THE UNIVERSITY OF SYDNEY

School of Chemistry

2003 Research Report

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Names in parentheses following research project titles refer to joint researchers. Those names with an asterisk or other symbols refer to non-University of Sydney Chemistry researchers.
The School of Chemistry at the University of Sydney is one of the top research Chemistry Departments in Australia. In 2003, there were about 33 research groups spanning a wide range of Chemistry disciplines. Identified areas of research strength include: Biological and Medicinal Chemistry; Synthesis, Catalysis and Materials; Polymer and Colloid Chemistry; Computational and Theoretical Chemistry; Supramolecular Chemistry; Reaction Dynamics and Kinetics; and Chemical Spectroscopy.

The School is well-equipped with modern research instrumentation including major research facilities for NMR Spectroscopy, Mass Spectrometry, X-ray Crystallography, Optical Spectroscopy, Electrochemistry, High Pressure Liquid Chromatography, Analytical and Preparative Gas Chromatography, and High Performance Computing. Research infrastructure (that underpins and supports all research programs) includes in-house mechanical and electronic workshops. The Madsen Library (as a branch of the main University Library) holds all of the main Chemistry titles and also provides on-line access to national and international databases.

In 2003, staff at the University of Sydney held 30 ARC Discovery grants, 8 ARC Fellowships and 26 ARC Linkage grants. The School earned $11.4M in total research funding, including $6.9M from the Australian Research Council (ARC). In addition, over $3.8M was obtained from other government sources and industry. Among the major developments in 2003 were the arrival of our first Federation Fellow, Professor Thomas Maschmeyer and the establishment of two new research centres: The Centre for Structural Biology and Structural Chemistry, and the Organic Synthesis Centre.

Collaborative links with industry continued strongly through the Centre for Heavy Metals Research with Professor Len Lindoy as Director, the ARC-supported Key Centre for Polymer Colloids with Professor Bob Gilbert as its Director and the Organic Synthesis Centre with Professor Damon Ridley as Director. All centres expanded already strong links with industry and other research organisations both locally and internationally.

In 2003 there were approximately 90 graduate students enrolled in higher degrees in the School of Chemistry as well as 30 honours students undertaking a year of research to complete their undergraduate degree programs. This large cohort of research students fosters a strong and vibrant environment for research and this continues to be a real strength of the School.

I would like to thank our Research Committee, chaired by Associate Professors Scott Kable and John Mackie (Associate Heads of School, Research), for managing research matters within the School.

Professor T.W. Hambley
Head of School
Advice to Postgraduate Candidates

The University of Sydney’s School of Chemistry is one of the largest chemistry departments in Australia with a strong record of achievement and an international research reputation. There are typically around 100 postgraduate students undertaking research towards doctorate and masters degrees.

The School offers postgraduate programs in all areas of contemporary chemistry leading to the following degrees:

i  Master of Science (MSc)
ii  Doctor of Philosophy (PhD)
iii  Graduate Diploma in Science (equivalent to 4th year of a BSc degree)

The School welcomes expressions of interest from both Australian and international students to undertake a postgraduate degree in Chemistry.

All information on how to apply for candidature, scholarships, research projects in the School of Chemistry and other information for both Australian and international students may be found at:


If you do not have Web access, please contact:

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New Faces for 2003
Thermodynamics, Statistical Mechanics, and Condensed Matter Modeling

The properties of matter are described at the macroscopic level by thermodynamics, and at the molecular level by statistical mechanics. The latter accounts for the collective interactions and motion of molecules by a variety of computational and mathematical techniques. The generic challenges are to find more efficient algorithms or more accurate analytic approximations that are applicable to different classes of problems, and to develop the fundamental theoretical formalism. In particular cases the problem is to account quantitatively for specific experimental measurements, or to identify the molecular basis of observed phenomena. A selection of recent research projects is reported upon below.

Nanorheometry (Tyrrell)

A theory for the response of viscoelastic materials to time-varying applied loads was developed. The theory is applicable to the interactions between deformable particles and substrates and has applications in diverse fields such as particle adhesion, surface force measurement, emulsion stability, and bubble-particle interaction. The theory can also be used to extract material properties on very fine length scales. To this end a nanorheometer was built by modifying an atomic force microscope. Results have been obtained for an agar gel substrate, poly(dimethylsiloxane) droplets, cellulose particles, and a polystyrene substrate. Detailed measurements for agar gel showed good agreement between theory and experiment, and the viscoelastic material properties (elastic constants, decay times) were obtained on submicrometer localized regions.

Nanobubbles (Tyrrell, Moody)

Over a number of years evidence has accumulated to show that nanobubbles exist and are relatively stable on hydrophobic surfaces in water. Nanobubbles were originally hypothesized by Attard and coworkers, and they account for the marked instability of dispersions of hydrophobic colloid particles, for the measured long-ranged interactions between hydrophobic surfaces, and for their strong adhesion, and for the rupture of macroscopic bubbles near such surfaces, as is important, for example, in mineral flotation. The evidence for nanobubbles has come mainly from direct surface force measurements, and from atomic force imaging. The outstanding puzzle with nanobubbles is their apparent
stability and longevity, since according to classical thermodynamics they ought be metastable. This problem of metastability is in fact quite general, and it occurs, for example, in fields as diverse as cloud formation, crystal nucleation, and emulsion stability. A key ingredient for quantitative calculations for nanobubbles and for all these fields is the interfacial tension, and in particular whether it differs from its value at the planar coexistence interface. A new formally exact statistical mechanical formula for the surface tension has been derived and it has been used in computer simulations of the liquid-vapor interface. It was shown that the surface tension decreased as the supersaturation increased. This finding is of interest in its own right, has application in the various fields mentioned above, and suggests the origin of the mysterious longevity of nanobubbles.

Stochastic Molecular Dynamics (Boinepalli)
A computational algorithm was developed for performing molecular dynamics simulations at constant temperature. A feature of the method, and what distinguishes it from many other isothermal algorithms, is that it samples the canonical Boltzmann distribution on its trajectory through phase space. The algorithm was generalized to the grand canonical case, wherein the number of particles in the system changes according to the applied chemical potential. This is particularly useful for simulations of fluids in pores or confined between surfaces, or for phase transitions. The algorithms were successfully tested for Lennard-Jones fluids.

Dielectric Image Charges
The simplest model of condensed matter is one of dielectric continua, in which case the classical electrostatic potential due to charges is given by Coulomb’s law in media, as modified by the dielectric boundary conditions. However in all but the simplest geometries analytic formulae are unavailable. Examples of complex geometries where it is desirable to know the influence of the dielectrics include the modeling of ion channels in membranes, the description of protein tertiary structure and biomolecular binding, the analysis of water structure at surfaces, the calculation of bond energies of large molecules, the computation of cavity polarization, etc. Recently, we have derived a general formula for the non-equilibrium thermodynamic potential for the polarization of dielectric media that is suitable for numeric computations. The result has three advantages over existing approaches: (1) it is variational in nature, so it lends itself to parametric minimization, (2) the volume integrals that occur in solving Poisson’s equation are reduced to surface integrals over the dielectric discontinuities, and (3) the derivative of the potential gives the actual force on the induced polarization, and so the potential can be solved on the fly in Carr-Parrinello molecular dynamics approaches.

Selected Publications
Our research interests include: (i) the development of new synthetic methodologies with particular emphasis on stereoselectivity; (ii) application of these methods to the synthesis of complex, biologically active natural products, and; (iii) design and synthesis of natural product analogues as potential therapeutic agents.

Anti-Cancer Drugs from the Sea: Synthesis of Highly Cytotoxic Marine Macrolides

Marine organisms, particularly invertebrates such as sponges, have become a key source of novel biologically active compounds. Many of these marine-derived natural products exhibit exceptional levels of biological activity, combined with unique modes of action. Additionally, with the increasing threat of antibiotic resistance in bacteria and fungi, and the problem of multi-drug resistance (MDR) in cancer chemotherapy, pharmaceuticals with new modes of action are desperately required. However, the pre-clinical and clinical development of many marine-derived natural products into pharmaceuticals is often hampered by a limited supply from the natural source. We are currently engaged in synthetic efforts towards two promising anti-cancer marine-derived macrolides, (−)-lasonolide A and amphidinolide H. Successful total syntheses of these potently cytotoxic natural products will allow for further biological evaluation and the systematic production and analysis of analogues in order to probe structure-activity relationships (SAR). A key longer-term objective is the design and development of structurally simplified analogues which retain or improve upon the biological properties of the parent natural product. Our approach to analogue design is based on the proposition that only certain structural features of these macrolides are involved in discrete interactions with the biological target while the remainder of the molecule ensures the appropriate three dimensional display of these functional groups.

Towards New AIDS Treatments Based on Inhibition of HIV-1 Integrase

The continual rise of HIV-1 infection remains a serious global health problem. Two viral enzymes, reverse transcriptase (RT) and protease (PR), have been the main focus of efforts to develop chemotherapeutic agents for the treatment of HIV-1 infection. Although the use of combination therapies, including both RT and PR inhibitors have led to prolonged life expectancies for HIV patients and delayed onset of AIDS, the incidence of HIV resistance to current RT and PR drugs is rapidly increasing. Hence, new anti-HIV drugs with novel modes of action are urgently required.
A third viral enzyme, HIV-1 integrase (IN), has recently been identified as a highly promising target for anti-retroviral therapies. HIV-1 IN is responsible for integration of the HIV genome into the host genome. Integration is a unique event, necessary for propagation of the virus, and is absent from the host. Therefore, HIV-1 IN represents a safe and attractive target for the development of new anti-HIV chemotherapeutics for sole use or in combination with existing therapies.

Integramycin is a recently reported hexacyclic natural product, isolated from the fermentation extracts of *Actinoplanes* sp., which inhibits HIV-1 IN coupled and strand transfer reactions with IC_{50} values of 3 and 4 μM, respectively, whilst exhibiting no activity in DNAse assay at 100 μM. Synthesis and biological testing of the various segments of integramycin will provide invaluable structure-activity relationship (SAR) data and will provide the basis for a successful total synthesis. We are also interested in the anti-HIV integrase properties of lithospermic acid, isolated from the water soluble extracts of the herbal plant *Salvia miltiorrhiza* (Danshen).

In collaboration with Professor Chris Burrell (University of Adelaide) and Dr Li Peng (Institute of Medical and Veterinary Science, Adelaide) the compounds produced during this project will be evaluated for their anti-integrase activity in a powerful cell-based assay.

**Stereoselectivity in Organic Synthesis**

We are interested in developing efficient new methods to address certain current issues of stereoselectivity in organic synthesis, with a broad range of potential applications. Areas of interest include the design and stereoselective construction of new, sterically-congested chiral frameworks, an operationally simple and effective method for the synthesis of medium to large ring (Z)-cycloalkenes and a hybrid chiral pool/asymmetric catalytic strategy for the synthesis of stereochemically diverse C-disaccharides as hydrolytically stable carbohydrate mimics.

**Selected Publications**

**SYNCHROTRON TECHNIQUES IN BIOINORGANIC CHEMISTRY**

**New Synchrotron Techniques**

The application of synchrotron radiation to solving problems in bioinorganic chemistry has become more sophisticated over time in line with technological advances at facilities across the world. EXAFS, XANES, and crystallography of synthetic model compounds has given way, to some degree, to those same techniques being performed on purified proteins thanks to increased brightness of X-ray sources and improved isolation and purification methods for bioinorganic species. Now the arrival of even brighter third-generation synchrotron facilities, the penetrating nature of X-radiation and the elemental specificity of X-ray absorption spectroscopy (XAS) allows us to probe directly the chemical environment of bioinorganic systems *in vivo*.

Whilst crystallography cannot be applied in such a way, the lack of sample preparation required for XAS and derivative methods makes them almost perfect techniques for the field. This project focuses on the use and development of these techniques including: fingerprint identification of biotransformation products of low dose toxins and drug candidates in intact tissue by comparison to model XANES spectra, including the mathematical quantitation of complex mixtures where they exist; two- and possibly three-dimensional elementally (SRIXE or XRF) and chemically specific imaging of intact or sectioned tissue producing maps of the distribution of elements and chemical species in biological samples. Several systems currently under investigation are listed below.

**Organic Selenium Compounds as Anti-Cancer Chemopreventative Agents (Dillon)**

Recent studies indicate that various selenium compounds show considerable chemopreventative anticarcinogenic effects in both humans and laboratory animals. However the efficacy of different species varies significantly, with inorganic selenium being less effective than organoselenium compounds, whose properties in turn are affected by whether or not they become involved in the selenoprotein assimilatory pathway. Monomethylated species are proposed as the active agents, with the unstable methylselenol the most likely suspect. Methylselenol is suggested to be produced endogenously from either Se-methylselenocysteine or methylseleninic acid via different mechanisms. Elucidation of the chemopreventative mechanism of Se compounds is exceedingly valuable and is a problem eminently suited to study with XAS. Preliminary results after treating mammalian cells with inorganic forms of Se indicate that whilst uptake of selenite is minimal, selenite is readily absorbed and reduced to an organic form.

**Cellular Carcinogenic Mechanism of Cr(VI) (Levina, Lay, Mulyani, Dillon, Milsmann, Foran*, Stampfl*, Lai*)**

The group of Professor Peter Lay has previously determined using SRIXE imaging and micro-XANES analysis of single mammalian cells that the uptake and metabolism of the now well-known workplace and environmental carcinogen
Cr(VI) involves reduction to Cr(III) and detrimental binding to DNA in the nucleus. Renewed efforts involving time-course treatments and XAS of bulk cell cultures treated with Cr(VI) are providing new insights into the cellular and molecular mechanisms that are involved in this process. Cr(VI) is quickly reduced to one form of Cr(III) in all cell treatments, however we have shown using SRIXE imaging that significant changes in the spatial distribution and cellular content of Cr and other elements such as Ca and K occur with variations in the length of exposure to Cr. The nature of the Cr coordination in cells has also been characterised using EXAFS and by comparison of the XANES spectra to an ever-increasing library of Cr(III) model compound spectra.

**Imaging Heme Proteins in Porcine Aorta Endothelial Cells (Aitken, Lay, Witting*, Thomas*, Stocker*, Lai*)**

The expression of the heme protein indolamine 2,3-deoxygenase (IDO) has been promoted in porcine aorta endothelial cells (PAEC) and the resulting Fe chemistry and biomechanism after treatment with NO and the substrate tryptophan has been probed using sub-micron SRIXE imaging and microXANES. Similar experiments have been performed on PAEC after treatment with peroxide and myoglobin as a mimic of oxidative stress.

**Biotransformation of Arsenic in Mammalian Cells (Foster, Dillon)**

Current work involving As includes analysis of genetically engineered plant lines designed as bioremediation tools using XANES analysis of mixtures and research into the mammalian cellular mechanism of As detoxification. Initial XANES fingerprinting results on cells indicate that several different inorganic As species are converted to arsenite in a short time-frame. We continue to search for evidence of sulfur-coordinated As at longer exposure times.

**Selected Publications**


Helium nanodroplet spectroscopy is a new and exciting field in physical chemistry. Helium droplets are formed by expanding high pressure helium at low temperatures into vacuum. This produces a beam of helium droplets with a size range of several hundred to several hundreds of thousands of atoms or, on average, a few nanometers in diameter. They are extremely small, significantly smaller than, e.g., atmospheric aerosoles (micrometers), but still large enough to capture and dissolve several molecular species. It is the ease with which the droplets can be ‘doped’ with molecules that makes them a very useful experimental tool. Dopant species are introduced by passing the droplets through a small scattering region where a slightly elevated background pressure of the compound of interest is maintained. The beam of doped helium droplets can then be probed via laser spectroscopy and mass spectrometry.

**Superfluid Dynamics**

One unique property of liquid helium droplets is that they are superfluid. A result of this superfluidity is that a molecular dopant can rotate freely inside the helium. Although the helium will attempt to move with the molecule (and thus affect its moment of inertia), no energy is exchanged between the dopant molecule and the surrounding solvent. The motion is non-dissipative as opposed to motion in any other (classical) liquid which is rapidly frictionally dampened. Studying the spectroscopy of various molecular species in helium droplets can teach us much about the nature of superfluidity at the microscopic level and how it interacts with and is affected by the presence of the molecule.
Reactions at Zero Kelvin

Well, not exactly 0 K, but close enough. The extremely low temperature inside helium droplets and the facility with which they can be doped with a wide variety of species opens up the possibility to capture and stabilise molecular complexes that in another medium, or in the gas phase, at higher temperatures, would not be stable. A famous example is the dimer of the OH radical which theory predicts should be stable but has yet eluded experimental observation. Helium droplets might be used to bring two cold (0.37 K) OH radicals together to form a weakly bound, metastable complex that cannot react (too cold!) without being externally triggered. Once formed, the complex may be excited via laser radiation to give it just enough energy to overcome the barrier to rearrangement, and reaction. Many radical-radical and radical-molecule reactions exist in nature and often these are very hard to study due to the transient nature of the intermediate complexes.

A second method of studying chemical reactions in helium droplets is by preparing the reactants in situ, i.e. through photolysis of a precursor molecule. In a sense, this is the reverse chemical reaction and by studying the photolysis reaction in detail, much can be learned about the way in which a solvent influences reaction dynamics.

Unique Stuctures

Because individual molecules are each dissolved in their own helium droplet, from which they cannot escape, helium droplets have sometimes been termed ‘nanoscales laboratories’. Where more than one molecule dissolves in a single droplet, the dopant species combine to form a van der Waals complex whose structure is governed by relatively long range forces, e.g. dipole-dipole interaction. The internal temperature of the droplets, and hence the dopant molecules, has been measured at 0.37+/−0.03 K. At these temperatures, even small barriers on the potential energy surface can be enough to prevent rearrangement of one structural isomer into another. Studies have shown that unique van der Waals complexes are indeed formed inside helium droplets and often the resulting structures closely resemble the structural motif of the corresponding bulk (liquid or solid) phases of the dopant species. An example is the observation of a cyclic water hexamer, the structural motif of plain water ice and an isomer of water that is not stable by itself in the gas phase.

Current Status

The helium droplet experiment is currently still under construction. A vacuum chamber and helium droplet source are nearly assembled and work is progressing on building the additional sections of the apparatus, a scattering region, laser interaction chamber and a mass spectrometer. The helium droplet source is expected to be finished in the middle of 2004 and experiments shall commence soon thereafter.

Selected Publications

General

The world is standing at the technological threshold of an industrial revolution that is driven by the need for hydrogen as an energy carrier and the need for truly sustainable (industrial) processes. Meeting these challenges by developing new catalysts and functional materials as well as by devising strategies for waste reduction, energy optimisation and process intensification represents the ultimate set of aims in Prof. Maschmeyer’s group. Thus, the mission is to tackle some of the major global technological problems (e.g. waste generation/pollution, green-house effect, depletion of fossil-based energy sources) by generating and using new fundamental insights on the molecular and nanoscopic level to develop feasible leads.

In particular, the objective is to initiate the development of novel processes for catalysis and for hydrogen generation/reversible storage, with a strong emphasis on (a) the efficient usage of raw materials and energy and (b) the minimal generation of unwanted by-products. This approach is based on a solid molecular understanding of reactions, catalysts and processes. Much of the work takes into account the often overlooked, but essential, need to build up functional structures into macro-structures addressing all length scales with the application in mind, so that they can be integrated into appropriate reactors or devices successfully.

Examples of project areas:

• Novel single-site heterogeneous oxidation catalysts
• Preparation, characterisation and testing of nanoparticles stabilised and supported in mesoporous hosts as catalysts and functional materials
• Conversion of batch reactions into continuous flow reactions using immobilised homogeneous catalysts and/or membranes (e.g. fermentation)
• Preparation, characterisation and testing of hierarchically structured catalysts
• Exploring ionic liquids as new reaction media using high throughput experimentation approaches
• Converting biomass to biofuels (HTU process)
• Developing new photocatalysts with low bandgaps for reactions with natural light as integrated reactor systems
• Functional coatings on microstructured reactors

Brief Curriculum Vitae
In 1994, as Australian Bicentennial Fellow, Thomas went to the Royal Institution, London. Subsequently, he was made Assistant Director of their Davy Faraday Laboratories and also Associate Lecturer and Affiliated Fellow (Peterhouse) at the University of Cambridge. In 1998, at the age of 31, he was appointed Professor and Head of the Department of Industrial Organic Chemistry at the Delft University of Technology, making him the youngest Professor of Chemistry in Europe at that time. Additionally, in 2000, Thomas became Vice-Chairman of the Delft Institute of Chemical Technology. During this time he was also advisor to the Dutch Federal Ministry of Finance and Economic Affairs. He returned to his alma mater in late 2003, when he commenced his new positions as Federation Fellow and Professor of Chemistry.

Recent highlights include: his founding role in ‘Avantium’ (a Dutch spin-off company with ca. 100 employees, specialising in High-Throughput Experimentation Research), the design of the ‘grafting approach’ (leading to highly selective catalysts via the use of molecularly confined spaces) and the design of new types of mesoporous materials. Both design approaches lead to catalysts that are superior to their industrial counterparts and are part of on-going industrial development/up-scaling programmes. He also devised and commissioned ceramic membrane reactors that represent new technological solutions to many chemical process problems, as they allow conversion and separation to occur simultaneously, with the added benefit of being able to operate beyond the reaction equilibrium.

Selected Publications
Chemistry is traditionally an experimental science. However, recent advances in computer technology and the development of highly efficient computer algorithms have opened the way for a viable alternative approach to chemistry: chemistry by computer. We use such computer calculations to determine the structures of molecules and to help understand how molecules react with one another.

Enzyme-Catalysed Reactions (Sandala, Topf †, Smith †, Wetmore †, Coote †, Easton †, Schofield ‡, Golding ‡)
Vitamin B12 is one of nature's essential vitamins. We have used ab initio calculations to model reactions mediated by coenzyme B12. Although these reactions have been extensively studied experimentally, there is certainly no consensus as to how they proceed. We have proposed mechanisms involving partial-proton-transfer (donation or acceptance) provided by enzymatic hydrogen bonding. Supporting evidence for our proposals has come from site-directed mutagenesis experiments. These and other recent examples provide strong encouragement for the use of such computer calculations in a predictive manner in the study of enzyme reactions. Pursuing this direction further, we have also been examining the mechanism for the conversion of (3S,5S)-carbapenam (1) to the biologically active beta-lactam antibiotic, (5R)-carbapenem (2), catalyzed by the enzyme carbapenem synthase. Our calculations suggest that the reaction proceeds via initial abstraction of the C5 hydrogen atom, followed by epimerisation at C5 and desaturation at C2/C3.

Free Radical Chemistry (Gomez-Balderas, Coote †, Henry †, Wood, Fischer ‡)
Radicals are ubiquitous in chemistry, biology, and polymer science. Because they are reactive species, they are often difficult to study experimentally and therefore theory has a potentially useful role to play in their characterisation. We have been using theory to determine radical stabilisation energies, with the important aim of seeing how individual substituents stabilise or destabilise a radical centre. We have also been examining the details of addition, abstraction and rearrangement reactions of radicals. These are very important in biological chemistry and polymer chemistry.

Development of Improved Theoretical Procedures (Henry †, Sullivan †, Wood, Petersson ‡)
The ability to predict reliable thermochemistry represents a very important application of ab initio molecular orbital theory. We have recently been designing and assessing methods that are suited for predicting accurate thermochemistry for free radicals because these represent particular challenges for theoretical investigation. Our latest work has been concerned with methods that we have designated G3-RAD, G3X-RAD, G3(MP2)-RAD and G3X(MP2)-RAD. We are also developing an improved procedure for examining radicals within the complete-basis-set (CBS) formalism, designated R-CBS-QB3.
**Oxidative Damage to Proteins (Wood, Moran, Jacob, Coote, Easton, Rauk, Davies, O’Hair, Gordon)**

An understanding of the oxidation of proteins by free radicals is of great importance because of its implication in a number of human disorders such as Alzheimer’s disease, atherosclerosis, and diabetes, as well as aging. We have been using *ab initio* molecular orbital calculations to address the problem. Initial targets have included the cleavage of the peptide backbone following radical formation, and migration of the radical site within the peptide. We have also examined solvation effects.

**Oxides and Hydroxides of Alkali and Alkaline Earth Metals (Haworth, Sullivan, Wilson, Curtiss, Martin, Kass)**

We have been examining the alkali metal oxides and hydroxides as a preliminary to investigating their interesting acid and base properties. Reliable experimental data are very sparse for these molecules. Their theoretical description is not entirely straightforward either and has necessitated incorporation of several new features and the development of new basis sets.

**Interaction of Metal Ions With Biological Systems (Corral, Yanez, Mo, Tortajada)**

Metal ions are of great importance in biological function. We have embarked on a broad-based theoretical study to probe the interaction of metal ions with prototypical biological molecules. Our initial investigations have focussed on the interaction of calcium dications with simple model systems in order to establish suitable theoretical procedures that can be applied to larger molecules. Calculations on the interaction of calcium dication with urea have been carried out in parallel with experimental mass spectrometric studies, and used to help interpret the observed mass spectrometric fragmentation patterns.

**Metal-Free Hydrogenation (Chan)**

Hydrogenation is a very important process in chemical systems. It is generally brought about by transition metal or heavy metal catalysts. However, in recent years it has been demonstrated that catalytic hydrogenation can also be accomplished in the absence of such metals. We are using theory to try to design systems in which metal-free hydrogenations can occur with low energy requirements. Our initial studies involve the acid-catalysed hydrogenation of ethene.

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† Research School of Chemistry, ANU. ‡ Coworker not associated with University of Sydney or ANU.

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**Selected Publications**

Platinum-Carborane Complexes as New Agents for Boron Neutron Capture Therapy (Todd*, Woodhouse*)

The principal goal of this research program is to expand the clinical efficacies of platinum chemotherapy and radiotherapy by coupling the potent DNA-binding characteristics of certain platinum compounds with the remarkable neutron capture properties of the non-radioactive $^{10}\text{B}$ nucleus that have been exploited in an experimental cancer treatment known as Boron Neutron Capture Therapy (BNCT). BNCT is currently undergoing Phase I/II clinical trials in several countries for the treatment of the brain tumour glioblastoma multiforme and malignant melanoma. The therapy utilizes $^{10}\text{B}$-containing drugs and thermal neutrons of low kinetic energy ($< 0.025$ eV), although epithermal neutrons allow for deeper tissue penetration. The very large, effective nuclear cross-section of the $^{10}\text{B}$ nucleus (3837 barns, natural abundance = 19.8%) makes it highly amenable to the neutron capture process. The major (94%) reaction is shown in eq. 1:

$$^{10}\text{B} + \gamma \rightarrow [^{11}\text{B}] \rightarrow ^4\text{He}^{2+} + ^7\text{Li}^+ + \gamma + 2.4 \text{ MeV} \quad (\text{eq. 1})$$

The primary nuclear fission products that are produced in the neutron capture reactions have a high rate of linear energy transfer and they cover a short range (ca. 10 μm, or one cell diameter). As a result, the immense amount of energy derived from the nuclear reaction is dissipated in a very small volume. Therefore, the selective destruction of tumour cells is feasible with this type of therapy since nearby cells that are free of the $^{10}\text{B}$-containing drug are spared except for the minor contribution of background $^1\text{H}(n,\gamma)^2\text{H}$ and $^{14}\text{N}(n,p)^{14}\text{C}$ processes.

$^{10}\text{B}$ compounds that are localised near chromosomal DNA cause maximum cell damage in the presence of thermal neutrons. The proof-of-principle for the synthesis, DNA-binding, and tumour cell uptake of the archetypal Pt-B complexes 1 and 2 has already been established in our laboratory. Complexes 1 and 2 represent two new classes of DNA-binding agents for potential use in BNCT, and an international patent (PCT/AU02/00943) was filed on these compounds in 2002. This work has also lead to innovative synthetic and design strategies that, for example, overcome the facile decomposition of many complexes in the presence of water as a consequence of redox reactions involving the metal centre and carborane.

DNA Nanoshuttles: Electrostatic Models of Toroidal Proteins and Potential Topological Probes of DNA Structure and Function (Harding)

Toroidal, or ring-shaped, proteins are used in a variety of ways by the cell. Almost all classes of enzymes involved in DNA metabolism have a toroidal motif that is central to their function. It has been postulated that protein quaternary structures involved in DNA metabolism have converged to the toroidal motif as a consequence of the unique structure and nature of the common substrate DNA. A well-known example of a toroidal protein known as the DNA sliding-clamp is a key subunit of the DNA polymerase holoenzyme complex, the central enzyme of DNA replication.
A key feature that characterises the structure of toroidal DNA-binding proteins such as the DNA sliding clamp is the central hole (~35 Å) which is large enough to accommodate double-helical nucleic acid with little steric hindrance for B-DNA (~20 Å diameter). In general, the DNA-protein interaction is purely topological, and it is greatly stabilised by powerful electrostatic interactions between the polyanionic phosphodiester backbone of DNA and a region of high positive potential that surrounds the inner surface of the toroid. In this research program, we have sought to answer whether linear DNA can thread nanoscale cationic macrocycles of platinum that we have termed DNA Nanoshuttles (Figure 1).

The interaction of nanoscale platinum complexes with DNA, as depicted in Figure 1, is unprecedented and it would represent a significant advance in the field of metal-DNA chemistry. As a direct consequence of the nanoscale dimensions, shape and charge that allow the DNA Nanoshuttles to interact with DNA in a topological manner, there exists the exciting possibility of developing them into electrostatic models of toroidal DNA-binding proteins and a new class of synthetic probes of DNA structure and function. Furthermore, it is feasible that DNA Nanoshuttles may eventually find useful applications in the rapidly developing field of “DNA Nanotechnology”.

Organotransition Metal Complexes as Synthetic Receptors for Nucleobase Recognition (Crisp*)

Molecular recognition is central to most biochemical processes, and the development of synthetic molecular receptors for biologically-relevant molecules is an area that lies at the frontiers of supramolecular chemistry. We are interested in new types of metal-based “molecular tweezers” for the recognition of nucleobases via molecular chelation involving non-covalent interactions. One can envisage the development of such receptors into new probes for molecular biology, with numerous potential applications including the selective targeting of nucleobase sites in biomolecules such as ssDNA, ssRNA and tRNA.

Recently, we initiated studies into the molecular recognition of adenine derivatives with simple mononuclear organoplatinum(II) complexes containing nicotinic and isonicotinic acid. We also studied analogous dinuclear species with the aim of developing a new class of platinum-based “molecular tweezers” for the recognition of nucleobases via molecular chelation. A favourable 1:1 interaction between a dinuclear host and adenine, as determined by molecular mechanics calculations (Figure 2), involves simultaneous Watson-Crick and Hoogsteen binding with the formation of four strong H-bonds between the nucleobase and the platinum receptor.

Selected Publications
Research Report
Fullerenes: Their Complexes, Conjugates and Derivatives (Boyd,* Carter, Cheng, Gallagher, Lay, Reed,* Sen Gupta, Sun*, Thompson, Zeng)

Research has continued into studies of the spectroscopy and bioinorganic chemistry of fullerene/porphyrin conjugates, including water-soluble species. These conjugates have been shown to be very potent potential anti-cancer drugs, with higher activity than cisplatin against a series of cell lines, including Pt-resistant lines. Detailed vibrational spectroscopic measurements have been performed on C_{60}, C_{60}O, C_{120}O, C_{59}N^+, and (C_{59}N)_2. They show new and interesting spectroscopic features, both in the solid state and in solution. Solute-solvent studies of C_{60} continued to give evidence of unusual vibronic coupling effects in their Raman spectra. Photophysical studies of Ru fullerene complexes have revealed interesting optoelectronic properties.


XAFS structures (at 10 K) of human hemoglobin (Hb, including mutants from thalassemia patients), indolamine 2,3-deoxygenase (IDO) and their adducts with O2 and NO were determined. Structural work has also been performed on the nitroxyl (NO) adduct of horse heart myoglobin and other heme proteins. Further work has also been completed on the unfolding of cyt c as a function of pH, and the characterisation of NO adducts of the unfolded protein. Resonance Raman spectroscopy is being used to probe the active sites of heme proteins, in particular IDO and normal and thalassemic Hbs, and their small molecule adducts. Finally, research has been performed on the binding of CO to CooA and some mutants to investigate how CO acts as a signal molecule to allow binding of this protein to DNA during transcription.

Cancer Diagnosis in Tissues and Identification of Microbes by Vibrational Spectroscopy (Ali, Carter, Lay, Mountford,* Russell,* Sorrell,* Tam)

Infrared (IR) and Raman imaging techniques are being used in conjunction with principle component analysis (PCA) to develop new methods for distinguishing breast tissues that are normal from those that are benign tumours or malignant tumours. IR and Raman images indicate that benign and malignant tissues differ in their protein secondary structure, amide I band around 1650 cm⁻¹ and the content of the lipid in the tissues. Strong correlations have been obtained for
vibrational imaging diagnosis with diagnoses obtained from standard pathology studies and NMR techniques. Vibrational spectroscopic techniques are also being developed to identify pathogenic microorganisms and to examine their susceptibility to new drugs.

Selected Publications
Quantum Chemical Studies of Binaphthyls in Ground and Excited Electronic States (Kable, Zhang)
Following the extensive laser induced fluorescence studies of 2,2′- and 1,2′-binaphthyls carried out by Kable et al. at Sydney, the spectroscopy of these systems, as well as of 1,1′-binaphthyl, was investigated by theoretical methods, in an effort to aid with the assignment of the observed spectra. The theoretical studies included naphthalene as well as the benzene and biphenyl systems, which allows useful pararallels to be drawn between the different biaryl systems.

This study focused on the determination of equilibrium geometries and vibrational frequencies of the three binaphthyls, along with benzene, biphenyl and naphthalene, in their ground and lowest two to three electronically excited states using current techniques of computational quantum chemistry, which range from Hartree-Fock and density functional methods (for ground states) to configuration interaction with single excitations, time dependent density functional and complete active space second order perturbation theories (for excited states) in conjunction with the 3-21G and 6-31G(d) basis sets.

The calculations demonstrated that in the biaryls π-electron delocalization has the greatest stabilizing effect in excited states where the HOMO → LUMO excitations are predominant. Thus, while the ground states of biaryls are non-planar, due to steric hindrance, the 1B1u state of biphenyl and the analogous 1La state of cis-2,2′-binaphthyl are planar. All three binaphthyls in their 1La states are significantly more planar than in their ground or 1Lb excited states.

Utilizing the findings of the computations, the experimentally observed spectra of 2,2′- and 1,2′-binaphthyls were reassigned as S0(1La) ← S1 rather than S1(1Lb) ← S0 as previously assumed. With this reassignment it became possible to provide definitive assignment of a number of the observed low frequency torsional and out-of-plane bending modes, as well as a more confident identification of the conformation of the observed excited states.

The Spectroscopy and Photochemistry of Halocarbenes (Guss, Kable)
Following our earlier theoretical studies of a range of triatomic halocarbenes, such as CF2, CFCl, CCl2, and CBr2, a quantum chemical study of CClBr has been carried out, focusing in particular on the prediction of accurate a(3A″) ← X(1A′), and A(3A″) ← X(1A′) excitation energies. The geometries, vibrational frequencies and molecular energies were determined by the application of a range of quantum chemical techniques, including coupled cluster, equations of motion coupled cluster, multi-reference configuration interaction and density functional methods, utilizing basis sets of cc-pVTZ and cc-pVQZ quality. The computed excitation energies include corrections for core-valence correlation and scalar relativistic effects. The potential energy surface of the singlet excited state was investigated to determine the stability of the molecule to dissociation and whether it could undergo internal conversion to the ground state by Renner-Teller coupling. The results of these computations are in good agreement with the available experimental LIF measurements carried out by Guss and Kable in the School of Chemistry. The computed results provide a theoretical underpinning to the assignment and interpretation of the observed spectroscopic data.
The Relative Stabilities of \textit{Cis}- and \textit{Trans}-Platinum Dichloride in Aqueous Solution (Schamberger, Hush)

An extensive quantum chemical study of the relative thermodynamic stabilities of \textit{cis}- and \textit{trans}\-[Pt(Cl)\_2(H\_2O)\_2] in aqueous solution was completed in an effort to establish the theoretical and computer resource requirements associated with the accurate description of the thermochemistry of transition metal complexes in aqueous solution. The computations utilized a range of methods including density functional and coupled cluster theories, concentrating largely on the role of solvation. The latter was modelled by the Effective Fragment Potential method and by the COSMO solvation model. The basis sets used range from double zeta to 6-31+G(2df,\;p) on the ligands and a multiply polarized basis on Pt, in combination with a relativistic effective core potential. In the gas phase at 0 K, the \textit{trans} - \textit{cis} energy difference, as computed by coupled cluster methods, was determined to be 0.1 kcal mol\(^{-1}\). The analogous value at 298 K in aqueous solution, obtained by density functional theory, in conjunction with COSMO, is -0.8 kcal mol\(^{-1}\), while modelling solvation by a combination of discrete (quantum chemical) and continuum (COSMO) methods, whereby four H\_2O molecules are explicitly accounted for, yielded a value of -1.5 ± 1.0 kcal mol\(^{-1}\). These results are in acceptable agreement with the experimental value of -0.1 kcal mol\(^{-1}\). It is concluded, therefore, that Density Functional Theory and polarizable continuum methods with appropriate basis sets are capable of yielding relative thermodynamic stabilities in solution of near chemical accuracy.

Selected Publications
7. Spectroscopic constants of the X (\textit{A}\_1), \tilde{\textit{a}} (\textit{B}\_1) and A (\textit{B}\_\textit{g}) states of CF\_2, CCl\_2 and CBr\_2 and heats of formation of selected halocarbenes: An ab initio quantum chemical study. K. Sendt and G.B. Bacskay. \textit{J. Chem. Phys.}, 112, 2227-2238 (2000).
Planar-Chiral Metal Complexes for Asymmetric Catalysis (Whitby*)

Asymmetric synthesis, and in particular asymmetric catalysis, remains one of the most active areas of current research in organic chemistry. Planar-chiral cyclopentadienyl metal complexes feature amongst the most successful asymmetric catalysts, but they are often very difficult to prepare in enantiomerically pure form. We have devised a new type of chiral cyclopentadienyl ligand, incorporating axial chirality, which allows the preparation of planar-chiral metal complexes in enantiomerically pure form. We have recently prepared a wide range of axially chiral chelating indene ligands, such as 1–6, and are currently exploring the preparation of a number of transition metal complexes (e.g. 7 and 8) using these ligands. In addition to our ability to prepare these complexes in enantiomerically pure form, we have observed that the constrained chelation afforded by our ligand design can in some cases generate metal complexes having unusual coordination environments, and therefore potentially unique reactivity. The screening of these complexes for potential applications in asymmetric catalysis is underway.

1. $X = \text{CH}_2\text{OH}$
2. $X = \text{CH}_2\text{NMMe}_2$
3. $X = \text{CH}_2\text{PPh}_2$
4. $X = \text{NH}_2$
5. $X = \text{OH}$
6. $X = \text{PPh}_2$
Metallocene-Based Catalysts for Olefin Polymerisation and Asymmetric Catalysis (Alt,† Schilling)†

Polyolefins are a multi-billion dollar a year industry. Recently, there has been enormous interest in the use of metallocenes as single-site homogeneous catalysts for the polymerisation of olefins. We have prepared a number of unique fluorene-based metallocenes such as the *ansa*-zirconocene complexes 9 – 11, which have been used as catalysts (in combination with methylalumoxane) for the preparation of polyethylene and stereoregular polypropylene; e.g. highly syndiotactic polypropylene (which cannot be prepared using traditional heterogeneous Ziegler-Natta catalysts) was obtained using complex 9 as the catalyst. We are also currently investigating the preparation of chiral non-racemic versions of these complexes (using our axially chiral cyclopentadienyl ligand design) for use as asymmetric catalysts for synthetic organic transformations.

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Selected Publications
Electroacoustics Of Colloidal Suspensions (Djerdj ev, Owen, Walker, Warr)
An electroacoustic effect is created when an alternating electric field is applied to a concentrated (> 1 vol%) colloidal suspension. The charge on the particles (their zeta potential) causes them to jiggle in the field. Because of their density difference from the surrounding fluid this oscillatory motion creates a sound wave of the same MHz frequency as that of the applied electric field. By measuring the phase as well as the amplitude of this sound wave a dynamic mobility spectrum is obtained which can be analysed to give the mean size of the colloidal particles as well as their charge. This development, made in Sydney over the last decade, allows measurements of the properties of many different concentrated colloidal suspensions, which previously could only be studied under dilute conditions by optical methods. As well, new electroacoustic phenomena continue to be revealed.

Unusual dynamic mobility spectra are observed with porous particles. If the pores are larger than the double layer thickness, electroosmotic flow can occur within the particle as well as around the outside. This leads to an entirely different electroacoustic signature and provides a means of probing the interior of mesoporous materials. Microporous particles such as zeolites give characteristic signals due to the shape of the electric field around the particles which is affected by their internal conductivity (Figure 1).

Oil-in-water emulsions can be produced with different droplet sizes depending on the force and length of the homogenisation process, the temperature, the concentration of the stabilising surfactant and other factors. The effects of all of these can be observed directly in real time as the homogenised emulsion passes through a flow-cell electroacoustic device. New time-dependent phenomena are observed that only become apparent because we can measure concentrated emulsions.

This has enabled us to confirm quantitatively for the first time the long-standing belief that the oil/water interface is negatively charged spontaneously by the autolysis of water and the preferential adsorption of hydroxide ions. We conducted a pH-stat experiment in which the increasing surface area of the emulsion as homogenisation occurred could be correlated with the hydroxide ion adsorbed on the newly formed surface.
The rapid measurement cycle of the AcoustoSizer allows kinetics studies. We have observed the growth of flocs created by osmotic depletion pressures and the formation of latex particles in emulsion polymerisation.

The electroacoustic spectra of emulsions stabilised by polymeric surfactants is affected by the hydrodynamic drag of the chains extending into the aqueous phase. Application of a two-layer model developed by O'Brien allows analysis to determine the extent of this polymer shell around the droplet. Neutron scattering studies with contrast-matched oil-in-water emulsions carried out at BENS in Berlin have confirmed the validity of this model (Figure 2).

Homogeneous Oxidation With Metal Acetate Complexes (Masters, Guo, Klepetko)
Cobaltic acetate is a widely used industrial homogenous oxidation catalyst but its mechanism of reaction and the species responsible for the catalysis are not known. New complexes continue to be isolated in our laboratories from the mixture that is ‘cobaltic acetate’. Remarkably, the µ3-oxo centred CoIII trimer was found to undergo a reversible one-electron oxidation to a CoIV species, introducing new possibilities for the catalytic mechanism.

In the homogeneous oxidation of tert-butyltoluene by hydrogen peroxide catalysed by cobalt acetate the catalytic activity dies after about 30 minutes by transformation of the active catalyst into an inactive complex. We have determined that the product, tert-butylbenzaldehyde, is partly responsible for this inhibition, as is the water that is added with the 30% hydrogen peroxide.

Ultimately heterogeneous catalysts may be preferred if they can be as selective as homogeneous catalysts and remain active over many catalytic cycles. New mixed metal catalysts based on the AlPO-5 and SAPO-5 zeolite structures have been prepared and tested for activity for cyclohexane oxidation at Delft University of Technology and DSM in The Netherlands (Figure 3).

Selected Publications
Kinetics of the $\text{Na}^+,\text{K}^+$-ATPase (Starke-Peterkovic, Cornelius*, Apell², Else³, Froehlich^)

The $\text{Na}^+,\text{K}^+$-ATPase, which is found in the plasma membrane of all animal cells, utilizes the free energy derived from ATP hydrolysis for the transport of $\text{Na}^+$ ions out of and $\text{K}^+$ ions into the cell. The concentration gradients of $\text{Na}^+$ and $\text{K}^+$ thus generated across the cell membrane have numerous important physiological functions, e.g. maintenance of the resting potential in nerve cells, cell volume regulation and nutrient reabsorption in the kidney. The aim of this project is to determine the kinetics of the individual reaction steps of the enzyme's complex reaction cycle and thus obtain a deeper understanding of the mechanism of ion pumping and how it is coupled to ATP hydrolysis. A major tool involved in these investigations is stopped-flow fluorescence spectroscopy, which allows conformational changes and charge translocation steps of the enzyme to be resolved on the millisecond timescale.

Recently we have been carrying out measurements of the enzyme's kinetics using kidney tissue derived from a range of warm- and cold-blooded animals in order to correlate enzyme activity to membrane composition. It was found that the degree of fatty acid chain saturation was a significant factor in determining $\text{Na}^+,\text{K}^+$-ATPase function.
Regulation of the Na⁺,K⁺-ATPase (Kong, RasMussen#, Hansen#)

The Na⁺ concentration gradient built up across the membrane is essential in driving numerous physiological processes, including heart muscle contraction and glucose uptake. The enzyme has, thus, been implicated in diseases such as congestive heart failure and diabetes. In order to locate possible mechanisms of in vivo regulation of the enzyme we have been constructing kinetic models of the enzyme’s steady state activity based on the kinetic constants of its partial reactions. The results of such theoretical simulations are then compared to experimental data of the enzyme’s activity obtained from either whole-cell patch clamp measurements performed at the Royal North Shore Hospital on isolated rabbit heart muscle cells or activity measurements on purified membrane preparations.

Molecular Origin and Magnitude of The Membrane Dipole Potential (Starke-Peterkovic, Hibbs)

The membrane dipole potential is an electrical potential of several hundred millivolts situated within phospholipid membranes. It has been postulated to play an important role in controlling the kinetics of ion transport processes in biological membranes (ion channels and pumps). Its origin is, however, still unclear. According to one hypothesis it may be due to orientated water molecules on the surface of the membrane. Dipolar groups from the lipids themselves could however also be contributing. The aim of this project is to investigate each of these hypotheses using theoretical calculations as well as spectroscopic and electrical methods specifically developed for the quantification of the dipole potential.

Using fluorescence spectroscopy with the voltage-sensitive fluorescent probes RH421 and di-8-ANEPPS, it has been found that the dipole potential can be modified by changing the degree of saturation of the membrane lipids and by incorporation of either charged or dipolar hydrophobic species into the membrane. We have recently found that cholesterol significantly enhances the value of the dipole potential. In order to understand the molecular basis of this effect we are currently investigating a range of cholesterol derivatives and attempting to correlate their effects on the dipole potential with the magnitude and direction of their molecular dipole moments, calculated quantum mechanically.

Voltage-Sensitive Fluorescent Membrane Probes (McLeod, Amoroso, Sebban^)

The kinetics of ion transfer across lipid membranes can be conveniently studied using voltage-sensitive styrylpyridinium dyes, such as RH421 and di-8-ANEPPS. So far these dyes have been particularly successful in resolving the mechanism of the biologically important ion-transporting membrane protein, the Na⁺,K⁺-ATPase. The current dyes do, however, suffer from problems of photochemical instability and lack of specificity. We are presently investigating synthetic modifications to the dyes to suppress their photochemical reactions as well as to increase their specificity, in particular to allow measurements to be carried on the proton transfer reaction of the photosynthetic reaction centre.

Selected Publications

Metalloproteins from Cold-Adapted Bacteria (Simpson, Maher, Nichols, Santini)
The extreme temperatures present on the Earth, such as those found in hydrothermal vents (>90 °C) and in Polar regions (<5 °C), have forced resident bacteria to adapt to these seemingly inhospitable temperatures. Proteins (both non-metallated and metallated) expressed by these 'extremophilic' life forms have unusual structures and may have applications in biotechnology; proteins expressed by hypothermophilic (more commonly known as psychrophilic, 'cold-loving') bacteria (optimal growth temperature <15 °C), for example, have higher glycine contents, compared to the analogous mesophilic (optimal growth temperature 20-40 °C) proteins. We are examining the nature of cold-adapted metalloproteins expressed by psychrophilic bacteria isolated from Antarctic sea ice, focusing on classes of redox-active proteins that have been well characterised in mesophilic and hyperthermophilic organisms.

“Super-Siderophores” from Cold-Adapted Bacteria (Pakchung)
In order to survive in Antarctic regions, resident bacteria must adapt their biomolecular machinery to remain functional under cold conditions (refer to project above). In this project, we are isolating small-molecule organic chelates involved in microbial Fe(III) uptake (siderophores) from Antarctic bacteria grown under conditions of low Fe availability. We hypothesise that cold-adapted siderophores produced by Antarctic bacteria will have novel structures and extraordinary affinities towards Fe(III).

Modelling Tungsten, Molybdenum and Vanadium Metallo-Isoenzymes (Jordan, Hibbs, McKenny)
The metallo-oxotransferases and nitrogenase are two classes of redox-active metalloenzymes that exist as metallo-isoenzymes, containing either tungsten or molybdenum (oxotransferases) or molybdenum or vanadium (nitrogenase) at the active site. The active-site metalloclusters of select oxotransferases (I) and nitrogenase (II), as revealed by X-ray crystallography, are striking.
It is intriguing that Nature appears to preferentially express specific metallo-isoenzyme forms (e.g.; W-containing metallo-oxotransferase) under specific environmental regimes (at hydrothermal vents, where temperatures >90 °C). We are synthesising metal-ligand complexes that mimic the active sites of these two classes of metalloproteins in order to further explore the role that temperature plays upon the redox-dependent catalytic profiles. Experiments using EPR spectroscopy to measure equilibrium distributions of Mo(V) and W(V)-dithiolene complexes are also being conducted in concert with computational studies.

Metal-Sialic Acid Chemistry (Fainerman-Melnikova, Jolliffe, Lay, Rockenbauer)

Sialic acids (e.g., N-acetylneuraminic acid, III) are negatively-charged carbohydrates located at cell surfaces that play important roles in cell-recognition processes. These extracellularly located polyfunctional molecules, present in both animals and humans, are potential metal chelates. Molecular mechanics calculations are being used together with EPR and NMR spectroscopy to build models for speciation profiles between transition metal ions and III. We have shown that complexes between sialic acid and transition metal ions are readily formed and we are continuing to evaluate the biological relevance of species formed between sialic acid and endogenous (Cu, Fe) or exogenous (Cr, V) metals. In addition, a family of organic molecules that model specific regions of III are being prepared to assist in the deconvolution of complex metal-III speciation profiles.

Synthesis of Designer Resins (Greaves)

We are examining ways to synthesise resins that are tailored toward resolution chemistry by immobilising coordination complexes onto resins, using standard coupling techniques. These resins will be well suited toward resolution of many organic ligands, which has increasing significance in pharmaceutical applications, where resolved (100% e.e.) compounds are required for use in clinical trials.

Selected Publications

Porphyrin Arrays as Models for Light-Harvesting Systems and Charge Separation Involved in Photosynthesis (Absalom, McDonald, Blake, Kashiwagi, Suga, Fukuzumi*, Sundström*, Larsen*)

Light capture is the first step of photosynthesis. Artificial porphyrin systems designed to mimic light capture in Nature are currently under investigation. New multi-porphyrin arrays assembled on dendrimer cores are designed to mimic the LH1 and LH2 systems and the light-harvesting arrays of Photosystem I. Ultrafast spectroscopy is being used to study energy transfer in these systems. Use of other dendritic cores in the synthesis and their effect on the photophysical properties of resultant porphyrin-appended dendrimers is being explored along with variation of the porphyrin component.

A 16-porphyrin dendrimer that displays multi-photosynthetic reaction centre properties, see left, has been synthesised and its photophysics examined. Each unit acts as a donor-acceptor system leading to long-lived charge separation, lasting about 0.8 milliseconds. When less than a stoichiometric ratio of acceptor was used, photoinduced charge separation was still very efficient as an energy transfer pathway from uncomplexed porphyrin to acceptor-complexed porphyrin was found to operate.

A very long-lived charge-separated state produced by photoinduced electron transfer was observed in a zinc imidazoporphyrin-C₆₀ dyad designed and synthesised in this project. Methodology for selective metallation and selective partial metallation of the porphyrin units has been further developed.
Porphyran-based Photovoltaic Cells (Blake, Absalom, Thordarson, Dastoor*, Fukuzumi*, Hasobe*, Franzon*)
A solid-state and a solution photovoltaic cell were constructed using thin films and nano-clusters of porphyrin arrays on optically transparent electrodes as light-harvesting units. Both cells were found to have desirable properties for further investigation. A new approach to aligned donor-acceptor systems was explored.

New Advanced Materials (Hough, Khoury, Reimers, Hush, Hersham*)
The design and synthesis of new advanced materials based on metalloporphyrins was continued. A novel approach to rigid extended aromatic systems has been further developed to include the synthesis of novel polymers with the potential to behave as electrical conductors and semi-conductors. Studies in the areas of molecular switching devices and molecular shift-registers and novel molecular circuitry were continued. Additional methodology for construction of porphyrin building blocks that allow up to four attachments of molecular wire components was established.

Synthesis and Photophysics of Models for the Photosynthetic Reaction (Sintic, Blake, Ghiggino*, Fukuzumi*, Kadish*)
Two tris-and tetrakis-porphyrin chemical mimics of the chromophore arrangement of the photosynthetic reaction centre (PRC) has been designed and synthesised. Photophysical studies show that it results in long-lived charge separation upon being irradiated. The kinetic and thermodynamic properties of the synthetic PRC are under investigation using ultrafast and ESR spectroscopy and electrochemistry. A long-lived charge shift state has been detected. In related studies, when gold(III) porphyrins were used as acceptor molecules it was found that gold(III) porphyrin π-radical anions are not formed, contrary to the claims of others for more than 30 years, but that gold(II) porphyrins are produced. More elaborate models that incorporate an additional non-porphyrinic acceptor unit were designed and synthetic studies were commenced. These are the closest mimics of the natural systems to be developed anywhere.

Porphyran Analogues as Gingivitis Inhibitors (McDonald, Yap, Hunter*)
The black-pigment Gram-negative bacterium Porphyromonas gingivalis is an important etiological agent of adult periodontal disease. This bacterium has been reported to display an absolute requirement for either hemin or hemoglobin as growth factors. In this work, a porphyrin-antibiotic conjugate designed to be recognised by HA2 receptors of the gingipains and to kill the P. gingivitis bacterium selectively has been designed and is being synthesised.

Selected Publications
X-Ray Nanoprobe Investigations of Intracellular Arsenic Species for Understanding As-Induced Genotoxicities (Foster, Harris)

Chronic As poisoning, arsenicosis, is a problem associated with drinking As-contaminated water (as little as 0.05 mg As/L for a period of 6 months). It is a worldwide problem predominantly affecting third-world countries where groundwater is the major source of drinking water; e.g., Argentina, Chile, China, India and Mexico. In Bangladesh and West Bengal alone, more than 70 million people are at risk of drinking this water and it is estimated that more than 4 million people currently suffer the effects of arsenicosis; namely, cancers of the skin (keratosis), kidney, bladder, lung and liver, and black foot disease (gangrene resulting from severe disease of blood vessels).

While the potential incidence of As-induced cancer is clearly phenomenal, its mechanism of action is poorly understood. This project aims to determine the modes of As carcinogenesis and toxicity, by determining the intracellular targets of As and its associated biotransformation products. Scheme 1 shows the species that have been identified from plasma and urinary analyses of As-exposed humans and animals. Two main chemical reactions are evident: reduction of As(V) to As(III) with associated oxidation of two glutathione molecules to form the oxidized form GSSG, and the biomethylation of As(III) by $\text{S}$-adenosylmethionine to form the monomethylated As(V) species. The As(V)/(III) reduction/oxidation cycle continues following further reactions with GSH and $\text{S}$-adenosylmethionine to produce dimethylated arsenic species, and, in some animals, trimethylated arsenic species. Unsurprisingly, debate exists as to whether biomethylation of As is a detoxification or toxification process.

Scheme 1. Proposed biotransformation reactions of As species in vivo.
Nanoprobe synchrotron-based techniques are opening up unprecedented avenues of research as they are now capable of providing chemical information at nanoscale resolution and parts per million sensitivity. Techniques such as micro-SRIXE (synchrotron radiation induced X-ray emission) and micro-XAS (X-ray absorption spectroscopy) have been used to offer new insights into the intracellular As species. Figure 1a shows the distribution map of intracellular As. Micro-XAS was performed at the point indicated in the map of an arsenate-treated cell and a spectrum (Fig. 1b) indicative of a As(III) species was obtained. This information shows that following 4 hr exposure of lung cells to arsenate (and arsenite), there is no evidence of substantial As methylation. Correlation of this result with genotoxicity assays of a number of inorganic As species indicates that the damaging species is unlikely to be methylated As.

Further studies involving longer exposure times, liver cells and other As complexes are being performed to further elucidate information regarding the biotransformation reactions of As, and the damaging species.

Other areas of research in this laboratory include intracellular studies of metal-containing potential anti-cancer drugs and analyses of the targets of these drugs.

Selected Publications
Activation of Metal-Coordinated N₂ (Hazari, Li, Luck, Tronoff)
The reactions of molecular nitrogen (N₂) coordinated to transition metals were examined with the aim of providing new methods for reducing N₂ or incorporating nitrogen into organic substrates. Transition metal complexes of N₂ (containing Mo, W and Fe) were synthesised and characterised.

Reduction of N₂, coordinated to an iron hydrido phosphine complex, was examined in detail. The reaction presumably proceeds via intermediate complexes with coordinated diazine and hydrazine to yield eventually free ammonia. Experiments were initiated to establish details of the reaction mechanism.

Transition Metal Activation of H₂ and Hydrocarbons (Smernik, Li)
A number of different metal hydrides (containing Rh, Ir, Fe, Ru) were synthesised to form potent organometallic reagents that react with C-H bonds in organic compounds to form alkyl- and aryl-metal compounds. New polydentate phosphine ligands were synthesis and complexed to metals to form reactive complexes which were fully characterised the examined as reagents for C-H activation of alkynes, alkenes, arenes and alkanes.

The chemistry of iron complexes of dihydrogen (H₂) was examined both to establish the nature of the metal-H₂ bonding but also to study the exchange dynamics of the coordinated dihydrogen with other hydride ligands.
(a) the cyclisation of aminoalkynes to N-containing heterocycles

(b) a new route to the indole skeleton from functionalised aryl acetylenes

Transition Metal Catalysis of Organic Transformations
(Shasha, Li, Messerle)
New organometallic rhodium and iridium complexes with carbene ligands were developed as catalysts for a number of organic transformations including:

Selected Publications
THE STRUCTURE AND FUNCTION OF METALLOPROTEINS

Many biological processes depend on types of protein, whose molecular structure includes one or more essential metal atoms. Research on the crystal structures of such proteins was initiated in the (then) Department of Inorganic Chemistry in about 1975. An early success was the structure analysis of plastocyanin, a ‘blue’ copper protein with unusual spectroscopic properties and an essential electron-transfer function in photosynthesis. Current research is focussed on the crystal structures of auracyanin, a ‘blue’ copper protein from the primitive photosynthetics bacterium *Chloroflexus aurantiacus*; copper amine oxidases, a widely distributed class of copper enzymes; proline aminopeptidase, an enzyme whose active site includes a dinuclear manganese(II) cluster; and a related enzyme, prolidase, from the thermophilic bacterium *Pyrococcus furiosus*. In order to explore the mechanism and specificity of the copper amine oxidases, we are undertaking crystal structure analyses of three types of derivative: complexes of the enzymes with inhibitor molecules, complexes prepared by snap-freezing crystals of the enzymes under a high pressure of xenon gas, and complexes of the enzymes with electronic ‘wires’. The xenon derivatives probe hydrophobic cavities that may act as a transient binding site for dioxygen molecules prior to the catalytic reaction. The electronic ‘wires’ are synthetic compounds that enable electrochemical measurements on a catalytic site buried deep in an enzyme molecule, by connecting the catalytic site to the surface of an electrode. Complementary studies include spectroscopic (XAFS/XANES, EPR) and electrochemical measurements. International collaborators in 2003 included Prof. M.W.W. Adams, University of Georgia (prolidase), Prof. R.E. Blankenship, Arizona State University (auracyanin), Prof. D.M. Dooley, Montana State University (amine oxidases), Dr. P.J. Ellis, Stanford Synchrotron Radiation Laboratory (protein-xenon complexes), and Prof. H.B. Gray, California Institute of Technology (‘wire’ complexes).

The University's protein structure laboratory, originally located in the School of Chemistry, was Australia’s first centre for the study of macromolecular crystal structures. It was moved to the Department of Biochemistry (now the School of Molecular and Microbial Biosciences) in 1995. The study of metalloprotein structures is a continuing collaboration with the Director of the laboratory, Dr J. Mitchell Guss.
Selected Publications


Organometallic catalysis (Frey)
The project aim is to use the porphyrinogen and calixpyrrole structure as a ligand for metals engaged in catalysis reactions. By providing a cavity for the metal we intend to extend the lifetime of the catalyst and have the ability to modify the reactivity of the metal through a variety of interactions with the calixpyrrole host. Large radii lanthanoid metals, such as samarium, will be coordinated in the cavity. Syntheses of a range of these cavity materials are being developed.

Education in Chemistry (Engelsman, Read)
Chemistry, to the practitioner, is a web of inter-related concepts yet it is traditionally taught to students as a linear progression of topics. This project has probed the perceptions that students have of the linkages between topics in chemistry and has examined how these linkages are portrayed in the resource material available. Part of the project has involved the development of problem sheets that are designed to highlight the integrated nature of chemistry with the aim to facilitate student learning. Student perception of their understanding of topics within first year chemistry is being examined and how this correlates with assessment performance in those areas determined.

Detection of steroid use in sports (Cawley)
Dehydroepiandrosterone (DHEA), a naturally produced androgen, may be administered by athletes with the aim of increasing levels of the more active androgens such as testosterone (T) and dihydrotestosterone (DHT). The International Olympic Committee (IOC) prohibits DHEA administration in athletes, however its detection remains difficult due to an incomplete understanding of DHEA metabolism as well as inter-individual variations.
In this study, Gas Chromatography-Mass Spectrometry (GC-MS) demonstrated that a single oral administration of DHEA (100 mg) to a subject altered the urinary steroid concentrations of androsterone (A) and etiocholanolone (Et). The ratio of the concentration of A to Et (A/Et) may provide a screening marker of DHEA administration. Values of A/Et less than 0.5, measured following DHEA administration, were compared to a reference distribution of A/Et values obtained from 858 urine samples. Only 3 of these had A/Et values less than 0.5.

The urine samples collected after DHEA administration were also analysed by Gas Chromatography-Combustion-Isotope Ratio Mass Spectrometry (GC-C-IRMS) to determine the Carbon Isotope Ratio (CIR, d^{13}C) of A and Et. This technique demonstrated that d^{13}C A and d^{13}C Et were reduced following the single administration of DHEA. The difference between d^{13}C Et and d^{13}C An increased from 1.6 ‰ at the time of administration to a maximum value of 5.2 ‰, which corresponded to a minimum A/Et value of 0.4.

Multiple oral administrations of 100 mg DHEA, morning and night for seven days to a separate subject resulted in Et being ^{13}C depleted in relation to the DHEA that was administered. Also, an unknown compound, detected in many of the GC-C-IRMS traces was shown to have d^{13}C values similar to those of Et. This compound, identified as 3a-5-cyclo-5a-androstan-6b-ol-17-one, may prove to be an effective indicator of DHEA administration.

Selected Publications
Polymers and Emulsion Polymerization: Novel Structure and Properties (Ferguson, Pham, Sangster, Vosloo, Thickett)

The relationship between molecular and mesoscopic structure on the one hand and mechanical and other end-use properties on the other is a major unsolved problem in the science and technology of polymer colloids. The study of how changes at the molecular level affect physical properties incorporates projects ranging from the preparation of novel clay-polymer and coal-polymer composites to the development of new methods for living radical polymerization in emulsion systems. Other ongoing projects include the preparation of nanoscale particles through emulsion polymerization, synthesis and characterization of novel polymer colloids with grafted architectures, effects of molecular architecture on mechanical properties (with University of Queensland and University of Stellenbosch), and the preparation of next-generation environmentally-friendly surface coatings (with Dulux Australia). Fundamental investigations have explored the effect of mobile surfactants and electrosteric stabilizers on the kinetics of particle growth and formation, as well as examining their effects on the end-use properties of surface coatings derived from polymer latexes. Studies have been completed on the effect of grafted in-situ stabilizer on the effect of entry and exit of monomeric polymeric radicals. A novel means of using polymer colloids in electrosensing electrodes has also been completed (with UNSW). Work continues on the fundamental science of free radical polymerization with a project on reversible addition-fragmentation chain transfer using emulsion polymerization (with Dr E Rizzardo, CSIRO Molecular Science) and involvement in IUPAC initiatives to develop more rigorous protocols for determination of propagation and termination rate constants.

Modelling and Control of Emulsion Copolymerization (Lamb, Zeaiter, Elgebrandt)

A universal problem in the industrial manufacturing of polymer colloids is that a process which works well on a 1 litre laboratory scale can fail when scaled up to 20 tonnes. Some fundamental reasons for this are understood: many of the steps in an emulsion polymerization are such that the process is sensitive to small fluctuations, e.g., in shear or amounts of inhibitor. This project aims to create a unified approach to the understanding of this problem by combining the scientific knowledge becoming increasingly available in the kinetics and mechanism of the conventional free-radical synthesis of polymer colloids with the requisite chemical engineering science (experimental and computational fluid dynamics and reactor engineering, in collaboration with the Department of Chemical Engineering). Other work includes the first comprehensive study of redox-initiated emulsion polymerization (with BASF Australia and Germany) which has now been completed.
Polymer Colloids in Natural Systems (Castro, Chiou, Perry, Warrender, Rouilly, Rea, Youssef, Chang)
The aims of this project are twofold. First, to apply the experimental and theoretical techniques developed for the characterization of synthetic polymer colloids, and for investigation of their behaviour in multiphase and interfacial systems, to natural polymer colloids. This is leading to the development of models for natural polymer colloid structure (e.g., molecular architecture of starch hydrocolloids) or natural polymer colloid processes (e.g., flocculation of polysaccharide particulates). Second, to carry out strategic basic research for novel applications of synthetic polymer colloids in natural systems. Extensive new knowledge has been produced on how the molecular weight distribution of starches affects physical properties such as “mouth-feel”, and how these molecular weight distributions may be used to infer biological pathways in starch synthesis (with CRC for Quality Rice and NSW Agriculture). The last-named work has produced the exciting discovery of the presence of a third form of starch (in addition to the well-known amylose and amyllopectin) in grain food.

Selected Publications
Tuning the Chemistry of Platinum(IV) Drugs (Alderden, Amjadi, Callaghan#, Dolman, Deacon#, Failes, Hall, Turland#)

Platinum(IV) complexes are more inert than their Pt(II) analogues and therefore have the potential to be less toxic. Means for targeting Pt(IV) complexes to DNA were investigated. $^1$H,$^{15}$N HSQC spectroscopy was used to follow the reactions between Pt(IV) and biomolecules. The use of X-ray absorption near edge spectroscopy (XANES) to provide information about the relative proportions of platinum(II) and platinum(IV) complexes by analyzing the XANES edge height was further developed. The intracellular reduction of platinum(IV) complexes in cancer cells was observed directly, and the proportion of reduction after 2 h was found to correlate with the reduction potentials of the complexes. The distribution of platinum in tumours implanted in mice and treated with platinum(IV) complexes was examined using elemental analysis (SRIXE). Tumour spheroids were investigated as models for hypoxic tumours and the effect of platinum(IV) complexes on cellular growth in spheroids was studied.

Stereochemical Influences on the Binding of Novel Complexes to DNA (Bullus, Diakos, Fenton, Messerle#, Sadler#, Waller)

The primary aim of this project is to establish the role steric interactions and hydrogen bonds play in influencing the coordinative binding of Pt complexes to DNA. A full 2D NMR structural study of the two isomers formed when $[\text{PtCl}_2(\text{3-ahaz})]$ ($R_1 = R_2 = R_3 = H$) binds to a 14-mer duplex oligonucleotide was continued in collaboration with Professor Peter Sadler of Edinburgh University. NMR spectra of both isomers revealed strong nOe’s that enabled isomer determination. The spectra have been fully assigned and structural modelling using the NMR was completed and the results are being prepared for publication. The effect of substituents (R) on the structural and dynamic properties of the d(GpG) ligand in complexes of the type $[\text{Pt}(d(GpG)(R_2-1,10-phenanthroline))]$ and $[\text{Pt}(d(GpG)(R_2-2,2’-bipyridine))]$ was commenced. Rotational isomers were separated by HPLC and studied by NMR spectroscopy.

Sequence Selective Targeting Metal Complexes to DNA (Whan, Young)

The targeting of metal complexes to DNA has numerous applications such as the delivery of radionuclides, anticancer agents and DNA cleavage agents. A project to achieve sequence selective targeting using intercalators bound to metal complexes was continued. Preparation of a new series of intercalator/macrocycle complexes was continued with a series of new macrocycles prepared and attached to anthraquinones.

Targeting Tumours using Matrix Metalloproteinases (Failes, Hall, Underwood)

Inhibition of matrix metalloproteinases (MMPs) reduces cancer growth and metastasis and the fact that MMPs are overexpressed in metastasising tumours makes them ideal for targeting tumours. A cobalt complex of marimastat was confirmed as being more effective than marimastat itself at inhibiting tumour growth, but to be less effective at inhibiting metastasis. XANES spectroscopy was used to investigate the oxidation state of cobalt complexes in solution and in tumour cells.
Structural Insights in Metal Ligand Bonding (Hocking)

A project on the use of structural databases and theoretical methods to gain insights into metal-ligand bonding was continued. An examination of the relationship between TM-C and C≡≡≡≡≡O bond lengths using more than 20,000 crystal structures revealed three novel observations relating to TM-carbonyl interactions. The curves representing plots of TM-C vs C≡≡≡≡≡O bond lengths are chair shaped, having three distinct regions of gradient. The steeper gradient in region 1, with very short TM-C bond lengths is consistent with the effects of π-bonding dominating over those of σ-bonding. The shallowest gradient occurs in region 2, with intermediate TM-C distances where the σ- and π- contributions to bonding have largely counteracting effects. Finally, an increase in gradient is observed in Region 3, where C≡≡≡≡≡O bond lengths are shorter than those of gaseous carbon monoxide. In this region the σ and ionic contributions to the bonding dominate and presumably are not balanced by the effects of π-bonding. The second novel observation is that a region of large gradient change is coincident with the C≡≡≡≡≡O bond length being equal to that in carbon monoxide gas. The final novel observation emerges from a comparison of the results for 2nd and 3rd row elements of the same triad. The curves overlap in region 3 but increasingly diverge through regions 2 and 1. The overlap in region 2 is consistent with the similarity of the ionic radii of 2nd and 3rd row elements and with the bonding in this region being dominated by σ and electrostatic contributions. The divergence in regions 1 and 2 begins where the C≡≡≡≡≡O bond length is the same as in gaseous carbon monoxide or as the contribution of π-bonding begins to have a net effect.

Selected Publications

Antifreeze Proteins and Glycoproteins (McGann, Anderberg, Hutchins, Kwan, Mackay, Haymet)

Antifreeze proteins and glycoproteins permit many species of fish to survive in sub-zero oceans without freezing. These antifreeze compounds have potential applications in the frozen food industry (e.g., maintaining the texture of ice cream), medical science (e.g., cryosurgery) and veterinary science (e.g., storage of sperm). Commercial applications are limited by the amounts of compounds available from fish and the lack of understanding of how these proteins work.

Preliminary results crucial to allow the design of new synthetic AFPS have been obtained. A range of derivatives of the sculpin APF SS3, in which the overall charge, dipole, and capping groups were varied were prepared by selective modification of Lys residues. These derivatives were designed to test the hypothesis that AFPs interact with the charge inhomogeneity at the ice/water interface. While determination of the thermal hysteresis values was hampered by poor aqueous solubility and low hysteresis values, the results are consistent with a role of charge in the mechanism of action.

The first NMR structures of any natural or synthetic type I AFP have been determined. These NMR studies have been possible through expression of doubly labelled $[^{13}C, ^{15}N]$-sculpin APF. These structures have been contrasted at 5 and -5 degrees and included the acetylated and non-acetylated sculpins and have allowed the role of structure, including the N-acetyl group, in hysteresis to be determined.

Studies with model membranes have provided important insight into the design requirements to tailor new AFPs with cryoprotectant and other commercial properties. The effect of hydrophobic AFP analogues on the stability of model membranes showed that additional salt bridges incorporated in the synthetic sequences destabilize model membranes, while natural AFPs stabilise membranes.

Key model glycopeptides required to assemble AFGPs have been prepared. Synthetic routes to model glycopeptides in which the stereochemistry, and galactosamine sugar have been developed. The chemical route was identified as the superior to enzymatic glycosidation of peptides.

Antitumour Metalloccenes (Waern, Dillon)

The biological chemistry of the metalloocene dihalides has attracted significant interest and titanocene dichloride is the first non-platinum metal complex to enter clinical trials. In contrast to the titanium complex, there is insufficient biological and structure-activity data on the other metalloocene dihalides to propose mechanisms of action, and current
evidence strongly suggests that the different metallocene complexes interact differently with cellular components, and therefore probably have different antitumour mechanisms of action. Although molybdocene dichloride coordinates to nucleotides, molybdocene-oligonucleotide adducts are not formed under physiological conditions, and hence a direct relationship between anticancer activity and formation of stable molybdocene-DNA adducts in vivo is unlikely. We have shown that molybdocene dichloride interacts strongly with thiols including cysteine and glutathione and that these complexes are stable in the presence of competing biological nucleophiles. On the basis of these results, the design and synthesis of a range of thiol derivatives that have allowed the influence of overall charge, aqueous solubility and lability of the Mo-X bond on transport into cells and cytotoxicity to be evaluated. These studies, along with visualisation of the cellular distribution of the metal through the use of micro-SRIXE and microscopy techniques, have provided insight into the active species present in blood plasma, and provided important data on the role of the halide ligands that needs to be taken into account in the design of novel organometallic complexes as new anticancer drugs.

**Streptonigrin (Middleton)**
Streptonigrin is an aminoquinone antitumour antibiotic with broad spectrum activity against a range of cancers. The mechanism of antitumour action of the drug is related to free radical-mediated DNA strand cleavage due to reductive activation of streptonigrin, in a process that involves metal ions and oxygen. Synthetic routes to streptonigrin analogues, that overcome low-yielding oxidation and biaryl coupling reactions were investigated. Molecular Clefts (Tsai, Turner, Hutchins)
The stereoselective assembly of metallomacrocycles from the optically active bisbipyridyl ligand L that incorporates the chiral molecular cleft, dibenzobicyclo[3.3.1]nona-5a,6a-diene-6,12-dione has been achieved. This cleft is reminiscent of Tröger’s base but contains different dimensions and additional carbonyl (or alcohol) groups that may be utilised in molecular recognition studies. This cleft was incorporated into the ligand design as it allows entry into optically active ligands, and as the dimensions and recognition properties of the resultant metallomacrocycles offer new opportunities to target the molecular recognition of different classes of substrates. In the presence of zinc(II), racemic ligands undergo an unusual slow equilibration to form the thermodynamic [2+2] metallomacrocycles which contain a single ligand enantiomer.

**Selected Publications**
Glass Transitions (Fernandez, Widmer-Cooper, Padilla, Fynewever)
Our aim is to develop physically accurate theoretical descriptions of the glass transition and all its accompanying phenomenology in specific glass-forming liquids. This problem represents a major challenge in both materials science and the fundamental theory of condensed matter. Our tools are computer simulations of the dynamics of model liquids and the theoretical methods of statistical mechanics. In simulation studies of a model liquid mixture we have demonstrated that the glassy dynamics involved an increasing inhomogeneity in the spatial distribution of relaxation kinetics. This insight has proved a valuable approach to the analysis of structural relaxation and diffusion in supercooled liquids and has led to explanations of the breakdown of Stokes-Einstein scaling, the extended momentum memory near the glass transition and the phenomenon of solute-enhanced diffusivity (the ‘plasticiser’ effect). In simulations of amorphous silica, we have shown that UV irradiation can result in densification and, hence, long-lived changes in the refractive index. We have also established the collective particle motions in the glassy liquid associated with the sharp increase in heat capacity in heating the glass. Recently, we have determined the crystal structures of a range of glass-forming mixtures and are now examining the role played by these complex structures in stabilizing the amorphous state. We are also completing work on glass-formation in 2D. One study involves the crystallization of a large unit cell structure in which substantial supercooling is also possible. We have also developed a novel isoconfigurational ensemble that allows for the clear connection between dynamic heterogeneity and particle configurations in simulated glass-formers.

Crystal Growth (Wild)
We are interested in developing statistical theories of the molecular dynamics associated with crystallization from the melt. Our current work involves looking at two questions directly associated with colloidal crystallization. The first is the description of crystallization involving density change under conditions of constant N and V. Under these conditions the supercooling is, itself, varying with time. Our current work is aimed at extending the theory to include a second component, immiscible in the crystal. The second problem considers the relationship between a crystal surface’s ability to organize the adjacent liquid and the kinetics of the growth process. We have shown that a gap can exist between the density at which the crystal becomes stable and the density at which a given surface can advance. Specifically, close packed surfaces with short range interactions were found to be unable to fully break the symmetry of the adjacent liquid and hence the growth of these surfaces was impeded. We are carrying out simulations of the crystallization of a hard sphere liquid to understand the role of liquid structure and stacking faults in determining the crystal growth rate.

Shear Induced Transitions in Liquids and Crystals (Butler)
Using nonequilibrium simulations, we have recently demonstrated that a strained crystal can coexist with a shearing liquid. The criteria that define this nonequilibrium coexistence remain unknown despite its central importance with regards the rheology of materials characterised by ‘soft order’. We established for the first time that popular extensions of thermodynamics to these nonequilibrium systems can not account for the observed coexistence. Instead we have
proposed that the two phase states represents the balance between the rate of crystallization and the rate of erosion of the crystal. This represents the first molecular theory of erosion. We have developed a theory of the nonequilibrium coexistence in which we couple the equations of the motion of the heterogeneous crystal structure with the strain field. This theory successfully reproduces the behaviour observed in simulation, including the erosion-based explanation of the coexistence. In a related problem we are studying origin of rigidity in thin liquid films confined between two amorphous walls (i.e. lubrication films).

Structure and Stability of Ionic Clusters and Reverse Micelles (Wootton)
Small clusters represent a fascinating window onto how atoms and molecules behave at surfaces and the enhanced possibilities for structures once long range order is no longer necessary. Using computer simulations we are currently studying the following three questions. i) Can ions form polyhedral clusters that are stable with respect to crystal fragments? ii) How are ion clusters hydrated by water? iii) What is the structure and phase behaviour of small clusters of liquid crystal forming molecules? A systematic study of silver halide clusters has indicated that polyhedral clusters (ionic analogues of buckyballs) are stable when the anion is considerably larger than the cation. Reverse micelles formed from ionic surfactants are, at low water concentrations, ionic clusters and we are currently working on resolving the long-standing problem of what determines their equilibrium size in terms of stable ordered structures.

Selected Publications
Physical Chemistry of Flavonoids (Overgaard, Hanrahan, Hambley, Johnston)
The primary objective of this project is to contribute to the design and development of new drugs via a study of the experimental charge distribution in molecular crystals. This has involved the high resolution X-ray crystallographic study of a number of novel receptorial drugs of the flavonoid class, using a multipole refinement procedure to determine the electron distribution.

Flavonoids are polyphenolic compounds found extensively in plants:
Recently, it has become clear that some flavonoids have effects on the central nervous system and it is this group that will be the subject of the project outlined here. GABA (g-aminobutyric acid) is the major inhibitory transmitter in the brain and it has been shown that the anxiolytic flavone apigenin has a novel mode of action on GABA receptors in the brain. This project relates the structural and electronic characteristics of this novel mode of action, and how flavonoids may influence actions of other molecules in order to design and develop potentially useful therapeutic agents for CNS disorders.
Computational Studies of Platinum Complexes (Hambley, Waller)

Platinum anticancer drugs such as cisplatin (cis-[PtCl₂(NH₃)₂]) effect their action by binding to DNA. It has been suggested the incoming platinum complex recognises different sequences and that design of compounds capable of targeting different sequences will depend on the ability to model this recognition process. Before such modelling can be reliably undertaken, charge distributions of the platinum complexes need to be determined. Theoretical methods are available for producing charge distributions but they have had no experimental verification as yet. Therefore, an important goal of this project has been to develop methods for determining the electronic distributions in platinum complexes of the type involved in binding to DNA.

Insights into Hydrogen Bonding (Overgaard, Waller)

The primary outcome of this project has been to contribute to the understanding of the nature of hydrogen bonding in biological systems via a study of the experimental electron distribution. The hydrogen bond is the most versatile intermolecular interaction in the biological and material worlds and is responsible for molecular aggregation, protein folding and enzyme activity. Conventionally strong hydrogen bonds such as O – H …O, N – H …O and O – H …N have been extensively exploited in the areas of supramolecular chemistry and crystal engineering. In contrast, the somewhat weaker N – H …N hydrogen bonds have been scarcely studied, but clearly have important roles in nature. For example, the gross structure of protein molecules, the structures of the genetically important DNA and RNA molecules, as well as drug – receptor binding.

Chemical Mineralogy of Secondary Base Metal Species (Williams)

This project concerns secondary copper(II) arsenates and phosphates and related species. Relevant stoichiometries are Cu₂XO₄(OH). Structural relationships are well-established, with many being isomorphous. However, subtle differences in space group symmetry are known for certain related phases, in part due to solid solution phenomena. The secondary phosphates and arsenates of Cu(II) are very common minerals in oxidized base metal orebodies and a thorough understanding of the solid solution phenomena is lacking.

In a second related area, we have focussed attention on “simple” oxyanion mineral salts of the Cr triad MXO₄ (M = Ca, Pb; X = Cr,Mo,W), and associated species such as anglesite (PbSO₄) and cerussite (PbCO₃). Recognition of the structural variation has solved a decades-old problem associated with the true symmetry of the scheelite (CaWO₄) group and the phenomenon of hemihedrism observed for individual crystals of the PbWO₄-PbMoO₄ series.

A combination of synthetic, structural, analytical and solution thermodynamic studies will be employed to:

- determine the true extent of solid solution in the systems using single-crystal X-ray, powder X-ray and powder neutron diffraction methods;
- explore the detailed nature of any structural transitions that may accompany any of the above solid solution series and in particular investigate structural effects on anion and cation ordering with respect to structural variations;
- explore the extent of such solid solutions in naturally occurring minerals.

Selected Publications

Colloid Chemistry

Many, if not most, industrial and commercial materials consist of dispersions of particles of a solid or a liquid immersed in another liquid. Cosmetics, food and many pharmaceuticals are in this category as are also some mineral ores. Soils, paint, inks, polymer latex and ceramic materials are also of this kind and all are examples of colloidal dispersions. Although strictly limited to systems in which the particles are of order 1 mm or less in size, there is no real demarcation between such systems and those with rather larger particles (called suspensions). The latter tend to be unstable and to separate into their components unless the density difference is small. Colloid chemistry concerns itself with the understanding of the behaviour of dispersions and fine suspensions, particularly in respect of their sedimentation, flow and stability properties.

Electroacoustics

When a very high frequency (MHz) electric field is applied to a colloidal dispersion, the (charged) particles oscillate backwards and forwards in response to the field. This generates a sound wave of the same frequency, and by measuring the properties of the sound wave we can determine the particle size and effective charge on the particles. The theoretical basis of such measurements was developed here in Sydney in the mid 1980s by Dr Richard O’Brien, who has since gone on to establish a company (Colloidal Dynamics Inc) which produces and markets, world-wide, several highly sophisticated devices for measuring these colloidal properties. The company’s R & D program is partly housed in the National Innovation Centre of the Australian Technology Park near Redfern and we continue part of the program in the School of Chemistry in the laboratory of Assoc Professor James Beattie.

Electroacoustic measurements have proved of value in characterising many systems including the slurries used to polish the latest generation of computer chips to the necessary level of planarity to enable the development of high processing speed. The electroacoustic method is also particularly useful for studying emulsions since they can be analysed without dilution. The usual methods for determining particle size and charge involve light scattering procedures which require the emulsion to be diluted and this can change its surface properties. Since electroacoustics involves only sound waves, it works quite well in opaque systems. Our most recent studies have been on semiconductor materials and on emulsions. The method is also applicable to ceramic slips, pigments and many other industrially significant materials.
Selected Publications


Our research interests are in the area of environmental geochemistry with special emphasis on the chemical reactions taking place in caves. Some studies in progress are:

**Paleoclimatic Studies from Speleothems and Cave Sediments**
We are obtaining paleoclimatic records from speleothems and sediments throughout Australia using uranium/thorium radionuclide methods. The average temperatures at the time of deposition are established by stable isotope measurements. Submerged calcite deposits found under the Nullarbor Plain are being studied for their association with bacterial colonies and the variation in surface temperature and sea level changes over the last 300,000 years. These results are important in modelling future changes in sea-level from the greenhouse effect.

**Trace Organic and Trace Metal in Speleothems Studies**
Extraction and identification of trace metals and organic materials and their complexes from within the calcite matrix are being carried out. We have established that amino acids are present in many speleothems and are using amino acid racemisation dating techniques to study the geochemical record of specimens up to one million years old.

**The Chemistry of Cavern Development**
The chemistry of cavern development in unusual environments is being studied and modelled. Of specific interest are caves developed by high pressure and temperature waters associated with igneous activity, sulfuric acid and mixing corrosion. The chemical processes leading to the development of caves in non-karst rocks is also being studied.

**Selected Publications**
New Methods for the Cyclisation of Small Peptides (Skropeta)

There has recently been a great deal of interest in the synthesis of small cyclic peptides. Naturally occurring cyclic peptides exhibit a wide range of biological activities and are often more resistant to enzymatic hydrolysis than their linear counterparts. Additionally, the restricted conformational flexibility of cyclic peptides allows them to present functional groups in a spatially well-defined manner and is of use in the study and mimicry of protein folding. Current methods for the head-to-tail cyclisation of linear peptides are often slow and low-yielding. The aim of this project is to develop widely applicable methodology for the efficient head-to-tail synthesis of small cyclic peptides. The use of removable backbone modifications, in the form of pseudoprolines, to stabilise a linear peptide conformation that is amenable to cyclisation is currently being investigated. Introduction of such modifications into a linear peptide has been found to improve both the rates and yields of peptide cyclisation. Installation of a pseudoproline residue at the C-terminus of the linear peptide has also been found to prevent epimerisation during the cyclisation reaction. Once cyclisation is complete, the backbone modifications are readily removed, thereby providing efficient access to a wide range of cyclic peptides.

Design and Synthesis of Fluorescent Sensors for Apoptotic Cells (Johansson, Smith*)

The ability to detect apoptotic cells has numerous applications in biomedical research. The aim of this project is to design and synthesise a cheap and reliable sensor for cell surface phosphatidylserine, which is an early marker of cell apoptosis. A series of peptidic compounds containing two or more divalent zinc ions and tethered to a fluorescent tag have been synthesised for this purpose. Such compounds should be capable of detecting cell surface phosphatidylserine.
Cyclic Peptides as Platforms for Supramolecular Chemistry (Ly, Lee, Larsson)
Backbone rigidified cyclic peptides appear to be ideal platforms for use in the preparation of enzyme mimics and molecular receptors. We are investigating the use of azole-heterocycle containing cyclic peptides for this purpose. The primary aim of this project is to design and synthesise molecules that allow both the preorganisation of functional groups and a degree of flexibility. This will provide us with compounds capable of mimicking enzymes such as serine lipases and phosphatases. Our initial studies have led to the synthesis of a phosphatase mimic bearing two zinc(II) centres that has been found to hydrolyse an RNA model compound at a greatly enhanced rate. The synthesis of a family of lipase mimics is also underway. The relative catalytic properties of these mimics will be evaluated and the importance of flexibility versus preorganisation will be assessed. This should allow the design of enzyme mimics with optimal catalytic activity.

Design and Synthesis of Selective Inhibitors of Fungal Virulence Factors (Ng, Sorrell*, Widmer*, Wright*)
Pathogenic fungi are increasingly implicated as a cause of serious and potentially fatal disease, especially in immunocompromised hosts. Many of these fungi have been found to secrete enzymes that contribute to their virulence and therefore present new targets for drug discovery. The primary aim of this project is to design and synthesise selective inhibitors of fungal phospholipases for use as therapeutic agents. Several classes of compound are under investigation and our best compound has comparable antifungal activity to the currently marketed antifungal drug, Amphotericin B.

Selected Publications
Computational Drug Design (Chebib¹, Crittenden)

γ-aminobutyric acid (GABA) is the major inhibitory amino acid in the brain. Understanding how GABA works will aid in the development of new drugs to treat diseases such as epilepsy, depression, anxiety and Alzheimer’s disease. GABA exists as a neutral molecule in the gas phase but as a zwitterion in solution and in vivo. Models of its biological activity must therefore provide a realistic description of its zwitterionic structure. The goals of this work are to develop accurate and transferable models for the structure and interactions of zwitterions. This will allow the dynamics of their interactions to be investigated and, specifically, will allow interactions of different zwitterionic conformers to be studied. Such dynamic drug design is a major step forward from the static descriptions of structure commonly used at present.

Molecular Potential Energy Surfaces (Collins*, Thompson, Crittenden)

Molecular potential energy surfaces (PES) describe how the energy of a molecule changes as the positions of its constituent atoms change. Accurate PES are crucial to our understanding of molecular structure and reactivity. We have developed new interpolation techniques for constructing PES that allow the PES to be iteratively improved until convergence in any desired molecular property occurs. A computer package “Grow” has been released making these techniques freely available. The “Grow” package has recently been combined with quantum diffusion Monte Carlo methods for determining the ground state nuclear wavefunction of a molecule.

Molecular Reactivity (Crittenden, Kable, Thompson, Codd, McKenny)

We have described, for the first time a chemically accurate PES for the photodissociation of triplet state acetaldehyde. We have also used these and related techniques to describe the structure and dynamics of Mo and W metallooxotransferases, metallo enzymes important in hyperthermal environments.

We are currently implementing path integral Monte Carlo techniques, that will enable temperature effects on molecular structure and properties to be investigated, as well as approximate time-dependent quantum methods appropriate to large systems that will enable quantum dynamical effects to be investigated and for spectra of large molecules to be determined.

Molecular Environments (Thompson)

Molecular environment affects both molecular structure and reactivity. Typically, long-range solvent effects are modelled using electric fields. Determining how structure changes as the field (or the nature of the solvent) changes is computationally intensive and is not feasible for large molecules or at high levels of ab initio theory. However, the response of a molecule to an external electric field can also be expanded as a power series in the field. We have recently shown quantitative accuracy using this approach, at first order, in a model system. That is, we have shown that environmental effects can be modelled by considering the interaction of the molecular dipole with the external field.
We are currently examining the usefulness and limitations of this method and plan to use this technique to model spatially anisotropic electric fields, for example the field generated by a number of amino acid residues in an enzyme active site, and time-dependent electric fields, for example what happens to a molecule in an enzyme active site as conformational change occurs in the enzyme.

Molecular Structure (Chebib, Crittenden, Thompson)

We have applied these methods to describe the structure of a number of systems including the water dimer, ethanediol:water complexes, which provide a model for antifreeze, glycine and the glycyl radical: smaller molecules than GABA that allow solvation effects to be better evaluated, and GABA:water complexes. We have also developed the first chemically accurate PES for the CH₅⁺ system, the structure of which has been the subject of much debate in recent years. Our calculations have allowed Chemistry’s “Cheshire Cat” to be unambiguously characterised as a fluxional molecule with no distinct structure. Two views of the most probable configurations of CH₅⁺ are illustrated below:

![Molecular Structure](image)

1. Faculty of Pharmacy, The University of Sydney

Selected Publications


Laser Induced Chemistry

Lasers have revolutionised many aspects of chemistry, including our understanding of chemical reactivity, synthesis and characterisation of new materials, all forms of spectroscopy and even mass spectrometry. The reason for the large diversity of chemical applications that lasers have found lies in the wide range of effects that strong light has on different materials; breaking bonds, ablating solids, ionising materials, and tickling molecules to behave in certain ways. The research interests of our group include photochemistry, spectroscopy, mass spectrometry and polymerization. A brief description of this work is below. More details can be found on our web page.

Spectroscopy and Structure of Radicals (Bacskay, Nauta, Guss)

Free radicals have proven elusive to study because of their inherent reactivity. Consequently, the chemistry and structure of many radicals remains unknown and has been the subject of active research for many years. Over the past few years we developed three different free radical sources, involving pyrolysis, photolysis and electric discharge. With these sources we can create a wide variety of radicals in a molecular beam, where they cannot react with anything, and can therefore be studied using laser spectroscopy. For the past several years we have been exploring the spectroscopy and structure of small carbenes in the gas phase. Our interest lies in elucidating the fate of these species where irradiated with light. We have found that their fate depends sensitively on the specific halogen substituent: CBr and CCl photodissociate into CF plus an atom; CHF and CCl mix with the ground state and have extended lifetimes for emission; CF and CBrCl are photochemically and photophysically stable. In 2003, we completed work on the CHF [5] and CBrCl [1] radicals, and completed a substantial amount of experimental work on the CCl species.

Photodissociation Dynamics (Jordan, Nauta, Yin)

During 2003 we continued work on the photodissociation dynamics of aldehydes. In this work we are learning what the rotation of a polyatomic fragment can tell us about the reaction process. Such a fragment can rotate in 3-dimensions, which complicates the analysis, but returns 3-D information about the transition state in the reaction. Over the past several years we have built up a considerable body of experimental data covering a range of molecules and conditions. In 2002/3 we have published a model to explain the data, based on classical mechanics [1] (in collaboration with Greg Metha at U. Adelaide) and Dr Meredith Jordan in this department has performed ab initio and semi-classical trajectory calculations to explain the experimental observations, and provide a predictive theory.

We are now in a position to predict the reaction dynamics of reactions that have not yet been determined. We have returned to the simplest aldehyde – formaldehyde – to explore how the reaction changes with increasing energy. We have predicted what should happen on the basis of our theory and during 2003 have collected substantial experimental data that is being analysed currently. We hope to report on our progress in this regard in the 2004 report.
Novel methods in Mass Spectrometry (Hammer, Hughes)

Time of flight mass spectrometry involves the separation of ions of different masses by their flight time rather than by conventional methods (e.g. magnetic sector). In 2000, we developed and patented a new type of mass analyser for ToFMS, shown at right. This analyser is significantly smaller (for the same resolution) than traditional ToF analysers. Since then we have been extensively testing and characterising the analyser. We have tried the analyser with different ionisation sources and different ion detection methods. This project is a collaboration with Varian Australia.

Multiphoton Spectroscopy (Smith (U. Melb.), Richmond)

The phenomenon of two-photon absorption (2PA) as a single quantum transition was first predicted in 1931, however it wasn’t until the advent of lasers in 1960 that it became experimentally feasible. 2P processes have found application in many areas of research, including spectroscopy, multiphoton ionisation, and multiphoton microscopy. In any experiment that utilises 2P processes, one of the most fundamental properties to know is the two-photon absorption cross-section. Most methods that have been developed thus far to measure 2P absorption cross-sections utilise indirect methods, and all require tightly focussed laser beams. During 2003 we have been developing a direct method to measure the 2P cross section. Calculations predict that the method is theoretically feasible and preliminary experiments performed at the Univ. of Melbourne also demonstrate that it is experimentally feasible. [8] The main experimental obstacle is that normal one-photon absorption in the solvent can cause thermal lensing of the laser beam, which affects the measurement of the 2P cross-section. The figure at right shows how the laser beam diameter changes as it passes through three different neat solvents.

Selected Publications

Phase Transitions in Perovskite Oxides (Li, Zhou, Carpenter*, Howard*, Knight*, Vogt*, Wallwork*)
We are undertaking comprehensive experimental studies of the structures and phase transition behaviour of perovskite-type oxides. Metal oxides having structures based on the mineral perovskite, CaTiO$_3$, display a vast array of interesting and technologically important properties including superconductivity, ferroelectricity and magneto-resistance. In general these properties are associated with a structural instability and in this project we seek to understand the nature of these structural instabilities. Systems are studied over a wide range of temperatures (2-2000K) and pressures using both neutron and synchrotron X-ray diffraction methods. As part of this project we have recently temperature, pressure and composition dependence of novel valence transitions in the oxides Ba$_2$PrRu$_{1-x}$Ir$_x$O$_6$.

Structure and Electronic Properties of Bismuth Containing Oxides ((Macquart, Li, Zhou, Ismunandar*, Howard*, Vogt*)
This project is concerned with understanding the importance of the sterochemical activity of the Bi $6s$ electrons on the structural and electronic properties of Bi containing oxides. We have recently demonstrated the static disorder of Bi cations in a number of pyrochlore oxides of the type Bi$_2$Yb$_x$Ru$_{2-x}$O$_6$ can influence the onset of metallic behaviour in these oxides. High resolution diffraction studies have demonstrated the behaviour of the layered oxides ABi$_2$M$_2$O$_9$ (A = Ca, Sr, Ba, M = Nb, Ta) is much more complex than initially believed.

Chemical Applications of Powder Diffraction (Hester, Howard, Vogt*)
Until the development of single crystal diffractometers all crystal structures were solved using powder diffraction methods. Unfortunately many compounds do not form diffraction quality crystals and their precise structures remain unknown. Recent advances in instrumentation have seen a major resurgence in powder diffraction methods. In this project we use an array of advance instruments, in Australia and overseas to examine the structures of novel compounds, including coordination compounds and metal containing drugs.

Oxides as Hosts for Heavy Metals (Tong, Carter, Thorogood, Auora*, Singh*)
The success of nature to immobilize heavy metals, either in biological systems using minerals such as apatite Ca$_{10}$(PO$_4$)$_6$X$_2$ or in the environment using minerals such as Goethite (FeOOH) has lead us to examine the interaction of heavy metals with such minerals so to establish the sites they occupy and the basis of their stability.
Orthorhombic-Tetragonal Transition in CaBr₂ (Howard*)
The nature of the orthorhombic-tetragonal transition in CaBr₂ has been investigated using high resolution powder synchrotron X-ray diffraction methods between room temperature and 800 °C. The temperature dependence of the spontaneous strain in the lattice or octahedral tilt angle, suggests that the transition is close to second order in nature.

Selected Publications
4. Structural and Electronic Properties of the Ru Pyrochlores Bi₂₋ₓYbₓRu₂₋ₓ₋₀₋ₓ₋₀₋ₓ₋₀₋ₓ₋₀₋ₓ₋₀₋ₓ₋₀₋ₓ₋₀₋ₓ₋₀₋ₓ₋₀₋ₓ₋₀₋ₓ₋₀₋ₓ₋₀₋ₓ₋₀₋ₓ₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋₀₋_x₋0 (2003).
Chiral Nanoporous Phases (Weeks, Thiyakesan, Faiz, Chapman, Rosseinsky)
Materials with the ability to recognise molecular handedness have long been sought due to their potential for application in chiral separations and syntheses. Previously we discovered two extensive families of chiral framework, \(^\text{9}\) which provided the only homochiral nanoporous materials known. Recent efforts made to enhance robustness by the modification of these phases and develop new phases using auxiliary ligands have resulted in the formation of several new 3-D and 2-D nanoporous materials. We have investigated the sorption properties of these materials to determine how these structural variations affect the robustness of the frameworks, and discovered a range of interesting guest-driven structural transitions.

Guest-Exchange Studies (Halder, Southon, Bevitt, Weeks, Rosseinsky, Thomas)
We have recently achieved some ground-breaking developments in the study of molecular sorption through the use of single crystal X-ray diffraction. By cooling crystals of the nanoporous phase \([\text{Co}^{II}(\text{bpy})_{1.5}(\text{NO}_3)_2]\) in the presence of solvent vapour we have followed the up-take of several different adsorptives into the 1-D nanopores of the host (eg. THF, CH\(_2\text{Cl}_2\), CH\(_3\text{CH}_2\text{OH}\), N\(_2\)). In addition to determining the location of the guests in the framework (see electron density plots) the adsorption kinetics for N\(_2\) were determined (see graph). Sorption studies on bulk samples of nanoporous frameworks were carried out by gravimetric techniques \(^\text{8}\) and by volumetric techniques and \textit{in situ} powder X-ray diffraction.

Switching Nanoporous Materials (Halder, Hughes, Amoore, Ganesan, Hudson, Murray, Moubaraki, Cashion, Toftlund)
The incorporation of molecular electronic switches into nanoporous frameworks is leading to materials having unique physicochemical properties and potential applications in molecular sensing and data storage. \(^\text{5}\) We have recently synthesised the first porous materials, Fe\(^{II}(\text{L})_2(\text{NCS})_2(\text{guest})\) (\(\text{L} = \text{bridging ligand}\)), that exhibit guest-dependent spin-crossover. \(^\text{4}\) Through the systematic variation of the bridging ligand and counter-ion we have developed an extensive family of materials, allowing fine-tuning of guest-exchange (pore size and shape) and switching (transition temperature) properties.
Negative Thermal Expansion, NTE (Goodwin, Chapman, Kozlowski, Kennedy, Withers, Dove, Hagen, Hester, Knight)

Following the report of NTE in a number of 3-D oxide lattices we have extended the search for this exotic and highly useful property to molecular framework materials. Notably, the investigation of a wide range of cyanide-bridged systems has led to the discovery of the most pronounced isotropic and anisotropic NTE behaviour discovered to date. We attribute the extreme NTE in these systems to two different modes of transverse vibrational motion of the linear cyanide bridge (see picture), each one leading to a decrease in the M–M distance with increasing temperature.

Porous Magnetic Frameworks (Hughes, Chapman, Kurmoo, Murray, Rosseinsky, Rujiwatra)

We are exploring an alternative avenue to electronically switching porous materials through a range of metal-organic frameworks which order magnetically at low temperature. Efforts are focusing on the formation of materials where guest-exchange may be used to perturb the magnetic properties, thereby providing a unique technique for studying structure-property relationships, and where magnetic interactions between host and guest may be observed.

Porous Mineral Formulations for Controlled Release Applications (Antill, Green, Khalil, Thomson, Matthews, Anderson, Wells)

In this project we are collaborating with an industrial partner on the generation of new technologies for the controlled release delivery of agrochemicals from porous mineral phases. Commercially relevant details of this research are subject to confidentiality agreements and may not be disclosed here. In parallel with this project we are using halloysite nanotubes (HNTs) (geometric analogues of the more expensive carbon or boron nitride nanotubes) as templates for fabrication of nanostructures such as nanowires, rods and clusters.

Selected Publications

Mechanisms of Cr(VI/V) oxidations of organic substrates, and the biochemistry and cell biology leading to Cr-induced cancers, have been studied. The structure of Cr(V) complexes with citrate, peptides, hydroxamic acids, sugars, and catechols have been assigned by EPR spectroscopy and/or XAFS. Such complexes damage DNA and are mutagenic, which supports their potential roles as the active species in Cr-induced cancers. The Cr(VI/V/IV) chemistries in aqueous solutions have been compared and the structures of their complexes determined by XAFS and electrospray mass spectrometry. This work has resulted in the characterisation of new intermediates and a more detailed understanding of the mechanisms of the reactions than was known previously. Similar studies have been performed on Cr dietary supplements, which are widely available, but have questionable efficacy for healthy humans and possibly deleterious side-effects. We have established that Cr(III) dietary supplements are oxidised to carcinogenic Cr(VI) by certain enzymatic processes and that Cr(VI) and Cr(V) inhibit the same phosphatase enzymes and, in the same manner, as well-known vanadium anti-diabetic complexes. Hence, it is postulated that the anti-diabetic effects exhibited by certain Cr(III) dietary supplements are due to their in vivo oxidation to carcinogenic Cr(VI), which is a considerable concern in terms of a carcinogenic hazard.

XAS Studies of Isolated and Intracellular Heme Proteins (Aitken, Armstrong, Cheng, Dillon, Harris, Farmer,* Freisleben-Udyananingsih, Lai,* Levina, Rich, Stocker,* Thomas,* Witting*)

XAFS structures (at 10 K) of human hemoglobin (Hb, including mutants from thalassemia patients), leghemoglobin, myoglobin, cytochrome c, indolamine 2,3-deoxygenase (IDO) and their adducts with NO and O2 were determined. Structural work has also been performed on the nitrosoyl (NO−) adduct of horse heart myoglobin. Further work has also been completed on the unfolding of cyt c as a function of pH. X-ray elemental mapping has been achieved at a sub-micron spatial resolution on single porcine aorta endothelial cells in which IDO has been induced by γ-interferon in order to mimic an immune response. Micro-XANES (X-ray absorption near-edge structure) at different regions of the cell has also been examined in order to determine the structures of the heme proteins induced in different regions of the cells and under different conditions. Similar experiments have been performed on the effects of myoglobin and/or hydrogen peroxide in order to mimic the effect of oxidative stress (ischaemia reperfusion injury) on endothelial cells lining the arteries after stroke or a heart attack.

Fullerenes: Derivatives, Conjugates and their Complexes (Armstrong, Boyd,* Cheng, Carter, Gallagher, Reed,* Sen Gupta, Thompson, Sun,* Zeng)

The photophysical properties of Ru fullerene complexes have been studied and they exhibit some interesting optoelectronic properties. Fullerene/porphyrin conjugates have been shown to have the potential to be anti-cancer drugs, with higher activity than cisplatin against a series of cell lines, including Pt-resistant lines. Detailed vibrational spectroscopic measurements have been performed on C_{60}, C_{80}O, C_{120}O, C_{59}N^+, and (C_{59}N)_{2}. These “simple” compounds continue to throw up new and interesting spectroscopic features.
Cu Anti-inflammatory Drugs (Aitken, Bonin, Davies,* Dillon, Hackett,* Hambley, Haque, Kennedy, Lai,* McConaghy,* Morgan, Ramadan, Sinha, Turner, Zhou)

Cu-indomethacin veterinary pharmaceutics were characterised by spectroscopic, magnetic, and XRD techniques. EPR spectroscopy and MS XAFS have been used to determine the purity and stability of the drugs in pharmaceutical preparations. The Cu complexes are much less ulcerogenic than indomethacin and cause less renal damage than the much-touted COX-II inhibitors. Micro-SRIXE and micro-XANES techniques have been used to study the entry of the drugs into cells and tissues, and their biotransformations within the cells. Detailed studies of the pharmacology of these drugs in rats have been undertaken, and new drugs with even higher efficacy and lower side effects have been developed and are being patented.

X-Ray Absorption Spectroscopy Studies on Melanoma Cells, Antimelanoma Drugs and Melanin (Aitken, Farmer,* Harris, Lai*, Meyskens*)

Microprobe X-ray beams have been used to determine the elemental distributions within melanoma cells and the effect of Cu-based drugs on the elemental distribution. These experiments are the first X-ray images of melanoma cells and have provided insights into the mechanisms by which these anti-cancer drugs work. We have also performed X-ray absorption spectroscopy on Cu in artificial melanin in order that we can identify regions of Cu melanin within the cells using micro-XANES.

Cancer Diagnosis in Tissues and Identification of Microbes by Vibrational Spectroscopy (Ali, Armstrong, Carter, Mountford,* Russell,* Sorrell,* Tam)

Microprobe vibrational spectroscopy is being used in conjunction with multivariate analysis to develop new techniques for distinguishing breast tissues that are normal from those that are benign tumours or malignant tumours. Strong correlations have been obtained for vibrational spectroscopic diagnosis with diagnoses obtained from standard pathology studies and NMR techniques. Vibrational spectroscopic techniques are also being developed to identify pathogenic microorganisms and to examine their susceptibility to new drugs.

Selected Publications

3. Competition Between 1,2-Diol and 2-Hydroxy Acid Coordination in Cr(V)-quinic Acid Complexes: Implications for Stabilization of Cr(V) Intermediates of Relevance to Cr(VI)-Induced Carcinogenesis. R. Codd and P. A. Lay. Journal of the American Chemical Society, 34, 7864-7876 (1999).
Covalently Linked Supramolecules Incorporating Macrocycles as Structural Components (Ando, Chartres*, Dong, Fainerman-Melnikova, Meehan*, Ramli, Wei)

This project has involved the design and synthesis of novel multi-component supramolecules incorporating both identical and non-identical macrocyclic rings as structural elements. The new systems display a range of molecular architectures that include linear, branched, stacked and dendritic arrangements of the macrocyclic components. For example, dendritic structures incorporating up to nine linked N,S₂-donor macrocyclic rings have been prepared. In most cases, the nanometre-scale structures synthesised in this project have been designed to bind two or more metal ions (both homo and hetero) simultaneously.

Metallo-supramolecular Chemistry: Metal-Directed Synthesis of Discrete Molecular Architectures - Triangles, Squares, Tetrahedrons, Catenanes and Capsules (Beves, Bray, Clegg, McMurtrie, Perkins, Price)

The synthesis of unusual supramolecular architectures employing metal template procedures has been carried out. This project is aimed at using the latent directional and electronic information in molecules and ions (including metal ions) to assemble new supramolecular structures. Representative examples are given below.
Self-Assembly and Molecular Recognition. Hydrogen Bonded and Metal-ion Linked Macrocyclic Ring Arrays (Bishop, Kepert, McMurtrie, Mulyana, Wei)

The project is concerned with the design and synthesis of new molecular architectures incorporating linked macrocyclic rings as structural components – with emphasis being given to the use of hydrogen bonded or metal-donor atom links in the bridges between macrocyclic rings. As such, the project represents an extension of our other studies in which a number of different macrocyclic rings have been linked covalently by means of conventional organic synthetic procedures. In particular, the new species are designed to form linked products by means of self-assembly processes - thus offering synthetic economy in the construction of the novel materials.

Ligand Host-Guest Assembly and Metal Ion Complexation (Gasperov, Tasker*)

In this project a subtle new effect in metal coordination chemistry - termed the assembly effect - has been investigated. Host-guest formation between species which are themselves potential metal-ion ligands may lead to enhanced metal-ion binding. The assembly concept yields a means for systematising previously reported synergistic metal-ion solvent extraction behaviour as well as providing a basis for the design of improved metal-uptake systems.

New Cage Receptors for Metal Ions and Small Molecules (Meehan*, Perkins, Turner)

We have undertaken the construction of new cage and cage-like molecules for the selective binding of small molecules and metal ions. These include the inherently chiral supra-cage (see below) which has been demonstrated to form 1:1 complexes with a number of transition ions. Molecular modelling and X-ray studies indicate that the cage interacts with a single octahedral metal ion such that a helical twist extends about 22 angstroms along the axial length of the system. Such behaviour is unusual relative to other helical structures recently reported for which multiple metal-ion coordination is required to induce a helical twist.

Macrocyclic Ligand Design for Metal Ion Recognition (Atkinson*, Charter, Chia, Fainerman-Melnikova, Hoshikawa, Price, Wei)

We have focussed on the design and synthesis of new macrocyclic ligands for metal ion recognition. The subtle factors underlying different discrimination mechanisms have been investigated using a range of techniques that include thermodynamic and computational studies. The use of new macrocyclic and pseudo-macro cyclic species as reagents for achieving metal ion discrimination in solvent extraction experiments and in bulk liquid membrane transport experiments has been investigated.

Selected Publications

A Study of Metal Salt Solutions as Environmentally Safe Flame Suppressants to Replace Halons (Masri*)

This project is investigating the possibility of using inorganic salt solutions as fine water mists for fire suppression. Mists of water droplet sizes less than about 10 microns have been shown to be more efficient in fire suppression than sprinklers which deliver droplets of much larger size. Metals have also been shown to be effective flame inhibitors, especially alkalis which produce stable monohydroxides under flame conditions. We are investigating possible synergistic effects of combining water mists and inorganic suppressants via a study of droplets of inorganic salts in flames. We are also investigating the applicability of measuring shifts in ignition delay times in the shock tube as a means of studying the inhibition properties of potential inhibitors.

To investigate the flame suppressant ability of a wide range of inorganic salts, a laboratory cupburner has been constructed using liquid heptane as the fuel. The inhibitor coflow with air around the flame and the inhibitor mole fraction which extinguishes the flame is measured. The flame inhibition chemistry is also being modelled using a flame and chemical kinetic computer code.

Salts of several metals have been found to be particularly effective flame suppressants. Lithium salts, particularly halides and hydroxides are useful inhibitors as are iron (II) and iron (III) chlorides. Phosphates and slurries of insoluble salts are also being trialled as potential flame suppressants. Small concentrations of surfactants together with the inorganic suppressant salts have been found to be effective in reducing blockage in the nebulizers used to produce the fine water mists.

Recently we have constructed a laminar opposed flow flame instrumented with state-of-the-art laser diagnostics to enable particle sizes and particle velocities to be measured when the flames are seeded with droplets of aqueous solutions of potentially active inorganic fire suppressants. We are able to determine the most efficient droplet sizes and suppressant concentrations. Simultaneous laser induced fluorescence measurements of OH, an important flame gas radical, can be measured and used as a criterion of flame suppression. The opposed flow flame can be readily modelled using large chemical kinetic reaction mechanisms for the flame and suppression phenomena.

How Important is the NNH + NO → NO + NH Route in NOx Production? (Bacskay, Haworth)

From a detailed quantum chemical and RRKM study of the NNH + O reaction potential energy surface rate coefficients for reaction into products NO + NH, N2O + H, N2 + OH and HNO + N have been determined. The quantum chemical calculations revealed that the reaction proceeds via three stable N2OH adducts which are able to undergo isomerisations and rearrangements leading to the above product channels. A multiwell RRKM kinetic model has been used to obtain rate coefficients to the individual reaction channels. Our calculations indicate, for the title reaction, previous literature estimates of its rate coefficient are about × 3 too large, leading to overestimation of NOx formation.
in premixed and diffusion flames and completely stirred reactors. Modelling of NO\textsubscript{x} formation from several combustion environments with our new NNH + O kinetics leads to greatly improved predicted levels of NO\textsubscript{x}. These include modelling of premixed flames of low calorific value waste gases, completely stirred reactors, flow reactors and opposed flow flames of methane/air and hydrogen/air. We have also carried out modelling of the reverse reaction, i.e., NO + NH \rightarrow all products and found that our theoretically derived rate coefficients agree well with experiment.

**Selected Publications**

Our research interests include the chemical synthesis of biologically active organic materials and the development of new synthetic methods.

The Total Synthesis of (-)-Tetrahydrolipstatin (Bodkin, Humphries).
We have recently completed the enantioselective total synthesis of the pancreatic lipase inhibitor (-)-tetrahydrolipstatin. The synthesis discovered and capitalised on previously unreported influences on the regioselectivity and diastereoselectivity of the bromolactonisation to construct the β-lactone ring of the target. This work has been reported in *Tetrahedron Letters* and a second full paper in the *Australian Journal of Chemistry* as part of a Cornforth Foundation for Chemistry Symposium special issue.

Studies Toward the Total Synthesis of the Cytotoxic Macrolide (-)-Zampanolide (Humphries, Louis).
The aim of this study is to provide a complete structural assignment of (-)-zampanolide by diastereoselective total synthesis and to provide quantities of this scarce resource for further biological testing. The project was awarded an ARC Large Grant in 2001. Excellent progress has been made on two key aspects of the synthetic approach under study. Work on the synthesis of the E,Z-diene ester system has been completed and a short efficient synthesis of the cis-pyran ring system is in progress. A second focus of investigation has seen the development of methodology for the synthesis of the sensitive N-acyl carbinolamine sidechain of zampanolide.

Controlling the Regioselectivity of the Sharpless Asymmetric Aminohydroxylation Reaction (Bodkin, Harding, Morrissey, Shuter, Bacsay, Hutton).
Recent contributions to methodology include the development of strategies for substrate control of the Asymmetric Aminohydroxylation reaction leading to dramatic improvements in the regio- and stereoselectivity of this transformation for complex synthetic intermediates. This project arises from observations made during research funded by ARC Large Grant 1999. The current research project significantly expands the scope of this powerful method of asymmetric catalysis for the synthesis of amino alcohol products, including amino sugars and unusual amino acids. The project forms a central plank of the
Towards the Total Synthesis of the Fumonisins (Issa).
This project was funded by an ARC small grant in 2000. Significant progress has been made on the enantioselective synthesis of the mycotoxin fumonisin B₁. The research has culminated in the completion of a fumonisin B₁ backbone structure. However, the approach has delineated some limitations associated with the key aldol and directed reduction steps proposed for the synthesis. Work to correlate the synthetic material with the natural product and towards an improved approach to the natural product arising from our investigations is under investigation in 2004.

Chemistry and Biology of Nicotinic Acetylcholine Receptors (nAChRs) (Barker, Behrends, Cheah, Lin, Brimble*, Collins*).
Nicotinic acetylcholine receptor (nAChR) chemistry and biology is currently of enormous interest in the field of drug development. The receptors have been implicated as playing a key role in conditions such as epilepsy, Alzheimer’s disease and schizophrenia. However, few compounds selectively differentiate between the different nAChR subtypes. Methyllycaconitine is a selective and potent α7 nAChR antagonist. A range of small molecule analogues of methyllycaconitine suitable for therapeutic applications have been synthesised and evaluated at nAChR ligands. Novel chemistry developed includes the application of new techniques for the double Mannich ring synthesis from β-keto esters and the development of new reagents for MLA sidechain synthesis. One of the analogues tested in 2002 against the α7 nAChR expressed in Xenopus oocytes shown significant activity and acts as a competitive antagonist (10 µM ligand acts inhibits 50% of the response of 300 µM acetylcholine). The project was awarded a University of Sydney Near Miss Grant 2003 and is the subject of an NHMRC Project Grant application in 2004.

Synthesis and Analysis of Anabolic Steroid Metabolites (Hungerford, Pu, Ridley, Stenhouse*, Westwood*)
This project has resulted in the synthesis of steroid conjugates for use as authentic standards and the development of antibodies for use in immunoassays for illicit drug detection. The initial collaboration involving a research agreement with AGAL (human metabolites) and has since been expanded to include the ARFL (equine metabolites) and resulted in the award of two ARC Linkage Projects in 2002.

Selected Publications
Photosynthesis (Dahlbom, Canfield, Shapley, Hush)
The conversion of optical to chemical energy by plants is central to most forms of life on this planet. More detailed information is available, however, concerning a closely related process in purple bacteria. Our work concerns the “special pair” of chlorophyll-type molecules that induce primary charge separation, converting the absorbed solar energy into internally stored electrical energy. Primary charge separation is important not only in biology but also is central to all photovoltaic devices such as silicon photocells that convert solar to electrical energy. The absorption spectrum in the key region of the bacterial “special pair” was first measured in 1992 and its qualitative interpretation led to the first complete picture of the processes controlling primary charge separation. Our aim is to quantitatively understand this spectrum and in so doing form a model of all the chemical, mutagenetic, and electrochemical properties of the system. In 2003 we completed the first full simulation of the spectrum. This required the assignment of some previously unidentified electronic transitions in the special pair, calculations that deduced the form of its vibrational modes, calculations of the coupling between electronic and nuclear motions, and full simulations, without use of standard chemical approximates such as the Born-Oppenheimer assumption that is at the core of all undergraduate chemistry teaching.

Molecular Electronics (Bilic, Lambropoulos, Solomon, Allen, Crossley, Hush)
A rather large research field has opened in the area of molecular electronics, the exploitation of the electrical conductivity properties of single molecules, and a major review book was produced. The forefront of electronics research by companies such as IBM, HP, Bell Labs, and Hitachi is in this area, and we have been involved in the development of the field since its first conception. During 2003 we were involved in a collaborative experimental project that bound molecules to a silicon surface at selected locations with the aim of one day being able to assemble complex logic circuits made of single molecules. Other work concerned the properties of porphyrin molecules for use in molecular electronic circuits, including photosynthetic mimic systems. These studies showed that the enormous synthetic flexibility available within porphyrin chemistry allows for the tailoring of molecules to meet a range of specific needs.

Basics Spectroscopy (Cai)
Molecular Electronics involves the passage of electrons through molecules and is not an equilibrium phenomenon. To understand such processes, often in very complex solid-state or biological (eg. photosynthetic) systems it is hence essential that we first understand in great detail the optical and electron-transport properties of model systems. In 2003, we collaborated with two sets of experimental groups to obtain high-quality spectra that we subsequently analysed. This includes very high-resolution UV spectra of pyrimidine, a simple aromatic molecule that forms a core of DNA bases, and the newly discovered photosynthetic pigment chlorophyll d. In both cases, the results yielded key information
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concerning flow and trapping of electrons within the molecules. Evidence was also obtained depicting a more general failure within triplet manifolds of one of the cornerstones of our understanding of aromaticity, the Perfect Pairing Theorem from 1940 of Coulson and Richardson. This will have wide ranging effects on our understanding of triplet-excited aromatic molecules.

Fundamentals (Cai)
Density-Functional Theory is now the most commonly used method for molecular electronic structure evaluation. Its weaknesses are often poorly known or understood, however. In 2003 we developed a review of these weaknesses, highlighting in particular their relevance to applications in molecular electronics.

Selected Publications
Metabolic Studies of Drugs in Horses and Analysis of Metabolites
The use of drugs in horses continues to present a major problem to the racing industry. New drugs are continually being developed to overcome existing laws, so the industry constantly needs to monitor racing animals. Not only are detailed studies of the drug required, but also we need to understand the pathways for drug metabolism and the effects the metabolites have on performance. Metabolism of anabolic steroids in the horse differs significantly from other animals. We currently are exploring the metabolism of a number of key steroids in the equine, and are investigating new methods, involving immunoassays, for their detection.

Design and Synthesis of Light Absorbing Compounds
The ability of organic compounds to absorb light of various wavelengths is well known, and light absorbing properties of substances have numerous commercial applications. However there is a need to obtain compounds that absorb in specific parts of the spectrum and that are transparent in all other regions. We are developing computer programs to predict the absorption maxima of novel compounds and are involved with their synthesis.

Chemical Information Retrieval
Scientists publish research papers and patents in what is known as the primary literature. However the value of this primary literature is considerably increased by chemical abstracting and indexing services, who not only collate the original data but also create search tools (for example for searching of structure or chemical reactions). Our research is in this area is to develop an understanding of these search tools and in particular to understand how they can be used creatively to solve research problems.

Selected Publications


INORGANIC SOLID STATE CHEMISTRY

Systems that form modulated structures are a fascinating class of materials, which lack lattice periodicity but may still be perfectly long-range ordered. Such systems exist not only for samples with exotic compositions but for many simple compounds as well and across the whole range of chemical disciplines from organic conductors to high-T\textsubscript{c} superconductors and minerals. Research projects encompass a wide range of both synthetic chemistry (Inorganic Coordination Chemistry and Inorganic Solid State Chemistry) and characterisation techniques, in particular X-ray and neutron powder and single-crystal diffraction as well as electron microscopy using in-house equipment as well as instrumentation at major research facilities.

X-Ray Powder Diffraction of Modulated Structures

Single-crystals from compounds forming modulated structures are not always readily available. It is therefore necessary to extend the capability for solving and refining modulated structures to powder data. Very recently a powder module was added to the main program package for modulated structure work. It is envisaged that some transition metal oxide systems, which form wide-range non-stoichiometric solid solutions with modulated structures, are ideal candidates to test the new features of the program. This is due to the fact that all structures in such a solid solution are ‘very similar’ and if data are available from a single-crystal structure refinement it should be possible to use powder data for the remainder. Work on the solid solution of tantalum pentoxide and tungsten trioxide has begun (see Figure 1). It will be necessary to synthesise specimens across the solid solution field, collect powder diffraction data and refine the modulated structures for suitable examples.

Fig. 1: X-ray diffraction pattern from the ANBF, Tsukuba ($\lambda = 0.7$ Å; rel. intensity vs. 2\theta). Black markers are for main reflections of the metal substructure, while grey markers are for satellite reflections thereof. From this typical pattern the weakness of satellite reflections is easily appreciated.
Synthesis of Novel Metal Nitrides

Many known metal nitrides have extremely useful physical and/or chemical properties that are exploited in a variety of technological applications. Nitrides of Group 13 (AlN, GaN, InN), for example, are currently receiving a tremendous amount of attention as potential components of high temperature electronic and short-wavelength (shorter than orange) optoelectronic devices. However, compared with oxides, relatively few nitrides are known, principally due to difficulty of synthesis. This research project aims to establish a route to bulk synthesis of early transition metal nitrides from appropriate inorganic coordination compounds via low temperature pyrolysis. The new synthetic route will then be employed to synthesise novel nitrides with respect to stoichiometry, structure and properties. Characterisation of the resulting nitrides will involve detailed compositional and structural analysis of novel compounds using a wide range of suitable techniques. This detailed knowledge of composition, structure and microstructure will be related to the properties of the materials. The suitability of novel nitrides for various applications, e.g., microelectronic or optoelectronic devices, will be investigated more closely.

Modulated Structures in the \( \text{Ta}_2\text{O}_5-\text{WO}_3 \) Solid Solution (Binder)

The wide-range, non-stoichiometric solid solution \((1-x)\text{Ta}_2\text{O}_5\ast x\text{WO}_3\) \(0 \leq x \leq 0.267\), forms a composite modulated structure. An elegant description is possible in terms of two coherently intergrown, mutually incommensurable, component substructures. The two average substructures (an M substructure containing the metal and apical oxygen atoms and an O substructure containing the basal plane, or equatorial, oxygen atoms - see Figure 2) both have \(C_{mmm}\) space group symmetry and identical \(a\) and \(c\) axes but are, in general, mutually incommensurable along their common \(b\) axis direction with a relative periodicity \(b_M/b_O = \beta\) which ranges from \(\approx 1.635\) for \(x = 0\) (i.e. \(\text{Ta}_2\text{O}_5\)) to \(\approx 1.615\) for \(x = 0.267\) (i.e. \(\text{Ta}_{2.2}\text{W}_{4}\text{O}_{67}\)). Initially X-ray and neutron powder diffraction data were collected on two compositions within the solid solution range. It has been shown that refinements using those data lead to reasonable results. Especially the powerful combination of powder neutron and X-ray diffraction data ensures that good refinements are achieved. The final modulation functions are certainly entirely compatible with previous results for other compositions, refined using single-crystal X-ray diffraction data.

Selected Publications

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AREAS OF INTEREST:

Mechanochemistry
Mechanical processes, e.g., ballmilling, can provide the energy needed for chemical reactions to proceed. Initial results indicate that rather unexpected reactions (e.g., transfer of hydrogen atoms) occur under such conditions and the primary aim of this project is to investigate them in a systematic manner. Practical possibilities include the destruction of persistent environmental pollutants, such as DDT.

Induction of Chirality in Mesophases
Mesophases, i.e., forms of matter intermediate between crystalline solids and liquids, may be made chiral by addition of small amounts of chiral inducers or dopants. Initial results gave a number of desirable structural characteristics for efficient dopands and include the most powerful dopands yet reported. Practical possibilities include better materials for liquid-crystal based display panels.

Selected Publications
Research centres on chemical and biological aspects of natural products. The aims are:

(i) to study the constituents of plants in relation to their taxonomy (chemotaxonomy) and identify intermediates including novel products in biogenetic pathways;

(ii) to isolate and study useful substances including pharmacologically active compounds.

(a) The plant *Schefflera lucantha* (Araliaceae) is used widely in Thailand and China as an antiasthmatic. The active bronchodilator principle is a mixture of saponins; the pure components have been isolated in order to establish the structures and to study the biological properties.

(b) The seeds of the Indonesian plant, Chydenathus sp. contain significant quantities of saponins which are toxic to fish. The pure saponins are being isolated and their structures elucidated by NMR and MS studies.

(c) Members of the Guttiferae family [e.g. *Garcinia mangostana* (mangosteen)] are rich in xanthone derivatives, some of which have been found to be active as antibacterial/antifungal agents. Other members of the Guttiferae occurring in southern Thailand are being examined with a view to developing useful compounds.

(d) Antiviral constituents of *Clinacanthus nutans* and anti-hypotensive constituents of *Tacca chantrieri* are being studied.

Extensive collaborations exist with universities in Indonesia, Myanmar, Nepal, Thailand and Vietnam with botanists, chemists and biologists studying local floras used in traditional medicine. Six papers were published in 2003.

Current Projects:

- Bronchodilator constituents of *Schefflera lucantha*, fish toxins of Chydenanthus spp. and anti-hypertensive constituents of *Tacca chantrieri*.
- Antiviral constituents of *Clinacanthus nutans*
- Constituents of *Garcinia* spp.; antibacterial derivatives of mangostin
- Constituents of Thai medicinal plants
- Constituents of Vietnamese medicinal plants
- Constituents of medicinal plants of Myanmar
**Selected Publications**

Development of Non-Peptide Agents for the Diagnosis and Treatment of Metastatic Melanoma Tumours (Indusegaram, Katsifis*, Ridley)

Integrins are a class of transmembrane cell surface receptors that mediate cell-cell and cell-matrix interactions. Of particular interest is the vitronectin receptor αvβ3, which is expressed on the surface of a variety of cell types including human tumour cells where they have been shown to mediate angiogenesis. The vitronectin receptor recognizes certain proteins containing the RGD peptide sequence. As a result, αvβ3 antagonists containing RGD mimetic sequences have been proposed as therapeutic agents in the treatment of cancer. In this project we are examining a range of halogen-containing non-peptide RGD mimetics as vitronectin antagonists, the aim being to find agents that will inhibit angiogenesis and hence halt or suppress tumour growth. During 2001 seven 123I-labelled drug candidates were successfully synthesised. These are currently undergoing biological evaluation.

Sydney Organic Synthesis Unit

The Sydney Organic Synthesis Unit (SOSU) was established by Dr Simone Vonwiller as a business specialising in custom synthesis, contract research and consultancy. There is a great demand in the biotechnology, medical and pharmaceutical industries for short to medium term access to chemical expertise and state-of-the art facilities and SOSU meets these demands by drawing on extensive experience of its personnel in research and the exceptional range of facilities offered by the School of Chemistry and the University of Sydney as a whole. During 2001 the unit has largely focussed on major research projects commissioned by two Sydney-based companies. These projects are continuing.
Our research is aimed at understanding the behaviour of surface-active compounds in bulk phases (solutions, liquid crystals, complex fluids), in colloidal systems (emulsions, foams, dispersions), and at interfaces. In a wide range of projects we examine the structure and dynamics of bulk phases and dispersions using techniques including neutron scattering, optical microscopy, rheology and calorimetry, and interfacial structure by neutron reflectometry, adsorption isotherms, atomic force microscopy, and surface force measurements. By combining these techniques we are discovering new structures formed when surface-active molecules adsorb at the solid/liquid interface or when complex fluids abut an interface, and use this to design new nanostructured materials.

**Surfactant Structures at the Solid/Solution Interface (Blom, Richetti,* Wanless*)**

Using atomic force microscopy to make nanometer-resolution images of the surface film in equilibrium with bulk solution, we have established conditions under which a surface mesh is formed by a large variety of different surfactants (Blom). We have also discovered techniques for tuning adsorbed layer structure and composition in mixtures of surfactants with block copolymers (Blom, Richetti, Wanless) as well as fluorinated compounds.

**Surfactant-Templated Growth of Calcite (McAlpine)**

We have used atomic force microscopy to examine the effect of surfactants on the growth of calcium carbonate crystals in supersaturated solution. Cationic surfactants can template cylindrical mesoporous structures similar to surfactant-templated silicates.

**Self-Assembly in Novel Ionic Liquids (Araos, Guerchet)**

We have prepared and examined surfactant self-assembly into micelles and liquid crystals in a number of new salts that melt below room temperature. We have found that ethylammonium nitrate (m.p. = 13°C) supports the formation of micelles and a wide variety of lyotropic liquid crystals by poly(oxyethylene) non-ionic surfactants. A variety of novel alkylammonium salts that melt below room temperature yield similar results.
Shear Response of Membrane Phases (Hamilton,* Butler,* Porcar*)

Together with collaborators at Oak Ridge National Laboratory and the U.S. National Institute of Standards and Technology, we are using time-resolved small-angle neutron scattering to investigate how micelles, microemulsions and sponge phases reorganise when subjected to a shear field. Sponges gradually re-form themselves into shear-aligned lamellae with a critical shear rate determined by phase composition and continuous phase viscosity, then relax with an activation energy determined by the cost of forming tightly curved necks when membranes fuse. Microemulsions exhibit similar rheology, which suggests that some shear-induced alignment may also occur.

Polymerisable Surfactants in Bulk and at Interfaces (Topp,* Kurihara,* Barner-Kowollik,* Prud'Homme*)

In two related projects we are examining self-assembly structures formed by polymerisable cationic surfactants (surfmers). We are using controlled radical polymerisation techniques as a route to a generic synthetic method for surfactant oligomers with tunable properties (Topp, Barner-Kowollik, Prud'homme). These should yield micellar solutions with unique flow properties. Adsorbed layers of surfmers are being polymerised to form ultra-thin, laterally nanostructured films as permanent coatings on solid substrates (Kurihara). The performance of these films as water-based lubricants is being assessed with collaborators at the Centre de Recherche Paul Pascal in Bordeaux.

Stability of Inverted Emulsions (Jain, Hawkett, Guerchet, Rounsley,* Tolliday*)

We are preparing water-in-oil emulsions containing magnetic nanoparticles (aqueous ferrofluid emulsions) in order to measure the colloidal forces that stabilise such emulsions. This project is being carried out in collaboration with industry partners Dyno Nobel Asia Pacific and Clariant Australia with the objective of designing improved surfactants as emulsifiers for these systems.

Selected Publications

We work on constructing inorganic nanostructures with colloid particles of metal hydrates. Currently the following projects are conducted:

**Manipulating the Morphology of Boehmite Nanoparticles by Soft Chemistry Approaches**

Boehmite nanofibers can be formed from a precipitate of aluminium hydrous oxide in the presence of non-ionic surfactants at 373K. By a calcination above 723K, the boehmite nanofibres can be converted to \( \gamma \)-alumina nanofibres. The boehmite nanofibres grow when fresh precipitate of aluminium hydrous oxide is supplied continually to the reaction mixtures. It has been found that the structure of the boehmite nanoparticles are sensitive to the experimental conditions and we can obtain diverse structures such as porous laths (Figure 1), porous plate and particles of grass leave morphology by manipulating the experimental parameters. The aim of this project is to clarify the formation mechanism of the boehmite nanoparticles.

**Reactions of titanates nanofibres and nanotubes**

Titanate nanofibers and nanotubes are relative reactive: they react with mineral acids and organic ammoia at moderate conditions. They also have an ion exchaning capacity. Therefore, we can utilize the chemical reactions and ion exchange ability to develop functional nanostructures of TiO\(_2\) as well as their composites, such as fibers and particles. These nanostructures are of potential for many applications, such as the photocatalysts for splitting water by sunlight to produce hydrogen, decomposing organic pollutants in environment, and using in photovoltaic cells by which 10% of solar
energy can be converted to electricity. Some delicate TiO2 nanostructure (Figure 2) have been developed from hydrogen titanate by wet chemical process below 120°C. The investigation will conducted aiming to understand the mechanisms of titanate fibre formation and phase transition, prepare new nanostructures of titanate and TiO2 and study their properties as photocatalysts and electrode materials of lithium batteries.

![Hydrogen titanate nanotube](image1)

![Delicate structure of hydrogen titanate nanofibres covered anatase crystals](image2)

![Rutile nanoparticles](image3)

**FIGURE 2**

**Highly Porous Composites of Metal Oxide and Silicate Nanoparticles**

Porous composites of metal oxide and silicate nanoparticles were prepared by a wet chemistry reaction between clay suspension and acidic aqueous solutions of metal salts. Introducing PEO surfactants in the synthesis results in mesoporous nanocomposites with very large surface areas (400 -900 m²/g) and porosity. Such synthesis has distinct features from the process of pillaring intercalation and template synthesis. The obtained porous solid have large porosity, specific surface area and ion exchange capacity and are mainly used as catalyst and catalyst supports. For instance, TiO2-nanocomposites are used for photodegradation of organic pollutants in water and air, iron oxide-nanocomposites for photo-assisting Fenton reaction for degradation of organic dyes in polluted water, ZrO2-nanocomposites as nickel catalyst supports for reforming CO2 with CH4. Gold ions can be load onto the ZrO2-nanocomposites, the obtained catalysts are active can oxidize formaldehyde (HCHO) to CO2 at water at a temperature below 300°C.

We will design new nanocomposites of various metal oxides and mixed metal oxides, investigate the mechanisms of the synthesis which involve hydrolysis and the acid leaching process, introduce the metal ions to develop new catalysts and characterize the structure of the composite solids with various techniques in EMU and find new catalysts with superior performance.

**Selected Publications**

Research Centres
In this fifth year since its establishment, the Key Centre for Polymer Colloids (KCPC) has continued to be one of the most dynamic and exciting research centres in Australia, and is recognized internationally as the world's leading research centre in emulsion polymerization and related fields. In 2003, we made substantial contributions to Australian science in all of our major programs, including publications, training, industry collaboration, and outreach. This would not have been possible without the high levels of professionalism and expertise of the Centre’s staff.

Researchers at the Centre reflect our cultural diversity: over the last five years, our researchers have come from every continent. Over a 15-month period, two-thirds of our 63 researchers, staff and visitors were Australian, and a third were from France, South Africa, the Netherlands, the US, the UK, NZ and Sweden. In 2003, our researchers included 14 postdoctoral fellows, 12 PhD students, and three Honours students. We have started a new cotutelle (joint) PhD program with a sibling centre at the Technical University Eindhoven in the Netherlands, and will soon forge a similar relationship with two other major sibling centres, at the University of New Hampshire and Universidad del Pais Vasco (San Sebastián), Brazil. We continue to enjoy strong links with academic, government, and industrial researchers in France, Thailand, Malaysia, and South Africa.

From January 2003 to March 2004, the KCPC produced 36 papers in refereed journals, 34 conference presentations, one patent, seven PhD and three honours theses at University of Sydney, one PhD from the University of Stellenbosch (South Africa), one PhD from FAENQUIL (Brazil), and one MSc thesis from Universiti Malaya.

Our research covers a wide range of basic and applied aspects of polymer colloids in synthetic and natural systems. Our continuing advances in controlled radical polymerization in emulsion systems, in collaboration with Dulux Australia and the ARC's SPIRT program, has led to the first successful method of performing this new way of making polymers in water-based dispersions. This permits the creation of polymer colloids with virtually any desired molecular architecture, such as where all colloidal stabilizers are bound to a particle—i.e., are soap-free—and are composed entirely of core–shell particles comprising only block copolymers stretching from core to shell. These new materials have improved end-point physical properties and environmental impact, and are currently being developed by Dulux as potential new-generation surface coatings. Our collaborative work with the Rice CRC and NSW Agriculture on the molecular weight and structure–property relations of starches has led to new understanding of the enzymatic pathways in starch biosynthesis, in particular of the crystallinity constraints controlling the molecular architecture of starch, and hence its cooking properties.

KCPC courses enjoyed good attendance from researchers across industry and academia. The KCPC website received 4.6 million hits in 2003. Its comprehensive equipment list has attracted global interest from researchers seeking analytical expertise and instrumental capabilities.

The biennial Gordon Research Conferences, held in New Hampshire, is the premier research conference in the field. The 2003 GRC on Polymer Colloids was chaired by the Centre Director. A large cohort of KCPC junior and senior researchers attended—the largest from any research group in the world.

We have among the world's best equipment for the synthesis and characterization of polymer colloids. Thanks to a new ARC LIEF grant, we are about to acquire a multidimensional polymer characterization facility, which permits separation and characterization by molecular weight, hydrodynamic volume, composition, end-group, and the degree of branching. This acquisition, among others, furthers our aim of ensuring that polymer scientists in Australian industry and academia have access to world-class facilities.
These achievements are made possible by the ARC’s base funding—17% of our overall income—and the substantial leverage on this from industry and grant bodies.

The main focus of the KCPC is strategic basic research aimed at understanding the fundamentals underpinning present and future polymer colloid industries. Applied research is also conducted to meet shorter-term goals of interest to these industries. The core research of the KCPC is grouped into four main areas:

1. The structure-property relations of polymer colloids and of polymers from polymer colloids
2. Surfactants in the growth and properties of polymer colloids
3. Polymer colloid reaction engineering and production
4. Polymer colloids in natural systems

The relationship between the molecular and the mesoscopic structure of a polymer on the one hand, and its mechanical properties on the other, is a major unsolved problem in the science of polymer colloids. The key research questions involved concern the study of how changes at the molecular level affect physical properties. This involves creating a database for how a range of final properties for example, (e.g. the cohesive strength of an adhesive formed from a latex) depend on the parameters, and therefore the mechanisms, in experiments on conventional free-radical polymer colloid synthesis. These data are also used to develop qualitative and quantitative theories of structure–property relations. Researchers and projects in this area in 2003 were:

- Dr Kyle Ratinac and Lisa Stadmueller: Polymer nanocomposites (USyd Materials Initiative) with Dr Lin Ye, A/Prof Simon Ringer, Prof YuWing Mai, & Prof Robert G. Gilbert; Dr Franck Montagne: Bioactive polymer colloids with Dr Hamid Elaissari (CNRS-bioMérieux, Lyon) & Prof Robert G. Gilbert; Stuart Prescott: Novel synthetic procedures: RAFT in heterogeneous polymerizations with Dr Ezio Rizzardo (CRC for Polymers), Dr Mat Ballard (CSIRO Molecular Science), & Prof Robert G. Gilbert; Malan Calitz: ESR investigation of RAFT reaction processes with Dr Matthew Tonge (Honorary Associate), & Prof Ron Sanderson (Stellenbosch, South Africa); Vishal Goury: Synthesis and characterization of block co-polymers based on lactides and poly-peptides with A/Prof Dhanjay Jhurry (Mauritius); Joost Leswin: Mechanisms in controlled radical polymerization in dispersed systems (co-tutelle with Technical University, Eindhoven, Netherlands) with Prof Robert G. Gilbert and Prof A van Herk (Eindhoven); Stuart Thickett: Entry kinetics of emulsion polymerisation, supervisor: Prof. Gilbert, associate supervisor Dr M. Tonge; Ornsritir Aungsupravat: Structure-property relations of latexes for barrier products, supervisors: Prof. R. Gilbert, Dr M. Tonge and Prof. S. Kiatamjornwong (Chulalongkorn University, Thailand) in collaboration with Ansell (Malaysia); Dr Abraham Chemtob: Catalytic polymerization in dispersed media, working with Prof Robert G. Gilbert; Kris Thurecht (UQld): Inverse microemulsion polymerization in supercritical CO2, with A/Prof A Whittaker and Prof Robert G. Gilbert; David Sangster (Hon. Research Fellow) & Peter Hidi (Hon. Research Associate): Preparation and properties of sub-micron polymer particles; Dr Sheila Devasahayam: Stabilization of Titanium Dioxide, with Dr Brian Hawkett and Tiwest (Industry).

Surfactants play a key role in the synthesis and final properties of materials prepared by emulsion polymerization. A range of properties are sensitive to the amount and type of surfactant used, from the microscopic, such as particle-size distribution, to the macroscopic, properties such as the water permeabilities of films are sensitive to the amount and type of surfactant used. The effects of surfactants on polymerization kinetics are still poorly understood, but it is clear that controlling the surfactant regime offers one of the best ways for achieving greater control of emulsion polymerization processes.

Commercial emulsion polymerizations employ both conventional surfactants—anionic, cationic or nonionic surface-active agents—that can be added to a reaction mixture at the beginning of the reaction or as a continuous feed, and in situ surfactants generated by the polymerization of water-soluble co-monomers in the course of polymerization. Researchers and projects in this area in 2003 were:

- Kathryn Topp: Gemini and oligomeric surfactants by polymerization with Prof Greg Warr & Prof Bob Prud’homme (Princeton) and Kim van Berkel: Effects of surfactants on entry and exit in emulsion polymerization with Dr Greg Russell (Canterbury, New Zealand), & Prof Robert G. Gilbert.

A universal problem in the industrial manufacturing of polymer colloids is that a process that works well on a one-litre laboratory scale can fail when scaled up to 20 tonnes. Some fundamental reasons for this problem are already understood. For example, many of the steps in an emulsion polymerization are such that the process is sensitive to small fluctuations in such variables as shear or the amount of inhibitor. It is also clear that this is by no means the only reason for scale-up problems. This project is creating a unified approach to the understanding of this problem by combining (1) the increasingly available scientific knowledge on the kinetics and mechanisms of the conventional free-radical synthesis of polymer colloids, with (2) the requisite chemical-engineering science, i.e., (experimental and computational
Researchers and projects in this area in 2003 were:

Joseph Zeaiter: Reactor modelling and control systems for preparation of polymer colloids Dr Vince Gomes, Prof J Romagnoli (Chem Eng, USyd), & Prof Robert G. Gilbert. (PhD thesis submitted 2003); David Lamb: Redox reactions in emulsion polymerization (BASF) with Prof Robert G. Gilbert, & Dr Brad Morrison (BASF). (PhD thesis submitted 2004); Rebecca Elgebranidt: Shear and computational fluid dynamics in emulsion polymerization reactors, supervisors Prof J Romagnoli Dr David Fletcher, Dr Vince Gomes (USyd Chemical Engineering, USyd) & Prof Robert G. Gilbert.

We have two aims in our research involving polymer colloids in natural systems. The first is to apply to natural polymer colloids the experimental and theoretical techniques developed for the characterization of synthetic polymer colloids, and to investigate the behaviour of natural polymer colloids in multiphase and interfacial systems. This will lead to the development of models for natural polymer colloid structure (e.g., the molecular architecture of starch hydrocolloids) or natural polymer colloid processes (e.g., the flocculation of polysaccharide particulates). The second aim is to conduct strategic basic research for novel applications of synthetic polymer colloids in natural systems, such as the synthesis of (1) particles that are modified so as to have ‘proteinaceous’ functionality on their surfaces, with potential biomedical applications; and (2) hybrid particles containing both natural and synthetic components, with potential application as new ‘green’ materials. Researchers and projects in this area in 2003 were:

Dr Paul Perry: How does molecular architecture of starch determine viscosity of rice? (Supported by the Rural Industries Research and Development Corporation) with Dr Melissa Fitzgerald (NSW Dept of Agriculture/CRC for Sustainable Rice Development) & Prof. Robert G. Gilbert; Jef Castro: Biochemistry and polymer physics of rice hydrocolloids with Prof Robert G. Gilbert; Dr Chris Fellows, Dr Melissa Fitzgerald, & Dr Matthew Morell (CSIRO Plant Industry); Herbert Chiou: Molecular weight distributions and structure-property relations in rice hydrocolloids with Dr Melissa Fitzgerald & Prof Robert G. Gilbert (PhD thesis submitted 2004); Nathan Sinnathurai: Theory of molecular weight distributions in Starch with Prof. Gilbert, Celine Dumas: Molecular weight distributions of mutant starches with Prof. Gilbert and Dr M. Fitzgerlad; Steve White: Novel hydrocolloid membranes for biological systems; Garry Warrender: Acrylamide-based hydrocolloids in agriculture, with Prof Les Copeland & Prof Robert G. Gilbert; Antoine Rouilly: Synthesis and properties of composites of starch and chemically modified natural rubber, supervisors: Prof Robert G. Gilbert and Prof. Luc Rigal (ENSIACET, Toulouse); Gavin Rea: Diffusion of starch polymer in concentrated systems, supervisors: Dr Paul Perry, Dr Melissa Fitzgerald and Robert G. Gilbert.

With an eye to future opportunities, the KCPC is actively undertaking projects in a number of fields outside its core areas. We have achieved new architectures and topologies by using controlled radical polymerization, in particular through the Reversible Addition Fragmentation chain Transfer (RAFT) mechanism. This has included the first effective use of RAFT in generating electrosterically stabilized lattices by ab initio emulsion polymerization. These projects include applications of controlled radical polymerization that fall outside the core areas, such as the development of environmentally-friendly surface coatings in collaboration with Dulux, other studies of unconventional free-radical polymer colloid synthesis, and the development of novel branched-polymer architectures for rheological studies.

Other new areas in which the KCPC is active include the tailoring of surfactant systems for application to explosive emulsions (with Dyno-Nobel), a fundamental study of cross-linking in polyacrylamide gels (ARC Linkage with Gradipore), and the investigation of the rheological behaviour of complex high-solids suspension (with Selleys). We have also recently launched a major initiative on the development of novel biomaterials for use as paper coatings, was funded as an ARC Linkage Project with Dow and the NSW Department of Agriculture. This work is exceeding expectations, and a patent is being developed. Researchers and projects for 2003 were:

Dr Christopher Ferguson, Dr Binh Pham and Dr Duc Nguyen: Next-generation environment-ally-friendly surface coatings (ARC SPIRT project with industry) with Prof Robert G. Gilbert, Dr Brian Hawkett, Chris Such, & Dr Algi Serelis (Dulux); Shane Seabrok Fundamentals of acrylamide-based cross-linking reactions (ARC Linkage APA-I) with RGG; Jaco Vosloo: Synthesis of branched polymers (ARC Discovery and Gritton Fellowship); with Prof Robert G. Gilbert, Dr Chris Fellows, Dr Matthew Tonge, & Prof Ron Sanderson (Stellenbosch); George Liang: Rheological behaviour of highly concentrated aqueous dispersions (ARC SPIRT APA-I and Selleys Adhesives); with Dr Brian Hawkett, Prof RI Tanner, & Koogan Moodiar (Selleys); Rachelle Ward: Novel biomaterials from an improved understanding of the structure of starch (ARC Discovery), with Dr Melissa Fitzgerald (NSW Dept of Agriculture and the CRC for Sustainable Rice Development), Prof Robert G. Gilbert, & Dr Chris Fellows;Dr Ghislain David, Ewan Sprong and Doug Willoughby New-generation starch-based paper coatings (Dow and ARC Linkage grant) with Dr John Roper (Dow) & Dr Melissa Fitzgerald (NSW Dept of Agriculture and the CRC for Sustainable Rice Development), Andrew Koh, Novel acrylate latexes working with (BASF) and Prof Robert G. Gilbert; Nirmesh Jain and Jason Hong: Improving explosive emulsions by understanding surfactant interactions, working with: Prof G G Warr & Dr B Hawkett (Support: ARC Linkage with Dyno Nobel); Laurence Guerchet: Stability of high internal phase inverse emulsions, working with: Prof G Warr & Dr B Hawkett (Support: Dyno-Nobel/Clariant and ARC Linkage); Yanjunng Wang: working on industry related project for Sirtex. Supervisor: Dr B.S. Hawkett.
For more than half a century synthetic organic chemistry has been a focal point in the School of Chemistry. This tradition provided the platform for the formation of the Sydney Organic Synthesis Unit by Dr Simone Vonwiller which specialised in custom synthesis, contract research and consultancy. With the growth in demand for short to medium term access to chemical expertise and state-of-the-art facilities this unit was formally adopted as a Centre within the University in 2003. The aims of the newly formed Organic Synthesis Centre (OSC) are to provide focus and support for synthesis-related research programs in the University, provide an opportunity for contract synthesis to Government Organisations and to Industry, develop relationships with Industry and to establish funded research programs. In providing a professional services to industry and the chemical research sector, the OSC acts as one of the commercial enterprises of the School of Chemistry.

To better service the aims of the new Centre, in 2003, the University of Sydney and the School of Chemistry invested in new equipment for the OSC and initiated plans for the complete refurbishment of dedicated OSC laboratories and offices to house OSC staff and provide state-of-the-art facilities. These building works are now complete and will provide dedicated laboratories to maintain pace with the rapidly expanding demand for OSC services.

Beside these recent investments, the OSC draws on the extensive expertise of the academic and research staff within the School of Chemistry and the exceptional range of research facilities available within the Centre, the School of Chemistry and the University of Sydney as a whole. The OSC has been able to provide a wide and unique range of services in the last 12 months - these have included (i) the synthesis of high quality specialist organic chemicals for the pharmaceutical, biotechnology and materials industries; (ii) the development and formulation of synthetic strategies for new compounds; (iii) the active involvement in research programs such as the refinement and optimisation of new compounds to develop analogues that are better able to achieve desired goals; (iv) consultancy and the provision of expert witnesses; (v) the provision of expertise to support applications for external research funding; and (vi) the provision of research assistance (on a contract or long-term basis) for funded research programs that require the synthesis of organic compounds.

Furthermore, the OSC also provides services to the wider Australasian organic chemistry community. This includes the development and implementation of OrgNet Australasia; a sister network to OrgNet UK operated by Professor R. Whitby (Southampton). OrgNet is a free service provided by the OSC for Australasian Organic Chemists whose aims are to keep a central mailing list of practising organic chemists to enable the rapid dissemination of important messages and information.

In addition to the service functions performed by the OSC, staff within the OSC are also involved in primary research activities. These research programmes include investigations into the chemo-enzymic synthesis of chiral auxiliaries, the biomimetic synthesis of novel functionalities, and novel carbon-carbon bond formation methodologies (Dr Pat Stamford).
Key Personnel in the OSC are:

**Director:**
Professor L.D. Field FAA (School of Chemistry)

**Deputy Director:**
Professor D.D. Ridley (School of Chemistry)

**Executive Officer:**
Dr N.P.J. Stamford (School of Chemistry)
The Centre for Heavy Metals Research (CHMR) is based in the School of Chemistry with linkages to other units within the University, as well as to participating institutions both within and outside Australia. It has as its major goal the instigation and development of a substantial research program in the chemistry of heavy metals and to develop interactions with industry, hospitals and government institutions. The Centre is the first of its kind to be established in Australia.

The CHMR builds on a long tradition of internationally recognised expertise within the University on the chemistry of the ‘heavy’ metals. Through its three research interests, designated respectively as Bio-Metals, Industry-Metals, and Environ-Metals, it places emphasis on the social and economic benefits of such research to areas of Health, Industry and the Environment. Individual projects range from the discovery of novel metal-based human and veterinary pharmaceuticals or the development of new industrial catalysts to methods for recovery and recycling metal-containing waste streams and to modelling the fate and transport of heavy metals in the natural environment. This represents an identifiable grouping of many of the established research activities of the Centre’s academic staff.

Projects on the development of anti-cancer and anti-inflammatory drugs, and the design, synthesis and investigation of new materials based on silica gel for the removal of heavy metals from waste water systems were undertaken during the year. Preliminary work on the investigation of methods for the remediation of soils contaminated with hydrocarbons and heavy metals in partnership with the University of Newcastle and Innova Soil Technology Pty Ltd was continued. An aim of this study is the development of procedures for use with Innova’s high-temperature process for the treatment of metal contaminants from soils and sediments.

There has been much activity in the Centre concerned with the synthesis and testing of platinum-containing potential anticancer drugs within the Hambley and Fenton groups. The prospect of commercialisation of Dr Fenton’s patented research in the Centre on new compounds of this type has continued to be under negotiation with prospective commercial partners in association with the University’s Business Liaison Office. This project is being carried out in collaboration with the University of Western Sydney. The developed compounds interact with DNA in an entirely novel way and testing against cancer cell lines indicate that they exhibit a high level of activity - suggesting high clinical activity and low toxicity. Similarly, the University is patenting discoveries on metal complexes as anti-inflammatory drugs involving a collaboration with the Centre (Professors Peter Lay, Trevor Hambley, Associate Professor Brendan Kennedy and Dr. Carolyn Dillon) and Nature Vet Pty Ltd. One new veterinary product has been registered for use in treating horses and several other products are under development for treating horses and dogs. In addition, the University has established a shelf company, UCOM Seven, that is seeking capital to take the drugs to human clinical trials.

**Sydney Cancer Institute**

The Biometals Section of the CHMR was one of the founding and largest groups in the Sydney Cancer Institute that was established early in 2003 in a joint initiative of the Sydney Cancer Centre, The University of Sydney, the Central Sydney Health and National Sydney Cancer Foundation. The Associate Director (Biometals), Professor Peter Lay is on the Scientific Advisory Board of the new Institute.
Metals in Medicine Research Network
The Biometals Section of CHMR was also the central player in developing a seed network application for an ARC Network in Metals in Medicine. The seed application was successful and funded at a level of $30k, and formed the basis of a full application for a large network. This is currently under consideration by the ARC, with Professor Lay being the nominated convenor.

A selection of other current CHMR projects include the synthesis and characterisation of new porous materials that display reversible exchange of molecular guests for use in separation processes (Dr Cameron Kepert), negative-thermal expansion materials that are generating commercial interest (Dr Cameron Kepert), hydrocarbon oxidation catalysts (Dr James Beattie, A/Prof. A. F. Masters and collaborators in the Netherlands), the distribution of metal ions in synthetic clays (Assoc. Prof. Brendan Kennedy), polymerisation catalysts (Assoc. Prof. Tony Masters and Prof. Les Field), metal-based drugs, nutritional supplements and metal-induced cancers (Prof. Peter Lay), heme proteins (Assoc. Prof. Robert Armstrong and Prof. Peter Lay), arsenic bioinorganic chemistry (Dr. Carolyn Dillon) and studies of metallo-proteins expressed by extremophilic microorganisms and their potential applications in biotechnology (Dr Rachel Codd).

Collaboration has continued between the Centre and the Netherlands at the Department of Applied Organic Chemistry of the Technical University of Delft with Professor Thomas Maschmeyer and DSM Research in Geleen with Dr Wim Buijs. Dr Buijs was a visiting lecturer in the School in 2002. In 2003 Mr Paolo Pescarmona from Maschmeyer’s group spent several months in the School conducting research on silsesquioxanes in Professor Masters laboratory and Professor Masters subsequently was invited to be one of the examiners’ at Pescarmona’s PhD defence in Delft. As part of a collaborative project between Delft, DSM and Sydney, Mr Chris Guo spent two months in Delft and Geleen conducting activity tests on hydrocarbon oxidation catalysts prepared in Sydney as part of his PhD project, which is funded by DSM.

Most significantly, Professor Maschmeyer was awarded a prestigious Federation Fellowship and joined the School and the Centre at the end of 2003.

Research grants and publications by members of the CHMR are presented elsewhere in this publication and are not separately listed here. Over 40 research publications from the Centre appeared during the year. It is enough to say that 2003 has been a very successful year.

Key Personnel in CHMR are:

Director:
Professor L.F. Lindoy, FAA (School of Chemistry)

Associate Director (Bio-Metals):
Professor P.A. Lay (School of Chemistry)

Associate Director (Industry-Metals and Environ-Metals):
A/Professor J.K. Beattie (School of Chemistry)
Research Facilities
School of Chemistry

Summary of Facilities and Techniques

The School contains or is involved with joint facilities covering a diverse array of state-of-the-art instrumentation, worth well over $10M. In addition, we have extensive collaborations with major synchrotron radiation and neutron sources, allowing access to the some of most sophisticated and expensive instrumentation in the World, on a project specific basis. Further information on facilities and researchers in the School can be found on the Internet (http://www.chem.usyd.edu.au/).

AAS Spectrophotometry - Varian Spectra AA-20 including graphite furnace; Varian Spectra AA-800; Varian AA220; Flame photometers for alkali metal analysis.

Calorimeters - Capabilities for titrations of solution reactions.

Catalysis Laboratory - Range of small scale catalytic reactors with on line sampling GC.

CD Spectroscopy - Modern JASCO CD spectropolarimeters.

Computing and Molecular Modelling - High level computing facilities including access to VisLab, and covering diverse applications to industry, pharmaceutics, etc.

Electroacoustics - AcoustoSizer-II for analysis of sizes and charges of colloidal particles.

Electrochemistry - A range of electrochemical techniques, including: microelectrode, rapid scanning, and digital simulation techniques for polarography and voltammetry; bulk electrolysis and electrochemical synthesis (including BAS100B/W and PAR Potentiostat Model 273A instruments); spectroelectrochemical techniques (Electronic, EPR, FTIR, Raman, SERS, XAS); selective electrodes and oxygen sensors.

Electronic Absorption and Emission Spectroscopy - Various Cary instruments, including a Cary 5E system with UV/Vis and NIR optical fibre and diffuse reflectance capabilities; Hewlett-Packard Diode Array spectrometer; Emission spectrometers.

Electron Microscopy - Many researchers have access and experience with the advanced instrumentation in the Electron Microscopy Unit of the University of Sydney.

EPR Spectroscopy - 2 x Bruker EMX, and a Bruker ESP300 (updated to-state-of-the-art in 2002/2003), X-band, Q-band, L-band, ENDOR, fast scan, liquid He cryostat in a joint facility with UNSW.

Gas Sorption - Hiden Isochema IGA-002: gravimetric measurement of the adsorption isotherms for gases and liquid vapours, equipped for measurements up to 10 atm and at high temperature. Quantachrome Autosorb-1 (shared instrument located at Chemical Engineering): volumetric measurement of gas adsorption isotherms at 77 K.

High Pressure Equipment - Capable of solution phase synthesis of 2 x 5 mL samples at up to 8,000 atm and 100 °C.

Key Centre for Polymer Colloids - Gel-permeation chromatography for molecular weight distributions of organic- and water-soluble polymers, a wide range of polymerization reactors (including computer-controlled ones), capillary hydrodynamic fractionation (for particle size analysis), microfluidizer.

Laser Techniques: Nd:YAG laser (1064 nm, 532 nm, 355 nm, 266 nm, up to 20 Hz repetition rate); Excimer laser (308 nm, up to 50 Hz rep rate), Dye lasers (tuneable from ~215 - 800 nm, rep rate determined by pump laser above); Spectrometers (1 x high resolution, several lower resolution instruments); Detection (fluorescence or ionisation).
Magnetic Measurements - Including access to a SQUID.

Mass Spectrometry - 5 instruments including: Polaris-Q (CI/EI)GC-MS with autosampler; Hewlett Packard 5989A MS Engine (CI, GC/MS); Micromass TofSpec2E (MALDI-TOF); LCQ (Electrospray) and a LCQ Deca (Electrospray) with a HPLC system. There is also access to a QSTAR XL hybrid LC/MS/MS (in School of Molecular and Microbial Biosciences for high resolution measurements on proteins, DNA fragments, transition metal and organometallic species).

NMR Spectroscopy - Bruker 600 MHz, 2 x 400 MHz, 1 x 300 MHz, 1 x 200 MHz spectrometers, plus modern data manipulation and plotting stations.

Potentiometric Equipment - For accurate determinations of metal-complex stability constants.


Separations - Large range of equipment including GC’s, HPLCs, Dionex, gel electrophoresis, etc.

Stopped-Flow Spectrometers - Applied Photophysics SMV-17, UV/Vis, CD and emission detection, global analysis software; Hi-Tech Scientific SF-61, UV/Vis and emission detection.

Surface Analysis Facility (shared with UNSW) - Large range of surface techniques, XPS, Auger spectroscopy, PIXE etc.

Surface Characterisation - Atomic force microscopy, neutron reflectometry, small-angle x-ray and neutron scattering.

Synthesis - Diverse range of specialist equipment and laboratories for inorganic, organic, organometallic and polymer chemistry.

Thermogravimetric Analysis - TGA and modulated DSC; intelligent gravimetric analyser.

Two-Photon Spectroscopy - Microprobe fluorescence imaging of biological samples (joint with EMU).

Ultracentrifuge - Is used to separate polymers from supernatant in a polymer colloid, so that the polymer properties can be examined.

Vibrational Spectroscopy - Dispersive Raman spectrometer (Jobin-Yvon U1000, Ar+ ion and Kr+ lasers); FT-Raman spectrometer (Bruker RFS100) with 90° and 180° sampling. The FT-Raman is coupled via fibre optic probe to a microscope with 7x7 µm mapping resolution; Renishaw Raman Systems 2000 spectrometer equipped with a 3-axis motorised stage with ±1 µm repeatability. The instrument is capable of point spectroscopy, 2-D Raman imaging and 3-D Raman mapping with 1-5 µm spatial resolution. The Renishaw Raman can use any of the following excitation lines: 488, 514, 532, 567, 647, 752 nm; access to UV Renishaw Raman at Macquarie University with microprobe which has 325 and 406 nm excitation; FTIR Spectrometer (Bruker IFS66v) with DRIFT, ATR (single bounce diamond), grazing angle and photoacoustic accessories. The instrument is also equipped with a microscope with an MCT detector. NIR, MIR and FIR capabilities; plus a range of smaller FTIR instruments).

X-ray Absorption Spectroscopy - Access to various synchrotron radiation sources for XANES and XAFS analysis, microprobe and stopped-flow techniques on a project specific basis.

X-ray and Neutron Powder Diffraction - Benchtop and synchrotron X-ray instruments and access to ANSTO and overseas neutron sources on a project-specific basis; high temperature (1600 °C) capabilities.

X-ray, Single-Crystal Diffraction: Bruker SMART 1000 and an imminent installation of a Bruker-Nonius APEX II FR591 high flux and sensitivity system. Oxford Cryosystems cryostats for data collections between 230 deg C and –250 deg C. Microscopes for crystal and micro-crystal examination and manipulation. Access to diffraction facilities at synchrotrons such as the ChemMatCARS facility at the Advanced Photon Source and the European Synchrotron Radiation Facility.
Research Publications
Book Chapters


Journal Publications


Bernhardt, PV; Hambley, TW; Lawrence, GA; Maeder, M; Wilkes, EN (2003). Isomers of 1,4,8,11-tetraazocyclotetradecane-6,13-dicarboxylate characterized as cobalt(III) complexes. *Australian Journal of Chemistry*, 56:679-684.


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Coxall, RA; Lindoy, LF; Miller, HA; Parson, S; Tasker, PA; White, DJ (2003). Solvent extraction of metal sulfates by zwitterionic forms of ditopic ligands. *Dalton Transactions*, 2003:55-64.


D’Agosto, F; Charreyre, M-T; Pichot, C; Gilbert, RG (2003). Latex particles bearing hydrophilic grafted hairs with controlled chain length and functionality synthesized by reversible addition-fragmentation chain transfer. *Journal of Polymer Science Part A-Polymer Chemistry*, 41:1188-1192.


Dillon, CT; Hambley, TW; Kennedy, BJ; Lay, PA; Zhou, Q; Davies, NM; Biffin, JR; Regtop, HL (2003). Gastrointestinal toxicity, antiinflammatory activity, and superoxide dismutase activity of copper and zinc complexes of the antiinflammatory drug indomethacin. *Chemical Research in Toxicology*, 16:28-37.

Dillon, CT; Kennedy, BJ; Lay, PA; Lai, B; Cai, Z; Stampfl, APJ; Illinski, P; Legnini, DG; Maser, J; Rodrigues, W; Shea-McCarthy, G; Cholewa, M (2003). Implementation of X-ray microscopy and micro-XANES analysis for investigations of the cellular uptake and cellular metabolism of transition metals. *Journal de Physique IV*, 104:293-296.


Emseis, P; Hibbs, DE; Leverett, P; Reddy, N; Williams, PA (2003). Solid state and solution structures of complexes of the type $\Lambda$-$\beta_1$-[Co(R,R-picchxn)(R-aa)]$^{2+}$ [picchxn = $N,N^1$-Di(2-picolyl)-1,2-diamino-cyclohexane; aa=aromatic aminoacidate. *Journal of Coordination Chemistry*, 56(8):389-395.

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Fukuzumi, S; Ohkubo, K; Wenbo, E; Ou, Z; Shao, J; Kadish, KM; Hutchison, J; Ghiggino, KP; Sintic, PJ; Crossley, MJ (2003). Metal-centered photoinduced electron transfer reduction of a gold(III) porphyrin cation linked with a zinc porphyrin to produce a long-lived charge-separated state in nonpolar solvents. *Journal of the American Chemical Society*, 125:14984-14985.


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Kashiwagi, Y; Ohkubo, K; McDonald, J; Blake, IM; Crossley, MJ; Araki, Y; Ito, O; Imahori, H; Fukuzumi, S (2003). Long-lived charge-separated state produced by photoinduced electron transfer in a zinc imidazoporphyrin-C60 dyad. Organic Letters, 5(15):2719-2721.


Kurmoo, M; Kumagai, H; Hughes, SM; Kepert, CJ (2003). Reversible guest exchange and ferrimagnetism ($T_c = 60.5$ K) in a porous cobalt(II)-hydroxide layer structure pillared with trans-1,4-cyclohexanedicarboxylate. *Inorganic Chemistry*, 42(21):6709-6722.


Lindoy, LF; Mahinay, MS; Skelton, BW; White, AH (2003). Ligand assembly and metal ion complexation: syntheses and X-ray structures of Ni(II) and Cu(II) benzoate and 4-tert-butylenzoate complexes of cyclam. *Journal of Coordination Chemistry*, 56(14):1203-1213.


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Nieuwenburg, P; Clarke, RJ; Cai, Z; Chen, M; Larkum, AWD; Cabral, NM; Ghiggino, KP; Reimers, JR (2003). Examination of the photophysical processes of chlorophyll $d$ leading to a clarification of proposed uphill energy transfer processes in cells of *Aeropyoclora marina*. *Photochemistry and Photobiology*, 77(6):628-637.

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Rukachaisirikul, V; Rithiwigrom, T; Pinsa, A; Sawangchote, P; Taylor, WC (2003). Xanthenes from the stem bark of *Garcinia nigrolineata*. *Phytochemistry*, 64: 1149-1156.


Strauch, J; McDonald, J; Chapman, BE; Kuchel, PW; Hawkett, BS; Roberts, GE; Tonge, MP; Gilbert, RG (2003). Diffusion coefficients of the monomer and oligomers in hydroxyethyl methacrylate. *Journal of Polymer Science Part A-Polymer Chemistry*, 41:2491-2501.

Sullivan, MB; Iron, MA; Redfern, PC; Martin, JML; Curtiss, LA; Radom, L (2003). Heats of formation of alkali metal and alkaline earth metal oxides and hydroxides: surprisingly demanding targets for high-level ab initio procedures. *Journal of Physical Chemistry A*, 107: 5617-5630.


Tolhurst, V-A; Cookson, D; Turner, P (2003). A synchrotron study of $\mu_1$-chloro-tri-$\mu_2$-chloro-$\mu_2$-sulfido-hexakis(triphenylphosphine)triruthenium(II) - tetrahydro-furan - water. *Acta Crystallographica Section E-Structure Reports Online*, E59:m218-m219.


**Conference Publications**


**Cawley, AT; Rogerson, J; Rahman, K; Trout, G; Kazlauskask, R** (2003). Preliminary results on the carbon isotope ratios of ketonic steroids in urine samples collected from different countries. Proceedings of the Manfred Donike Workshop 21st Cologne Workshop on Dope Analysis, 1:183-194.

**Abstracts**

**Alderden, RA; Hall, MD; Amjadi, S; Hambley, TW**: Beale, P; Zhang, M; Lai, B; Stampfl, APJ (2003). Increasing the cellular accumulation of platinum(IV) complexes. *Journal of Inorganic Biochemistry*, 96:89-89.


**Hall, MD; Hambley, TW**: Beale, TW; Zhang, M; Dillon, CT; Foran, GJ; Stampfl, AP; Lai, B (2003). Does platinum(IV) survive in tumour cells? *Journal of Inorganic Biochemistry*, 96:141-141.


Research Fellowships & Grants
Fellowships

Attard, P (ARC Australian Professorial Fellowship)
Nanotribology and nanorheometry

Harris, HH (ANSTO/ASRP Professorial Fellowship)
XANES Mixtures Speciation and XAS Imaging Techniques in Drug Design, Disease Mechanisms, and Bioinorganic Chemistry

Hibbs, DE (ARC Australian Postdoctoral Fellowship)
Experimental charge density studies and drug design

Jolliffe, KA (ARC Queen Elizabeth II Fellowship)
Backbone modified cyclic peptides: scaffolds for supramolecular chemistry

Lay, PA (ARC Professorial Fellowship)
The chemistry and biochemistry of chromium: cancer and nutrition

Maschmeyer, Th (ARC Federation Fellowship)
From nanostructural fundational materials to sustainable processes

Nauta, BK (ARC Postdoctoral Research Fellowship)
Superfluid helium nanodroplet spectroscopy

Reimers, JR (ARC Australian Senior Research Fellowship)
Theoretical modelling of chemical systems, with applications to excited states, intermolecular interactions, bacterial photosynthesis and molecular electronics

Thordarson, P (Sesqui Postdoctoral Fellowship)
Energy- and electron-transfer in bio-hybrids

Zhu, HY (ARC Queen Elizabeth II Fellowship)
Fundamental Study on Porus Clay Heterostructure

ARC Grants

ARC Discovery and Large Grants

Fullerenes, their complexes and materials
Armstrong, RS; Gallagher, SH; Reed, CA - $34,240

Nanotribology and nanorheometry
Attard, P - $112,867

Nanotribology and nanorheometry: A fundamental study of the dynamic interactions of particles and surfaces at the molecular level
Attard, P - $30,443

Electroacoustics of concentrated oil-in-water emulsions: Small angle - and ultra small angle neutron scattering tests
Beattie, JK, Warr, GG - $51,360
Function and regulation of the Na+,K+-ATPase
Clarke, RJ; Else, PL; Cornelius, F; Apell, H - $49,227

Molecular recognition and self-replication by porphyrin systems
Crossley, MJ - $69,550

Molecular electronics: from electron transfer through photosynthesis towards functional nano devices
Crossley, MJ; Reimers, JR; Hush, NS; Hersam, MC - $366,585

Organometallic transformations of organic compounds
Field, LD - $83,791

Novel biomaterials from improved understanding of the structure of starch
Gilbert, RG - $61,419

Structure-property relationships of polymers with controlled architecture
Gilbert, RG; Whittaker, AK; Fellows, CM; Monteiro, M - $117,307

Development and biological chemistry of novel platinum anti-cancer agents
Hambley, TW; Deacon, GB - $51,148

Antifreeze proteins and glycoproteins
Harding, MM; Haymet, ADJ - $92,128

Experimental charge density studies of hydrogen bonding
Hibbs, DE - $68,080

Cross-linked tyrosine residues in peptides and proteins
Hutton, CA - $60,620

Backbone modified cyclic peptides: Scaffolds for supramolecular chemistry
Jolliffe, KA - $128,235

Hydrogen bonds: types, structures and IR and NMR spectra
Jordan, MJT; Del Bene, JE - $38,520

Photodissociation dynamics of radicals and molecules
Kable, SH - $106,459

Structural and electronic properties of layered bismuth oxides
Kennedy, BJ - $87,010

Structural variants and phase transitions in perovskites
Kennedy, BJ - $49,220

Nanoporous molecular frameworks: Chirality, host-guest chemistry and nanoscale templation
Kepert, CJ - $102,365

The chemistry and biochemistry of chromium: Cancer and nutrition
Lay, PA - $146,634

Nanoprobe and microprobe spectroscopic techniques in drug design, probing mechanisms of diseases, and bioinorganic chemistry
Lay, PA; Armstrong, RS; Stampf, A - $108,507

Metal directed assembly of new supramolecular systems
Lindoy, LF - $94,265
Nanoscale molecular architectures - New metallo cages and capsules  
**Lindoy, LF; Meehan, GV** - $80,899

Organometallic catalysts for olefin polymerization  
**Masters, AF; Field, LD** - $39,590

Total synthesis of the microsclerodermins: Anti-fungal cyclic peptides  
**McLeod, MD; Hutton, CA** - $80,081

Cooperativity in spin-crossover systems: Memory, magnetism and microporosity  
**Murray, KS; Kepert, CJ; Toftlund, H** - $133,868

Superfluid helium nanodroplet spectroscopy  
**Nauta, B** - $66,537

Computational quantum chemistry study of molecular structures, stabilities and reactions  
**Radom, L** - $102,365

Composite mesoporous solids of TiO₂ nano-crystals and silicate as photo-catalysts for degradation of organic contaminants in water  
**Zhu, H-Y** - $62,843

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**ARC SPIRT and Linkage - Projects**

New-generation starch-based paper coatings  
**Gilbert, R; Fitzgerald, M; Fellows, C; Roper, J** - $255,257

Mechanisms and modelling of gels for protein separation  
**Gilbert, R; Seabrook, S; Monteiro, M** - $33,148

Next-generation environmentally-friendly surface coatings  
**Gilbert, RG** - $128,150

Next-generation environmentally-friendly surface coatings  
**Gilbert, RG; Hawkett, BS** - $25,000

Design, evaluation, and selection of novel Pt(IV) complexes as anti-cancer agents  
**Hambley, TW** - $109,760

Enhanced biocatalysis in organic solvents for pharmaceutical biotransformation  
**Hutton, CA** - $27,283

Pulsed oscillating mass analyser  
**Kable, S** - $56,148

Porous mineral formulations for controlled-release applications  
**Kepert, C** - $114,307

New metal complexes of NSAIDs as veterinary eye ointments, anti-cancer drugs and general anti-inflammatory agents  
**Lay, P; Hambley, TW; Kennedy, B** - $156,490
New metal complexes of NSAIDs as veterinary eye ointments, anti-cancer drugs and general anti-inflammatory agents

**Lay, PA; Hambley, TW; Kennedy, B** - $75,000

A new synthesis of steroid conjugates for illicit drug detection

**McLeod, M; Ridley, D** - $23,556

Total synthesis of the cytotoxic macrolide zampanolide

**McLeod, MD** - $59,920

Design of supramolecular structures for use in nanoelectronics

**Reimers, J** - $10,000

Understanding the chemistry of molecular excited states and their intermolecular interactions

**Reimers, JR** - $39,590

Synthesis and analysis of equine anabolic steroid metabolites

**Ridley, DD; Stanley, AM; McLeod, MD; Stanley, AM** - $76,310

Streamlining product development by understanding the rheological behaviour of highly concentrated aqueous dispersions

**Tanner, RI, Hawkett, BS** - $6,000

Improving explosive emulsions by understanding surfactant interactions

**Warr, GG, Hawkett, BS** - $106,322

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**ARC Linkage - Infrastructure Equipment and Facilities (LIEF)**

LIEF grants are multi-institutional, often involving a large number of researchers. In 2003, members of the School were involved in the following successful LIEF grants:

Ultra-sensitive CCD diffractometer with high intensity X-ray photon generator

**Hambley, TW, Kepert, CJ, Turner, P, Hibbs, DE, Spackman, MA, Williams, PA, Pyne, SG, Try, AC** - $399,466

Fluorescence detector for the Australian National Beamline Facility

**Lay, PA, Foran, GJ, Ridgway, MC, Gentle, IR, Best, SP, Riley, MJ, Berry, AJ, Gerson, AR, Hambley, TW, Bhargava, SK, Garrett, RF, Creagh, DC** - $507,000

Neutron-beam techniques

**Mather, D, Gray, EM, White, JW, Gentle, IR, O'Connor, B, Kisi, EH, Kennedy, BJ, Campbell, SJ, Hicks, TJ** - $240,000

Circular dichroism spectrometer system

**Riley, MJ, Krausz, ER, Lay, PA, Pace, RJ** - $390,000
ARC Linkage - International

Inhibitors of enzymes in the lysine biosynthetic pathway
Hutton, CA - $2,757

Cooperativity in spin-crossover systems: Memory, magnetism and microporosity
Murray, KS; Kepert, CJ; Toftlund, H - $6,142

Structure of polymer surfactant lubricant layers
Warr, GG; Richetti, P - $19,701

International research exchange
Gilbert, RG - $63,217

ARC Key Centre of Teaching and Research

Key Centre for Polymer Colloids
Gilbert, RG - $432,243
Other External Competitive Grants

Australian Antarctic Science Grant

Chemical & biochemical characterisation of the cold-adapted metallo-enzymes expressed by Antarctic bacteria: Molybdooxotransferases from Shewanella species

Codd, R - $5,285

Horticultural Research and Development Corporation Grant

Cost effective UV protection for biological actives

Hawkett, BS - $33,000

Wellcome Trust - Major Equipment Award for Biomedical Research in Australia

L-Band EPR spectroscopic studies of radicals in mammalian cells and tissues and biological fluids

Lay, PA; Davies, MJ; Kennedy, BJ; Witting, PK - $466,000

International Joint Research Grants

New strategies for developing ultrathin nanostructured polymer films

Warr, GG; Gilbert, RG - $339,739

Innovation Access Programme - International Science & Technology

Value added material from Australian and French agricultural waste

Gilbert, RG - $64,601
Other International Grant Programmes

Hydrothermal liquefaction of biomass: reaction paths and kinetics (NWO, Netherlands)
Maschmeyer, Th, Peters, JA - $126,000

Enantioselective cyanohydrin synthesis catalyzed by bio-inspired catalysts (NRSCC, Netherlands)
Maschmeyer, Th, Hanefeld, U - $73,000

Enzyme-based membrane structures (NRSCC, Netherlands)
Maschmeyer, Th, Sheldon, RA - $73,000

Novel zeolitic/porous membranes (NRSCC, Netherlands)
Maschmeyer, Th, Sheldon, RA - $12,000

Novel zeolite compositions (Marie Curie EU Programme)
Maschmeyer, Th, van der Waal, JC - $83,000

Distillation of HTU products, (NWO/TNO, Netherlands)
Maschmeyer, Th, Peters, JA - $75,000
International Travel Grants

Access to Major Research Facilities Program

Isotropic negative thermal expansion in a molecular framework - ISIS Facility, UK
Kepert, CJ - $8,215
Experiments at ISIS, UK
Warr, GG - $ 1,625

Australian Synchrotron Research Program

Micro-SRIXE and Micro-XANES analyses of chromium compounds in lung cells: the beneficial (dietary supplements) and the detrimental (carcinogens) - APS, USA
Dillon, CT - $10,755
Investigations into the rate of biotransformation of inorganic chemotherapeutics - ANBF, Japan
Hambley, TW - $17,445
Structures and phase transitions in metal oxides and halides - ANBF, Japan
Kennedy, BJ - $13,120
Reversibility of negative thermal expansion in the MM'(CN)6 family - ANBF, Photon Factory, Japan
Kepert, CJ - $6,760
XAFS studies of bioinorganic systems - ANBF, Japan
Lay, PA - $24,455
Mo EXAFS as a probe of molybdenum speciation in the production of pharmaceuticals - ANBF, Japan
Masters, AF - $6,680
Charge density studies of drug molecules and their metal complexes - Photon Factory, Japan
Overgaard, J - $5,370
Ceramic materials with modulated structures - ANBF, Japan
Schmid, SA - $2,180
Specialist crystallography at the Advanced Photon Source: SCrAPS 2003, USA
Turner, P - $6,253
XAFS study of negative thermal expansion in ZnII(CN)2 and ZnIIPtIV(CN)6 - ANBF, Japan
Kepert, CJ - $4,280

Other Travel Grants

Ian Potter Foundation Travel Grant
Jolliffe, KA - $2,000
University of Sydney - Sesqui Grants

Projects

Synthesis and biological testing of antifungal cyclic peptides
Jolliffe, KA - $25,000

Characterisation and optimisation of multiphoton microscopy dyes by multiphon cavity ring down spectroscopy
Kable, SH - $25,000

Anomalous expansion materials
Kepert, CJ - $36,000

Catalytic asymmetric synthesis of biologically significant carbohydrates
McLeod, MD - $25,000

X-ray powder diffraction investigation of the (1-x)Ta$_2$O$_5$·xWO$_3$, 0 = x = 0.267, solid solution and the modulated structure of the x=0 member L-Ta$_2$O$_5$
Schmid, SA - $10,000

Surfactant self-assembly in room-temperature molten salts
Warr, GG - $25,000

Major Equipment

Protein isolation equipment
$25,000

Ultra centrifuge
$96,500

Organic synthesis centre laboratory
$70,000

Conducting AFM: Nanoscope scanning probe microscope
$200,000

University of Sydney - Cancer Research Fund Grants

Developing and probing hypoxia-selective anti-cancer agents
Hambley, TW - $47,500

Diagnosis of breast disease using vibrational spectroscopy and multivariate analysis
Lay, PA - $47,500

Titanium-based anticancer agents
Harding, MM - $47,000
Scholarships

Australian Institute of Nuclear Science and Engineering (AINSE)

Experimental charge density studies of hydrogen bonding
Hibbs, D - $13,750

Negative thermal expansion in molecular framework materials
Kepert, C - $7,500

Synthesis and development of radiolabelled MMP inhibitors for imaging and therapeutic applications on the treatment of metastatic tumours
Hambley, TW; Alexander, M - $6,500

Australian Nuclear Science and Technology Organisation (ANSTO)

Molybdenum-Alumnia interactions
Masters, AF - $45,000
Industrial Research Partnerships

Beattie, JK, Masters, AF, Maschmeyer, Th (DSM)

Field, L (NSW Department of Education, Science and Technology)

Gilbert, RG, Seabrook, S, Monteiro, M (Gradipore Ltd)

Gilbert, RG, Fitzgerald, M; Fellows, C, Roper, J (Dow Chemicals Pty Ltd)

Gilbert, RG (BASF Aktiengesellschaft)

Gilbert, RG (Unite Mixte de Recherche, France)

Hawkett, BS (Kerr-McGee Chemicals Ltd)

Hawkett, BS (Nuplex)

Hawkett, BS (Pasminco)

Hawkett, BS (Silverbrook)

Hawkett, BS (Sintex Medical)

Maschmeyer, Th, van der Waal, JC (Avantium Technologies)

Maschmeyer, Th, van der Waal, JC (Avantium Technologies)

Maschmeyer, Th, van der Waal, JC, van der Water, LGA (Avantium Technologies)

Maschmeyer, Th, Jansen, JC (ABB Lummus, USA)

Maschmeyer, Th, Jansen, JC (Shell BV, Netherlands)

Maschmeyer, Th (DSM)

Maschmeyer, Th, Jansen, JC (Amylum)

Maschmeyer, Th, Bromley, S (Shell BV, Netherlands)

Maschmeyer, Th, Jansen, JC (Shell BV, Netherlands)

Ridley, DD; Stamford, NPJ (Silverbrook Research Pty Ltd)

Reimers, JR, Hush, NS (Molecular Electronics Research)

Vonwiller, SC (Clearcoll Pty Ltd)

Vonwiller, SC (Synthesis Contract)

Warr, GG (Dyno Nobel Asia Pacific Ltd)

TOTAL - $2,655,969
Bequests

Agnes Campbell Research Prizes
Chemistry - $72,790

Dr Joan Clark Research Scholarship
Chemistry - $43,309

GG Blake Radio Research Fund
Chemistry - $3,526

John A Lamberton Research Scholarship
Chemistry - $30,108

Professor Archibald Liversidge Bequest
Chemistry - $3,256

Schofield Bequest
Chemistry - $375,000
Awards, Scholarships & Prizes
External Awards (Staff)

Dr Rachel Codd  
Selby Research Prize

Professor Max Crossley  
Fellow of the Japanese Society for the Promotion of Science  
Centenary Medal  
Mahler Lecturer (University of Texas at Austin)

Professor Les Field  
Centenary Medal

Emeritus Professor Hans Freeman  
Centenary Medal

Professor Robert Gilbert  
RSC Australasian Lectureship  
Centenary Medal

Dr Dai Hibbs  
Cardiff Fellowship

Professor Robert Hunter  
Centenary Medal  
Order of Australia Medal

Emeritus Professor Noel Hush  
Centenary Medal

Dr Cameron Kepert  
Rennie Medal, Royal Australia Chemical Institute  
Le Fèvre Prize, Australian Academy of Science  
Australian Academy of Science International Travel Grant

Professor Leonard Lindoy  
Centenary Medal

Professor Thomas Maschmeyer  
ARC Federation Fellowship  
Tall Poppy Award

Dr Mal McLeod  
Royal Australian Chemical Institute Organic Division Lectureship for Recently Appointed Staff

Professor Leo Radom  
Dozor Fellow (Ben Gurion University, Israel)  
Lise-Meitner Lecturer (Hebrew University Jerusalem, Israel)  
Centenary Medal

Dr Louis Rendina  
Biota Medal, Royal Australian Chemical Institute

Emeritus Professor Sev Sternhell  
Centenary Medal
External Awards (Students)

Mr Greg Arrow, Honours Student
Winner of the RACI NSW Analytical Chemistry Prize.

Ms Jennifer Bodkin, PhD Student
Australian Journal of Chemistry Prize for the best student poster at the Royal Australian Chemical Institute NSW Organic Group, 23rd Annual One Day Symposium. Campbelltown Campus, University of Western Sydney, Australia.

Mr Adam Cawley, PhD Student
Best oral presentation prize at the International Association of Forensic Toxicologists (TIAFT) in Melbourne, Australia.

Ms Karena Chapman, PhD Student
AINSE Scholarship.

Mr Gregory Halder, PhD Student
Crystal Engineering Communications Prize for best student presentation at the AsCA ’03/Crystal-23 Conference, Broome, Western Australia.

Mr Nilay Hazari, PhD Student
Rhodes Scholarship.

Mr Peter Hughes, PhD Student
Best oral presentation (PhD student category) at the Royal Australian Chemical Institute, Physical Chemistry Division Student Conference, Albury, New South Wales, Australia.

Mr Edward Humphries, PhD Student
Royal Australian Chemical Institute Fuetril Prize for the best student oral presentation at the 19th Royal Australian Chemical Institute Organic Conference, Lorne.

Ms Philippa Simpson, PhD Student

Mr Craig Turner, PhD Student
Royal Australian Chemical Institute Cornforth medal for his PhD thesis.
Student Prizes and Scholarships

The School of Chemistry awards over $85,000 in Prizes and Scholarships each year to the best of its students. The following students were awarded prizes or scholarships in 2004 based on their academic achievements in 2003. Scholarships are awarded subject to the students satisfying conditions required for each of the individual scholarships.

Agnes Campbell Prize (Postgraduates)
Mark Anthony Absalom
Rebecca Ann Alderden
Jennifer Ann Bodkin
Adam Troy Cawley
Joshua Fischer
Joseph Stephen Guss
Nilay Hazari
Suzanne Marie Hughes
Edward Jason Humphries
Luke Hunter
Sutharsiny Indusegaram
Tony Khoury
Louis Ignace
Bich San Ly
Matthew James McGann
Andrew Ronald McKinney
Clarissa Ka Lai Ng
Fan Pu
Adelle Shasha
Emily Clare Shuter
Ojia Skaff
Appadurai Thiyakesan
Ashley Tronoff
Jennifer Jane Turner
Jenny Brigitta Waern
Mark Waller
Renee Megan Whan
Geoffrey Paul Farra Wood
Alexander Kah Liem Yuen

Iredale Prize
Anna Frances Garsia

Arthur Hollis Memorial Prize
Thomas Owen Prince

Australia-USA Foundation Prize
Matthew Johnson Wong

Hush Prize
Suan Maree Corley

RJW Le Fèvre-DAASN Rao Prize for Physical Chemistry
Andrew Peter Symons

RACI Student Prize
Paul Bonnitcha

Janet Elspeth Crawford Prize in Chemistry
Tanya Maria McKenny

C.H. Wilson Prize
David James Bray

Edna Maude Goulston Prize in Organic Chemistry
Timothy Middleton

Levey Scholarship 2
Bradly James Webster

Levey Scholarship 3
Lachlan James Young

Walter Burfitt Scholarship No.1
Paul Bonnitcha

G S Caird Scholarship
Paul Saines
Katie Cergol
Andrew Peter Symons

Frank E. Dixon Scholarship
David Schilter

Inglis Hudson Scholarship
Natasha Fleur Sciortino
Kate Sarah Campbell
Jill Irene Halliday

Kate Sarah Campbell
Jill Irene Halliday

George Harris Scholarship
Matthew Hall
Tony Khoury
Deborah Crittenden