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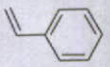

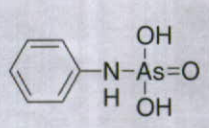

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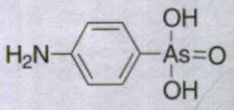

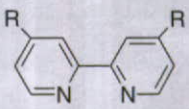

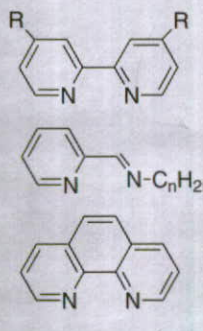

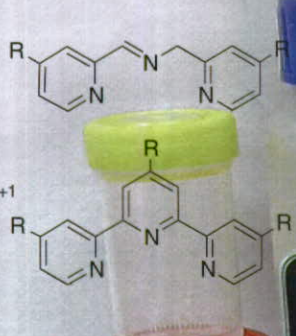

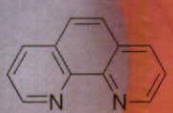

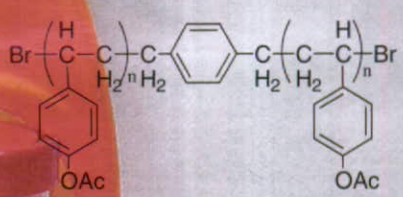

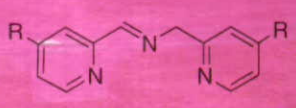

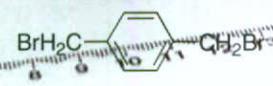

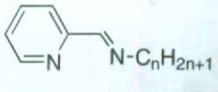

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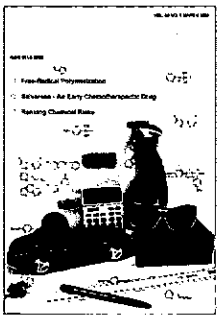

Volume 69, No. 1
March 2005

NZ Science Scene

CALL FOR 2005 RUTHERFORD MEDAL NOMINATIONS

The Royal Society is calling for nominations for the 2005 New Zealand Rutherford Medal, nominations close on 30 June 2005.

The Rutherford Medal is the highest award instituted by the Royal Society of New Zealand at the request of the Government to recognise and honour those who have made exceptional contributions to New Zealand society and culture through activities in the broad fields of science, mathematics, social science, and technology. The Rutherford Medal recognises a significant contribution to the advancement and promotion of public awareness, knowledge and understanding in addition to eminent research or technological practice by a person or group in any field of science, mathematics, social science, or technology. A group award shall only be made in very meritorious circumstances.

When considering the award of a Rutherford Medal, the Royal Society will be looking for people of distinction who will stand in high public esteem. They will have demonstrated more than purely scientific or technological achievement within their scientific or technological discipline. To qualify, the research needs to be recognised internationally as significantly advancing understanding of the field. They will also have made a substantial contribution to the advancement and promotion of public awareness, knowledge and understanding of science, mathematics, social science, or technology, public service within the scientific community, or on behalf of research, science, mathematics, social science, or technology in the wider community.

Nominations must be via the form on the Royal Society website at <http://www.rsnz.org/awards/rutherford/>. Nominations may be made by any person, but must be supported by at least one member of the Royal Society Council. Nominations must be accompanied by a curriculum vitae, as well as a supporting statement signed by the seconding Council member. Any person may be nominated as long as he or she meets the requirements in accordance with the guidelines. Nominees will normally be expected to be living and working in New Zealand, but people living overseas with strong New Zealand connections, either personally or through their work, will also be eligible.

AGRESEARCH SCIENTIST NAMED EMERGING BIOTECHNOLOGIST OF THE YEAR

An AgResearch Scientist has been named Emerging Biotechnologist of the Year. Dr Sue McCoard, who is in the Food and Health Group based at the CRI's Grasslands campus, received the accolade at an awards dinner at the inaugural NZBio Conference.

Dr McCoard is currently involved in research to identify genes that regulate protein production in the mammary gland of cows. Using genomics techniques, the project team has now identified pathways and candidate genes thought to be important to protein synthesis which may determine the amount of protein in milk. Dr McCoard's focus is now on functional testing of those genes with a view to applying for patent registration in a year's time.

The Emerging Biotechnologist Award is only available to candidates under 35 years of age and is targeted at scientists who display potential to be a future leader of their field of biotechnology endeavour.

HONOUR FOR NEW ZEALAND ANIMAL WELFARE & ETHICS SCIENTIST

Distinguished scientist Professor David Mellor from the Institute of Food, Nutrition and Human Health, Massey University, has been elected an Honorary Associate to the Royal College of Veterinary Surgeons. The award to Professor Mellor has attracted praise from the veterinary profession in New Zealand and from the Minister of Agriculture Jim Sutton. Professor Mellor is the first New Zealand resident to achieve such an honour from the Royal College, the leading veterinary body in the world and the regulatory body for the United Kingdom veterinary profession.

Election to Honorary Associate is the highest honour conferred by the College, for eminent service to the profession. There have been only 64 Honorary Associates since the first election in 1963. The RCVS was established in 1844 by Royal Charter to be the governing body of the veterinary profession in the United Kingdom

Professor Mellor will travel to London in July to accept the award.

SCIENTIST HONOURED AT VICTORIA

Professor Shayle Searle, an eminent Cornell University statistician, will be awarded an honorary doctorate from Victoria University during May's graduation ceremonies. Professor Searle has a long-standing association with Victoria University and established a Visiting Fellowship in Statistics in 2003, to enable leading international statisticians to visit Victoria to undertake research and seminars. He is also an active member of the US Friends of Victoria, and endowed a prize for the best student in first-year applied statistics, which has been awarded since 1999.

Professor Searle was elected as a fellow of the American Statistical Association in 1968 and was awarded a US Senior Scientist Award from the Alexander von Humboldt Foundation in Germany in 1985. In 1999 he was made an Honorary Fellow of the Royal Society of New Zealand, a rare honour for New Zealand scientists who are resident overseas.

Professor Searle joins Professor Albert Wendt (CNZM) and Judith Hanratty in receiving Victoria's highest honour at the first of the graduation celebrations for 2005.

PERFORMANCE BASED RESEARCH FUND UPDATE

As the redesign process for the 2006 PBRF Quality Evaluation reaches its end, the final consultation paper is now available. It covers issues surrounding the use of PBRF data by TEOs. The consultation document is available on the TEC website at <http://www.tec.govt.nz/funding/research/pbrf/consultation_documents.htm>.

NZ SCIENCE AND TECHNOLOGY MEDALS: CALL FOR NOMINATIONS

The New Zealand Science and Technology medals were instituted by the Royal Society of New Zealand at the request of the Government to recognise and honour those who have made exceptional contributions to New Zealand society and culture through activities in the broad fields of science, mathematics, social science, and technology. The award of any medal recognises contribution beyond the bounds of the discipline or immediate work environment. This may take place through novel ways such as the media (print, radio or television) to audiences such as children, selected interest groups, Maori, or the general public.

Nominations close on 30 June 2005 and must be made via the form on <http://www.rsnz.org/awards/st_medals/>. Further information on the medals and nomination requirements may be obtained from the website or via Email: <awards@rsnz.org>.

CALL FOR NOMINATIONS FOR 2005 PICKERING MEDAL

The Royal Society is calling for nominations for the 2005 Pickering Medal. Offered for the first time in 2004, the Pickering Medal has been established to recognise excellence and innovation in the practical applications of technology. The medal will be awarded annually to a person who, while in New Zealand, has through design, development or invention performed innovative work, the results of which have been significant in their influence and recognition both nationally and internationally, or which have led to significant commercial success.

The nomination form is available at <http://www.rsnz.org/awards/pickering/index.php> and the closing date is 30 June 2005.

JAMES COOK RESEARCH FELLOWSHIPS: CALL FOR APPLICATIONS

The James Cook Research Fellowships are administered by the Royal Society of New Zealand on behalf of the Government. They are awarded to researchers who are recognised leaders in their respective fields, have the requisite qualifications and experience, and are able to demonstrate that they have achieved national and international recognition in their area of scientific or technological research.

Applications are now being sought in the following two research categories:
*Physical Sciences
*Engineering Sciences and Technologies

The primary intention for the award of Fellowships is the recognition of sustained excellence in research. The normal term of a Fellowship is two years and the stipend offered for those awarded in this round will be NZ$110,000 inclusive of GST per year. This increased stipend will hopefully make tenure overseas for all or part of the Fellowship more viable. Reimbursement of relevant expenses to a maximum of $10,000 annually will also be offered. Those appointed will be required to take up their Fellowships by March 2006.

Eligibility: New Zealand citizens or permanent residents. Host Institution: Fellowships will be tenable in a location and institution of the applicant's choosing, whether in New Zealand or overseas. Closing date for applications: 1 September 2005. For further information, please contact: Executive Officer - Awards, Email: awards@rsnz.org> or see <http://www.rsnz.org/awards/james_cook/index.php>.

JULIUS VON HAAST FELLOWSHIP AWARD

The New Zealand Government has established the Julius von Haast (JvH) Fellowship Award. Under a JvH Fellowship, German scholars and scientists will be able to undertake research in New Zealand, for a minimum of four weeks per year over a three-year period. The Alexander von Humboldt Foundation supports this programme and has incorporated the JvH Fellowship into the Humboldt Research awards based on reciprocity for top German researchers. This JvH scheme is funded through New Zealand's International Science and Technology (ISAT) Linkages Fund, and is administered by the Royal Society of New Zealand.

This Fellowship is open to all fields of research including social science and humanities. Fellowships will be awarded upon excellence and the benefits for New Zealand research, science and technology. The applicant must be a German national with an international reputation as an innovative researcher, and must be currently working within the German research/science sector and have been employed for no less than five years in public or private German research or academic institutions. A JvH Fellowship will be awarded for three years. It is intended to appoint one new Fellow in each financial year (July to June).

Applications close with the Fund Manager, Royal Society of New Zealand at 4.00 p.m. on Wednesday 1 June 2005. Guidelines and application forms are available at: <http://www.rsnz.org/funding/vonhaast/>.

SIR PETER BLAKE ENVIRONMENTAL EDUCATOR AWARD

The Sir Peter Blake Environmental Educator award was set up in 2005 in partnership with the Royal Society of New Zealand and the Ministry of Education. The Award is open to fully qualified, practising primary, intermediate and secondary teachers.

The objective of the Award is to contribute to the development of the future human resource in the wise and sustainable use of natural resources, the promotion of the wise and sustainable use of natural resources and to enhance the delivery of environmental education curricula in schools.

Guidelines and conditions at <http://www.rsnz.org/funding/peterblake/Guidelines.pdf> and application forms

at <http://www.rsnz.org/funding/peterblake/appform.doc>.

ANZCCART STUDENT AWARD

In conjunction with its 2005 annual conference entitled "Animal Ethics Committees and animal use in a monitored environment: is the ethics real, imagined or necessary?", to be held in Wellington from 26 to 28 June 2005, ANZCCART is offering a student award to encourage attendance and involvement at the conference by Honours and Postgraduate students.

The award is open to New Zealand and Australian students of all disciplines and is worth A$1,000. It is intended to provide for conference travel costs, accommodation and registration. Students are required to submit a short paper (no more than 3000 words, including an abstract of about 400 words) on a theme related to the conference. The paper should be compatible with the goals of ANZCCART. The award will be given to the best paper submitted, as judged by members of the conference planning group. Assessment will be based on excellence, originality and relevance. The winner will be asked to present the paper at the conference, either in the form of a short talk or a poster.

Applications should be submitted by 27 May 2005 to Executive Officer, ANZCCART, C/- Royal Society of New Zealand, P O Box 598, Wellington.
Email: <mailto:anzccart@rsnz.org>.

LIGGINS INSTITUTE FELLOWSHIP FOR TEACHERS (LIFT) PROGRAMME

The Liggins Institute recognises the need to share knowledge across traditional boundaries and offers teachers an opportunity to become familiar with modern biomedical research. The programme will let you learn new skills and knowledge through working side-by-side with scientists to enable them to motivate young people to develop an interest in science and biotechnology. Through LIFT, secondary school science, technology, health or social science teachers undertake a 4-week project with university mentors in academic research laboratories. At the end of the programme, the teachers' students are invited to the Liggins Institute to hear the findings presented, and the Liggins Institute researchers follow up with visits to school classrooms.

For more information, contact: Programme Leader: Associate Professor Bernhard H. Breier, Liggins Institute, The University of Auckland and National Research Centre for Growth and Development. Email: <bh.breier@auckland.ac.nz> or Peter Spratt, Royal Society of New Zealand, Email: <peter.spratt@rsnz.org>.

100 YEARS AT AGRESEARCH WALLACEVILLE

One hundred years of science was celebrated at AgResearch's Wallaceville campus in Upper Hutt this past Easter. Wallaceville is one of the country's oldest agricultural research facilities. About 400 people, including many former staff from as far afield as the United States, the UK and Australia returned to the Wallaceville campus for a reunion with New Zealand colleagues with a link to AgResearch's Animal Research Centre.

Wallaceville, which was established in 1905, was the first veterinary research centre set up in the Southern Hemisphere. It has played a critical role in a number of agricultural problems over its 100-year history including tackling blackleg, brucellosis, bush sickness, hydatids, and toxoplasmosis. Its scientists pioneered research that led to the use of mixed vaccines for diseases like blackleg, pulpy kidney and scabby mouth. Now part of AgResearch, the Centre's current research is focused on infectious diseases, parasitology and reproductive biology. The campus is also home to MAF's National Centre for Disease Investigation.

APPLICATIONS FOR GENESIS ONCOLOGY TRUST GRANTS

The Genesis Oncology Trust invites applications for grants to support New Zealand-based initiatives that will lead to improvements in the prevention, detection, diagnosis or treatment of cancer, or improvements in the palliative care of cancer patients. These initiatives can be biomedical, clinical, epidemiological or psychosocial. The closing date for applications in 2005 is Friday 26 August and the grants will be announced in early December. The total amount available for distribution in 2005 is up to $500,000. Grants to be awarded will include: Postgraduate Scholarships; Professional Development Awards; Research Project Grant; Special Purpose Grant.

The Genesis Oncology Trust fund was established with a settlement from Genesis Power Limited in May 2002. The Trust fund has been invested and, as a registered charity, the Trust welcomes donations from individuals and firms. Application forms and information are available from the Genesis Oncology Trust web site: <http://www.genesisoncology.org.nz> or by Email to : <oncology.research@genesispower.co.nz>.

SEAFOOD INNOVATIONS: REQUEST FOR RESEARCH PROPOSALS

Seafood Innovations Ltd is a research consortium company that has recently been established to promote research relating to the seafood industry in New Zealand. Seafood Innovations' mission is to promote industry-initiated research and development projects primarily aimed at increasing the value of existing harvests; reducing harvesting and processing costs; and enhancing consumer-driven product attributes. Seafood Innovations plans to more than double its existing research programme via a Request for Proposals (RFP) process. The RFP is aimed at securing enough detail for a Research Advisory Group to evaluate each proposal and make recommendations to the Board. Projects eligible for consideration should fall in a budget range of $50,000 to $500,000 per annum and focus clearly on one or more of the above priority research areas. All research projects put forward for funding must include one or more project sponsors including at least one levy-paying member of SeaFIC (The New Zealand Seafood Industry Council Ltd).

The closing date for proposals is Friday 20 May 2005. A copy of the Request for Proposal form can be obtained from: Seafood Innovations Ltd, Private Bag 24-901, Wellington. Attention: Mark Loeffen, Acting CEO, Email to: <loeffenm@seafoodinnovations.co.nz>.

Ranking the Risks Due to Chemicals

Peter Cressey and Rob Lake
Institute of Environmental Science and Research (ESR), Christchurch Science Centre
P O Box 29-181, Christchurch, Email: Peter.Cressey@esr.cri.nz

Consumers regularly list the chemicals present in food as an important concern. Pesticides, additives, growth hormones, heavy metals, acrylamide, dioxins, natural toxins, packaging contaminants are common examples. The sources of potential risk are many, and not all can be addressed at once. To effectively manage risks from chemicals effectively, it is necessary to rank the risks in some way. The ESR Food Group has been examining approaches to risk ranking for chemicals as part of its science programme for the New Zealand Food Safety Authority. However, ranking risks from chemicals is a broader issue that will be important to those involved with all potential sources: food, air, water, *etc.* This article presents general considerations about ranking chemical risks.

Risk ranking is driven by the premise that if the relative risks of a range of problems can be established, then efforts to reduce the risks can be directed at the worst problems first. While a variety of different risks may exist in relation to chemicals, in this article *risk* will refer to the public or human health risk due to exposure to the chemical of concern, although, for some interest groups, *risk to the environment* may be of equal or greater importance.

A risk ranking exercise has three main components:[1]

- The problem list.
- The criteria for evaluating problems. Criteria must consider the types of risks analysed (human health, quality-of-life, trade, economic), the scope of the risks considered (inherent, residual), and the participants conducting the ranking (public, expert). Criteria may be a mixture of quantitative and qualitative descriptors.
- The ranking process. Data must be sorted and conclusions drawn on the relative severity of problems. This inevitably involves comparing problems against several criteria at once.

The current discussion takes the problem list to include all chemicals to which humans may be exposed, and will focus discussion on criteria for evaluation and approaches that may be taken to combining criteria to provide a ranking of risk.

Human health risk may be defined as a function of the probability of adverse health effects and the severity of those effects in the exposed population. The probability of adverse health effects is, in turn, a function of the magnitude of the exposure to the chemical and the characteristics of the dose-response relationship. This immediately suggests three criteria for use as a basis for chemical risk ranking, namely exposure, hazard or potency (a function of the shape of the dose-response curve), and severity of outcome.

A further factor that must be considered when assessing the human health risks associated with chemicals is the degree of uncertainty associated with any assessment. While there may be uncertainty due to lack of hard data, the greatest problem in assessing chemicals is in defining the characteristics of the relationship between exposure dose and specific adverse health outcomes. For example, although aflatoxins (secondary fungal metabolites) are known to be potent liver carcinogens it is not possible to attribute individual human cases of primary liver cancer to specific aflatoxin exposure scenarios. Therefore, much of the information connecting a chemical to an adverse health state comes from toxicological experiments, mainly on rodent species, or epidemiological studies considering broad trends in populations. The uncertainty in the evidence linking exposure to a chemical to a particular human disease state is often expressed in a reciprocal form as *strength or weight of evidence* and is usually judged by international expert panels, often convened by UN agencies.[2,3]

Exposure assessment

Exposure has been defined as the contact of a chemical with a hypothetical outer boundary of the human body, constituted by the skin, the mouth, the nostrils, and punctures and lesions in the skin.[4] Exposure assessment is a quantitative or qualitative evaluation of that contact, including consideration of the route of exposure (oral, respiratory or dermal), the frequency, duration and intensity, *i.e.* the concentration of the chemical at the point of exposure, the amount that crosses the outer boundary (the dose), and the amount absorbed (the internal dose).

The total exposure or potential dose can be expressed as the integral over time of the product of the concentration of the chemical (C_i) and the intake rate (IR_i) (a measure of consumption of the matrix in which the chemical is present). This equation can be expressed in a discrete form as:

Total exposure (or potential dose) $= \Sigma\, C_i \times IR_i \times ED_i$
where ED_i is the exposure duration for exposure event i.

For chronic exposures C_i and IR_i are often represented by averages, and the exposure duration is standardized to a daily basis, to reduce the exposure equation to:

Average daily exposure $= \Sigma\, C\,average_j \times IR\,average_j$
where j represents the different possible routes of exposure (oral, respiratory, dermal).

The exposure estimate will usually be further normalized by dividing by the body weight of the exposed person or

the average body weight of the exposed population, to give an exposure in mass units/kg body weight/day.

Theoretically, exposure to chemicals can be determined with a reasonable degree of accuracy. Concentrations of chemicals in foods, water, air, and soil can be measured by various analytical techniques, while intake rates can be determined by observing the amount of food eaten, the amount of water consumed, the frequency and volume of breathing, *etc.* However, the different toxicological characteristics of different chemicals mean that exposure estimates in isolation are not a suitable measure for ranking. It is first necessary to relate the exposure to dose levels at which human health effects may occur (dose-response).

Hazard, dose response relationships and benchmark doses

In the risk ranking context, hazard refers to the capability of a chemical to cause harm, without particular reference to the type of harm caused or the actual level of exposure in human populations. Hazard is thus an inherent characteristic of the chemical. It is often considered in terms of the dose of the chemical required to cause harm (dose-response) and the weight of evidence that this harm is relevant to humans.

A major distinction is made between dose-response relationship for genotoxic carcinogens, and non-genotoxic carcinogens and chemicals with other health endpoints. For the latter class it is assumed that there will be some level of exposure below which no adverse health effects will occur – a threshold limit. This assumption appears to be based on the premise that the body's detoxification mechanisms are able to deal with low-level insult, but saturate at higher levels. For genotoxic carcinogens it is assumed that there is some probability of adverse outcomes at any level of exposure (non-threshold).

A benchmark dose is a dose that corresponds to a particular standardized level of risk. For non-genotoxic chemicals, the most common type of benchmark doses are those corresponding to *notional zero risk*, derived from a *No Observable Adverse Effect Level* (NOAEL) – the highest dose at which no response is seen when considering the most sensitive endpoint in the most sensitive species. For genotoxic carcinogens benchmark doses are more likely to be related to a particular probability of cancer, such as *an excess lifetime cancer risk of one in one million* or to the slope of the dose-response curve, often expressed in terms of *carcinogenic potency*.

The simplest of benchmark doses is the LD_{50} – the single administered dose that will result in death for half of the exposed population. Benchmarks such as this can be used for risk ranking in one of two ways, either the chemicals can be ranked on their LD_{50} values or the exposure situation can be ranked based on comparison of the exposed dose to the LD_{50} or another benchmark dose.[5-7]

Severity and Toxicological Endpoints

Chemicals may elicit a range of reactions from the human body ranging from transitory changes in enzyme levels to major organ failure and death. The response may also depend on the magnitude of the dose, the shape of the dose-response curve and the reactive characteristics of the chemical. Risk ranking of chemicals may treat severity in one of two ways. The toxicological endpoints may be graded, with certain endpoints being considered to be more severe than others.[8,9] This approach requires certain value judgements to be made, such as *is cancer more or less severe than kidney failure?* The other approach is to treat different toxicological endpoints separately, without any attempt to integrate across different endpoints.[2,3] Under this approach a chemical may have quite a different risk rank when considered in terms of acute toxicity, than when considered in terms of, *e.g.* the effects of chronic exposure on reproductive toxicity or neurotoxicity. Common toxicological endpoints used in this approach include:

- Acute toxicity
- Short-term toxicity
- Subchronic toxicity
- Chronic toxicity (non-cancer)
- Carcinogenicity
- Mutagenicity
- Reproductive and developmental toxicity
- Neurotoxicity
- Allergenicity

Ranking – bringing it all together

The preceding sections have discussed three potential criteria for chemical risk ranking: the inherent hazard of the chemical with respect to various toxicological endpoints, the severity of potential toxicological endpoints, and the level of exposure of the population of interest. Development of a ranking methodology requires decisions on which criteria to use and how to assess them to achieve a ranking.

Surprisingly, many attempts to rank or classify chemicals deal with only two of these three criteria at most. Ranking approaches generally fall into two groups: scoring methods (where the diverse information is used to generate a scaled numerical score for the risk due to the chemical) and categorization methods (where the chemical is assigned to a risk category based on the available information).

Scoring Approaches

Scoring approaches have been popular in the large number of environmental risk ranking exercises that have been carried out.[8] These assign a numerical value to a ranking criterion and then combine across different ranking criteria with or without weighting.

The EU has developed a chemical risk ranking method (EURAM), primarily for setting priorities in relation to high production volume chemicals (HPVCs).[7] The human health ranking component of EURAM generates a human exposure score (HEX), which is derived from an estimate of emissions and a distribution factor, related to the volatility of the chemical. HEX is scaled to give a value between zero and 10. A human health effect score (HEF) is also assigned based on the *worst* health effect resulting

from exposure to the chemical – also on a scale of zero to 10. The combined exposure and effect score (HS) is the product of HEX and HEF. This approach does not consider the dose-response characteristics of the chemicals and, hence, whether HEX is sufficiently high to result in the effect represented by HEF.

Categorization Approaches

The WHO have used a single endpoint - acute toxicity measured by the LD_{50} - to classify pesticides by hazard, using rodent bioassay data. A weight of evidence approach has been used by the International Agency for Research on Cancer (IARC) for potential carcinogens. The IARC classification scheme assigns categories to chemical substances and mixtures based on the level of evidence for the carcinogenicity.

The OECD has developed a broader approach, using a wider range of endpoints. Their classification system for human health and environmental hazards of chemical substances and mixtures[2] considers chemicals in terms of nine toxicological endpoints: acute toxicity, skin irritation/corrosion, eye irritation/corrosion, respiratory or skin sensitization, mutation in germ cells, cancer, reproductive toxicity, specific target organ oriented systemic toxicity following a single exposure, and the same following repeated exposure. Within each of these systems chemicals are categorized based on the dose required to reach the endpoint, the weight of evidence that the chemical is able to cause the specified endpoint, or a combination of both.

Weight of evidence is generally determined by *expert judgement*. This is a common approach used to synthesise diverse information in risk ranking exercises and is widely used for them.[1]

The Society for Environmental Toxicology and Chemistry (SETAC) took a more systematic approach to the use of quantitative data for categorization.[3] They considered three human health endpoints, namely acute, sub-chronic/chronic, and carcinogenicity. For each endpoint, a measure or a range of measures were selected and the potential range segmented to produce ranking categories based on hazard potency. For example, in one approach for subchronic/chronic toxicity the oral *No Observed Effect Level* (NOEL) range, expressed in mg/kg body weight/day, was segmented into categories of >1000, 100-1000, 10-100, 1-10, 0.1-1 and <0.1. For the carcinogenicity endpoint, chemicals are categorized into a two-dimensional matrix, one being a segmentation of potential cancer potency factors and the other a weight of evidence classification. The SETAC authors discussed the concept of aggregating ranking across different toxicological endpoints, but concluded that *it generally makes little sense to aggregate acute and extended exposure effects because they are seldom relevant to each other.*[3]

Conclusions

Categorization approaches to chemical risk ranking are most useful for preventative risk management, *e.g.* identifying suitable measures to prevent or minimise exposure of the human population. A chemical risk ranking for an actual population, *e.g.* a nation, will involve a combination of exposure and severity or toxicological criteria.

The disparate nature of criteria employed for chemical risk ranking make combination of these data problematic. For instance, how can a chemical with a high exposure level effective at low dose, but with relatively non-severe consequence, be compared to a chemical for which the exposure level is very low, the level at which it exerts its effect is low, but the consequences are severe? Many of the approaches adopted to accommodate these problems can be criticized as being *values laden*. For example, any scoring and weighting system will inevitably reflect the opinions (and hence the values) of those devising the scheme. Similarly, expert judgement approaches will be influenced by the values of the experts. As the *experts* are often from similar professional backgrounds the potential for value bias can be significant. This potential bias can be countered by running the ranking exercise using both expert and public panels and comparing results.[1]

Approaches that maintain the integrity of quantitative data would appear to be less open to criticism of value bias. Such approaches are likely to result in graphical or matrix representation of risk criteria, such as a plot of exposure against NOEL for chemicals exhibiting subchronic/chronic toxicity. Clustering of problems in such a graphical representation would provide a potential basis for risk ranking.

Acknowledgement

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Living Free-Radical Polymerization

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Introduction

At the end of the 19th century it was remarked famously that there was nothing left to discover in physics. In recent times, many chemists have had the same dismissive attitude towards free-radical polymerization (FRP). Just as with the physics forecast, so this attitude towards FRP is proving to be highly mistaken, in two major ways. Firstly, it confuses invention with scientific discovery. For example, commercial production of polystyrene began 8 years before it was recognized that the process had a free-radical mechanism. Even today the underlying science behind many market products of FRP is not well understood. So even about conventional FRP there remains much fundamental science to be unearthed. Secondly, and more importantly, far from FRP being a completely explored landscape, much new and inventive chemistry has emerged over the last two decades.[1,2] In particular, living free-radical polymerization (LFRP) has been developed,[1-3] and it promises to revolutionize polymer production. This article outlines the story of LFRP to date.

Today, many commercial polymers are prepared by conventional FRP (CFRP). The popularity of the method is high as a wide range of monomers can be used under mild conditions but one sacrifices a large degree of control over the polymer product. This is explained by Fig. 1, which shows a conceptual outline of CFRP. Radicals are continuously formed from initiator (I), and as a radical forms it quickly adds to monomer, a process that is repeated many times until at some stage a (macro)radical is converted into a *dead* polymer chain by participating in either combination, disproportionation (together called *termination*) or chain transfer. Human populations are a good analogy for this: babies are born at all times (akin to initiation), people inexorably age (propagation), and at some time they die (termination and transfer). Just as human death can occur at any age, resulting in a *distribution* of ages at death, so too the dead-chain-forming reactions of FRP can occur at any stage of a radical's life. For CFRP carried out over constant conditions, one typically obtains a Boltzmann-like distribution of molecular weights (Fig. 2). Although *average* size can be controlled through choice of reaction conditions, nothing can be done to eradicate the *polydisperse* nature of the polymer product, *i.e.* one must accept that the dead chains have a wide variety of sizes, even if they are otherwise chemically identical.

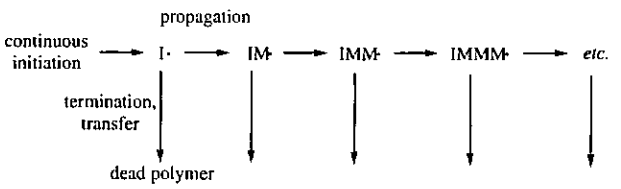


Figure 1. Conceptual representation of free-radical polymerisation (FPR). (*I* denotes the initiating species, *M* monomer, and the arrows a reaction).

Implicit in Fig. 1 is an even more important way in which CFRP is lacking: once a dead chain has been formed, there is no easy way for its growth to be reinitiated (hence *dead*!). For example, there is no easy way of forming *block copolymers* by FRP, *i.e.* polymers that consist of a long block of residues of one monomer followed by a long block of residues of another monomer. Such polymers are highly prized because they possess properties of both the corresponding homopolymers. For example, poly(styrene-*block*-isoprene-*block*-styrene) is a so-called *thermoplastic elastomer* because it behaves like a plastic (ex-styrene) and a rubber (ex-isoprene). However, there is no easy way of making such polymers by CFRP.

With the above in mind one can grasp the impetus for developing *living polymerisation* (LP). This term, defined in the 1950s to describe a chain-growth process that proceeds in the absence of irreversible chain-termination and chain-transfer steps,[4] provides only *living* chains so that after initiation chains grow in a continuous manner

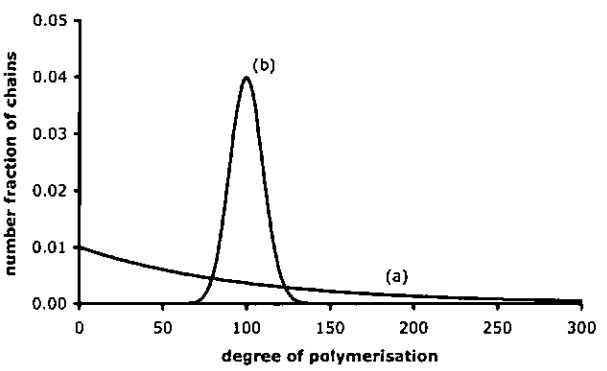


Figure 2. (a) An *exponential* distribution of chain sizes typically of CFRP over constant conditions, and (b) a *Poisson* distribution of chain sizes from ideal LP. The distributions are normalized and have number-average degree of polymerisation of 100.

until the supply of monomer is depleted (Fig. 3). If initiation is rapid on the timescale of monomer consumption, then all chains are (approximately) the same size. To use once again the analogy of human populations, this is like a multitude of babies being born at the same time: forever after they will be the same age. With LP the situation is not exactly the same, because the stochastic nature of chemical kinetics means that some chains undergo more propagation events than others. However, the distribution of sizes is still relatively narrow and, if ideal, the molecular weight distribution is a Poisson distribution (Fig. 2).[5] The distributions of Fig. 2 have a number-average degree of polymerisation of = 100. This makes it clear just how much more *monodisperse* is the product polymer of LP.

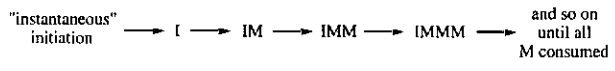


Figure 3. The concept of the ideal living polymerisation (*I* denotes the initiating species, *M* monomer, and the arrows a reaction).

A further characteristic of LP is that, even after monomer supply is exhausted, the chains remain active (unless a terminating agent is introduced). Thus one may synthesize a block copolymer simply by introducing a second monomer *after* polymerisation of the first monomer is complete. This exemplifies how LP also offers greater control over microstructure and architecture than does CFRP.

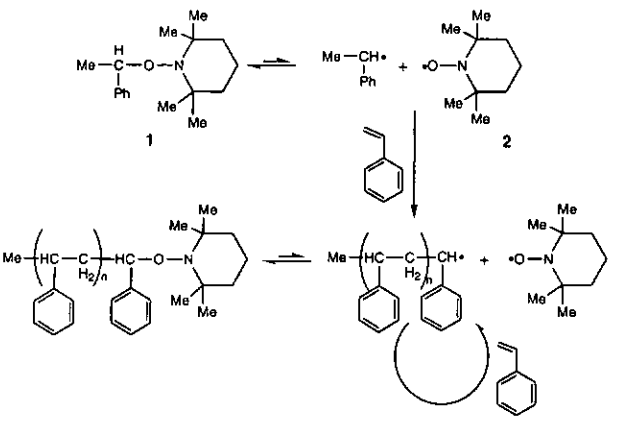
LP is most commonly realised by *anionic polymerisation* but it has two debilitating disadvantages. Firstly, it is synthetically demanding and prey to trace quantities of impurities; all reactants and solvents must be rigorously pure and the polymerisation performed under inert conditions in scrupulously-clean, sealed apparatus.[5] For this reason LP is very expensive to carry out commercially. Secondly, polar monomers undergo side reactions that lead to loss of control such that anionic polymerisation is applicable only to a small number of monomers.

For the polymer chemist the Holy Grail is facile polymer synthesis with a high degree of control of the product polymer. In general, a narrow molecular weight distribution (MWD) is desirable, and certainly it is always desirable to have control of microstructure and architecture. Thus one needs to marry the best features of CFRP (synthetically easy, widely applicable) with the best of LP (narrow MWD and control of composition and topology). For a long time it seemed that there was no way of using free radicals (which react easily and multitudinously) to mediate LP but in 1980s living free-radical polymerization emerged.

The Paradigm of Living Free-Radical Polymerisation

The key to LP is to eliminate termination. Of course it is impossible to prevent free radicals from reacting with each other but, as propagation is first order in radical concentration [R·] and termination second order, it follows that one can promote propagation over termination by lowering the radical concentration. One way of achieving this is to include a reagent that can *reversibly deactivate* a radical. Both words here are pivotal: the reagent must *deactivate* the radical so as to protect it from termination, but the process must be *reversible* so that the radical can spring back to life sporadically and grow a bit more before reverting to hibernation. After many such deactivation/ activation cycles a radical will have grown to polymeric size, and be capable of further growth as long as monomer is present; this sounds like living polymerisation!

Various reagents that more or less achieve the above paradigm were experimented with in the early 1980s.[2] However, it was not until the employment of alkoxyamines[2] by Rizzardo and coworkers in the mid-1980s that people became fully cognisant of what they were doing, and that *living* FRP (LFRP) was born. Scheme 1 illustrates the principles involved and shows how the activation/ deactivation equilibria lie toward the deactivated (*dormant*) TEMPO species **1**, (and adducts). This is because the reaction between TEMPO **2** (2,2,6,6,-*tetra*methyl*p*iperidinyl-1-*oxy*) and a carbon-centered radical is fast (close to diffusion-controlled) whereas the reverse bond cleavage is much slower (even if the bond involved is labile). Thus radical concentration is low and termination suppressed. At the same time the activation reaction remains fast enough for a long polymer to be obtained on a practicable timescale, *viz.* hours.



Scheme 1. Use of 1-phenylethyl-TEMPO **1** to effect LFRP of styrene.

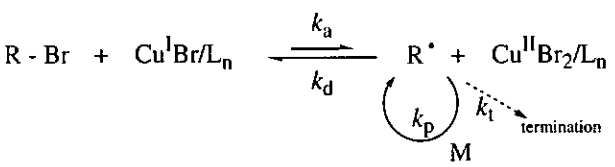
So-called *nitroxide-mediated polymerization* (NMP) was the first form of LFRP to find widespread use and, as implicit in Scheme 1, a key to its successful use is that nitroxide radicals, *e.g.* **2**, do not self-react, *viz.* they are stable free radicals as discussed below. In contrast, polymerizing radicals do react with each other even when they are present in very low concentration. Thus conventional radical-radical termination is unavoidable in LFRP, emphasizing that the process can never function as an ideal living polymerisation. Nevertheless, it has been established in (literally) thousands of experiments that successful LFRP provides polymer with a MWD almost as narrow as the Poisson distribution of Fig. 2; close enough is good enough!

Although he did not discover NMP, Hawker has been its main champion,[6] and he has invested much effort into developing an alkoxyamine that is a *universal initiator*,[7] *i.e.* one that may be successfully employed for a large

number of monomers over a wide variety of conditions. However, Hawker was never destined to succeed because, with the exception of styrenes, other superior forms of LFRP have emerged. Specifically, NMP paved the way for the development of so-called *atom transfer radical polymerisation* (ATRP) and *reversible addition-fragmentation (chain) transfer* (RAFT) polymerisation.

ATRP – Atom Transfer Radical Polymerisation

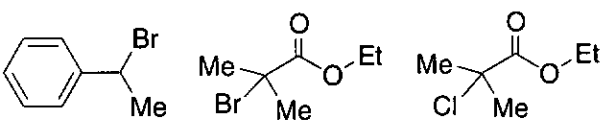
Sawamoto *et al.*[8] were the first to recognize that the activation/deactivation equilibria of Scheme 1 can be effected by transition metal complexes, using the Ru(II)/Ru(III) couple to demonstrate this. Their idea was almost instantaneously seized upon by Matyjaszewski who, without delay, showed that Cu(I)/Cu(II) systems seem to do an even better job.[9,10] The chemistry involved is shown in Scheme 2 where active radicals R· are generated when a copper(I) complex $CuBr/L_n$ undergoes a one-electron oxidation to a copper(II) complex $CuBr_2/L_n$ with simultaneous extraction of a bromine atom from an initiator R-Br. The reverse of this process is extremely fast so that the radical only has a short time to react with monomer before it is reconverted into alkyl halide. However, this cycle may occur repeatedly thereby providing LFRP.



Scheme 2. Cu-based ATRP.

Because the process of Scheme 2 is simply the application to polymerising systems of atom transfer radical addition, it has become known as *atom transfer radical polymerisation* (ATRP). By now it has been shown that many other metals can be used to bring about ATRP so that Scheme 2 is correctly described as illustrating *Cu-based* ATRP. However, Cu catalysts in ATRP are superior in terms of versatility and cost[11] and have achieved a pre-eminence such that the term ATRP is generally taken as implying the use of Cu(I). ATRP is extremely versatile because many components can be varied in striving for optimum results:[11]

Initiator - Usually an alkyl halide, *e.g.* **3**; an α-bromoester, *e.g.* **4**; or an α-chloroester, *e.g.* **5**.



3 **4** **5**

Monomer - ATRP is generally superior for LFRP of methacrylates. It has been used successfully also for the controlled polymerisation of many other monomers,[11] a selection of which are shown in Chart 1. ATRP gives good results for a greater number of monomers than does NMP.

Ligand (L) - Addition of a suitable ligand to the ATRP mixture often improves the solubility of the metal catalyst in organic solvents by forming a complex with the latter. It is the complex solubility that determines the actual

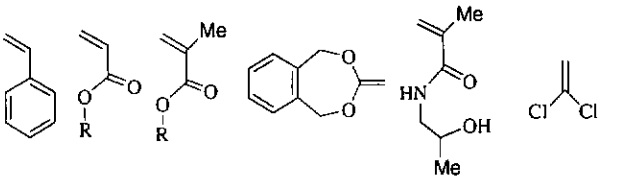


Chart 1. Monomers successfully polymerised by ATRP.

concentration of catalyst in the reaction mixture, thus affecting the position of the equilibrium of Scheme 2. In turn, this influences the polymerisation kinetics as well as the MWD of the produced polymer. The nitrogen-based ligands of Chart 2 have been used successfully in Cu-mediated ATRP with a variety of bidentate and tridentate ligands used giving polymer with a narrow MWD. The key appears to be the need for the ligand to form a strong complex with the metal centre, thus avoiding ligand displacement by solvent or monomer molecules in a labile complex.

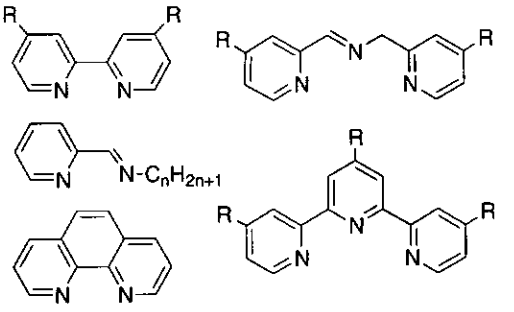


Chart 2. Ligands used for Cu-based ATRP.

Solvent - Different solvent systems affect the rate of polymerisation by altering the homogeneity of the catalyst and shifting the position of the ATRP equilibrium. In turn this may affect the polydispersity of the final product. Solvents such as MeCN, PhCN, and DMF combine high polarity with a ligand capability and the overall effect on the kinetics of polymerisation depends upon which property dominates. Additionally, the solvent must be able to dissolve the polymer that is formed.

Kinetics and Molecular Weights

As presented above the idea behind LFRP may seem obvious. However, a conundrum emerges: if the process is started by a reaction that generates radicals and stable species (nitroxide radical, Cu(II) complex, *etc.*) in equal numbers, and if cross-reaction of these products occurs essentially as quickly as self-reaction of radicals (both processes are essentially diffusion controlled), then why is it that the former reaction is so heavily favoured over the latter? In other words, how is it that LFRP works? In a series of brilliant articles, Fischer developed the answer.[12-14] In summary, it is that the extreme selectivity is a *concentration* effect rather than a reactivity effect that is at the heart of LFRP – radical-radical reaction is suppressed almost to the point of non-occurrence while cross-reaction between radicals and stable species occurs almost exclusively. What happens is that conventional radical-radical termination does occur in the early stages of LFRP, and this process is indispensable in that it depletes the radical concentration while the stable species, not being

able to self-react, rises and rises in concentration. Thus an extreme imbalance in concentration develops, and as long as this happens relatively quickly on the timescale of polymerisation, LFRP will subsequently take place. Because the situation just described relies on the production of a stable species, it has been named the *persistent radical effect*.[12-14]

For ideal living polymerisation one has that

$\overline{DP}_n = x[M]_0/[\text{Initiator}]_0$ and $PDI = 1 + 1/\overline{DP}_n$

where M denotes monomer, x is the fractional conversion of monomer into polymer, and *PDI* is the *polydispersity index* (the quantity by which the broadness of a MWD is characterized). For example, in Fig. 2 the *PDI* is 2 for the exponential distribution, is 1.01 for the Poisson distribution, and is 1 when all polymer molecules are exactly the same size. Fischer was able to show that to a reasonable approximation the two expressions given hold also for LFRP.[13,14] They are plotted in Fig. 4 and the behaviours displayed are considered the hallmark of *successful* LFRP. Firstly, there is a linear increase of average polymer size ($\overline{DP}_n$) as the reaction proceeds with the final value simply equating to the starting ratio of monomer to initiator; it is obvious how this affords easy control of polymer size. Secondly, *PDI* is low and decreases slightly during the polymerisation. In practice it is not possible to achieve a *PDI* as low as in Fig. 4, but the range 1.1-1.2 is routinely obtained with LFRP. Fischer[12-14] also derived that LFRP has an unusual dependence of monomer consumption with time: $\ln([M]_0/[M]) \sim t^{2/3}$. We have verified this prediction as shown in Fig. 5.[15]

A fascinating aspect of Fischer's recent review[14] is the historical perspective he gives of the persistent radical effect. He shows the concept to be present in organic and inorganic chemistry from the 1930s. Of course, workers were only intuitively aware (at best) of why they were obtaining such unusual preference for their particular unsymmetrical coupling reaction. Now that physical chemists have shown the concept to have a sound

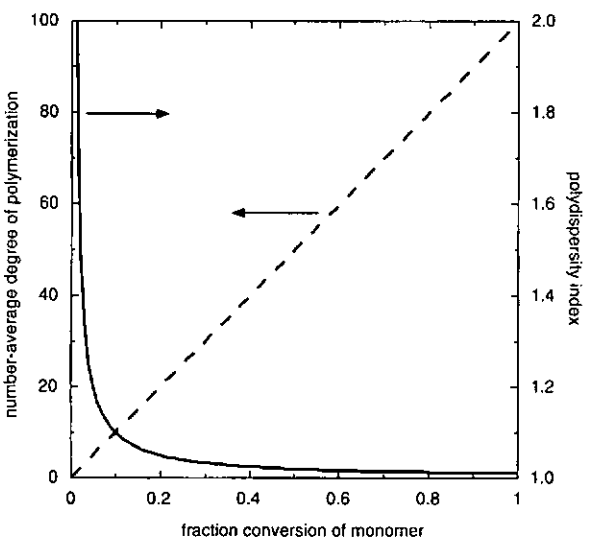


Figure 4. Evolution of the number-average degree of polymerisation (; broken line) and polydispersity index (*PDI*; full line) with fraction of monomer conversion (x) for ideal LP in which $[M]_0/[I]_0 = 100$.

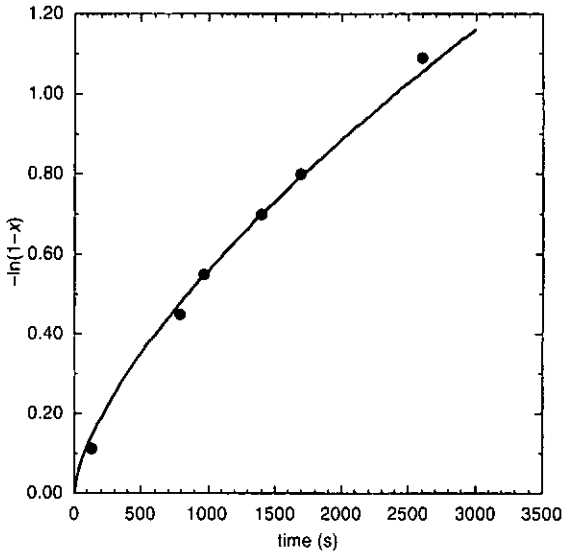


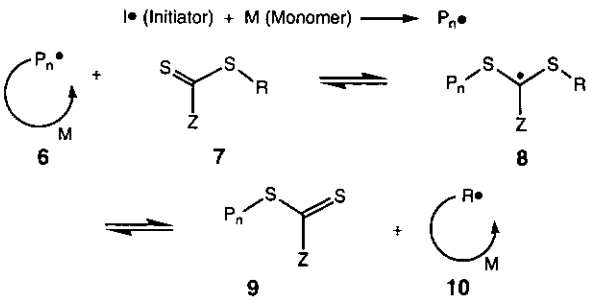
Figure 5. Kinetics of LFRP: fraction conversion of monomer x [plotted as $-\ln(1-x)$] *vs* t for measurements from an ATRP of methyl methacrylate (see ref. 15); curve: theory (see refs. 12-14).

theoretical basis and polymer chemists have demonstrated just how potent an idea it is, one wonders if it might find wider use in organic and inorganic chemistry.

RAFT – Reversible Addition-Fragmentation (Chain) Transfer Polymerisation

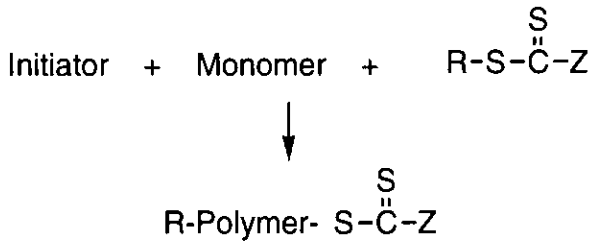
Both NMP and ATRP involve reversible *termination*. However, so-called *transfer agents* such as thiols are routinely employed in conventional FRP in order to bring about dead chain formation in preference to termination. It follows, therefore, that reversible transfer might equally bring about LFRP. The first truly successful demonstration of this was by Rizzardo *et al.* in the late 1990s using *dithioesters* (Scheme 3)[16,17] and involves reversible addition-fragmentation (chain) transfer - hence the name RAFT polymerisation.

Scheme 3 shows the generation of free radicals by a conventional free-radical initiator (as opposed to the alkyl halide and alkoxyamine initiators described earlier). The subsequent addition of the resulting propagating radical P_n (**6**) to the thiocarbonyl compound or dithioester **7** (also termed RAFT agent) results in formation of an adduct radical **8** that can fragment to a polymeric thiocarbonylthio compound **9** and a new propagating radical R• **10**; each



Scheme 3. General mechanism of reversible addition-fragmentation (chain) transfer polymerisation, as mediated by a dithioester. Note: Initiator here refers to a conventional free-radical initiator.

step is reversible. Equilibrium between the propagating radicals **6** and **10** and the dormant (polymeric) thiocarbonylthio species **7** and **9** is established. An excess of **7** (relative to initiator) is used so that at any instant the majority of polymer chains are capped by a dithiocarbonyl group and thus are dormant. Exactly as with NMP and ATRP, radicals come briefly alive, add a few monomer units, and then go back into hibernation. In this way termination is suppressed and a narrow molecular weight distribution is obtained. While all the above may seem complicated, the overall representation of Scheme 4 reveals a simpler and highly elegant picture. Indeed, it shows that RAFT polymerisation is nothing more than a conventional free-radical polymerisation to which is added a transfer agent with the special property of being able to react reversibly with radicals.



Scheme 4. Dithioester-mediated RAFT polymerisation.

Various components, *e.g.* polymerisation conditions and monomer, determine the effectiveness of a RAFT polymerisation, but the choice of the RAFT agent is the most important. Its effectiveness depends on the nature of its leaving (R) and stabilising (Z) groups (Chart 3). In a successful RAFT process there is a rapid transfer between free radical (**6** and **10**) and intermediate **8**, *i.e.* the rate of addition and fragmentation is high. The rate of addition of radicals to RAFT agents **7** and **9** depends upon the nature of the stabilizing group Z; radical stabilising groups appear to enhance the rate of addition. The rate of fragmentation is affected by the nature of the leaving group R, and it needs to be a better leaving group than the polymeric chain P_n. A number of commonly used RAFT agents[18] is shown in Chart 3. By choosing an appropriate RAFT agent, successful LFRP of a variety of methacrylates, styrenes, methacrylamides and even of troublesome vinyl acetate has by now been carried out.[19]

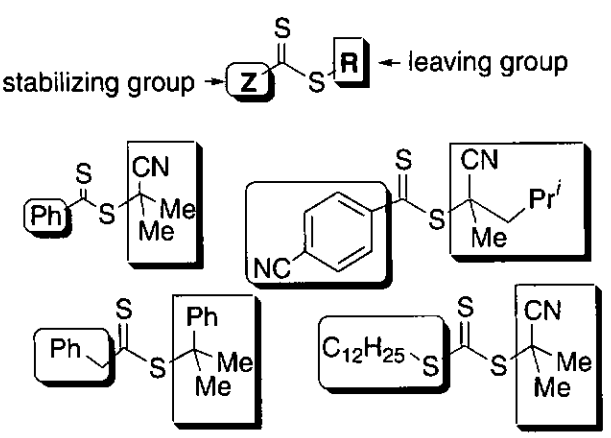


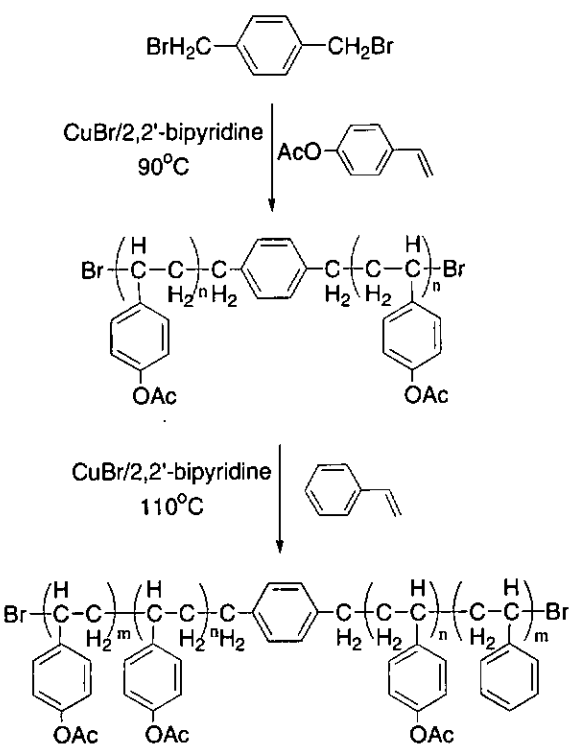
Chart 3. General representation of a RAFT agent (upper) and some RAFT agents currently used in polymerization of methacrylates and methacrylic acid.

One should properly refer to the process as dithioester-mediated RAFT, because there are other compounds that act as reversible chain transfer agents, *e.g.* xanthates and dithiocarbamates.[19] In fact the xanthate promulgators refer to their system as MADIX – *ma*cromolecular *d*esign via *i*nterchange of *x*anthates – as if the paradigm involved were distinct. Of course it is not, for they are simply performing xanthate-mediated RAFT. But this does give a feeling for the extraordinary versatility of RAFT.

Macromolecular Design

In addition to giving a narrow distribution of polymer sizes and great control of the average size (Fig. 4), LFRP also affords unprecedented command over other aspects of macromolecular design. This is illustrated well by Scheme 5, which shows the use of ATRP to synthesize a *triblock* copolymer.[11,20] From this example one can readily envisage how easy it is to use LFRP for the synthesis of *graft copolymers, e.g.* by carrying out ATRP from halogen atoms incorporated along a polymer; *star polymers, e.g.* by carrying out ATRP using an initiator with 3 or more halogen atoms; *functional polymers, e.g.* by use of an initiator that also contains a desired functional group; *etc.* Of course these are accomplished with control also over size (of block, graft, arm, *etc.*). This newfound capacity to tailor macromolecular design is leading to many novel polymeric materials and thus promises an age of 'smart' polymers (see below). A vast literature on this exciting aspect of LFRP has arisen, and the reader is referred to notable reviews for many spectacular examples of macromolecular architectures now possible.[1,3,6,11]

Because of the above, LFRP is sometimes called *controlled free-radical polymerisation.*[3,9,10] While there is no disputing that LFRP opens many new doors in this regard, the term



Scheme 5. Poly(styrene-*block*-4-acetoxystyrene-*block*-styrene) synthesis using ATRP (see refs. 11, 12).

controlled FRP is misleading in that complete control of macromolecular design is not offered, and it implies that conventional FRP lacks control. In fact, the latter is not the case, *e.g.* with CFRP one can control average molecular weight and average copolymer composition, one can incorporate functionality by use of an initiator or chain transfer agent, and one can create different architectures. What LFRP offers is the capacity to do these things even better.

Polymer Therapeutics

Of many possible applications of LFRP only one is discussed here, namely *polymer therapeutics*. It is an area examined at the University of Canterbury.[18] Ringsdorf's seminal idea[21] was that by attaching a drug molecule to a polymer, the efficacy of the drug could be increased, through what has become known as the EPR effect (enhanced permeability and retention).[22] A number of polymer therapeutics are approaching clinical development,[23] but progress would be promoted by an ability to synthesize polymer components of uniform size. This is because cellular uptake of small conjugates is disfavoured, and the kidneys cannot excrete conjugates that are too large. Thus there is an optimum size of about 20-30 kDa for *all* conjugates.[22] Furthermore, regulatory authorities frown on pharmaceuticals that consist of molecules of a variety of sizes. Because LFRP can deliver polymers of close-to-uniform size, the potential for better polymer therapeutics exists, which would lead to superior treatments for cancer and other diseases.

In employing LFRP, we and others find that ATRP and RAFT are not the panaceas that their advocates make them out to be. Poly(2-hydroxypropyl methacrylamide), the drug-carrying polymer of choice, is not obtained in controlled size by either LFRP method, but better recipes are being developed with time. Our feeling is that RAFT is the more user-friendly and versatile synthetic method and is perhaps the one of greater long-term potential.

Conclusion

In less than ten years, the original papers on ATRP by Sawamoto *et al.*[8] (Ru) and Matyjaszewski and Wang[10] (Cu) have been cited 827 and 1044 times, respectively (to 20 January 2005). These numbers indicate an extraordinary interest in LFRP from within the polymer science community and beyond, with people from outside areas, *e.g.* the biomedical community, sensing the new opportunities on offer. Of course practical issues remain. For example, polymers made by ATRP need to have *all* metal removed from the product before sale, while the colour of RAFT agents means that post-polymerisation decolouration of commercial products is needed. Such problems can be overcome and LFRP processes are already being commercialised. In the coming era of smart materials, LFRP will be to the fore because of its ability to deliver polymers of precisely controlled architecture, functionality, and size. Free-radical polymerisation is not a closed book; it *lives*, literally.

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Editorial

We frequently hear pessimistic predictions for the future of chemistry, but I believe that there are encouraging signs for its future in New Zealand.

The number of university level chemistry students has shown a steady increase over recent years. Much of this increase has been at the first year level, indicating that chemistry is seen as an important basic component in several degree courses. Increases in advanced and postgraduate chemistry student numbers have been smaller, although more substantial increases have occurred in some areas of the subject, particularly those such as organic and medicinal chemistry, which lie at the interface of chemistry and biology. In a *CHEM NZ* article last year, Jan Giffney pointed out that the proportion of students sitting Bursary chemistry had not decreased over the previous eight years, and that there was a significant increase in the absolute number of such students. Last year the results of the New Zealand's first research assessment exercise (Performance-Based Research Fund: PBRF) were published with chemistry as one of the higher ranked subject areas (6th of 41 subjects).

There has been a considerable investment in the infrastructure for chemistry teaching and research. Most of the university chemistry departments have been refurbished recently to modern standards, and upgrades of some of the essential major items of equipment necessary for the study of chemistry (NMR, XPS, X-Ray Diffraction, *etc.*) are currently underway in several centers.

Major government research contracts have been awarded in chemistry-related areas such as materials science, which received a considerable boost with the award of the 2000 Nobel Prize in Chemistry to former New Zealander Alan MacDiarmid and two of his co-workers. The resulting publicity has tended to counter the negative image that is sometimes associated with chemistry, and there are other positive signs that this process is continuing. For example, excellent promotional work is done by Allan Blackman in his monthly topical chemistry column *Chemistry Matters* in the *Otago Daily Times*, and is reproduced on the University of Otago web site. Another example is a recent article in the *Sunday Star Times* on developments in research on superacids by Professor Chris Reed, a New Zealand graduate at the University of California.

Employment opportunities in chemistry are increasing. For example, a major Australian pharmaceutical manufacturing company will move all of its operations from Sydney to Auckland this year (following the example set by this President several decades earlier, even to the extent of moving from the same Sydney suburb!). On a lighter (and musical) note, a British pop group that recently performed in New Zealand calls itself the *Chemical Brothers*. The reasons for their doing so probably don't bear close scrutiny, but we might at least take some hope from the fact that young people are encountering the word *chemical* in other than a negative context!

Given these positive signs for our subject, what are the prospects for the Institute? In several articles last year our Immediate Past President, Andrew Brodie, posed searching questions about the future of the NZIC, and these concerns were discussed at Branch and Council meetings last year. After considerable discussion and input from members, it was decided not to implement the more radical changes that had been proposed, such as a change in the name of the organization, or a focus on operation at the National rather than at the Branch level. One of the clearest responses from the Branches was the importance of the Institute's operations at that level, and the clear message to Council is to find ways in which it can assist and enhance Branch activity.

Council will now assign areas of responsibility (specialist groups, prizes and fellowships, conferences, publications, web site, chemical education, strategic planning, membership, *etc.*) to individual Council members for liaison directly with Branch representatives to strengthen the link between Council and the Branch. Concerns about the future of the Institute derive from its declining membership; clearly our main priority is to address this question and find a solution. As a member of the national chemical societies of New Zealand, Australia, and the UK I can clearly see the comparatively difficult task that we face with our much smaller population base. However, I am sure that the benefits of membership (see A. Brodie, *Chemistry In New Zealand*, **2004**, *68*(3), 6-10) are as valid today as they have been in the past. Our main challenge is to make these benefits clear to members and prospective members, to enhance them, and to find other areas where we can improve the status of the NZIC and the benefits of membership. Council is always keen to hear members' views on these matters, and encourages you to discuss them with your Branch Delegate.

Graham Bowmaker, NZIC President 2005

IUPAC NEWS

New Online Submission And Peer Review System For PAC

An online submission and peer-review system has been implemented for Pure and Applied Chemistry. The new web-based workflow for manuscript handling will enable Scientific Editor James Bull to implement peer review of manuscripts from IUPAC-sponsored conferences and also provides support to John Lorimer and Bernado Herold, editors of IUPAC recommendations and technical reports and respectively chairperson and secretary of the Interdivisional Committee on Terminology, Nomenclature and Symbols. <http://www.iupac.org/publications/ci/2005/2702/pac7_online.html>.

IUPAC Prize For Young Chemists - 2006 Solicitation

The IUPAC Prize for Young Chemists has been established to encourage outstanding young research scientists at the beginning of their careers. The prize will be given for the most outstanding PhD thesis in the general area of the chemical sciences, as described in a 1000-word essay. Deadline: February 1, 2006 - for entrants that receive their PhD (or equivalent) degree during the calendar year 2005. <http://www.iupac.org/news/prize.html>.

supporting chemical sciences

NEWS

About the President
Professor Graham Bowmaker

Graham Bowmaker showed an early fascination with chemistry as a pupil at Canterbury Boys High School in Sydney (the not so well known school where the current prime minister of Australia was educated) with school experiments often followed by more adventurous explorations of the subject in his father's workshop at the back of the family home in Sydney (with only one unexpected explosion). He gained BSc (Hons) (1964) and PhD (1968) degrees from the University of Sydney, was appointed to a Lectureship at the University of Auckland and is now Professor of Chemistry and Head of Department. He is a Fellow of the RSNZ, RSC, and RACI. He has held visiting appointments at the Universities of Oxford and Durham and the Technical University of Munich.

His main research interest is molecular structure and bonding from magnetic resonance and vibrational spectroscopic studies. He has worked mainly on inorganic-based materials, particularly those involving the coinage metals, but also has interests in organic materials such as electrically conducting polymers.

He has been involved in a range of NZIC activities (Auckland Branch Committee and then its Chairperson, Secretary of the Inorganic/Organometallic Group and Chairperson of the Physical Chemistry Group. He is the New Zealand Representative of the RSC, a position that involves the appointment of, and programme for, the RSC Australasian Lecturers. He is a strong believer in the importance of the national chemical societies in promoting chemistry and in developing professional links between practising chemists.

NZIC Prizes

Council is pleased to announce and offer its congratulations to the recipients of the 2004 prizes. The 2004 Nufarm Prize for Industrial and Applied Chemistry is jointly awarded to **Drs. Richard Furneaux** and **Gary Evans** of Industrial Research Limited. The 2004 Hort Research Prize for Chemistry is awarded to **Professor David Officer** of Massey University and the 2004 NZIC Chemical Education Award is made to **Dr. Suzanne Boniface** of St. Margaret's School, Wellington.

Closing date for the 2005 Prize nominations/applications is 30 June 2005 and includes the Easterfield Award [for which a period of 10 years post-latest degree (up to PhD) work applies]; conditions and full details appear on the web site: <www.nzic.org.nz>.

New Fellow

Council is delighted to announce election to Fellowship of **W. F. Grayson** (Auckland).

By-Line Competition

The winning by-line adopted from the competition entries is ***Supporting Chemical Sciences*** submitted by **Dr. Kate McGrath** (Wellington Branch) who receives the $100 prize.

Presidential Report

Professor Andrew Brodie's *2004 Presidential Report* and the *Audited Accounts* for the operation of NZIC, as accepted at the 2004 AGM, are now available for perusal on the web site; they will no longer be published in *Chemistry in New Zealand.*

11th Asian Chemical Congress (FACS)

This congress, scheduled for August 24-26, 2005 in Seoul (Korea), encompasses a Federation of Asian Chemical Societies General Assembly. Any NZIC member planning to attend the Congress and willing to serve as NZIC representative is asked to contact the President <NZIC.President@NZIC.org.nz>; registration and other benefits can apply.

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Auckland: Chair: **Brent Copp**; Secretary: **Gordon Miskelly**: Treasurer: **Alistair Nielson**; Council Delegate: **Gordon Rewcastle**; Branch Editor: **Alastair Bingham**.

Waikato: Chair: Bob Wilcock; **Secretary:** Kitty Lee; **Treasurer:** Michael Mucalo; **Council Delegate:** Richard Coll; **Branch Editor:** Michele Prinsep.

Manawatu: Chair: Jeremy Dombroski; **Secretary:** Justin Bendall; **Treasurer:** David Shillington; **Council Delegate:** Grant Boston; **Branch Editor:** Ben Mulchin.

Wellington: Chair: Ken MacKenzie; **Secretary:** Kate McGrath; **Treasurer:** Alan Turner; **Council Delegate/ Branch Editor:** Brian Halton.

Canterbury: Chair: Jan Wikaira; **Secretary/Council Delegate:** Rebecca Hurrell; **Treasurer/Branch Editor:** Cassandra Hinton; **Events Coordinator:** Andy Pratt.

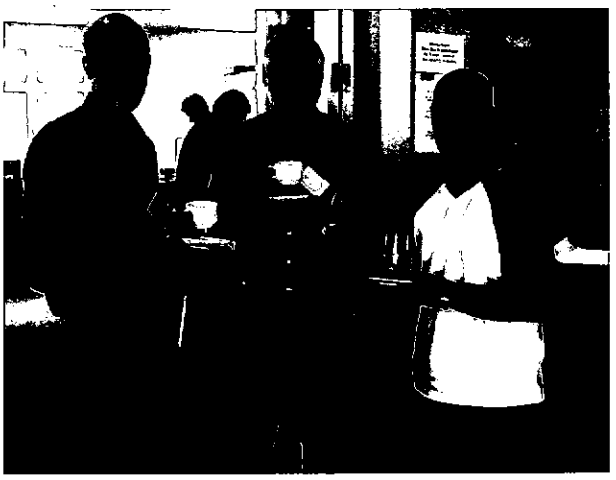
Otago: Chair/Council Delegate: **Allan Blackman**; Secretary: **Lyall Hanton**; Treasurer: **Kim Currie**; Branch Editor: **Julian Eaton-Rye**.

Inorganic and Organometallic Specialist Group

The Inorganic and Organometallic Specialist Group held a conference, organised by **Owen Curnow** (University of Canterbury) with some assistance from **David Weatherburn** (Victoria University), at the Portage resort in the Marlborough Sounds in early December 2004. The more than 60 chemists from six different countries were blessed by three days of perfect weather. The mornings and the evenings were devoted to the scientific business with the afternoons free for other activities. Plenary lectures were presented by **Jim Collman** (Stanford University), **Phalguni Chaudhuri** (Max-Planck Institüt - Bioanorganische Chemie), **Bruce Wild** (ANU), **Paul Low** (Durham University), **Andy Hor** (National University, Singapore), and **Peter Schwerdfeger** (Massey University - Albany). Some 24 additional oral presentations and 32 posters made up the rest of the programme. The student poster competition was won by **Ali Hosseini** (University of Auckland) with **Robyn Abernethy** (ANU) as runner-up. Highly commended awards went to **Siew Huang Chong** (National University, Singapore), **Maryka Gaudio** (Adelaide University) and **Never Tshabang** (ANU).

Above: Portage in the Marlborough Sounds.

Above: Conference Organisers Owen Curnow (left) and David Weatherburn.



Above: Tea break at the conference at Portage.

BRANCH NEWS

AUCKLAND

The 2005 Committee was elected at the November AGM when long standing Branch Chairman **Gordon Rewcastle** retired after six years of dedicated service; he remains the Council Delegate. The new chairman is **Brent Copp**. The rest of the Committee remains largely unchanged with officers as listed above.

Professor Ted Baker (Molecular Biodiscovery, The University of Auckland) gave an inspiring overview (at the AGM meeting) of the contribution that structural analysis has made to our knowledge of biological materials, particularly enzymes. Ted outlined the historical development of X-ray crystallography and the significant pace at which improvements in the field are occurring. The more recent applications of techniques such as NMR were

also discussed. Increasingly, structural analysis is being used to gain insight in medicine and biotechnology. Ted illustrated his talk with examples of protein structures solved by his group that included an enzyme structure complete with substrate bound in its active site! Current research interests of the Centre were described including its participation in an international study elucidating the structures of the 250 or so enzymes coded by the now known genome of the tuberculosis bacterium.

The University of Auckland

Charmian O'Connor has retired from the University and been accorded the title *Professor Emeritus* in recognition of her outstanding contribution to the university over many years. **Prof. Russ Hille** (Ohio State University) visited **Bob Anderson** for two weeks in February under the ISAT Linkage programme to collaborate on pulse radiolysis studies.

Ali Hosseini won 1st prize in the Student Poster Competition at the Portage NZIC Inorganic and Organometallic meeting (see above); his poster was entitled *Calix[4]arene Linked Bis-porphyrins Designed to Host Fullerenes*. Five Auckland staff members with seven students and postdocs attended the meeting. **Anja Bierstedt** has joined the Roper/Wright research group as a Postdoctoral after completing her PhD (Technical University, Dresden) under the supervision of **Prof. Dr. Metz**. **Jan Hegelwald** (Dresden University of Technology) has joined the Polymer Electronics Research Centre to do his PhD studies on developing micro-actuators based on conducting polymers.

CANTERBURY

The 2004 fundraising cookbook, **NZIC Canterbury Branch Cookbook**, sold over 80 copies and a December rush suggested it was a popular stocking filler. Copies are still available for $5.00 from the Editor, **Michael Edmonds** <edmondsm@cpit.ac.nz>.

Barbara Thomson (Food Safety Group, ESR) gave a seminar entitled *Boys, Baked Beans, and Babies* for the Branch's JOINT October meeting with the local Branch of the Institute of Food Science and Technology. Barbara's seminar outlined work on exposure to estrogen mimics in diet and the implication of this for humans. She also detailed considerations of the chemical constituents in food that have hormonal activity, the concentrations of these in foods, aspects of gut microfloral activity that affect bioavailability, and consideration of fetal exposure. After talking about the estrogen mimics, Barbara went on to introduce the audience to the new field of *Envirogenomics*.

Dr. Alisa Roddick-Lanzilotta, Research Leader, Applied Sciences Division, Canesis Network Ltd) spoke on *Functional Personal Care Ingredients Derived from Wool* at the Branch's December meeting. She gave a profile of Keratec Ltd, a young company set up to utilize New Zealand's natural resources in creating functional ingredients for the personal care market, and detailed the science behind getting a new ingredient ready for marketing by illustrating the recently launched product, Keratec IFP.

The December Branch **AGM**, guised as a Christmas Morning Tea, raised several issues for the Branch to pursue, both locally and with Council. Several changes to the Committee occurred and we thank outgoing members for their contributions, particularly our student and postdoctoral members whose enthusiasm and commitment has been greatly valued.

Chemistry Department, University of Canterbury

The Chemistry Department has had **Dr. Hartmut Spiering** (Mainz, Germany) working with **Craig Tennant** and **Dr. Rod Claridge** over the summer months. Hartmut is a specialist physicist in single-crystal studies and synchrotron applications of Mössbauer spectroscopy, crystal physics, and low-temperature-spin-trapping optical spectroscopy. **Dr. David Charutz** has joined the Department for a sabbatical year to collaborate with **Prof. Leon Phillips** on scattering of molecules from a liquid/gas interface. David was born in Jerusalem (PhD, Hebrew University - **Prof. R. D. Levine**) and, since 1995, worked in the Israeli National Laboratory SOREQ NRC in Tel Aviv. His work includes quantum-scattering calculations on double-electronic surfaces coupled by a conical intersection. **Dr. Matthew Polson** has been awarded a *2005 FRST Postdoctoral Fellowship* to work with **Prof. Peter Steel** and will be joining the group this year. Matthew obtained a PhD from Otago in 2000 and has since held postdoctoral positions in Montreal (Canada) and Ferrara (Italy).

Prof. Peter Steel, a recipient of a *2004 University of Canterbury Teaching Award* for excellence in teaching of undergraduate chemistry, has joined the editorial board of the *Journal of Coordination Chemistry*, and was recently been appointed to the Physical Sciences and Engineering Marsden Fund panel. Together with Cameron Kepert (Sydney), **Keith Murray** (Monash) and **Hans Toftlund** (Southern Denmark), he has been awarded an *Australian Research Council Discovery Grant* of $A925,000 over five years for a collaborative programme entitled *Polynuclear Spin-Crossover Molecular Switches; Host-Guest Chemistry, Magnetism and Memory*. **Prof. Leon Phillips'** Onsager Project *Understanding the Gas-Liquid Interface*, was successful in gaining a 2004 *Marsden Fund* award. **Dr. Greg Russell** became chairperson of the *Polymer Division of the Royal Australian Chemical Institute* in December and **Prof. Andrew Abell** joined the editorial board of *Protein & Peptide Letters*.

The Department congratulates **Alison Downard** on her recent appointment to Associate Professor and **Dr. Owen Curnow** who was appointed to Senior Lecturer above the bar.

Several students have recently completed their studies and taken up postings. **Marie Squire** has assumed a postdoctoral position with **Dr. Ben Davis** (University of Oxford) to investigate the synthetic potential of glycosyltransferases in the construction of glycoproteins. **Liz Reid** has gained a position with Fonterra in Palmerston North, **James Cambridge** and **Sean Devenish** have stayed on in the Department, and **Kim Van Berkel** is assisting with the Outreach programme. **Greg Francis** has been

awarded a *TIF Fellowship* to pursue PhD research with the ion-molecule group under **Prof. Murray McEwan's** supervision and **Anna McConnell** was awarded a UC Summer Scholarship for work with **Dr. Richard Hartshorn**; **Jocelyn Starkey** has been awarded a Carlisle Trust Scholarship.

The Department was successful in securing 2005 *University Canterbury Doctoral Scholarship* - to **Sam Edwards** and a *University of Canterbury Research Award* - to **Jennifer Burgess**.

Syft Technologies Ltd, the spin-off company undertaking the commercialization of SIFT-MS for trace gas analysis, won the *Most Innovative/Best Product* award for 2004 at the *Westpac High Tech Awards.*

ESR

In late 2004, ESR welcomed to its staff **Dr. Lou Gallagher** who has over 15 years experience as a toxicologist, research scientist, environmental risk assessor, and epidemiologist. Lou is based in the Population and Environmental Health group in Wellington. Christchurch-based ESR groundwater scientist **Murray Close** was invited to become an adjunct Senior Fellow in the Department of Geological Sciences at the University of Canterbury in November 2004.

MANAWATU

Fonterra

Dr. Lawrie Creamer, Principal Research Scientist at Fonterra's marketing and innovation division in Palmerston North has been awarded the world's top dairy honour for his contribution to the industry as announced by the *International Dairy Federation* (IDF) at its annual conference in Melbourne in association with the Global Dairy Summit. Lawrie is the first New Zealander to be awarded the *IDF Award*, which he shares with **Prof. Resmini** (Food Science & Technology, State University of Milan).

Dr. Creamer, a milk protein chemist with a distinguished career in dairy science spanning more than forty years, joined the then NZ Dairy Research Institute, as a protein chemist in 1963 after graduating with a PhD from the University of Canterbury. At that time the New Zealand dairy industry was facing a major challenge – the prospect of the UK joining the EEC and the loss of its previously secure market for dairy products. This prompted a substantial change of direction at NZDRI, with the addition of a team of internationally trained scientists and technologists to build the science and technology needed to diversify into new markets with products that suited those markets.

> *"The only significant exports in 1960 were a salted butter and a Cheddar cheese to feed post-War Britain* says Dr. Creamer. *It was a bit of a gamble to invest in a nucleus of young research scientists but the dairy industry's survival depended on the development of new and often unique products and techniques and it paid off".*

Lawrie's early work led to many improvements in the manufacture of traditional dairy products such as cheese and milk powders. A major focus was to influence the industry to manufacture consistently high quality Cheddar cheese and to develop a range of non-Cheddar cheeses. His innovative studies on the relationship of texture and flavour in cheese helped define its compositional characteristics. He attracted a group of scientists and the team tackled a number of the basic questions in dairy chemistry such as, *What happens when milk is heated?* and *How does that impact on a product?* The team's fundamental work on milk protein structures has not been surpassed, led to the Miles-Marschall Award in 1984, and established the New Zealand–led team as the pre-eminent research group in this area.

Since 1990, when he was appointed Principal Research Scientist, Lawrie has focused more intensively on the structure of the major whey protein, ß-lactoglobulin, and the effect on it of heat and its ability to bind vitamins. He says his later work reflects the separation of protein science into the more practical studies on cheese, milk protein products and milk powder, and the examination of the more fundamental basis of the interactions between the milk proteins that will drive development of value-add products with the characteristics major dairy customers want.

Recent research, in collaboration with scientists from the Massey University Riddet Centre and **Profs. Lindsay Sawyer and Paul Barlow** (Edinburgh University), showed that there are high temperature changes to the structure of ß-lactoglobulin to form a new protein that reacts with smaller milk proteins. This forms the basis for the heat stability of milk powders and slower coagulation of heated milks.

Lawrie is a Fellow of NZIC, a former Editor of this *Chemistry in New Zealand*, and was awarded the NZIC *ICI New Zealand Prize* in 1973. He was elected a FRSNZ in 1995 and awarded the Royal Society RJ Scott Medal in 1999. He is married with three sons and a daughter and, in keeping with his strong community service ethic is a Justice of the Peace.

Massey University

It was a great pleasure to welcome the **Rt. Hon. Helen Clark** to the Institute of Fundamental Sciences on 9 December 2004 to officially open the 700 MHz NMR. A welcome in the Marsden Lecture Theatre by the Vice Chancellor **Prof. Judith Kinnear** preceeded the official unveiling of the plaque outside the entrance to the NMR area. **Prof. Geoff Jameson** must take a great deal of the credit for putting the business case for the NMR instrument together; **Dr. Steven Pascal** has been appointed as Research Director of the BioNMR Laboratory.

The prestigious RSNZ Thomson Medal was awarded to **Assoc. Prof. John Ayers** *in recognition of his outstanding contribution to the application of science and technology.* John's development and application of ion exchange resins, for which 12 patents are in place, has been phenomenally successful. The resins are used by the dairy industry worldwide, especially for the recovery of whey protein

for hum consumption.

Above: New lecturer Paul Plieger.

Prof. David Officer and **Assoc. Prof. David Harding** have both been awarded NZIC Fellowships. **David Officer** is clearly on a roll at present with his Fellowship, the HortResearch Prize, and his Marsden award! This follows on from **Geoff Jameson's** success last year when the HortResearch Prize was known as the SGS Medal. Former postdoctoral fellow **Paul Plieger** has been appointed lecturer in analytical chemistry, previously working with **David Officer** and **Tony Burrell** after completing his PhD at Otago with **Sally Brooker. Patricia Shields** is now a teacher at Manawatu College in Foxton and **Malcolm Pahl**, having performed similar duties at Otago University, replaces her in the 100 Chemistry Lab.

A special farewell was held for **Paul Buckley** and **Len Blackwell** in December. Both have retired following 36 years of loyal service to Massey, each having made special contributions to teaching and research. Their combined farewell function featured the IFS/IMBS choir singing all of the songs composed by Paul over the years to farewell other members of staff! Paul led our Publicity Committee outstandingly, was also been an outstanding teacher and a recipient of the IFS Distinguished Teaching Award. Len made a number of specific contributions to research, especially in his ideas; against innumerable obstacles he showed great determination.

Monday 15 November 2004 saw a large group of postgraduates and staff head to Wellington for the annual Victoria/Massey Chemistry Student Symposium. The oral presentations began after morning tea and concluded in the afternoon with awards for the most original abstract, the talk with the coolest pictures, and the best overall talk decided by audience vote (to **John Ryan**, VUW, for the talk containing the least chemistry). Our own **Geoff Jameson** won the prestigious prize for the most questions asked!

OTAGO

The Otago Chemistry Department began 2005 under new management, with **Keith Hunter** taking over from **Jim Simpson** as HoD. Jim has been in charge since 1998 and has chosen this year to take a well-earned sabbatical both here at Otago and overseas. He has recently been instrumental (no pun intended) in obtaining funding for a new Bruker Apex diffractometer which is due for delivery in April. **Lyall Hanton** is currently training to be our diffractometer guru, which has involved a couple of lengthy stays at Canterbury under **Ward Robinson's** tutelage, and a trip to Karlsruhe will follow delivery of the machine.

Four students, **Marco Klingele**, **Julia Hausmann**, **Rongqing Li** and **Yanhua Lan** completed their PhDs in Brooker's Bunch during 2004. In July 2004 Rongqing (thesis in hand), Lan (full first draft of thesis in hand), **Dr. Markus Weitzer** (PhD under **Prof. Siggi Schindler**), **Dr. Jason Price** (PhD under **Prof. Len Lindoy**) and **Sally Brooker** represented Otago at the International Symposium on Macrocyclic Chemistry in Cairns. Sally went on to spend three months as a Visiting Professor in Karlsruhe with **Prof. Annie Powell**. While there she continued her slow recovery from major ear surgery, worked on a number of manuscripts that included a *Chem. Comm.* half-spin crossover paper featured on the front cover (with **Michael Crawford**) - and just out in perfect timing for her birthday! She also enjoyed a visit from her former postdoc **Dr. Udo Beckmann** (who has begun Habilitation in Dusseldorf) and establishing collaboration with **Prof. Philipp Gütlich** in Mainz. On the way home she visited **Prof. Han Vos** and **Dr. Grace Morgan** (Dublin) and **Vickie McKee** (Loughborough). Lan completed her PhD in Sally's absence with a successful oral once Sally was back in December – congratulations Lan! Currently **Vickie McKee** is visiting for March and April and **Dr. Grace Morgan** and visited in February 2005. **Jon Kitchen** has joined Brookers Bunch for his Honours project on iron triazole complexes and **Vikas Aggarwal** (Karlsruhe) is to join us for a 5-month project on porphyrin-like complexes. **Dr. Robyn Handel** (PhD with **Prof. Ed Constable**) has just heard that she, her husband, and their daughter have been granted permanent New Zealand residency – congratulations to you all! Sally has a Marsden-funded PhD scholarship on *Controlled self-assembly of arrays of communicating transition metal ions* available to a suitable candidate.

Henrik Kjaergaard has been promoted to Assoc. Prof. His former PhD student **Timothy Robinson** is now working with the Manchester Super Computer Center, and new students **Joseph Lane** (PhD study funded by a Top Achiever Doctoral Bright Future Fellowship), **Ben Miller** and **Charles Champness** (MSc) have joined him. Collaboration with **Terrence Quickenden** (Perth) was included in an article entitled *H_2O-HO radical complex unveiled* in the January 31 issue of *C&EN*. Henrik's student **Daryl Howard** attended the 5th RACI Student Conference on Physical Chemistry in Wagga Wagga, where he presented a talk on *Hydrogen Bonding in Antifreeze: Vibrational Spectroscopy of Ethylene Glycol.*

Late last year **Keith Gordon** attended (with RSNZ support) the International Workshop on Quantum Transport in Synthetic Metals & Quantum Functional Semiconductors (QTSM & QFS 2004) in Korea. This workshop focussed on the unusual behaviour of semiconductors and conducting plastics, with Keith one of about 35 invited speakers (including Nobel Laureate **Alan Heeger**). In early February a number of Keith's group attended the Advanced Materials and Nanotechnology (AMN-2) conference in Queenstown. Run over a week, the meeting included **Cushla McGoverin**'s talk entitled *Predicting non-linear optical properties in push-pull molecules using vibrational spectroscopy and density functional theory* on work in collaboration with **Drs. Andy Kay** and **Tony Woolhouse**

(IRL) and **Keith Gordon** gave one on work with **Prof. David Officer** (Massey University) on *Experimental and computational studies of substituted terthiophene oligomers as electroluminescent material.* Posters were presented by: **Tracey Clarke**, **Natasha Lundin**, and **Penny Walsh**. In late February Cushla received a Bright Futures Scholarship for research on Raman spectroscopy-based chemometric analysis, which she will start in April. The group has also welcomed **John Earles** for his Honours project on extended terthiophene systems.

The 14th Queenstown Molecular Biology Meeting (organized from Dunedin) at the end of November last was combined with the Annual Meeting of the NZSBMB. Otago Biochemistry students **Andrew Cridge** and **Martina Jaenicke** won QMB poster prizes and **Rob Day** won an NZSBMB poster prize. The John Morris student speaker award was won by **Amy Dear**, a PhD student in the Molecular Pathology Lab in Christchurch.

WAIKATO

NIWA

Trevor Mathieson worked at the University of Munich for 3-months from October, supported by an Alexander von Humboldt *Resumption of Fellowship Award.* His work focused on using an HPLC/MS with a time-of-flight mass spectrometer, elucidating molecular structures of bioactive marine extracts. In addition, two well-publicised cyanoabacterial toxins - microcystin and cylindrospermopsin - were analyzed extensively by HPLC/MS(TOF).

Prof. Bill Maher, (Canberra University), attended the NZIC-organised *Trace Metals* workshop sponsored in part by NIWA. Bill was hosted by **Michael Ellwood** and also gave a seminar at NIWA.

University of Waikato

The Chemistry Department has ordered a new electrospray mass spectrometer, a Bruker MicroTOF which adds <5 ppm accuracy in mass determination to the local capability. A new mass spectral suite will house together the existing Finnigan LCQ LCMS, the Platform II electrospray mass spectrometer, the Bruker MALDI-TOF, and the new machine.

Several former students visited over the summer. **Cameron Evans** (postdoctoral - Glasgow) is using X-ray crystallographic methods to look at electron density associated with chemical bonding. **Wade Mace** has returned from a year of pharmaceutical synthesis in Cork (Ireland) and is presently looking for a position in New Zealand. **Lea Bonnington** is in Stuttgart working in a technical support position with the mass spectrometry division of Agilent.

Prof. Steve Riethmiller (Virginia Military Institute) is visiting for three months under an ISAT grant to work on the Raman spectra of polyarsines, in a collaboration that also includes **Graham Bowmaker** (Auckland). Congratulations go to MSc students **Sarah Devoy** (who took time off from research to get married), **Karen Love**, and **Daniel van de Pas** who have become engaged.

Richard Coll recently spent some study leave in Fiji working with **Dr. Sadaquat Ali** (USP) on a number of chemical educational issues at USP, including first-year chemistry performance, learning chemistry by distance education, and differences in learning styles between ethnic Indian and indigenous Fijian students. USP and AusAid fund the research.

WINTEC

The 2005 HPLC course takes place from 19-22 April. The course, presented on the WINTEC City Campus, is in conjunction with the NZIC Chromatography Group. Shimadzu Scientific Instrumentation supplies expertise and instrument support. Theory presentations are coupled with hands-on practical group work. The theory of columns, packings, mobile phases, detectors, and quantitation will be covered. Reverse Phase (RP) HPLC practical work with a variety of mobile phases/modifiers with emphasis on understanding the processes involved inside the HPLC column.

The 13-week Block course for food science students in the dairy industry, will run from 26 April until 22 July. Students will study a range of courses, including chemistry, physics, biology, microbiology, and food science; they may be awarded a Diploma in Technology (Science) after 3 years of such course study. Also starting on 26 April is the 10-week Block course, Certificate in Dairy Technology, for dairy industry workers with the equivalent of year-12 chemistry, physics, and mathematics that enables them to continue at Massey University in the following year for the Diploma in Dairy Technology.

WELLINGTON

The November 2004 meeting comprised of a short Branch AGM followed by a delightful address to a good-sized audience by Ross Grimmett on *Art Fakes and Forgeries* - a topic on which Ross is becoming well known. The talk covered the history of art forgery, famous forgers of the past and present, how they did it - and how they got away with it for a time. We were also advised how to avoid being taken in!

The 2005-year started with an excellent lecture on *Nanoparticles and Quantum Dots* from **Dr. Richard Tilley** (VUW). Nanoparticles are crystals less than 100 nm in size and hold much promise for new applications in nanotechnology because of their exciting and unique properties. The properties differ from those of bulk materials because of this small size. A general overview of nanoparticle research was given, focussing on semiconductor nanoparticles that are also known as quantum dots. Richard originates from Wales, received his undergraduate training at Oxford, and his PhD in Chemistry from Cambridge, where he specialised in transmission electron microscopy of nanoparticle systems. Following a period of postdoctoral research in the Toshiba Labs (Tokyo), he joined the academic staff of the SCPS at

Victoria a year ago; he is also in charge of the MacDiarmid Institute electron microscopes.

Industrial Research Ltd.

Cees Lensink and **Graeme Gainsford** attended and thoroughly enjoyed the NZIC INOG meeting at Portage in December (2004). Highlights included some excellent talks, making contacts with overseas (mainly Australian) scientists, enjoying some great *early* summer weather along with a chance to promote and discuss their asymmetric hydrogenation catalytic studies. The organizers picked an ideal venue, and the food set a new standard! Graeme has been awarded an ISAT Travel Grant ('05-'06) to work with eminent theoretician **Prof. Tom Ziegler** (University of Calgary). He will travel to Calgary in late May and subsequently attend the Canadian Chemical Society's annual meeting in Saskatoon to present joint results. It is hoped that Ziegler will visit New Zealand during the tenure of this grant.

Graeme Gainsford is to attend the triennial XX International Union of Crystallography Congress and General Assembly meeting in Florence (Italy) in August representing the New Zealand National Committee. He will also attend (as a current *Acta Crystallographica* Co-editor) the pre-meeting *Commission on Journal* session.

Victoria University

A recent visitor to the School was **Prof. Peter Tasker** (Edinburgh University) who provided an excellent and fascinating lecture on *High Added Value Co-ordination Chemistry by Ligand Design* - simple co-ordination chemistry applied to industrial problems!

The new academic year has seem **Almas Zayya** return from a summer studentship at ANU to begin PhD study with **Prof. John Spencer**. **John Beale** and **Teck Lim** have returned for PhD research with **Richard Tilley**, and **Mathew Cairns** has joined the **Johnston/Borrmann** applied chemistry group. Otago import **Lynton Baird**, who secured a Bright Futures Scholarship, has joined **Dr. Joanne Harvey**. **Lilly Campbell** and **Mathew Cairns** have returned to complete the research component of their MSc degrees.

NEW YEARS HONOUR FOR DENNIS HILLS

In the New Year Honours list, it was announced that Dennis Hills had been appointed an Officer of the New Zealand Order of Merit (ONZM), "for services to science and industry". Dennis has been associated with the New Zealand rubber and plastics industries for 47 years, and has set himself a target of 50 years of involvement! He has been a member of the New Zealand Institute of Chemistry for 45 years, and a Fellow since 1977.

He joined Empire Rubber Mills Limited (part of Skellerup Industries) in 1958, and rose to the position of Chief Chemist. He published articles in England from 1962, with his first book ("Heat Transfer and Vulcanisation of Rubber") appearing in 1971. He left Empire that year, and then worked for Sellotape Products (NZ) Limited until 1974, when he joined the DSIR's Christchurch Industrial Development Division. When the DSIR was disbanded in 1992, and closed its materials science operations in the South Island, he set up as a consultant, and still operates his company (Materials and Quality Consultancy Limited) on a part-time basis, dealing with non-metallic materials and QA systems.

He has been involved in research and consulting in the field of degradation of pipe materials and fittings for 40 years, in the main in relation to rubber pipe joint rings and asbestos-cement pipes. He conducted a Crown-funded project in 1996-98 on rubber joint rings and the *in situ* treatment of older rings to impart immunity to further microbial attack.

Dennis was instrumental in the formation of the New Zealand Branch of the Institution of the Rubber Industry, which existed from 1967 to 1971. Awards he has won have included the Institute's Morcom, Green & Edwards Prize (1968), the Institute/Australasian Corrosion Association's A C Kennett Award (1988 and 2001), and the Institute of Materials Hancock Medal in 1996. He has (thus far) published six books and more than 60 articles, and has presented almost 70 lectures on a variety of topics. Apart from his 1971 book, the other two on polymers have been "Basic Rubber Technology" (DSIR) in 1985 and "Plastics and Rubbers - How They May Fail" (Australasian Corrosion Association) in 1992. He is currently working on three books on local/family history, and won a heritage award in 2003 for an information/history book published the previous year on The Styx River in Christchurch. He has been active in local government, serving nine years on the Shirley-Papanui Community Board of Christchurch City, six as Deputy-Chairperson.

An interest in continuing education saw him complete a Certificate in Continuing Education in 1982 at the University of Canterbury, with an industrial education scheme for the rubber and plastics industries as his major topic. Other interests include astronomy, where he has been a member of the Royal Astronomical Society of New Zealand for 50 years.

Patent Proze

By John Landells and Helen Palmer

A NEW PATENTS ACT

After surviving more than 50 years of service the New Zealand Patents Act 1953 is drifting very close to retirement. 50 plus years of service is an extremely long time for legislation involved in the fast moving technological field. Equivalent patent legislation enacted in the UK in 1949 was replaced in 1977, and Australia performed a major overhaul of its 1952 patent legislation in 1990. After a very lengthy three-stage review process by the New Zealand Government, the long awaited Patents Bill, set to replace the Patents Act 1953, was finally released for public consultation on 20 December 2004. The Patents Bill will make its way through the select committee stage this year and is likely to be enacted into law sometime within the next 18 months.

The Patents Bill proposes many important changes from the existing law. Some alterations are still possible but the final version of the Patents Act is unlikely to look much different.

Some of the more important changes are summarized as follows:

- A patent must be novel, which essentially means the invention must not have been used or published before the patent application is filed. The current novelty standard is *local*, which means published or used *within New Zealand*. The proposed new higher standard is *absolute*, which essentially means published or used *anywhere in the world*.
- In addition to the current test for novelty, patent applications will be examined for *inventive step*. This would allow examiners at the Intellectual Property Office of New Zealand (IPONZ) to filter out patent applications that are obvious in light of what was known when the application was filed. This is a major undertaking by IPONZ and possible coordination with IP Australia has been indicated by the Ministry of Economic Development.
- IPONZ examiners will no longer have to provide applicants the '*benefit of doubt*' when assessing patentability. Patent applications are proposed to be examined on the basis of the higher '*balance of probabilities*' standard.
- Patent applicants will also be required to disclose to IPONZ the results of documentary searches conducted by overseas patent offices for corresponding overseas applications. Failure to disclose search results would jeopardize the ability to enforce the patent against infringers because amendments required to overcome prior art would not be allowed and would therefore invalidate patent claims. The obligation is similar to that required in Australia and applies to searches conducted up until the patent is granted.
- Exclusions from patentability are proposed to include the following types of inventions: where use is contrary to public policy or morality; inventions covering human beings or diagnostic, therapeutic, or surgical methods for the treatment of human beings.
- A Māori advisory committee will be formed to advise IPONZ as to whether the invention of a patent application covers and derives from Māori traditional knowledge or from indigenous plants and animals, and if so whether commercial exploitation of the invention is likely to be contrary to Māori values.
- Publication of the patent application currently occurs after acceptance, which varies but may not occur until 4 years or more from the first filing or priority date. Automatic publication is set to occur at 18 months from its first filing or priority date, in addition to publication after acceptance.
- The cheaper and expedient pre-grant opposition before the Commissioner of Patents is to be abolished. A post acceptance re-examination procedure will replace pre-grant opposition and be available to anyone before and after grant. Essentially novelty and inventive step will be re-examinable. However, unlike opposition, re-examination operates *ex parte* and does not provide a third party with any opportunity to rebut the arguments made by the applicant or patentee.
- Revocation actions will be able to be heard by the Commissioner of Patents at any time after grant on grounds currently available only to the courts. An application for revocation under the current legislation can be made to the Commissioner only within 12 months of the date of grant with the grounds being generally narrower than those possible before the Court. This proposed change will provide a permanent cheaper alternative route to challenge a patent's validity.
- Contributory infringement will be introduced, establishing that it will be an offence to supply or offer to supply anything that is an essential element of a claimed invention if the supplier knew, or ought reasonably to have known that it was suitable for and intended to be used for putting the claimed invention into effect.

John Landells

Helen Palmer and John Landells of Baldwins specialise in chemistry and biotechnology patents. Helen joined Baldwins in 2000. She has a PhD in chemistry from The University of Auckland and postdoctoral research experience. John joined Baldwins in 2003. He has a PhD in chemistry from the University of Otago and is in the final stages of completing an LLB at Victoria University of Wellington.

Helen Palmer

• A tribunal will also be established to hear complaints regarding the conduct of any registered Patent Attorney.
• The Ministry of Economic Development (MED) and the Intellectual Property Office of New Zealand are also currently in discussion with IP Australia over coordination of services, especially in order to reduce duplication of searching and examination.

The Patents Bill can be accessed on-line through the Ministry of Economic Development at <http://www.med.govt.nz/buslt/int_prop/patentsreview/draftbill/index.html>.

Traditionally New Zealand has viewed itself as a net importer of technology and drifted towards weaker patent protection. Unfortunately, New Zealand has opted for slightly weaker patent protection in the Patents Bill by providing further exclusions to patentability and by maintaining a regulatory approval exception to infringement without balancing this out with patent term extensions. Weaker patent protection discourages the importation of technology and local investment and development in new technology.

On the positive side, New Zealand's patent law is to be significantly aligned with our main trading partners, such as by providing for tougher examination procedures. However, there will still remain some significant differences with our major trading partners and any future free trade deal with the United States will require significant negotiation and comprise.

Getting the balance right with the Patents Act is very important, especially as the New Zealand Government has indicated its support of a knowledge-based economy. Strong patent protection will encourage and promote innovation and foreign investment in New Zealand. The Government's response to the Patents Bill is now keenly awaited.

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

Patent Proze
Baldwins
P O Box 852, Wellington.
Email: email@baldwins.com

Pacifichem 15-20 December 2005

Update

Abstract submission closes on the web on 13 April at: **www.pacifichem.org**

All delegates wishing to present a paper (invited or contributed, oral or poster) must submit an abstract online. Late submissions will not be accepted and every delegate will need to ensure that s/he complies with the requirements for the Technical Areas, and is aware of the type and limitation on audiovisual equipment and/or the poster board size provided. There will be a ***Student Poster Competition*** as at previous Pacifichem Congresses and entrants will need to ensure that their abstract submission is designated for entry to this.

The technical areas of the Congress that will consist of some 225 symposia, spread through 658 half-day sessions, have been published (see *Chemistry in New Zealand*, **2004**, *68*(4), 32).

Preliminary information on registration (opens on the web on 18 July 2005), visa issues, and hotels is provided on the website, and will be updated regularly as more details become available. Flights to and from Honolulu in December are limited and intending delegates are strongly encouraged to make their airline reservations as early as possible.

Should anyone require assistance please do not hesitate to contact the NZIC Pacifichem representative:
Professor Brian Halton
Ph: 04-463-5954 (direct)
Email: brian.halton@vuw.ac.nz

SALVARSAN – THE FIRST CHEMOTHERAPEUTIC COMPOUND

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Early History

If defined as the use of a specific compound discovered as the result of a systematic search for a cure for a specific disease, then chemotherapy is less than a century old. The first example was the introduction in 1910 by Paul Ehrlich[1,2] of an organoarsenic compound he named *Salvarsan*, which provided the first real cure for the extremely unpleasant disease syphilis (caused by the parasitic spirochete *Treponema pallidum*). As is well-known, the compound was also called Ehrlich 606 because it was the 606th compound tested by Ehrlich in conjunction with his colleagues Bertheim (synthesis) and Hata (biological testing) (Figs. 1 & 2).[3,4]

Figure 1. Ehrlich and Hata.

Salvarsan's origins can be traced to 1863, when Pierre Bechamp (famous for his discovery of the Bechamp process for the cheap production of aniline) isolated a compound from a reaction between arsenic acid and aniline. He characterised this compound as **1**, the anilide of arsenic acid. It was shown later that Bechamp's compound was less toxic that inorganic arsenic compounds and so it was given the informal name of *Atoxyl*.[3,4] In 1905, Thomas published a paper[5] which showed that Bechamp's compound was effective in the treatment of sleeping sickness, the greatest cause of death in Africa at the time. This paper caught the attention of Paul Ehrlich.

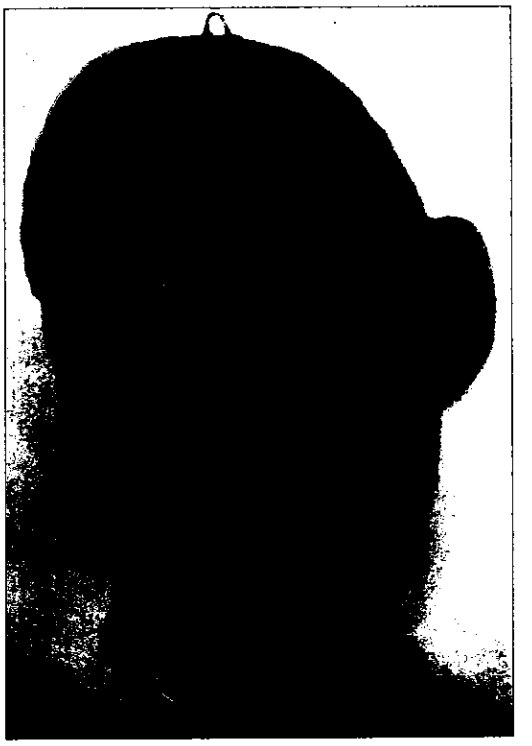
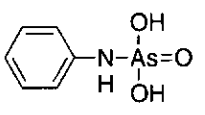
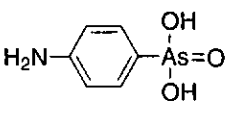


Figure 2. Ehrlich's death mask exhibited on the 150th anniversary of his birth at the World Conference on Dosing with Anti-infectives, Nurnberg, September 2004.

Ehrlich was born in 1854 in what is now Strzelin, Poland. He started his scientific career as a medical student, and became interested in the new dyes which were becoming available at the time. He started working in the field of immunology, convinced that *the body's immune system could be fortified by chemical means*. His interest in dyes – specifically their ability to selectively stain microbes – is what sparked his interest in chemotherapy. In simple terms, the idea was that if a dye could selectively target a micro-organism, and the functional groups responsible could be included in a molecule that was also toxic to the micro-organism then you would have a specific chemotherapeutic agent.[6]

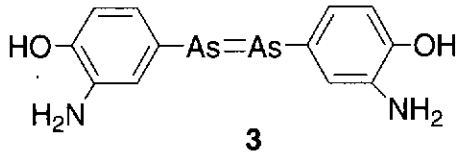


1 - Bechamp's Atoxyl



2 - Ehrlich's Atoxyl

When Alfred Bertheim arrived in Ehrlich's laboratory he worked on Bechamp's Atoxyl **1**, which was still thought to be an anilide of arsenic acid. It was quickly realised that the structure was incorrect and structure **2** was adopted, but not without controversy.[3] Ehrlich's lab then embarked on a systematic study of different compounds, starting from Atoxyl in order to find compounds with improved activity specifically against syphilis. The best candidate was *Salvarsan* for which Ehrlich assigned structure **3** (Fig. 3).[1]



3

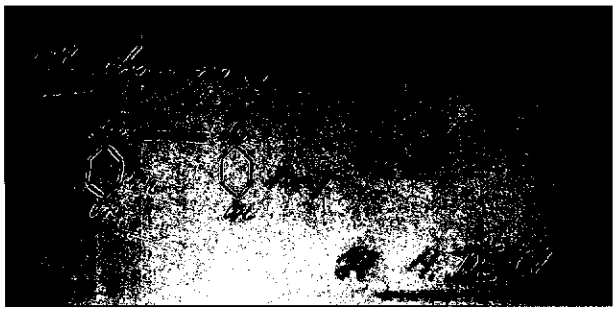
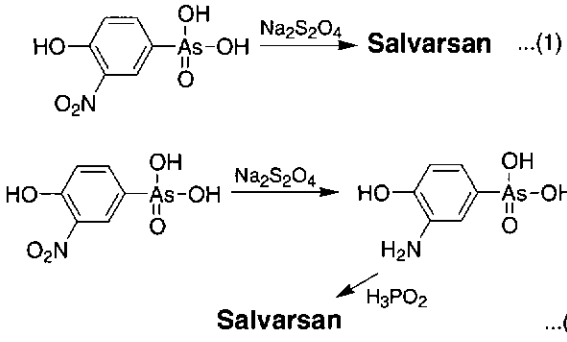


Figure 3., Entry in Ehrlich's book assigning **2** to "606"; 7 September 1909.

The introduction of Salvarsan was a major event, and the compound rapidly became the most widely prescribed drug in the world (necessitating emergency synthesis programmes in England, the US, and Japan after 1914 when the supply of German Salvarsan from the Hoechst plant was interrupted by the war). By 1920 Salvarsan had been shown to be effective against other parasitic disease[6] and 2 million doses a year were produced in the US alone.[7] Demand for Salvarsan remained very strong until 1943 when penicillin became available – an equally effective and more pleasant remedy.

Preparation of Salavarsan

Despite its wide use, Salavarsan has remained an enigmatic material. Ehrlich's synthesis involved the reduction of the substituted phenylarsonic acid with dithionite (Eq. 1)[1] in a reaction that was not straightforward; the products had variable toxicity such that up to 50% of batches from Ehrlich's operation were reported to be rejected.[8] This has been attributed to the presence of unidentified sulfur-containing impurities that were derived from the dithionite.[9] An alternative, two-step synthesis was more reliable (Eq. 2).[10]



Prepared in this way, Salvarsan is a pale-yellow powder. The neutral form is very easily oxidized so it was isolated as the HCl salt, which can be handled for short periods in air without deterioration. Administration of the drug by the physician was not straightforward – the typical average dose of 0.4 g of the salt was dissolved in water, neutralized by adding the exact calculated amount of aqueous NaOH, filtered to remove any undissolved material, and then made up to *ca.* 300 mL with saline solution. This solution was warmed to physiological temperature and injected. And all this with minimum exposure to air to avoid oxidation! Needless to say, there were many cases of medical misadventure, when the process was not followed exactly.

What is Salvarsan?

It is intriguing that despite its long history, and commercial and medical importance, the chemical constitution of Salvarsan is still undecided (try introducing a new pharmaceutical today without knowing exactly what it consists of!). The empirical formula of the material was well-established by Ehrlich's team as the arsenic(I) species, RAs.HCl.H_2O (R = 3-amino-4-hydroxyphenyl). While this is not in question, Ehrlich had assigned the structure **3**, with an As=As double bond, to the base (Fig. 3). This seemed reasonable at the time, since corresponding congeneric azo compounds RN=NR were well established. However, as inorganic chemistry developed it became apparent that this formulation was untenable[11] since As=As double bonds (unlike those of nitrogen) are only stable in exotic molecules with extensive steric protection.[12] Various attempts at measuring physical properties have been made over the years, but full chemical characterization has been elusive. Textbooks and reviews still quote **3**, the original incorrect Ehrlich structure;[13] various other suggestions for polymeric or oligomeric structures have been proposed but with little supporting evidence.[14] The reasons why Salvarsan has proved so intransigent include: i) it is actually a mixture of species, ii) it can only be isolated as an amorphous powder that precludes X-ray crystallography, iii) as a free base it is oxidized very readily to As(III), iv) in aqueous solution it is reactive and appears to undergo strong intermolecular hydrogen-bonding interactions that give gels at particular concentrations/pH values, and v) it is non-volatile so traditional mass spectrometry does not provide useful information. It is, therefore, a particularly difficult compound to deal with.

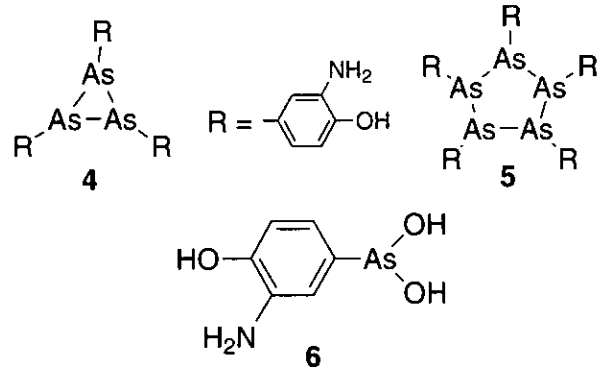
Why the current interest?

Given its widespread use as a cure for syphilis, surprisingly little is known about the mode of action. Discovering this and the site of action for a compound of uncertain composition is not easy. Since it is effective against a range of obligate pathogens, it must presumably affect a target present in the pathogen but absent (or reduced) in the human host. Advances in molecular biology and in our understanding of the structure of the active components of Salvarsan create new opportunities to detect the target and understand the mode of action. In 1997 the complete genome of the syphilis organism was sequenced[15] so that, in theory, every protein the pathogen synthesises can be identified and by molecular techniques it can be cloned

and expressed in large quantities in a suitable benign host, *e.g. E. coli.* Doing this for every protein would be an enormous task but two approaches can make it simpler. Firstly, one can mine the sequence database to look for key enzymes in the genome of the pathogen that have a different structure from equivalent enzymes in the human genome – these become prime targets for selective toxicity. Secondly, because we can now produce large quantities of the active component of Salavarsan in pure form, one can manufacture affinity columns with the active component attached. By passing protein extracts from the pathogen through this column those that interact will be separated from proteins which have no affinity. The former proteins can then be eluted, their amino acid sequence determined, and the corresponding gene (and possibly enzyme activity) identified from the genome sequence. Finally, tests of inhibition of these enzymes by Salavarsan can be conducted following cloning and expression. Therefore, we decided to reinvestigate the chemistry of Salvarsan and related species to establish their true chemical identity and to see if the target enzymes and mode of action could be established.

Waikato studies

The initial goal was to establish a reliable synthesis of Salvarsan. This was no trivial exercise but conditions have been established whereby both the direct Ehrlich method and the modified one (Eq. 1 & 2) give a consistent material that analyzes correctly for RAs.HCl.H_2O. In studies detailed elsewhere,[16] we used electrospray mass spectrometry to examine our material. This relatively new technique has the ability to analyse species directly from solution without the need for intrinsic volatility, and the chemical ionization involved occurs under very mild conditions so that ions are transferred generally without fragmentation. This makes interpretation relatively straightforward, even for mixtures, since each peak can be related to a single parent molecule or ion.[17] For Salvarsan this showed the compound to be a complex mixture with the main constituents as small ring cyclopolyarsines $[RAs]_n$ (n = 3-6), *e.g.* **4** and **5**, together with small amounts of larger rings. Variable amounts of partially oxidized materials $[RAs]_nO_{1-2}$, some sulfur-containing impurities $[RAs]_nS$ as well as the fully oxidized arsenic(III) compound $RAs(OH)_2$, **6**, were also present. Compound **6** is particularly important since it is generally assumed to be the active form, generated by *in situ* oxidation of Salvarsan, though this has still to be fully proved.



To provide a link to Ehrlich we were fortunate to be supplied with some original Salvarsan from the archives of the Georg Speyer Haus (the Frankfurt research institute established for Ehrlich by Frau Speyer) (Fig. 4). This was examined by electrospray mass spectrometry under the same conditions used for our own material; the resulting patterns were closely similar, showing that our syntheses had reproduced the original ones, and that Ehrlich's Salvarsan had survived essentially unchanged for 80 years or so.

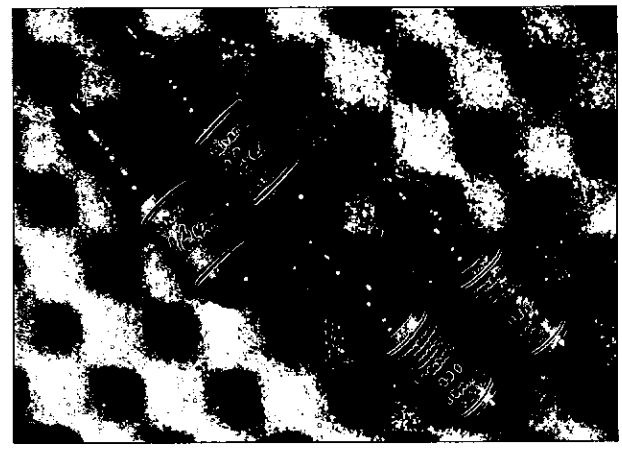


Figure 4. Ampoules containing Salvarsan and Neosalvarsan from Ehrlich's laboratory.

With a reliable source of Salvarsan we can turn our attention to further characterization of it and its close variants, and carry out tests to see if its mode of biological activity can be determined. Despite interest in this area having a strong historical component, the information obtained may lead to new disease treatments as organoarsenic drugs are still used for treating some Third World parasitic diseases,[18] and are reported to even cure Chronic Fatigue Syndrome in falcons and parrots![19] With developing resistance to antibiotics, Salvarsan itself may even one day return as a treatment for syphilis.

Acknowledgements

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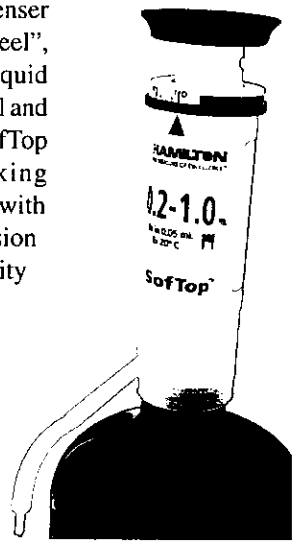

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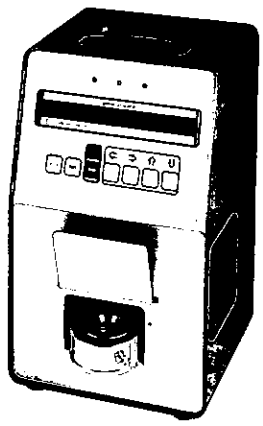

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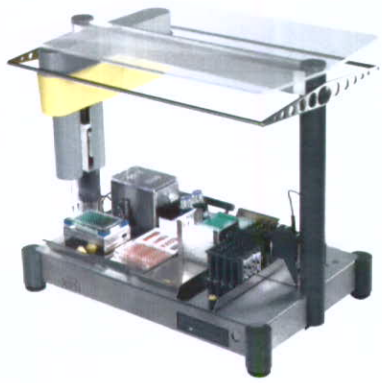

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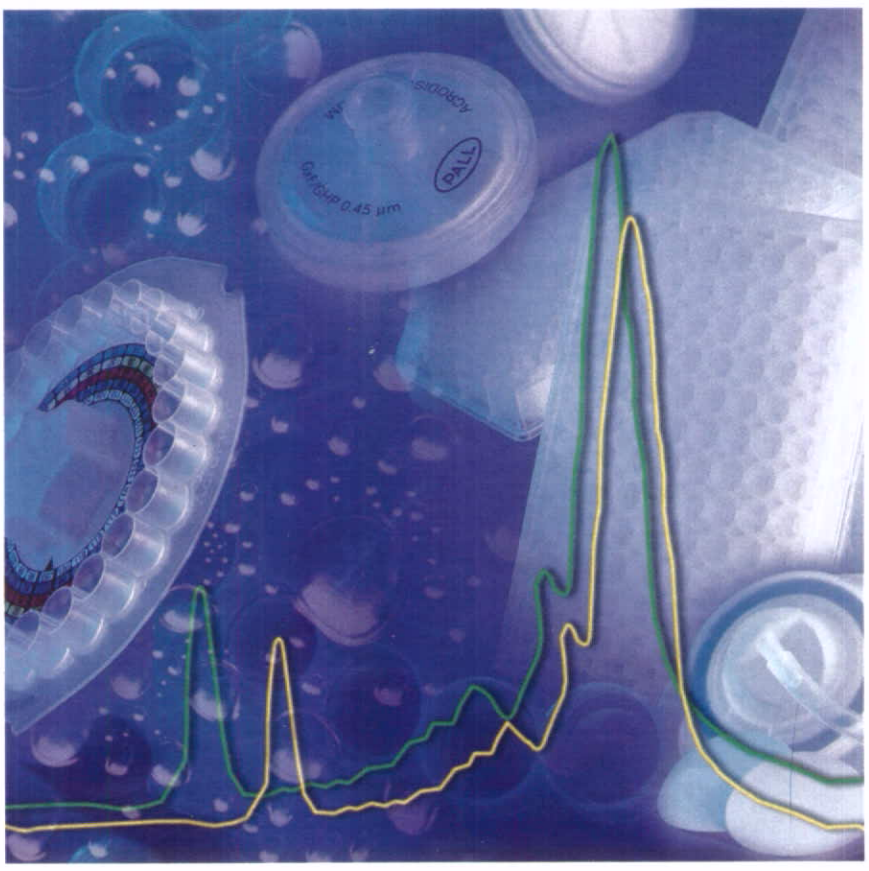

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