_L

Sometimes it will.

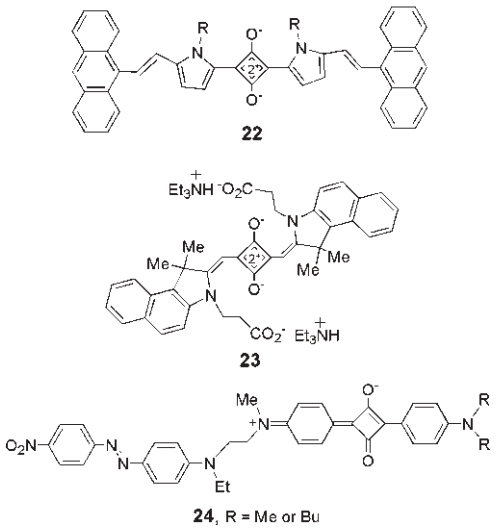
With a lot of effort we've managed to squeeze thousands of products into the latest Merck Product Catalogue. If that wasn't enough, we've also jammed in an impressive amount of detailed information on pack sizes, specifications and safety features. This all results in an invaluable reference for any laboratory.

For further information call 0800 46 37 25 or register for your copy on-line at **www.merck.co.nz**

MERCK

R

Chart 4



22

23

24, R = Me or Bu

molecular materials.[31] Differently functionalized derivatives have electron-transporting properties, some with both electron- and hole-transporting ability. One such compound, when inserted between a cathode and an anode, gave a single-layer-sandwich device with red light-emitting ability under both low negative and low positive driven bias.[32]

The novel blue squaraine dye **23** carrying two carboxylate groups has been successfully used in liquid- and solid-state NIR dye-sensitised solar cells.[33] Furthermore, a squaraine chromophore attached to a podand chain gives proton-controlled, intramolecular photoinduced electron transfer (PET)[34] that has application in the design of PET-based sensors. Finally, the coupling of the squaraine moiety with the azo dye Disperse Red 1 gives the dark green **24** (Chart 4) which has the rare combination of fluorescent and azo units within the same molecule, providing a promising system for optical data storage.[35]

Cohen, Lacher, and Park[5] could hardly have envisaged the potential importance of their squaric acid and the uses to which the squaraines have been put. Further advances in squaraine usage can be expected for some little while yet. This account serves to emphasise once again that pure research is the necessary forerunner to so much applied and technological development.

References

1. Carlson, C. F. US Pat. 2,221,776, **1940** (*Chem. Abstr.* **1941**, *35*, 8405).
2. Xerography: See: *http://a1851.g.akamaitech.net/f/1851/2996/1824h/chcheB.xerox.com/downloads/usa/en/s/Storyofxerography.pdf*
3. Law, K.-Y. *Chem. Rev.* **1993**, *93*, 449-486.
4. Perkin, W. H. *J. Chem. Soc., Trans.* **1887**, *51*, 1 - 28.
5. Cohen, S.; Lacher, J. R.; Park, J. D. *J. Am. Chem. Soc.* **1959**, *81*, 3480.
6. Park, J. D.; Cohen, S.; Lacher, J. R. *J. Am. Chem. Soc.* **1962**, *84*, 2919-1922.
7. Treibs, A.; Jacob, K. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 694.
8. Sprenger, H.-E.; Ziegenbein, W. *Angew. Chem. Int. Ed. Engl.* **1966**, *5*, 894.
9. Bigelow, R. W.; Freund, H. J. *Chem. Phys.* **1986**, *107*, 159-174.
10. Kampfer, H.; Verhille, K. E. US Pat. 3,617,270, **1971** (*Chem. Abstr.* **1972**, *77*, 158756).
11. Champ, R. B.; Shattuck, M. D. (IBM Corp.) US Pat. 3,824,099 19740716, **1974** (*Chem. Abstr.* **1975**, *81*, 9777).
12. See *e.g.:* Law, K. Y.; Bailey, F. C. *J. Imaging Sci.* **1987**, *31*, 172-177; Baranyi, G.; Burt, R. A.; Hsiao, C. K.; Kazmaier, P. M.; *et al.* (Xerox Corp.) US Pats. 83-493,114 4,471,041, **1984**, 84-570,563 4,524,218, **1985**, and Eur. Pat. 84-308,091 144,195, **1985** (*Chem. Abstr.* **1985**, *102*, 14790; **1985**, *103*, 161875, and **1986**, *104*, 43127); Fuji Xerox Co. Jp. Pat. 83-236,207 60,128,455, **1985** (*Chem. Abstr.* **1986**, *104*, 59376); and Law, K. Y. (Xerox Corp.) US Pat. 84-576,656 4,524,219, **1985** (*Chem. Abstr.* **1985**, *103*, 150922); Law, K. Y.; Bailey, F. C. (Xerox Corp.) US Pat. 83-558,248 4,508,803 **1985** (*Chem. Abstr.* **1985**,*102*, 195185).
13. Kazmaier, P. M.; Baranyi, G.; Loutfy, R. O. (Xerox Corp.) US Pat. 85-748,285 4,621,038 **1986** (*Chem. Abstr.* **1987**, *106*, 166137); Kazmaier, P. M.; Burt, R. A.; Baranyi, G. (Xerox Corp.) U.S. Pat. 85-749,857 19,850,628 **1986** (*Chem. Abstr.* **1987**, *106*, 205165).
14. Silva, C. E.; Dinez, R.; Rodriguez, B. L.; De Oliveir, L. F. C. *J. Mol. Struct.* **2007**, *831*, 187-194; Fu, J.; Padilha, L. A.; Hagan, D. J.; Van Stryland, E. W.; *et al. J. Opt. Soc. Am. B* **2007**, *24*, 67-76; Thomas, K. G.; Thomas, K. J.; Das, S.; George, M. V.; *et al. J.C.S. Faraday Trans.* **1996**, *92*, 4913-4916; Glidewell, C. *Chem. Scripta* **1988**, *28*, 299-302.
15. Law, K. Y.; Bailey, F. C. *Can. J. Chem.* **1986**, *64*, 2267-2273.
16. Law, K. Y.; Bailey, F. C. *J.C.S. Chem. Commun.* **1990**, 863-865; Law, K. Y.; Bailey, F. C. *J. Org. Chem.* **1992**, *57*, 3278-3286.
17. Terpetschnig, E.; Szmacinski, H.; Lakowicz, J. R. *Anal. Chim. Acta* **1993**, *282*, 633-641, *J. Fluoresc.* **1993**, *3*, 153-155.
18. Oswald, B.; Patsenker, L.; Duschl, J.; Szmacinski, H.; Wolfbeis, O. S.; Terpetschnig, E. *Bioconjug. Chem.* **1999**, *10*, 925-931.
19. Suzuki, Y.; Yokoyama, K. *Angew. Chem. Int. Ed.* **2007**, *46*, 4097-4099.
20. Ertekin, K.; Tepe, M.; Yenigul, B.; Akkaya, E. U.; Henden, E. *Talanta* **2002**, *58*, 719-727; Ertekin, K.; Yeniguel, B.; Akkaya, E. U. *J Fluoresc.* **2002**, *12*, 263-268.
21. Isgor, Y. G.; Akkaya, E. U. *Tetrahedron Lett.* **1997**, *38*, 7417-7420.
22. Ros-Lis, J. V.; Garcia, B.; Jimenez, D.; Martinez-Manez, R.; *et al. J. Am. Chem. Soc.* **2004**, *126*, 4064-4065; Martinez Manez, R.; Soto Camino, J.; Ros *et al.* (Universidad Politecnica, Valencia) WO Pat. **2005** 2004-ES504 2,005,047,225 (*Chem. Abstr.* **2006**, *142*, 493025).
23. Tatarets, A. L.; Fedyunyayeva, I. A.; Dyubko, T. S.; Povrozin, Y. A.; *et al. Anal. Chim. Acta* **2006**, *570*, 214-223.
24. Hsueh, S.-Y.; Lai, C.-C.; Liu, Y.-H.; Wang, Y.; *et al. Org. Lett.* **2007,** *9*, 4523-4526; Hsueh, S.-Y.; Lai, C.-C.; Liu, Y.-H.; Peng, S.-M.; Chiu, S.-H. *Angew. Chem. Int. Ed.* **2007,** *46*, 2013-2017.
25. Johnson, J. R.; Fu, N.; Arunkumar, E.; Leevy, W. M.; *et al. Angew. Chem. Int. Ed.* **2007,** *46*, 5528-5531, S5528/1-S5528/15.
26. Arun, K. T.; Ramaiah, D. *J. Phys. Chem. A* **2005**, *109*, 5571-5578.
27. Danaboyina, R.; Kalliat, A. T.; Das, S.; Epe, B.(Council Sci. & Ind. Res., India) Fr. Pat. **2002** 2001-3983 2,818,987 (*Chem. Abstr.* **2003**, *137*, 354395) and DE Pat. **2002** 2000-10,065,482 (*Chem. Abstr.* **2003**, *137*, 80282).
28 Jyothish, K..; Avirah, R. R.; Ramaiah, D. *ARKIVOC* **2007**, 296-310; Alex, S.; Basheer, M. C.; Arun, K. T.; Ramaiah, D.; Das, S. *J. Phys. Chem. A* **2007**, *111*, 3226-3230; Arunkumar, E.; Sudeep, P. K.; Kamat, P. V.; Noll, B. C.; Smith, B. D. *New J. Chem.* **2007**, *31*, 677-683; Danaboyina, R.; Kalliat, T. A.; Jyothish, K. WO Pats. 2007-IB30 2007077531 & 2005-IN457 2007077566 (*Chem. Abstr.* **2007**, *147*, 66736 & 144864)); Ramaiah, D.; Arun, K. T.; Das, S. Epe, B. WO Pat. 2000-DE1201 2000DE01201 (*Chem. Abstr.* **2007**, *147*, 66736).
29. Hotchandani, S.; Das, S.; Thomas, K. G.; George, M. V.; Kamat, P. V. *Res. Chem. Intermed.* **1994**, *20*, 927-938; Wang, M.; Xie, H.; Zhu, J.; Xie, M.; Li, T.; Li, Y. *J. Mat. Sci.* **2007**, *42*, 7678-7683; Otsuka, A.; Funabiki, K.; Sugiyama, N.; Yoshida, T.; *et al. Chem. Lett.* **2006**, *35*, 666-667; Alex, S.; Santhosh, U.; Das, S. *J. Photochem. Photobiol. A* **2005**, *172*, 63-71; Yum, J-H.; Walter, P.; Huber, S.; Rentsch, D.; *et al. J. Am. Chem. Soc.* **2007**, *129*, 10320-10321.
30. Marder, S. R.; Chen, C. T.; Cheng, L. T. (CIT) US Pat. **1996**, 94-225,582 5,500,156 (*Chem. Abstr.* **1996**, *124*, 355783).
31. Li, Z.; Xu, S.; Huang, L.; Huang, X.; Niu, L; *et al. Chem. Phys. Lett.* **2007***, 441,* 123-126; Fu, W.-w.; Zhou, L.-x.; Zhao, Y.-y. *Fuzhou Daxue Xuebao,* **2003**, *31*, 90-94 (*Chem. Abstr.* **2003**, *139*, 197022); Yang, M.; Li, S.; Ma, J.; Jiang, Y. *Chem. Phys. Lett.* **2002**, *354*, 316-323; Bueschel, M.; Ajayaghosh, A.; Arunkumar, E.; Daub, J. *Org. Lett.* **2003**, *5*, 2975-2978.
32. Liu, N.; Lu, Z. Y.; Xie, M. G.; Jiang, Q. *Chin. Chem. Lett.* **1997**, *8*, 403-406; Lu, Z.-Y.; Xie, M.-G.; Liu, N.; Jiang, Q.; *et al. Synth. Metals* **1997**, *91*, 233-235.
33. Burke, A.; Schmidt-Mende, L.; Ito, S.; Graetzel, M. *Chem. Comm.* **2007**, 234-236.
34. Arunkumar, E.; Ajayaghosh, A. *Chem. Comm.* **2005**, 599-601.
35. Liu, L-H.; Nakatani, K.; Pansu, R.; Vachon, J-J.; *et al. Adv. Mat.* **2007**, *19*, 433-436.

BestChoice: Interactive Web-Based Learning

Sheila Woodgate and David Titheridge

University of Auckland (*sd.woodgate@auckland.ac.nz*)

BestChoice is an open-access interactive web site (www.*BestChoice*.net.nz) that was developed initially to support learning in large first-year Chemistry classes at Auckland University. More recently, *BestChoice* has been expanded to provide learning opportunities for high school students in NZ and the UK. The model underpinning *BestChoice* learning activities is simulation of the interchange of a student with an experienced teacher. Thus, student responses on *BestChoice* question pages generate instant assessment and feedback. *BestChoice* is innovative in its emphasis on teaching both concepts and problem-solving strategies by guiding students in ways that promote their understanding. The design of activities, promotion of their usage, and evaluation of their effectiveness is described below along with outcomes relating to these three strands of the project.

Background to the Design of *BestChoice* Activities

Facilitating both teaching and learning using web-based activities

Teaching Chemistry to large first-year university classes is essentially the transmission of information to students who adopt a passive role. However, for quality learning to occur, the student must assume an active role and engage with the content through problem-solving. Often the subject expert is not readily accessible to offer guidance to the student during the learning process. This may cause

- uncertain learners to become discouraged and conclude that chemistry is *too hard*;
- confident learners to solve problems algorithmically without developing understanding.

It was envisaged that *BestChoice* activities could support the learning process by acting as a bridge between *hearing about it in lectures* and *doing it yourself*. Thus the activities would both connect with and be complementary to traditional learning resources, particularly in that usage of activities could be tracked in order to detect how better to support learning.

Connecting web-based learning activities and other study resources

Traditionally, students study using print materials. They solve problems using pen and paper. Many students prefer to have model answers readily accessible.

If *BestChoice* activities are to be valued as learning tools, their relationship to traditional study tools must be obvious. Authors can establish this connection by:

- constructing visually appealing pages using conventional symbolism in the display of mathematical and chemical concepts;
- developing activities that help students learn how to solve problems that appear on written assessments;
- giving users ready access to correct answers and to background material required.

Overcoming some of the limitations of fostering learning over the web

Reading from the screen is more difficult than reading from a printed page.

Information can be presented in a way that prevents cognitive overload with an emphasis on requiring users to answer questions. Content can be exposed in small quantities in the feedback generated by the user's response.

Waiting for downloads or for the computer to respond is frustrating.

A text-based web application that used graphics and animations only where necessary allows it to be used on slow internet connections.

Common web browser answer-input devices (text-boxes, dropdown lists) do not support subscripts and superscripts.

This limitation can be overcome by developing an authoring system that includes answer input devices with support for both images and formatted text.

The teaching model

Web-based activities that simulate a person-to-person tutorial with an experienced, patient teacher would complement existing learning resources. Implementation of this model would involve developing activities that mix explanation of concepts with questions to probe the student's level of understanding.

Implementation of *BestChoice*

BestChoice *for the web - 2002*

The web site went live in 2002, with a total of 1900 pages in 60 modules available. Some 90% of the pages were question pages; thus, as intended, the emphasis was on users entering responses that generate feedback.

In *BestChoice* activities concepts are presented in *Review Pages*. Typically these are brief and highlight only major principles. Most modules begin with such a page. The concepts are then developed further through:

- questions on pages that follow each Review Page;
- feedback displayed when users answer questions on *Question Pages*.

The feedback relates either to the previous review page (by reiterating principles) or presages the next review page by applying and extending the principles. Thus, during completion of a module, learning is monitored with the constant feedback and guidance provided by the system. Some students struggle to understand what the question requires or may not be able to enter the correct answer. Such users have the option for the system to show them the correct answer so that they can overcome this barrier and move on to complete the problem.

The use of *BestChoice* was recommended to students in two first-year courses at Auckland University in 2002. An end-of-semester survey in one of the courses endorsed the approach taken in the modules. The survey asked *What feature of* BestChoice *did you like best?* The two most common responses were *combination of questions and review pages* and *feedback*.

While we had put in place the structure described above, and had some validation of the approach to supporting learning, *BestChoice* 2002 was limited to one answer per question page. This meant that the stepwise solution of a multistep problem extended over several pages. Furthermore, an absence in control over positioning of the answer fields and the associated feedback severely hindered authoring.

BestChoice *for the web 2003-2008*

Both the content and system of *BestChoice* have been upgraded and expanded on a continual basis over the last five years. Currently there are more than 200 modules with 8000 possibilities for interaction that result in instructive feedback. An extensive web-based authoring system has been developed to enable authors to construct question pages with:

- any number of answer fields;
- answer fields and their associated feedback incorporated in the text of the page;
- a variety of types of answer fields;
- correct answers to one part of a page triggering the appearance of a second part.

Promoting Usage of *BestChoice* as Part of Course Materials

Connecting the BestChoice *activities with the student's course of study*

Teachers choose course resources to help students study. In order for *BestChoice* learning activities to be accepted as a course resource, customised courses have been constructed for target groups. In these courses the modules are grouped, and the groups are placed in a sequence that corresponds to the course outline. The number of target groups has grown in the last five years to include for 2008 students in Chemistry classes: at Auckland University (seven courses); in NZ high schools (NCEA Year 11-13, Scholarship and Olympiad courses); in the UK (AS/A2 levels courses for the four major exam boards); at Canterbury and Victoria Universities (one course each). Access is not limited to users in these target groups as anyone may register. Thus, two generic courses, General and Organic Chemistry, are also available.

Use of BestChoice *by chemistry students at Auckland University*

BestChoice was compulsory in two first-year courses at Auckland University in 2003; In 2008, modules are compulsory in six first-year courses. These courses range from foundation level to those compulsory for students trying to gain admission to Health Sciences programmes. In total, approximately 2000 users are involved.

Although one of the authors has had extensive experience teaching first-year chemistry, neither is currently lecturing in any of the first-year chemistry courses. Therefore, the support of course coordinators and teachers is crucial to:

- introduce their class to *BestChoice* and provide details of registration;
- promote *BestChoice* activities as learning experiences;
- encourage students to use *BestChoice* to support their learning during the entire course

For 2008, modules will be used in all of the first-year courses as both assignments and pre-laboratory activities. In general, course coordinators began to use *BestChoice* modules for assignments or pre- laboratory study and then, based on a successful experience, have extended its use in their course to include both assignments and pre-labs. It has been noted for a variety of courses that, when the compulsory requirement is increased substantially, an increased percentage of students complete the compulsory modules. Furthermore, an increase in the use of non-compulsory activities also occurs.

The *BestChoice* pre-laboratory activities replaced written material that was marked by supervisors at the beginning of the laboratory session. Because the *BestChoice* pages are marked as they are completed, supervisors now have more time to help students with practical work at the beginning of the session. Course coordinators also believe that there is less blind copying and more opportunity for learning than before.

How do teachers monitor their students' BestChoice *activity?*

BestChoice collects a variety of data for each user. These include demographic details (user-entered), registration date, number of logins, and a count of the pages on which answers have been entered, as well as the number of attempts required to get the correct answer, and the time interval over which the question was answered. These data are available to a teacher through the complementary application *BestChoice* Reports.

Use of BestChoice *by high school students*

During the period 2003–06, NZ high school teachers were made aware of *BestChoice* both through an electronic newsletter circulated by a high school teacher and through a series of presentations at Teacher's Days held at the universities around the country. In 2007 *BestChoice* and *BestChoice* Reports featured in a flyer in the package of educational materials distributed by the RSC to all schools in the UK. For the NZ 2007 and the UK 2007-8 school years, teachers in these two localities were offered use of *BestChoice* Reports at no cost.

Most high school usage is voluntary. Students are often introduced to the programme by their teacher using a period in the school computer lab. Teachers who are *BestChoice* Report users may assign *BestChoice* modules for homework. However, this practice is not widespread as yet. The pupils of teachers who are *BestChoice* Report users are the more likely to become active users, but some 53% of 2007 *BestChoice* use in NZ high schools was by students who are not enrolled in a *BestChoice* Reports class.

Evaluating *BestChoice* through usage data

Usage of BestChoice *has grown steadily*

Table 1 shows that there has been a steady increase in user numbers during the last four years. NZ high school students began using the programme in 2004 and usage in 2007 more than doubled from 2006. Active users are from 250 different NZ schools. Use by UK high school students from September '07 also contributed to the large increase in the number of users in 2007.

Table 1. Number of *BestChoice* users

Login year	*2004*	*2005*	*2006*	*2007*
Users (>1 mark)*	5109	6410	7040	13868
Active Users (>80 marks)	3380	4112	4546	7996

*Each answer in *BestChoice* is worth 1 mark.

The importance of the connection to the user's course of study

The distribution of users and activity for 2007 (Table 2) shows that 99% of usage is by three of the target groups for whom specific courses have been created. Teachers in these target groups actively promote use of *BestChoice*, and some have made completion of some *BestChoice* modules compulsory. Most of the remaining 1% of active use is by students from Canterbury University where some staff encourage voluntary usage.

Table 2. Distribution of users and usage in 2007

Institution	*Auckland University*	*High School*		*Other*
		NZ	*UK*	
Users	3186	6940	3579	163
Active users	2842	3344	1732	78
Total marks/1000	2240	1480	530	42

Evaluation of *BestChoice* using an on-line survey

Establishing mechanisms for on-line evaluation of BestChoice

One of the most important aspects of the *BestChoice* project is the extent to which our users have informed its development. In order to encourage student users to indicate what they liked best and how things could be improved, the survey displayed in Fig. 1 was included on the last page of each module. Thus, users may enter comments and rate modules on a six-point scale. This has provided continuous user feedback.

The comments entered in the survey indicate the student perception of BestChoice.

The on-line survey has been a very rich source of student comment, most of which is pertinent to teaching and learning. Of the 5133 complimentary comments entered during 2003-2007, six unedited examples appear below:

Fig 1. End-of-module Survey

User 1: Wonderful! Sooooo helpful! Best feature is that you can read the theory, then do the quiz! (Nov 03).

User 2: This was fun and helped me understand much easier. I was not placed under pressure at all, because I was allowed to make mistakes. I really enjoyed this. (Mar 04).

User 3: This has made so much that I didn't understand much clearer. The little amounts of information followed by heaps of questions makes it really easy to absorb! (Aug 03).

User 4: Awesome. Extremely helpful on specifics and terminology. It's great to be able to back up school resources with another reliable website that revises and teaches in an easy to follow format. (Aug 07).

User 5: This site is AWESOME!!! I'm really glad there's something like this up and running to help students who are willing to study at home. it gives a break from just reading and doing examples from books and really helps!!! I'm sure my marks are going to improve!!!! THANKS!!! (Apr 03).

User 6: I learnt a lot, & it went smoothly, gradually getting harder & making me learn much more efficiently; it is very helpful thank you (May 03).

The comments made have been assigned to categories. Three of these (complimentary, suggestion and critical) are relevant to teaching and learning; 70% of comments have been assigned among these. Some 6% do not pertain to *BestChoice*, and 24% highlight typographical errors and bugs that have been fixed.

Table 3 shows the distribution among the categories relevant to teaching and learning. Many of these comments have multiple threads. Any comment that includes a compliment is assigned to *compliment*. Critical comments that include a suggestion are assigned to *suggestion*. The fact that substantial increase in the quantity of feedback has made little change to the distribution provides endorsement of the enhancements that have been made to both the system and its content during these three years.

Table 3. End-of-module survey response summary

Year	*Total*	*Compliment*	*Suggestion*	*Criticism*
2007	3357	64%	19%	17%
2006	1658	70%	17%	14%
2005	1173	68%	15%	17%

The *comment* data indicate that, in general, learners perceive *BestChoice* to be beneficial to them and help them learn. Many of the suggestions made by users have been implemented. Some of the problems identified could be rectified easily and, in contrast to print-based materials, the revision is available immediately.

The ratings (out of 6) indicate that most students find the modules helpful

Students indicate how helpful they have found a module by choosing one of the six radio buttons at the end of the module survey form. The range is from *not at all* (1) to *fantastic* (6). The average response rate to this part of the survey over all modules and all cohorts of users is 30%. As shown in Table 4, the radio buttons corresponding to 4, 5 and 6 ratings are much more commonly chosen than those corresponding to 1, 2 and 3 ratings. The most frequent choice in each year is *fantastic* (6).

Table 4. Survey ratings response summary

Year	*Responses*	*Average out of 6*	*% positives (4,5,6)*	*% highest rating*
2007	19756	4.62	81	32
2006	9680	4.74	84	35
2005	6866	4.64	82	32

Outcomes in terms of the three strands of the *BestChoice* project

Instructional design

The construction of web-based activities consistent with our model of a one-on-one tutorial was a major challenge that required development of our own authoring system. Once this was in place, translation of pen-and-paper exercises to *BestChoice* activities became feasible.

Our project activities generally add value to the pen-and-paper exercise. Figs. 2-4 show how this is done for the task shown below, *viz*.:

Reaction of Cu (metal) with $Ag^+(aq)$ results in precipitation of silver metal, Ag. Write the half equation for this reaction.

The view on loading the *BestChoice* page is shown in Fig. 2. If the correct choice for each of the options presented is chosen, feedback associated with these choices is revealed as well as the next part of the problem (Fig. 3). The third part is shown in Fig. 4. Any incorrect choices can be changed without leaving the page and interrupting the flow of problem-solving.

These screen shots show that users do not simply answer the question posed on pen and paper. A *BestChoice* page based on this question forces the student to analyse the system involved and use appropriate terminology in doing so. Thus, *BestChoice* exposes the strategy that a subject expert would use to answer the question. The pages are as much about the thinking behind arriving at the right answer as they are about the answer itself.

The guidance offered by *BestChoice* pages such as this one (Fig. 4) makes successful completion of the problem more accessible for more learners who, over time, should gain the skills to answer the questions without guidance. Consider the unedited comments:

User 7: The main thing I liked is that it gave me the opportunity to practice and learn from my mistakes (Mar 06).

User 8: liked this topic. Being able to see and work everything out myself really helped me understand this. Thanks (Mar 06).

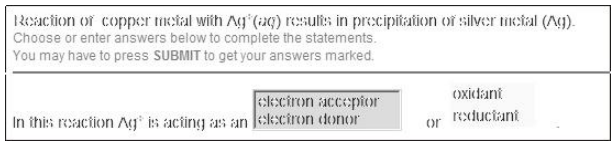


Fig. 2. *BestChoice* problem page view on loading

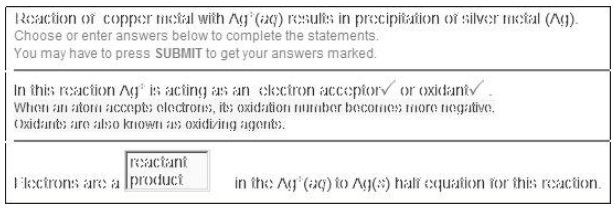


Fig. 3. *BestChoice* problem page view after making two correct choices

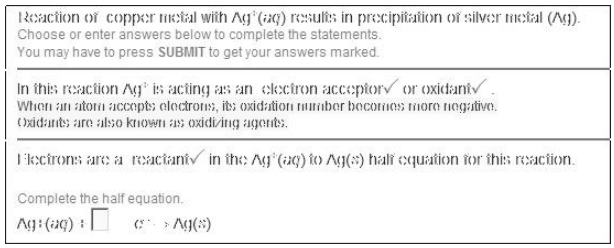


Fig. 4. *BestChoice* problem page view after making third choice

User 9: Very helpful, especially the first 8 questions, very good!! They were hard, but they made me think a lot and I ended up getting most of them right (Aug 07).

BestChoice activities also provide capable learners with an enhanced learning experience as insights are revealed during problem-solving and appear in the form of feedback just as the user has entered the answer that they thought was correct. Thus:

User 10: Very good, now I understand alot more little things I would've never thought of asking (Mar 06).

User 11: this was useful because it made me think logically about the electron configurations rather than just having a bit of a guess (Oct 07)

It is a challenge to accommodate the variety of learning styles and academic backgrounds in any class irrespective of whether it is high school or university. Web-based activities like those in *BestChoice* can add to the suite of tools available to help meet this challenge. A written survey in some of the courses where *BestChoice* is compulsory asked students *Which feature of the course helps to you to learn?* The results (Table 5) show that many of the responses indicated more than one feature. Thus, the students regard *BestChoice* as an effective learning tool for use alongside other traditional tools. It is not, and was never intended to be, a replacement for these.

Table 5. Student in-class survey response summary

Cohort	*Surveys/ Responses*	**Best-Choice**	*Labs*	*Lectures*	*Hand-outs*
BSc 1	100/62	47	21	5	
BSc 2	170/111	37	25	20	44
Pre-uni	80/63	25	NA	28	13

Evaluation

Unlike the most other learning tools, use of *BestChoice* by students automatically generates data that can provide information on how to support learning more effectively and efficiently. We have shown that, through these data, users can inform the design of systems to support their learning. The extent and quality of feedback entered by users has been overwhelming.

User 12: BC helps me understand chemistry in a way that is both faster and more convenient than tedious text book exercises - almost like having a personal tutor watching over my shoulder. Thank you and keep up the good work! (Apr 06).

User 13: *BestChoice* is simply the best learning technique i ever came across. It walks me through the important steps to follow inorder to solve a question and makes the theory more simpler (Mar 06).

User 14: really helpful, different way of looking at things than portrayed in the lecture, gave depth of understanding (May 07).

The most frequent suggestion entered in the survey is *more questions*. New question pages are being added on a continual basis. An important aspect of the writing of these is that new ways to present content interactively are being explored on a continual basis.

The foregoing discussion includes a broad analysis of data pertinent to student perception and usage. We have also considered student response data for individual modules and questions in order to identify areas found difficult. This process has informed the on-going updating of existing learning activies and authoring of new ones.

The data collection process makes it easy to see where students are going wrong, the authoring system makes it possible to create activities that address the student difficulties identified, and usage of these activities in turn generates data that provide evidence as to the success or failure of the *improvements*. This evidence-based methodology contrasts markedly with the *working blind* approach that one is forced to adopt when revising or creating most teaching resources.

The world-wide web has enabled communication and dissemination of ideas in ways that were beyond belief even 10 years ago. There is also a lot of talk about using the web to foster learning. However the extent to which most web-based content has moved beyond passive learning is minimal. *BestChoice* stands out from the rest both with respect to the emphasis on active learning, where student responses result in display of appropriate feedback, and the evidence-driven approach used to create and up-date content.

A web-based application like *BestChoice* could become an international resource informed by both educators and students world-wide. Our work for the UK-based RSC is a major step towards achieving this for high school students. The significant challenges at national level are to increase teacher participation in use of *BestChoice Reports* and to find ways and means of encouraging and supporting extensive use of *BestChoice* at other universities.

Both our experience in the journey to *BestChoice 2008*, and the substantial positive feedback from our users, lead us to believe that we have only just begun to exploit the potential of the web to deliver interactive learning. Therefore, extension and enhancement of *BestChoice* will continue. It is very exciting to be involved in the creation of a learning tool, the development of which is informed by the learners.

Acknowledgement

We acknowledge course coordinators, lecturing staff, and teachers who have recommended use of *BestChoice* to their students. The Chemistry Department and the Teaching Improvement Grants Committee of Auckland University have provided financial support throughout the project. The work with high school students has been made possible through support by the RSC in the UK (2006-2010) and in NZ by the Ministry of Education (2006-2008).

Obituary: Ken Seal (1923-2007)

Ken Seal, Hon. FNZIC and Past-President, died in Auckland on 29 October 2007, aged 84. He was a bright and enthusiastic member of the Auckland Branch for many years.

Ken was born in England. At primary school he won a scholarship to attend Kilburn Grammar in London. From there he was offered employment by GEC who agreed to pay his fees to attend Birkbeck College, University of London, which operated as a part-time university with courses and laboratory work on Saturdays and Sundays only. Ken graduated with BSc and MSc degrees in geology. At GEC he worked on a number of war-related scientific projects, which exempted him from military service when he reached conscription age later in the war.

He, and his wife Joy, migrated to NZ in 1952 where Ken took up employment with Amalgamated Brick & Pipe Company in Auckland. There, he was responsible for quality control and development work on their products, and this work was later extended to similar work for the later named company, Ceramco. Both companies were managed by the well-known Auckland entrepreneur, the late Sir Tom Clark.

In the early 1970s Ceramco was a shareholder of Geothermal Energy NZ Ltd., set up to utilise NZs expertise in producing electricity from geothermal steam. Ken was one of its geochemists who later became a director of the company. A major project was to assist Indonesia as part of the largest NZ aid project of that time. Ken served as its project manager from 1971-1975 returning to Ceramco and Auckland in 1975. He continued his geothermal consulting work around the world throughout the 1980s until his retirement.

Ken was a significant contributor to NZIC. At meetings he was always liked for his questioning nature and great enthusiasm for chemistry. He read widely, painted, and had a life-long interest in scouting. For his efforts as a young messenger in the early years of WWII he was awarded the Silver Cross for Gallantry. During a bombing raid he had, under the guidance of a doctor working nearby - himself unable to undertake the procedure - amputated the arm of a woman trapped in a burning building. He was awarded the CBE for services to New Zealand in 1977.

Ken is survived by Joy and their children Lesley, Kingsley and Heather.

Ashley Wilson

Article

MALDI-TOF Mass spectrometry of Cyanobacteria: a Global Approach to the Discovery of Novel Secondary Metabolites*

Jonathan Puddick and Michèle R. Prinsep

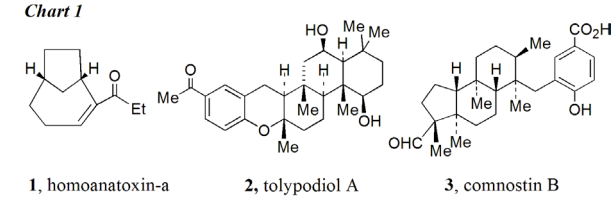
Department of Chemistry, University of Waikato, Private Bag 3105, Hamilton 3240
(e-mail: *m.prinsep@waikato.ac.nz*)

*This article, originally printed in the January issue of this *Journal* (**2008**, *72*, 25-28), was subject to major production errors with the loss of structural displays critical to its understanding. In fairness to the authors, and to you the reader, the article is reproduced here in full; the editors of *Chemistry in New Zealand* apologise unreservedly.

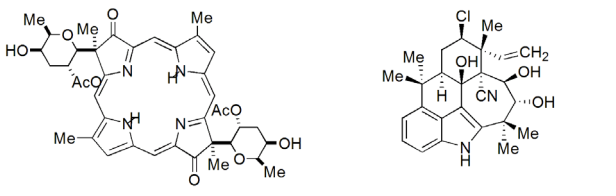
Cyanobacteria (blue-green algae) are a group of ancient prokaryotic organisms dating back between three and four billion years.[1] They have been attributed with oxygenating the earth's atmosphere[2] but, since the anthropogenic euthrophication of lakes, ponds and oceans, they have become synonymous with water hygiene issues.[3] This is due to the alteration of the nutrient composition of their habitat to one which is optimal for growth (or blooms). Cyanobacterial blooms may simply cause foul tastes and odours,[4] but they can also lead to the production of toxic secondary metabolites poisonous to humans and animals upon ingestion.[5] NZ has yet to suffer a human fatality, but the deaths of several dogs in Wellington was attributed to homoanatoxin-a **1** (Chart 1) from a *Phormidium* species.[6]

Although toxins are the most highly publicized cyanobacterial secondary metabolites, a vast array of compounds are produced which range in size, structure, and bioactivity. Terrestrial cyanobacteria have yielded diterpenes such as the anti-inflammatory tolypodiol **2**,[7] and the antimicrobial comnostins[8] such as comnostin B **3**, in addition to other unusual metabolites including tolyporphin A **4** (a porphyrin-like compound with multi-drug resistance reversal properties)[9] and the ambiguenes, *e.g.* ambiguene F **5**, which are antifungal chlorinated alkaloids (Chart 1).[10]

Chart 1



1, homoanatoxin-a **2,** tolypodiol A **3**, comnostin B



4, tolyporphin A **5**, ambiguene F

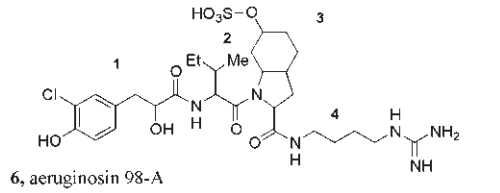
The major class of secondary metabolites produced by cyanobacteria is that of the oligopeptides, which are synthesised by non-ribosomal peptide synthetases.[11] These can be divided into six families depending on their structural characteristics,[12] namely the aeruginosins, the microginins, the anabaenopeptins, the cyanopeptolins, the microcystins, and the microviridins, as exemplified by metabolites **6-11** of Chart 2.

In the past, oligopeptides have been detected via enzyme-linked immunosorbent assays, enzyme inhibition assays, or according to their toxicity.[13] These assays have focused on obtaining quantitative data on the metabolites present, therefore the potential of these methods as discovery tools is limited. Analysis by high performance liquid chromatography (HPLC) is hindered by a lack of commercially available standards[14] so that time is wasted isolating known metabolites. Bioactivity-directed isolation has proved to be very effective in the past[8] but again limits the researcher to detecting molecules possessing a certain activity. More powerful still is liquid chromatography-mass spectrometry (LC-MS). Here, one can separate the components in a complex mixture and obtain their relative molecular masses. This allows one to assess the potential novelty of a compound according to both mass and elution time prior to large-scale purification and characterization. Most LC-MS instruments allow for tandem MS that enables structural clues to be deduced and the identity of known molecules to be confirmed.[15] However, separation by HPLC involves costly and time consuming sample preparation and, due to long run times, high throughput can be cumbersome. Analysis of cyanobacterial extracts by matrix assisted laser desorption ionization-time of flight (MALDI-TOF) MS can provide comparable data to those from LC-MS but with far simpler sample preparation.

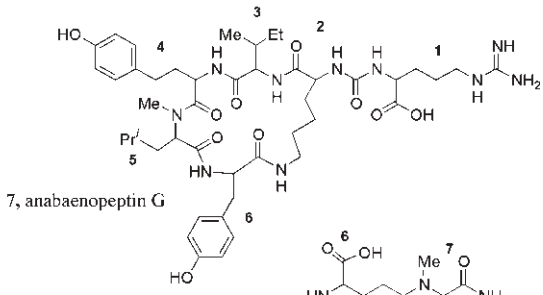
MALDI-TOF produces ions from laser irradiation of a sample co-crystallized with a matrix; the laser energy is absorbed and passed to the analyte molecules. This method of ionization predominantly produces singly protonated ions to *ca. m/z* = 5000, a range which encompasses the oligopeptides. Thus complex mixtures can be analyzed from a minute amount of sample without prior separation, and the relative molecular mass of each component present deduced from the protonated molecular ions.[16] Cyanobacterial extracts are assessed simply from mixing with the matrix, application of the mix to a target, and spectral recording.

The advantages described above make MALDI-TOF screening of cyanobacterial extracts particularly useful in the discovery of novel secondary metabolites. Due to the high sensitivity, low sample volumes, and speed of analysis, environmental samples can be assessed for the presence of novel compounds prior to culturing. Even single cyanobacterial colonies can be analysed by suspending them directly in matrix solution.[17] Novel compounds are easily detected using this method by comparing the

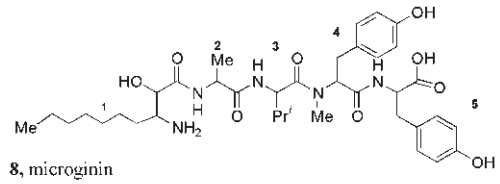
Chart 2



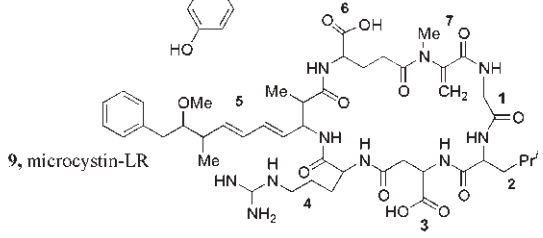
6, aeruginosin 98-A



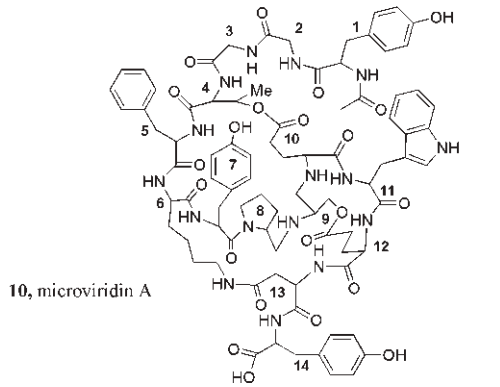
7, anabaenopeptin G



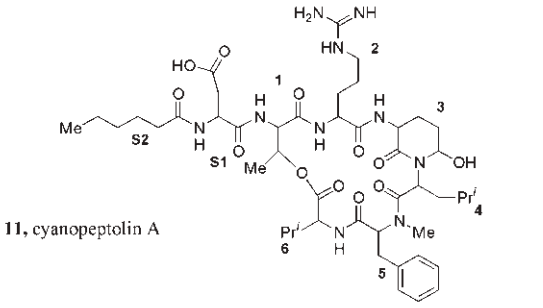
8, microginin



9, microcystin-LR



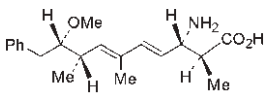
10, microviridin A



11, cyanopeptolin A

component masses recorded with those in an appropriate database. If the mass spectrometer is also equipped for the analysis of post source decay (PSD) species, it is then analogous to LC-MS with tandem MS, and the presence of known compounds can be confirmed from the masses of the fragment ions produced.

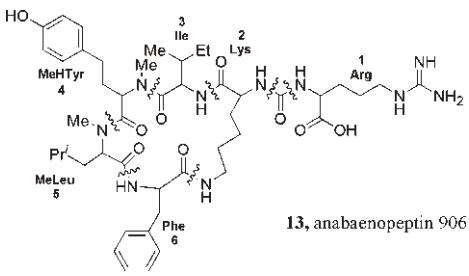
Since cyanobacterial oligopeptides are already well characterized, PSD allows for partial characterization of any novel compounds discovered. Often the subclass of oligopeptide present can be deduced by the presence of diagnostic fragment ions in the spectrum, e.g. the presence of a *m/z* = 135 ion ($PhCH_2CHOMe^{+\bullet}$) is characteristic of 2*S*,3*S*,8*S*,9*S*-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyldeca-4*E*,6*E*-dienoic acid (Adda, **12**), the unique amino acid found in microcystins.[16] The low mass daughter ions indicate the amino acids present in the molecule, while those at higher mass can indicate how the amino acids are joined together.



12, Adda

Oligopeptide characterization by MALDI-TOF MS has been undertaken successfully in Germany. Using the approach described above, von Dohren and co-workers were able to characterize a range of oligopeptides including aeruginosins, microginins, anabaenopeptins, and cyanopeptolins, whilst assessing the oligopeptide diversity of different cyanobacteria. They deduced structures for anabaenopeptin G, **7** (Chart 2) and anabaenopeptin 820 from analysis of the PSD fragments.[12,18,19]

The anabaenopeptins are cyclic peptides containing six amino acids. Each contains a D-lysine unit that has an ureido bond to a carbonyl that is linked to a side-chain amino acid. The D-lysine also forms a secondary peptide bond which encloses the ring. The CO-linked side-chain and the ring amino acids vary as does their degree of amino methylation.[11] There are 21 published structures of anabaenopeptins and these are listed in Table 1. The different compounds have varied biological activities including relaxation of norepinephrine-induced contraction,[20] protein phosphatase inhibition, and protease inhibition.[21-24] Like the German workers, we too have been able to deduce most of the structure of a new metabolite using MALDI-TOF MS, namely anabaenopeptin 906, **13**.



13, anabaenopeptin 906

An environmental sample containing cyanobacteria was collected from a North Island lake. The MALDI-TOF MS (Fig. 1) showed the presence of several known compounds as well as an unknown metabolite with *m/z* = 907. The PSD spectrum of this *m/z* = 907 ion is shown as Fig. 2 and the loss of 200 Da is clear. This is diagnostic for an anabaenopeptin possessing an arginine side-chain. The low mass/charge species indicate the presence of arginine (Arg; *m/z* = 70), lysine (Lys; *m/z* = 70, 84), isoleucine (Ile; *m/z* = 86), methylleucine (MeLeu; *m/z* = 100), and methylhomotyrosine (MeHTyr; *m/z* = 107, 164). Thus, five of the six amino acids present in the anabaenopeptins are identified, with the missing mass/charge entity correlating with that of a phenylalanine (Phe) residue. This

Table 1. Amino acid sequence of the known Anabaenopeptinsa

Compound	Mr (Da)	1	3	4	5	6	Ref.
Anabaenopeptin A	843	Tyr	Val	HTyr	MeAla	Phe	20
Anabaenopeptin B	836	Arg	Val	HTyr	MeAla	Phe	20
Anabaenopeptin C	808	Lys	Val	HTyr	MeAla	Phe	25
Anabaenopeptin D	827	Phe	Val	HTyr	MeAla	Phe	25
Anabaenopeptin E	850	Arg	Val	MeHTyr	MeAla	Phe	26
Anabaenopeptin F	850	Arg	Ile	HTyr	MeAla	Phe	26
Anabaenopeptin G	908	Arg	Ile	HTyr	MeLeu	Tyr	18
Anabaenopeptin G*	929	Tyr	Ile	HTyr	MeHTyr	Ile	23
Anabaenopeptin H	922	Arg	Ile	HTyr	MeTyr	Ile	23
Anabaenopeptin I	759	Ile	Val	HTyr	MeAla	Leu	22
Anabaenopeptin J	793	Ile	Val	HTyr	MeAla	Phe	22
Anabaenopeptin T	865	Ile	Val	HTyr	MeHTyr	Ile	24
Anabaenopeptin KT864	864	HArg	Ile	HTyr	MeAla	Phe	27
Anabaenopeptin 820	820	Arg	Val	HPhe	MeAla	Phe	12
Ferintoic Acid A	866	Trp	Val	HTyr	MeAla	Phe	28
Ferintoic Acid B	880	Trp	Ile	HTyr	MeAla	Phe	28
Nodulapeptin A	929	Ile	Met(O_2)	HPhe	MeHTyr	Ser(Ac)	29
Nodulapeptin B	913	Ile	Met(O)	HPhe	MeHTyr	Ser(Ac)	29
Oscillamide B	868	Arg	Met	HTyr	MeAla	Phe	21
Oscillamide C	956	Arg	Ile	HTyr	MeHTyr	Phe	21
Oscillamide Y	857	Tyr	Ile	HTyr	MeAla	Phe	21

[a]Numbering for anabaenopeptins amino acids is as for **7** of Chart 2; D-Lys is omitted as it is always present in position 2 in the known anabaenopeptins.

Table 2. Fragment ions of anabaenopeptin 906 observed by PSD.

m/z	Sequence
70	Arg/Lys-related ion
84	Lys-Immonium ion
86	Ile-Immonium ion
100	MeLeu-Immonium ion
107	Tyr-side chain
112	Arg-Immonium ion
129	Arg-Immonium ion
164	MeHTyr-Immonium ion
175	Arg + 2H
201	CO + Arg
275	MeLeu + Phe + H
305	Ile + MeHTyr + H
449	Arg + CO + Lys + Phe - CO + 2H
466	MeHTyr + MeLeu + Phe + H
579	Ile + MeHTyr + MeLeu + Phe + H
594	Lys + Phe + MeLeu + MeHTyr + 2H
603	Arg + CO + Lys + Phe + MeLeu + H
707	Lys + Ile + MeHTyr + MeLeu + Phe +2H
907	M + H

also matches well with anabaenopeptin G, **7** in that its mass is only 2 Da higher than the new **13**; it corresponds to the loss of a hydroxyl group from the tyrosine in position 5, and an additional amino methylation on HTyr in position 3.

The higher mass fragments provide the sequence of the ring amino acids in **13**. Thus, the *m/z* = 275 fragment shows that the Phe is joined to the MeLeu and the *m/z* = 449 fragment shows that the Phe is also attached to the Lys, thus placing it in either position 3 or 6. The *m/z* = 466 fragment can then be used to show that MeHTyr is attached to MeLeu as Phe is already attached to both Lys and MeLeu. This gives a final sequence of Ile-MeHTyr-MeLeu-Phe, and supports the presence of an Ile-MeHTyr fragment at *m/z* = 305.

None of the fragments observed confirm the order in which the amino acids are present in the ring and whether Ile or Phe is located at position 3. The structure proposed as **13** has been constructed according to the sequences of presently known anabaenopeptins, where Phe is commonly seen at position 6 and an aromatic amino acid, such as HTyr, is always at position 4. This illustrates the limitation in characterizing secondary cyanobacterial

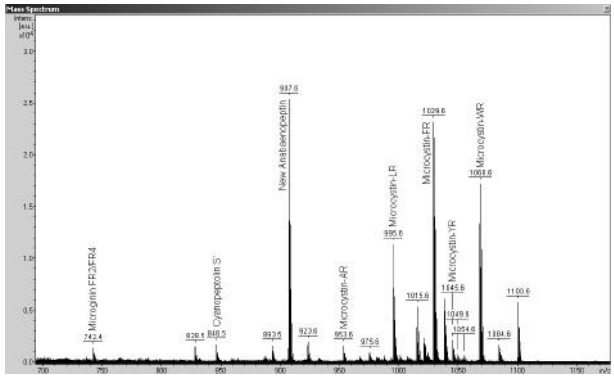


Fig. 1. MALDI-TOF MS of a NZ lake sample.

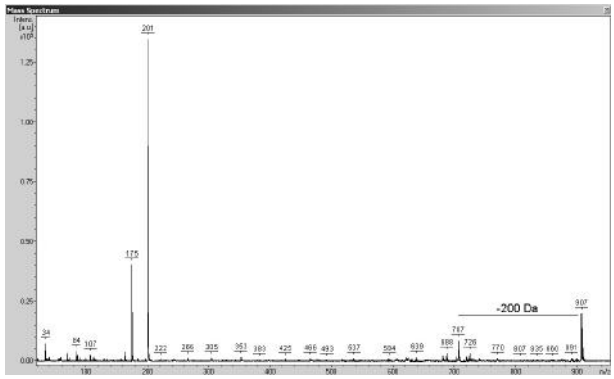


Fig. 2. The MALDI-TOF PSD spectrum of *m/z* = 907 from Fig. 1.

metabolites by MALDI-TOF MS as, at times, the complete structure cannot be elucidated and stereochemistry can never be deduced. Ultimately, full characterization of these novel compounds requires purification and NMR spectroscopic investigations.

The screening of cyanobacterial extracts for oligopeptides by MALDI-TOF MS is a very powerful technique that can lead to the discovery of new compounds. It is simple, quick and inexpensive. Its use requires only a minute amount of sample that gives a rapid assessment of the presence or absence of novel metabolites.

Acknowledgements

The contribution of Susanna Wood (Cawthron Institute, Nelson) is gratefully acknowledged.

References

1. Schopf, W. J.; Packer, B. M. *Science* **1987**, *237*, 70-72.
2. Whitton, B. A.; Potts, M. *The ecology of cyanobacteria, their diversity in time and space* Kluwer: Dordrecht, Netherlands, 2000.
3. Chorus, I.; Bartram, J. *Toxic cyanobacteria in water: a guide to their public health consequences, monitoring and management* Spon: London, 1999.
4. Jones, G. J.; Korth, W. *Water Sci. Technol.* **1995**, *31*, 145–151.
5. Codd, G. A.; Morrison, L. F.; Metcalf, J. S. *Toxicol. Appl. Pharmacol.* **2005**, *203*, 264-272; Azevedo, S. M.; Carmichael, W. W.; Jochimsen, E. M.; Rinehart, K. L.; *et al. Toxicology* **2002**, *181-182*, 441-446.
6. Wood, S. A.; Selwood, A. I.; Rueckert, A.; Holland, P. T.; *et al. Toxicon*. **2007**, *50*, 292-301.
7. Prinsep, M. R.; Thomson, R. A.; West, M. L.; Wylie, B. L. *J. Nat. Prod.* **1996**, *59*, 786-788.
8. Jaki, B.; Orjala, J.; Heilmann, J.; Linden, A.; *et al. J. Nat. Prod.* **2000**, *63*, 339-343.
9. Prinsep, M. R.; Caplan, F. R.; Moore, R. E.; Patterson, G. M.; Smith, C. D. *J. Am. Chem. Soc*. **1992**, *114*, 385-387.
10. Smitka, T. A.; Bonjouklian, R.; Doolin, L.; Jones, N. D.; *et al. J. Org. Chem.* **1992**, *57*, 857-861.
11. Welker, M.; von Dohren, H. *FEMS Microbiol. Rev*. **2006**, *30*, 530-563.
12. Welker, M.; Brunke, M.; Preussel, K.; Lippert, I.; von Dohren, H. *Microbiol*. **2004**, *150*, 1785-1796.
13. Xu, L. H.; Lam, P. K. S.; Chen, J. P.; Xu, J. M.; *et al. Chemosphere* **2000**, *41*, 53-58; Domingos, P.; Rubim, T. K.; Molica, R. J. R.; Azevedo, S. M. F. O.; Carmichael, W. W. *Environ Toxicol*. **1999**, *14*, 31-35.
14. Mountford, D. O.; Holland, P.; Sprosen, J. *Toxicon*. **2005**, *45*, 199-200.
15. Jemal, M. *Biomed. Chromatogr*. **2000**, *14*, 422-429.
16. Welker, M.; Fastner, J.; Erhard, M.; von Dohren H. *Environ. Toxicol.* **2002**, *17*, 367-374
17. Welker, M.; Marsalek, B.; Sejnohova, L.; von Dohren, H. *Peptides* **2006**, *27*, 2090-2103.
18. Erhard, M.; von Dohren, H.; Jungblut, P. *Rapid Commun. Mass Spectrom*. **1999**, *13*, 337-343.
19. Erhard, M.; von Dohren, H.; Jungblut, P. *Nat. Biotechnol.* **1997**, *15*, 906-909.
20. Harada, K.; Fujii, K.; Shimada, T.; Suzuki, M.; *et al. Tetrahedron Lett.* **1995**, *36*, 1511-1514.
21. Sano, T.; Usui, T.; Ueda, K.; Osada, H.; Kaya, K. *J. Nat. Prod.* **2001**, *64*, 1052-1055.
22. Murakami, M.; Suzuki, S.; Itou, Y.; Kodani, S.; Ishida, K. *J. Nat. Prod.* **2000**, *63*, 1280-1282.
23. Itou, Y.; Suzuki, S.; Ishida, K.; Murakami, M. *Bioorg. Med. Chem. Lett*. **1999**, *9*, 1243-1246.
24. Kodani, S.; Suzuki, S.; Ishida, K.; Murakami, M. *FEMS Microbiol. Lett.* **1999**, *178*, 343-348.
25. Fujii, K.; Harada, K.; Suzuki, M. *Occurrence of novel cyclic peptides together with microcystins from toxic cyanobacteria,* Anabaena *species* In: *Harmful and Toxic Algal Blooms* Yasumoto, T.; Oshima, Y.; Fukuyo, Y. (Eds.) Intergovernmental Oceanographic Commission of UNESCO Paris, 1996, 559-562.
26. Shin, H. J.; Matsuda, H.; Murakami, M.; Yamaguchi, K. *J. Nat. Prod.* **1997**, *60*, 139-141.
27. Beresovsky, D.; Hadas, O.; Livne, A.; Sukenik, A.; *et al. Isr. J. Chem.* **2006**, *46*, 79–87.
28. Williams, D. E.; Craig, M.; Holmes, C. F. B; Andersen, R. J. *J. Nat. Prod.* **1996**, *59*, 570-575.
29. Fujii, K.; Sivonen, K.; Adachi, K.; Noguchi, K.; *et al. Tetrahedron Lett*. **1997**, *38*, 5525-5528.

Dates of Note

April 22 marks the 150th anniversary of development of the fused salt electrolysis for commercial production of aluminium by ***Martin Killani***.

Born on 27 Apr 1913, ***Philip Hauge Abelson*** was the US physical chemist who proposed the gas diffusion process for separating ^{235}U from ^{238}U, which was essential to the development of the atomic bomb. Also on this day (in 1896) was born ***Wallace Hume Carothers***, the discovered of nylon.

Joel H. Hildebrand died on 30 Apr 1983. His monograph *Solubility* (1924; later editions, *Solubility of Non-Electrolytes*) was the classic reference for almost a half century.

John William Draper, the English-American chemist who pioneered in photochemistry, was born on 5 May 1811. He recognized that light initiated chemical reactions as molecules absorbed light energy.

May 15 marks the 150th anniversary of the death of 1858 ***Robert Hare***, the American chemist who devised the first oxyhydrogen blowpipe for the purpose of producing great heat. He melted sizeable quantities of platinum with this. His device is the precursor to the modern welding torch.

René-Just Haüy, the French mineralogist who founded of the science of crystallography through his discovery of the geometrical law of crystallization, died on 1 Jun 1822. In 1781, he saw an accidentally dropped calcite crystal break into rhombohedral pieces. Deliberately breaking various forms of calcite, he found the same result, concluding that all the molecules of calcite have the same form and it is only how they are joined together that produces different gross structures. He suggested that other minerals should show different basic forms. His theory predicted the correct angles of crystal faces in many cases.

June 19 is the 225th anniversary of the birth of ***Fredrich Wilhelm Sertürner***, the discoverer of morphine.

Richard Buckminster Fuller died on July 1 1983. He was the US engineer/architect who developed the geodesic dome.

Amedeo Avogadro published his memoir about the molecular content of gases on July 11 in 1811.

Tour Report

The 2007 Royal Society of Chemistry Australasian Lectureship Tour - Report

Prof. Peter Schwerdtfeger

Centre of Theoretical Chemistry and Physics, New Zealand Institute for Advanced Study, Massey University Auckland, PB 102904, North Shore City, 0745 Auckland (e-mail: *p.a.schwerdtfeger@massey.ac.nz*)

I was absolutely delighted when Professor Graham Bowmaker (University of Auckland) told me that I was to be the 2007 RSC Australasian Lecturer. This meant that, according to the RSC web-site, I should visit (theoretically) 32 universities in Australia and 6 in NZ. Well, after some careful planning, with the kind support of Professors Allan Bond (Monash) and Graham Bowmaker (Auckland), I made it to 11 universities in Australia and 6 in New Zealand, gave in total 21 talks on 7 different research topics (although 10 topics were offered, titles such as *Nuclear Multipole Moments* and *Electric Field Gradients* somehow were less popular). Most appropriately, I set the starting line at my home university (Massey) and finished not far away from were I started, at my former University of Auckland. And here is my report.

The most popular talks were *Left or right in Nature?* and *The Quest for Absolute Chirality*. The two talks are connected, as the main theme is symmetry breaking in nature. *Left or right in Nature?* describes the preference of L-amino acids and D-sugars in life (termed biomolecular homochirality). The fundamental question is how and when did nature choose one enantiomer over the other. My first talk at the Te Manawa Museum in Palmerston North was well attended (fully packed is the right term), and the 15 minutes of discussion went well. What I really enjoyed that evening was that a number of school children attended, and even sent me e-mail messages a week later asking some very good questions. My critical comments about creationism and intelligent design, where I used a well-known phrase by Aristotle - *Contra principia negantem disputari non potesti* – may have created a bit of controversy (fully intended, of course).

The talk on *The Quest for Absolute Chirality* held at the University of Queensland (Brisbane) dealt with the breaking of symmetry at the microscopic level. There is a tiny energy difference between the enantiomers of chiral molecules due to Z-boson exchange between electrons and nucleons. This is well known from the standard model, but has not yet been seen experimentally. At Griffith University, a joint chemistry/physics seminar was organized and the topic How to Pack Rare Gas Atoms was chosen. *How to Pack Rare Gas Atoms* is a very old problem dating back to Max Born in 1940, and was recently solved (and laid to rest) in our research group. Both Queensland and Griffith are wonderfully located and I enjoyed walking around the two campus sites.

The campus of the Charles Darwin University (CDU) is equally nice and, of course, located close to the famous Kakadu National Park. But science first! There are only a few chemists left at CDU and the word goes round that Darwin University does not need chemistry: Stage 1 teaching could be done by (retired) school-teachers. I find this quite unbelievable! It is an unnecessary cost cutting exercise, especially as the mining industry in this area now recruits qualified chemists from overseas (see below). My talk on super heavy elements was well received and well organized by the local Northern Territory Branch of the RACI. The talk gave an overview over the current activities in this area, mainly the synthesis of new elements (recently 118 was produced in Dubna), and atom-at-a-time chemistry to study the chemical behaviour of these new elements. On the weekend I took a trip with my wife to Kakadu National Park, which was certainly the highlight of the tourist part. On our way back to Darwin at night by car I almost hit a 3 m long crocodile dozing in the middle of the road. My suggestion to get out of the car and to chase it off met some fierce resistance from my wife, and I gave up this interesting idea. I really like the Northern Territory.

In Sydney I gave three lectures. *The Quest for Absolute Chirality* (University of New South Wales) was held in a brand new lecture theatre, and the physics section there took the opportunity to invite me for a seminar on *Small Effects, Large Consequences: from Relativity to Electroweak Interactions*. What I find amazing is that most physicists still believe that relativistic effects are not so important for chemical and physical properties of atoms, molecules or the solid-state; I hope I put that misconception to an end. At Sydney University *Relativistic Effects in the Chemistry of Gold* was presented to a department that has a very strong theoretical and computational chemistry section, and the talk was therefore more tailored towards theory.

The last stop of my first trip to Australia was Canberra, where I had spent two years as a research fellow 18 years ago. It was nice to be back and meet many of my former friends and colleagues (and they still tell stories about me …). Interestingly, I was told that they forgot to send an e-mail message around reminding people to attend the seminar, and I should therefore not be too disappointed if few turn up. Well, the lecture theatre was packed, with no seat left vacant; the discussion after my talk on *The Quest for Absolute Chirality* went on for a long time, and was very stimulating indeed. It was great to see some former members like Martin Bennett and Alan Sargeson asking the hard questions.

Back in NZ I gave two talks at Otago University. The theoretical group there chose *The Pseudopotential Approximation*. Pseudopotentials are the most widely used approximation for computing molecules containing heavy elements, and the talk addressed the advantages and pitfalls of this method. The physicists at Otago took the advantage to invite me to talk on *Parity Violation in Molecules*, which is really the *The Quest for Absolute Chirality* talk tailored for the theoretical physicist. On the same trip I visited Canterbury University and gave a talk on superheavy

elements.

I gave two talks in Wellington at VUW on *The Quest for Absolute Chirality* and *The Chemistry and Physics of the Superheavy Elements*. I find the chemistry and physics sections at Victoria an exciting place at the moment, with a lot of positive thinking and exciting research. Of course, this is largely due to the fact that the McDiarmid Centre of Excellence is located there, with a good number of young and excellent researchers. I also had a more political discussion with their Dean of Science (David Bibby) on the role of fundamental science in our society, which I really enjoyed. At Waikato University I gave the talk on *The Quest for Absolute Chirality*, which was well received.

My second trip to Australia started in Perth (University of Western Australia). I was impressed by the new chemistry building with its large ground floor area tiled in a Penrose pattern; in fact, the largest Penrose tiling in the world (and signed by Roger Penrose). The new lecture theatres, offices, and laboratories are carefully designed, and major equipment like NMR and X-ray facilities are state-of-the-art. The lecture choice was for relativistic effects in the chemistry of gold. Perth is a wonderful city and has a very nice botanical garden which is not to be missed.

Next stop was Adelaide with a talk on superheavy elements. In Hobart I gave two talks, one in the Chemistry Department (superheavy elements - again), and one in the Physics Department on *Kepler's Conjecture, Newton's Kissing Problems* and *How to Pack Rare Gas Atoms*. With the physicists there, I had some very interesting discussions on future collaborations.

Last stop was Melbourne where I gave two talks, one at Monash University (superheavy elements) and the other on *Left or Right in Nature?* at RMIT. I also participated at the Biannual Humboldt Meeting of the Australian Humboldt Association, where I gave another talk. As the NZ president of the Humboldt Foundation I delivered an after-dinner speech in which I emphasized the importance of fundamental science in our universities. As Humboldt fellows we celebrate Alexander von Humboldt as one of the true pioneers – and perhaps one of the last generalists – in the natural sciences. However, of equal importance is his brother, Friedrich Wilhelm Christian Karl Ferdinand Freiherr von Humboldt, born in 1767 two years before Alexander. He was a German linguist and philosopher, a government functionary and diplomat, founder of the Humboldt University in Berlin, and friend of both Goethe and Schiller. In his essay *On the Limits of State Action* he describes the development of liberalism and the role of liberty in the individual development and pursuit of excellence, where the state or government must not be allowed to limit these actions. What Humboldt called *the Enlightenment* is often closely linked with the Scientific Revolution emphasizing reason, science, and rationality against intolerance. It is the source of critical ideas, such as the centrality of freedom, democracy and reason as primary values to our society. Freedom to teach, the unity of teaching and research, and academic self-governance are key factors associated with his ideas. And here I come to my final (but may be most important) point.

Aside from delivering all these lectures - I gave my last talk at Auckland University on *Left or Right in Nature?* which was organized by the local NZIC Branch – I very much enjoyed talking to many of my colleagues about their current research activities, and the many difficulties they face in the current funding environment in the chemical sciences both in NZ and Australia. I carefully observed the *political* climate at each university, and met many researchers who seem not to be very happy (mildly put) with their's. Many Chemistry Departments have been turned up-side down (New South Wales and Auckland to mention but two), and others are at the brink of extinction, *e.g*. Darwin. There seems to be more emphasis now on materials science (*Nano* seems to be the magic word) and bio-sciences, with traditional chemistry disciplines going out the window, *e.g*. inorganic chemistry. I personally believe that such radical changes are quite damaging for the reputation of a university, and for the country as a whole, and I sincerely hope that most universities invest in excellence irrespectively of the research area. The future direction in many departments nowadays is determined by administrators who base their decisions on financial income, and not by (most of) the academic staff who base their decisions on excellence. Hence, a shift away from basic science to applied and even commercial science is clearly visible at many institutions, which (at least for me) is of great concern. We need to convince universities that the fundamental research of today becomes the technological application of tomorrows [see *This Journal* **2007**, *71*(July), 50-52]. ***If in your science you only look for business, then you risk finding neither knowledge nor business*** (Haldor Topsøe, Chairman of the Denmark-based catalysis and high-tech company). On a positive note, however, I found Otago, Sydney, and the Australian National University still in very good shape and most stimulating. They have not lost their touch with fundamental sciences, and the departments there may serve as future role models for all the others.

All in all it was a wonderful experience for me (and my wife), and I was overwhelmed with the generous hospitality everywhere. Financial support of the RSC is gratefully acknowledged. My special thanks goes to Profs. Allan Bond and Graham Bowmaker for organizing my complete lecture tour. The Royal Society of New Zealand financed my trip to Wellington, which is gratefully acknowledged. Financial support came also from the RACI and the NZIC. Finally, explicit thanks go to my hosts at each stop for their time and energy in facilitating this lecture tour: in Australia - Mark Riley, Debra J. Bernhardt and I. D. Jenkins (Brisbane), Kezia Lim and Naseem Peerzada (Darwin), David Black, Trevor Hambley, Jeff Reimers, Craig P. Marshall, and Victor V. Flambaum (Sydney), Martin Banwell (Canberra), Tak Kee and Michael Bruce (Adelaide), Sue Berners-Price (Perth), Paul Haddad and Peter Jarvis (Hobart), Alan Bond and Helmut Hügel (Melbourne); in New Zealand - Mark Waterland (Massey), Sally Brooker and Jevon Longdell (Otago), Jan Wikaira (Canterbury), Kate McGrath (VUW), Michele Prinsep (Waikato), and Graham Bowmaker, Gordon Miskelly and Brent Copp (Auckland). I also thank all the staff and students who attended my lectures and asked some very interesting questions, and giving me some good new ideas.

Introducing our Research at Massey University

The research in the Schwerdtfeger group at Massey University is concerned with all aspects of quantum chemistry and physics focused toward fundamental issues. Current research areas include: parity-violation in chiral molecules, relativistic effects, the chemistry of heavy and superheavy elements, simulation of metallic clusters, quantum-electrodynamic effects in atoms and molecules, solid state chemistry and physics including high-pressure materials, surface science, chemical evolution theory and mathematical and philosophical aspects of quantum theory. For further details see *http://ctcp.massey.ac.nz* and *http://www.nzias.ac.nz*.

New Zealand Science Scene: Communicating Science

One Site for All

In the last few issues of this journal climate change has caused some debate. A new website on the subject has been developed by two Canterbury Philosophers.

Climatedebatedaily.com includes both sides of the debate. Associate Professor Denis Dutton and lecturer Doug Campbell from the Department of Philosophy at Canterbury University, created the website after a tearoom debate on the subject. Professor Dutton was surprised no one had thought to put together such a website before.

The website has two main columns. The first links essays and research supporting the notion that global warming poses a threat to humans, that it is caused by human activity and that it can be solved. The second column links to essays and research challenging that view, and also whether the earth's climate is within human control. As well this, there are links to climate news articles, blogs written by people on both sides of the debate, and links to official sites.

Professor Dutton said scientists needed to drop the rhetoric and present the best, most balanced view of the facts. He did not think we needed moralizing about this issue but open discussion. He said "to stigmatise criticism as somehow immoral is intolerable for real science".

The site has a similar layout to *arts&lettersdaily.com*. This is no surprise since that site was also founded and edited by Professor Dutton.

The site will be updated daily by the philosophers. They have future plans of including a page to rank arguments and a predictions page. The predictions page would track scientists' predictions and note which turned out to be accurate.

The website has been supported by a grant from Dr Peter Farrell, a visiting professor at the University of New South Wales, who also has a number of business interests.

A First in New Zealand Science Communication

Communication of Science has been given a boost with the opening of New Zealand's first Science Communication Centre.

The Centre has opened at the University of Otago. Director, Professor Lloyd David, said the Centre's ultimate role was to enhance communication about science to the public.

The Centre would also run a new Master of Science Communication programme. It has three options; science and natural history film making, creative nonfiction writing in science and popularizing science.

The Centre was financed by a $1.6m donation by the Stuart Residence Halls Council and by the Government's Partnerships for Excellence Programme.

Professor Jean Fleming has returned to Otago to be a Professor of Science Communication at the Centre. She had a high profile role in the Royal Commission on Genetic Modification. Emmy award winner, Ian McGee, from NHNZ has been appointed Director of Filmmaking.

New Approach to Discussing Science

The genetic engineering debate proved useful in one student's research into new ways to communicate controversial science and technology to the general community.

Victoria University PhD Graduate, Karen Cronin developed new communication methods for scientists and community interest groups in workshops.

She said new communication methods were evolving from educating the public about science to involving the public in two-way communication about science.

This area of social engagement in science has become a big area of research worldwide.

Dr Cronin said not every technology would require this sort of approach but if there were uncertainties about outcomes or possible big systemic effects from research, it would be a more useful way to go.

The general idea would be to involve the public before large investments and commitment has been made in a technology, rather than waiting until something was commercialised, entered the public consciousness and there was an outcry.

Rather than debate her methods were based on dialogue and questions of inquiry.

She took six years to complete her PhD part-time and believes the research would be helpful in discussions on possible future issues like nanotechnology before they come topics of public controversy.

Dr Cronin is currently applying for funding to use her research with Crop and Food in the area of food technology.

Examples of using these techniques in New Zealand can be found at the bottom of the webpage;*www.morst.govt.nz/current-work/science-in-society/dialogue/fund/*.

Continued on page 77...

Protecting Cultural Heritage: Reflections on the Position of Science in Multidisciplinary Approaches*

Jan Wouters

Royal Institute for Cultural Heritage, Jubelpark 1, B-1000 Brussels, Belgium
(e-mail: *jan.wouters@kikirpa.be*)

*Reproduced from *Chemistry International* **2008**, *30*(1) with permission.

Introduction

Over the past 40 years, scientific research activities in support of the conservation and restoration of objects and monuments belonging to the world's cultural heritage have grown in number and quality. Many institutes specifically dedicated to the study and conservation of cultural heritage have emerged. Small dedicated laboratories have been installed in museums, libraries, and archives, and, more recently, university laboratories are showing increased interest in this field.

However, no definition has been formulated so far to identify the specific tasks, responsibilities, and skills of a conservation scientist or of conservation science. This is contradictory to the availability of a clear *Definition of the Profession of a Conservator-Restorer*, published by the Conservation Committee of the International Council of Museums (ICOM-CC) in 1984.[1] Conservation-restoration is also described as an academic discipline in the *Clarification of Conservation-Restoration Education at University level or equivalent*, published in the Clarification Document of the European Network for Conservation-Restoration Education (EnCoRE) in 2000.[2] At present, definitions on conservation and restoration, but not on conservation science, are under discussion in workgroup 1 of Technical Committee 346 of the European Committee for Standardization.

Hopefully, multidisciplinary research consortiums, *e.g.* executing research projects within European framework programmes, will promote the synergy between the cultural heritage field and the natural sciences, and will generate elements for defining conservation science. Important players in this field, which readily address interactivity and networking, are the recently started 'Episcon project' in the European Community's Marie Curie programme[3] and the five-year-old EU-Artech project.[4] The goal of Episcon is to develop the first generation of actively formed conservation scientists at the PhD level in Europe. EU-Artech provides access, research, and technology for the conservation of the European cultural heritage, including networking among thirteen European infrastructures operating in the field of artwork conservation.

The present absence of a recognised, knowledge-based identity for conservation science or conservation scientists may lead to philosophical and even linguistic misunderstandings within multidisciplinary consortiums created to execute conservation projects. This paper discusses sources of misunderstandings, a suggestion for more transparent language when dealing with the scientific term *analysis*, elements to help define conservation science, and the benefits for conservation scientists of becoming connected to worldwide professional networks.

Disputable Terminology Around *Analysis*

Modern analytical protocols involve ever-increasing sophistication of sample preparation procedures, instrumentation, and post-run data treatment. This, together with the frequent absence of explanatory terms around *analysis*, may create an alienating effect on those professionals who are not familiar with the inherent terminology and evaluation processes, yet are closely involved in the multi- or interdisciplinary approach that must lead to the preservation of cultural heritage. There is no doubt that this may generate reservations when analysis of art is at discussion, even when such analysis is considered essential to reveal an object's conservation condition or to establish a conservation treatment. Among the most notable of such explanatory terms are *destructiveness*, *invasiveness*, *representativeness* and *resolution*. Such terms tend to create a polarization between non-invasive/non-destructive interventions and destructive analytical approaches.

Inevitably, the withdrawal of a sample from an object of art or culture implies some kind of mutilation - even when executed in an inconspicuous area or when dealing with minute samples. Such handling is therefore called destructive to the object. On the other hand, there are analytical techniques available that may be applied directly to the object, without the removal of a sample being required. These techniques are often referred to as non-destructive and they are mostly applied to inorganic materials in art.[5] However, from a scientific point of view, any interaction between a material and an energy-bearing analytical vehicle is unlikely to leave that material, or an accompanying-one, totally unaltered after the interaction.

The key feature in this discussion is the way one interprets damage. Obviously, the least critical position may be expected from evaluations of damage by the naked eye: there is no damage if it cannot be *seen*. The most critical evaluation is from data generated at the molecular level by relevant

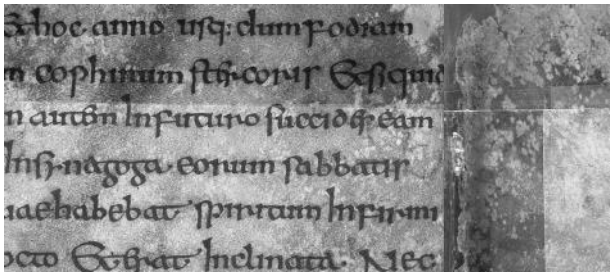


Fig. 1. Dyes in Preolumbian Peruvian textiles (reproduced with permission from the Royal Institute for Cultural Heritage, Brussels): A combination of medium destructiveness and high resolving power allowed for the identification of biological sources used for dyeing, and revealed changes in use as a function of cultural periods - see ref. 12.

spectroscopic techniques: There is no damage if the molecular compositional array at the spot of measurement has not changed beyond experimental deviations or beyond a preset level of tolerance. Sometimes, techniques applied directly to the object are called non-invasive. Although the term is correct since it is a non-sampling technique, the qualification may be misleading in terms of destructiveness for the reasons outlined above.

The complexity of the composition of artifacts such as paintings is expressed by their multi-layer architecture, by the high level of heterogeneity of each individual layer, and by the further contribution to that heterogeneity by natural ageing processes and human interventions. Having to reveal production technology or damage patterns of an object by observing analytical data produced from a microsample or a microspot may come into conflict with the low representativeness of such a sample or spot. Obviously, the only ways to increase representativeness are multiple sampling or increased spot size.

Multiple sampling increases damage to the object, but highly detailed results may be obtained by launching high-resolution mapping and imaging techniques to a set of microsamples.[6] Alternatively, non-invasive approaches may be applied, often with larger beam diameters than those used in high-resolution mapping and imaging. Such larger diameters are advantageous in terms of averaging and, hence, increased representativeness. But, due to the inherent lack of analytical resolution - both in the plane and in the depth of the artifact - they may miss phenomena vital to explain technology and/or damage that would require conservation measures.

It may be clear from this discussion that invasiveness/destructiveness alone is not a good criterion to select an approach for analysing artwork. One or more other parameters should be considered for evaluating the level and detail of information obtained.

Towards New Terminologies

So, should we stop using the often confusing terms that accompany *analysis* when discussing ageing, damage, and manufacturing technology of artifacts? The answer extends beyond the suspected yes![7]

Destructiveness could be replaced by ***degree of intervention***, which may be described at three levels: molecular (low change), microscopic (medium change), or visual (high change). This would imply, for instance, that the withdrawal of a microsample or the generation of a permanently discoloured microspot (as a consequence of prolonged remote radiation) reflect exactly the same degree of intervention. Using the older terms, micro-sampling would be called invasive, radiation non-invasive, but apparently destructive. However, the degree of intervention and its discussion should be time-related. Indeed, discolouration caused by radiation in a focused beam may be either permanent or limited in time, which means that the degree of intervention could be further classified as medium or low intervention, respectively.

However, the degree of intervention does not explain at all why analysis is proposed, requested, or executed, and by what party. More information is needed about the expectations of the requestor in terms of how analytical results will be used. It is suggested here that the terms ***usefulness*** and ***innovation*** can provide such information.

Fig. 2. High-level destructiveness analysis of synthetic membranes without touching the 8th century parchment of the Codex Eyckensis (reproduced with permission from the Royal Institute for Cultural Heritage, Brussels). This revealed a polyvinylchloride polymer with 30 % (w/w) monomeric plasticizer; after removal of the membranes, the Codex could be conserved by the application of an innovative parchment leafcasting technique – see ref. 13.

The assessment of the ***usefulness*** of the intervention should consider whether the intervention can establish what production technology was used, provide a damage assessment, and determine the best conservation practice to use. ***Innovation*** may be formulated in terms of progress beyond the state of the art. Eventually, innovation could be assessed according to the degreee of intervention[8] or usefulness[9] of analysis executed according to the newly developed approach. Hopefully, a high level of innovation shall create data, insights, and experience which, inr turn, would improve usefulness and probably even lower the degree of intervention in the longer term.

The terms intervention, usefulness, and innovation may be rightfully used and combined to estimate the balance between the degree or level of intervention and the analytical outcome. And it will be exactly this balance that must be discussed by all parties involved when selecting the most appropriate analytical approach. Transparency will be increased specifying the degree of intervention, usefulness, and innovation when discussing scientific analysis in a multidisciplinary environment. Use of these terms also may improve the source's credibility, the receiver's attention, and the quality of the decision.[10]

Towards a Definition of Conservation Science

The linguistic and philosophical issues discussed in the two preceding paragraphs illustrate how a natural scientist (chemist, physicist, biologist), working in the field of cultural heritage, must critically define pathways for proposing, executing, interpreting, and explaining analyses of art within a multidisciplinary and responsibility-sharing environment. To this must be added more specific research-related issues, including old manufacturing technologies, ageing phenomena, and social, cultural and political pressures to preserve the

past for the future. All of these elements constitute criteria for improving the understanding of the specific requirements of conservation science.

The major objectives of conservation science should be to study all aspects (chemical, biological, physical) of the manufacture, decay and preservation of objects of art and culture. Such studies require the following:

- reading and understanding the data present in historic literature (revealing the choice of sources, the preparation of products, and the combination of those products in the manufacturing technology of the final object), and the extrapolation of these data into a present day scientific framework (to prepare mock-ups or to develop an analytical strategy);
- recognition of phenomena, at any level of observation (visual, microscopic, molecular), related to manufacture and decay;
- creation of reference collections and databases of analytical results and standards;
- development of analytical approaches to enhance the ratio of information to destructiveness and taking into account levels of usefulness and innovation;
- understanding of usefulness;
- consideration and understanding of historical, geographical, and archaeological aspects of collections;
- appropriate applications of statistics;
- dedicated fundamental research and high-level interactivity with professionals from other disciplines.

A Multidisciplinary Research Forum in Cultural Heritage

Obviously, conservation scientists should have a strong interest in seeking and promoting interactions with other actors in their field. Such interactions will be more established within the framework of relevant professional organisations. A prominent player in this field is the *Conservation Committee of the International Council of Museums* (ICOM-CC).[11] This committee is the largest of 30 international committees of ICOM and is composed of 23 multidisciplinary working groups, covering all aspects of the investigation and conservation of museum collections. In this way, ICOM-CC helps to achieve ICOM's objectives, which are to exchange scientific information at an international level, to develop professional standards, and to adopt rules and recommendations. ICOM-CC membership, which is spread over 79 countries and has grown by 50 % over the last 7 years, is now more than 1500.

ICOM-CC organizes triennial conferences, where all working groups meet in dedicated sessions and where plenary sessions are organised on topics of general interest. At these conferences, working group members elect a coordinator and discuss a working programme for the next three years.

Conclusion

Multi- and interdisciplinary consortia established to preserve cultural heritage will benefit from a better integration of conservation science. This may be achieved through establishing a definition of conservation science and through the formulation of end-terms – formed at the Masters level at least – for conservation scientists. The terminology used nowadays to describe the potential damage to objects caused by analysis should be refined beyond the destructiveness/non-invasiveness polarisation. A terminology should include at least *degree level intervention* (low, medium, high), *usefulness*, and *innovation*. The further development and integration of conservation scientists will improve with their participation in international networks that encourage multidisciplinary approaches.

References and Notes

1. For the text on the *Definition of the Profession of a Conservator-restorer*, Conservation Committee of the International Council of Museums (ICOM-CC) 1984, see: www.icom-cc.icom.museum.
2. For The Clarification Document of the European Network for Conservation-Restoration Education (EnCore), see: www.encore-edu.org/encore/DesktopDefault.aspx.
3. See: www.episcon.scienze.unibo.it.
4. See: www.eu-artech.org.
5. *Ion beam study of art and archaeological objects*, Demortier, G.; Adriaens A. (Eds.), European Commission, Luxembourg, 2000.
6. Boon, J. J.; Ferreira, E. S. B.; Keune K. *Microscopy Microanal.* **2005**, *11*, 1370-1371.
7. Wouters, J. *Surrealism in science: the difference between analysis and analysis*. In *Proceedings of the De Mayerne Symposium*, NWO, The Netherlands, 2006, 13-20.
8. Verhoeven, M. A.; Carlyle, L.; Reedijk, J.; Haasnoot, J. J. *Exploring the application of solid-state Nuclear Magnetic Resonance to the study of the deterioration of paintings*. In *Proceedings of the De Mayerne Symposium*, NWO, The Netherlands, 2006, 32-42.
9. Della Gatta, C.; Badea, E.; Masic, A.; Usacheva, T.; Benedetto, S.; Braghieri A. *Environmental ageing of historical parchments: a DSC, SEM and unilateral NMR study of old bookbindings from the Historical Archives of the City of Turin*. In: *Improved Damage Assessment of Parchment*, School of Conservation, The Royal Danish Academy of Fine Arts, Copenhagen, 2005, 41-42.
10. Henderson, J. *The Conservator*, **2005**, *29*, 63-72.
11. For further regularly updated information see: www.icom-cc.icom.museum.
12. Wouters, J.; Rosario-Chirinos, N. *J Am. Inst. Conservation,* **1992,** *31*, 237-255**.**
13. Wouters, J. *The Paper Conservator*, **1995**, *19*, 5-22.

NZ Science Scene Continued....

Secondary School DVD Competition

The Royal Society of New Zealand is celebrating the 150th anniversary of Darwin's *On the Origin of Species* this year.

As part of the celebration the 2008 Freemasons Big Science Adventures, nationwide DVD competition has the topic of Darwin and the theory of evolution.

The competition is open to Year 11-13 students and has a two-week trip to the United Kingdom as a major prize as well as a trip to a remote offshore location.

Teams need to comprise of three students and one teacher to act as guide and facilitator.

Entries need to be in by 9 May. For more details see the website. *www.rsnz.org/events/bigsci/2008/*

In Science the credit goes to the man who convinces the world, not to the man to whom the idea first occurred.

Sir William Osler (1849-1919) Canadian physician.

To Patent, or to Publish, that is the Question!

By Blair Hesp and Jarrod Ward

Following the introduction of Performance-based Research Funding (PBRF), NZ universities are placing an increasing emphasis on the number and quality of publications produced by both academic and research staff. Consequently, researchers are encouraged to publish their results as often, and as quickly, as possible with the potential intellectual property (IP) contained in their discoveries sometimes being overlooked.

The implications of public disclosure of results

When a discovery is made it is important to understand the implications attached to the public disclosure of results. Premature public disclosure in any form will jeopardize the ability to obtain valid patent protection for an invention. Public disclosure not only includes publication in peer-reviewed journals, but also oral and poster presentations. Indeed, student dissertations and theses are also considered to constitute public disclosure.

Dissertations and theses often contain data that is commonly referred to as *unpublished*. However, any such documents are likely to be considered as available to the general public through the respective university's library. Even a single copy of a document that is available for public inspection will be sufficient to constitute public disclosure.

If you plan to disclose your research at a conference in NZ, it is possible to request that the event is gazetted by the Intellectual Property Office of New Zealand (IPONZ)[1]. If an event is gazetted, a six month grace period will be provided for filing a NZ patent application from the date of the event. However, whilst this grace period is available here, it is not universally recognised overseas.

The US, Canada, China, Russia, Australia and Japan have provisions for period of 6 to 12 months grace under certain circumstances, but other jurisdictions do not. Therefore, even if an event has been gazetted in NZ, inconsistencies across jurisdictions mean we do not recommend relying on these grace periods.

[1] Further information and suitable forms may be obtained from the IPONZ website: *http://www.iponz.govt.nz/iponz-docs/G/Gazetting_Info_Sheet_v2.pdf*

Thus arises the real dilemma for the academic researcher: how to balance the desire to patent an invention against the imperative of publishing results.

So when can my results be published?

There is a very simple answer to this question: as soon as you have determined whether or not patent protection for the invention is possible and/or warranted and if necessary, a patent application could be filed. Once a patent application has been filed, the public disclosure of your results will not impact on your ability to obtain patent protection in NZ or overseas.

Patenting and publishing do not have to be mutually exclusive activities. Key things to remember are:

- do not disclose the invention until any potential IP has been identified ;
- if disclosure is unavoidable, ensure it occurs at a gazetted event; and
- there are no restrictions on disclosure once a patent application has been filed.

One final point – lest it seem that even dreaming about an invention could constitute a public disclosure – remember that in order to impact patentability, the disclosure must contain a description of the invention. This must be detailed enough to enable a person skilled in that particular area of technology to understand and practise the invention.

If you are concerned about the effect of publication on your potential IP rights, we suggest consulting an IP specialist.

A reminder: if you have any queries regarding patents, or indeed any form of intellectual property, please direct them to:

Patent Proze
Baldwins
PO Box 852, Wellington

Email: email@baldwins.com

Blair Hesp and Jarrod Ward of Baldwins specialise in chemistry and biotechnology patents. Blair joined Baldwins in 2006, and has a PhD in pharmacology from the University of Otago as well as a NZDipBus with a management focus. Jarrod joined Baldwins in 2007, and has completed the requirements for his PhD in chemistry at the University of Auckland. Blair and Jarrod are currently studying towards law degrees and registration as patent attorneys.

Conference Calendar

Systems Chemistry, Bozen Symposium, Bozen, Italy, 26-30 May 2008

Further details available at the website: www.beilstein-institut.de

International Academy of Mathematical Chemistry, Math/Chem/Comp 2008 Conference, Verbania-Intra, Italy, 10-13 June 2008

Further details available at the website: http://michem.disat.unimib.it/chm/mcc08/index.htm

WHEC 2008, 17th World Hydrogen Energy Conference, Brisbane, Australia, 15-19 June 2008

Further details available at the website: www.whec2008.com/

International Symposium on Catalysis for Clean Energy and Sustainable Chemistry, Madrid, Spain, 18-20 June 2008

Further details available at the website: www.ccesc.es/

CESIO 2008, 7th World Surfactants Congress, Paris, France, 22-25 June 2008

Further details available at the website: www.cesio2008.com/

Dalton Discussion 11: The Renaissance of Main Group Chemistry, Berkeley, California, United States, 23-25 June 2008

Further details available at the website: www.rsc.org/ConferencesAndEvents/RSCConferences/DD11/index.asp

III International Conference on Colloid Chemistry and Physicochemical Mechanics, Moscow, Russia, 24-28 June 2008

Further details available at the website: www.icc2008.ru/en/

ICCE 2008: International Conference on Chemical Engineering, Paris, France, 4-6 July 2008

Further details available at the website: www.waset.org/icce08/

Gordon Research Conference on Polymer Physics, Newport, United States, 29 June - 4 July 2008

Further details available at the website: www.grc.org/

Drug Discovery & Development, Couran Cove Island Resort, Queensland, Australia, 13-17 July 2008

Further details available at the website: www.3datthecove.org/

BOSSXI, 11th Belgian Organic Synthesis Symposium, Ghent, Belgium, 13-18 July 2008

Further details available at the website: www.boss11.org

19th IUPAC Conference on Physical Organic Chemistry, Santiago de Compostela, Spain, 13-18 July 2008

Further details available at the website: http://www.icpoc2008.org/

17th International conference on photochemical conversion and storage of solar energy, Sydney, Australia, 27 July - 1 August 2008

Further details available at the website: www.ips17.com/

XXII IUPAC Symposium on Photochemistry, Goteborg, Sweden, 28 July - 1 August 2008

Further details available at the website: http://photoscience.la.asu.edu/Goteborg2008/

5th SETAC World Congress, The Society of Environmental Toxicology and Chemistry, Sydney, Australia, 3-7 August 2008

Further details available at the website: www.setac2008.com/

XXth International Symposium on Medicinal Chemistry, Vienna, Austria, 31 August - 4 September 2008

Further details available at the website: http://www.ismc2008.org

PSA2008, Particulate Systems Analysis 2008, Stratford Upon Avon, United Kingdom, 2-4 September 2008

Further details available at the website: www.psa2008.co.uk/

Praha 2008, The 20th International Conference on High Resolution Molecular Spectroscopy, 2-6 September 2008

Further details available at the website: www.chem.uni-wuppertal.de/conference/

23rd European Colloquium on Heterocyclic Chemistry, Antwerp, Belgium, 9-13 September 2008

Further details available at the website: www.echc08.org/

WATOC 2008, World Association of Theoretical and Computational Chemists, Sydney, Australia, 14-19 September 2008

Further details available at the website: www.watoc2008.com/

AACB 46th Annual Scientific Conference *Laboratory Medicine: Promoting Population Health*, **Adelaide, Australia, 15-18 September 2008**

Further details available at the website: www.aacb.asn.au/web/Meetings/Annual_Scientific_Conference/

XIV European Seminar on Computational Methods in Quantum Chemistry, Isola d'Elba, Italy, 2-6 October 2008

Further details available at the website: http://h2.ipcf.cnr.it/rizzo/XIV_ESCMQC.html

Functional Foods 2008: Functional Foods and Edible Oils - The Future, 8th Annual Functional Foods Symposium, Luxury Heritage Hotel, Auckland, New Zealand, 12-13 November 2008

Further details available at the website: www.foodworks.co.nz/oilsfats/news.htm

NZIC Conference 2008, Dunedin, 30 November - 4 December

RACI Organic 08, Wrest Point, Hobart, Tasmania, Australia, 7-12 December 2008

Further details available at the website: www.organic08.org/

Inorganic Chemistry Conference IC08, 14 - 18 December

Further details available at the website: www.chem.canterbury.ac.nz/ic08

AMN4, 4th MacDiarmid Institute for Advanced Materials and Nanotechnology Conference, University of Otago, 8-12 February 2009

Further details available at the website: http://macdiarmid.ac.nz/events/amn-4.php

PACIFICHEM 2010

Honolulu, Hawaii 15-20 December 2010

The Congress, scheduled to be held in Honolulu in December 2010, is jointly sponsored by the Canadian Society for Chemistry (CSC), the American Chemical Society (ACS), the Chemical Society of Japan (CSJ), NZIC, the Royal Australian Chemical Institute, the Korean Chemical Society, and the Chinese Chemical Society.

The goal of Pacifichem 2010 is to promote collaborations among Pacific Basin chemical scientists that will improve the quality of life around the world. It is a very large chemical congress attracting ~15,000 chemists and a similar number of papers. It is organised around several hundred symposia, suggested by chemists from the region, on the basis that they represent current cutting edge and 'hot' topics in chemistry.

The technical programme will embrace 13 key areas, each with its NZ Program Advisor as:

CORE AREAS OF CHEMISTRY:

Analytical - ***Dr. Gordon M. Miskelly***
(*g.miskelly@auckland.ac.nz*).

Inorganic - ***Prof Sally A Brooker***
(*sbrooker@chemistry.otago.ac.nz*).

Macromolecular - ***Dr J. Travas-Sejdic***
(j.travas-sejdic@auckland.ac.nz).

Organic - ***Prof Robin A. J. Smith***
(*rajsmith@chemistry.otago.ac.nz*).

Physical, theoretical & computational - ***Prof Peter Schwerdtfeger***
(*P.A.Schwerdtfeger@massey.ac.nz*).

MULTI- AND CROSS-DISCIPLINARY AREAS OF CHEMISTRY:

Agrochemistry - ***Dr Paul Kilmartin***
(*p.kilmartin@auckland.ac.nz*).

Biological chemistry - ***Dr Sigurd Wilbanks***
(*sigurd.wilbanks@stonebow.otago.ac.nz*).

Environmental chemistry - ***Prof Keith A. Hunter***
(*khunter@chemistry.otago.ac.nz*).

Materials & nanotechnology – ***A/Prof Keith C. Gordon***
(*kgordon@chemistry.otago.ac.nz*).

AREAS OF CHALLENGE & OPPORTUNITY:

Alternative energy technology - ***A/Prof Simon B. Hall***
(*s.b.hall@massey.ac.nz*).

Community outreach - ***Rebecca Hurrell***
(*rebecca.hurrell@canterbury.ac.nz*)

Health & technology - ***A/Prof Paul Teesdale-Spittle***
(*Paul.Teesdale-Spittle@vuw.ac.nz*).

Security - ***A/Prof Keith C. Gordon***
(*kgordon@chemistry.otago.ac.nz*).

CALL FOR SYMPOSIUM PROPOSALS

Pacifichem 2010 has issued its first call for symposia. Symposia proposal submissions will take place over two rounds. Round one is now open and closes on April 15. Notification of acceptance will be sent to symposium organisers in the late in 2008. There will be a second round in 2009. However, organisers suggest that it is best to submit proposals early as room for new symposia will decrease after the first round. Proposals must be submitted by members of sponsoring or participating societies and must include co-organisers from at least ***three*** Pacific Basin countries.

Guidelines for submitting proposals and more information on the Congress can be found on the official web site, *http://www.pacifichem.org/*

Prof. Rob Smith (rajsmith@chemistry.otago.ac.nz, phone 03 479 7924) is the NZ representative on the Pacifichem organizing committee. He, or any of the listed program advisors above, would be very pleased to answer any questions or comments about organizing a symposium within Pacifichem 2010.