Chem 3998/3997
2014
PREFERENCE FORM

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**List of Supervisor preferences (must include at least TWO academics):**

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*Students indicate order of preference (1 = highest, 3 = lowest). The form must be signed by the supervisor concerned. An email copy of this form must be submitted to Associate Professor Shelli McAlpine, School of Chemistry, s.mcalpine@unsw.edu.au by **February 1, 2014 for semester 1, 2014**, and June 15 for semester 2, 2014.*
Chem 3998 and 3997
SUPERVISORS
Currently crude oil and other materials are rapidly being depleted, pollution is accumulating everywhere in our biosphere, and our batteries just never seem to last long enough! My group therefore focuses upon introducing new, cleaner forms of energy, chemistry and resources. This generally involves biomass utilisation, green chemistry, hydrogen storage and analytical chemistry. Primarily, this focuses upon the intelligent application of ionic liquids, electrochemistry and nanomaterials.

a) Biomass: Sustainable Chemicals for the Future

Nature has created fantastic structures. To highlight two major Australian crops, rice is grown coated in a silica-based suit of armour, while Macadamia nuts have shells that are tougher than concrete, as strong as tempered aluminium but with only half the density; both are made up of a rich variety of chemicals. Once farmers remove these, they burn them! My research focuses upon using ‘ionic liquids’ to weaken and even dissolve these tough waste products, after which we can generate biofuel and platform chemicals for the chemical industry. Projects range from the design of new ionic liquids for special applications through to upgrading of dissolved biomass into new chemicals. An example project;

Which one to pick; can we design better ionic liquids? (in collaboration with Dr Jason Harper, University of New South Wales, and Dr Anna Croft, University of Nottingham, UK)

Some ionic liquids can dissolve wood; some can dissolve insect shells; some can dissolve neither. All ionic liquids will dissolve different quantities. If we are to get the best dissolution and extraction of useful materials, we need to choose the best ionic liquid - but unfortunately there are trillions of possible combinations! This project involves studying the solubility of various biomaterials in ionic liquids, in order to generate simple models that can inform us of which ionic liquid is best for which material.

b) Hydrogen Storage

Finding an effective system for the safe storage of hydrogen, followed by its easy release on demand, is one of the most important and challenging investigations of this century. We have two projects aimed at solving this;
Hydrogen Storage using Magnesium Hydride in Ionic Liquids

Magnesium Hydride is a fantastic material for hydrogen storage, but is unfortunately also incredibly flammable and reactive! Ionic liquids are non-flammable, very chemically stable, and have been known to protect very reactive compounds from the atmosphere. This project will involve combining the two to see if safe but effective hydrogen storage/release systems can be developed.

Hydrogen Storage using Ammonia Borane in Ionic Liquids

Ammonia borane (NH₃BH₃) contains three hydridic atoms (H⁻) right next to three protonic (H⁺) atoms, yet is stable and unreactive in air and water. If heated it can evolve large quantities of H₂, and contains one of the best %w/w H₂ storage records in the world. Unfortunately it is too stable, and evolves the H₂ slowly. Ionic liquids have been found to accelerate H₂ evolution from NH₃BH₃, but the mechanism is unknown and therefore the best ionic liquid is still unknown. This project will involve a study of NH₃BH₃ in a range of ionic liquids in collaboration with two experts on NH₃BH₃, in order to identify the best possible system.

c) Analytical Chemistry using Nanocarbon and Biomass-derived Carbon

Pollution is clearly accumulating in our biosphere, in areas such as our oceans, our food and even our own bodies. New techniques are required for the facile identification, quantification and removal of pollutants from the environment. I have various projects available, featuring detection in common samples (e.g. water), under severe conditions (e.g. the hot dry deserts of Afghanistan), and unusual environments such as food. Removal of pollutants from the environment is also important, and often new materials can be used in win-win situations, such as the below example project;

Nanoscale carbon: Awesome drug release, awesome sensor or awesome pollutant removal? (collaboration with Prof. James Clark, Green Chemistry Centre of Excellence, University of York, UK)

Nanoscale carbon can have a massive surface area, and many synthetic molecules (such as pharmaceuticals or drugs) can adsorb onto these materials. We are investigating ‘Starbon’, a range of mesoporous/nanoporous carbon powders made in the UK in a sustainable manner from polysaccharides (e.g. starch waste from rice). This project is aimed at screening these in the presence of different aromatic compounds such as are commonly found in drug architectures, in order to identify which properties and interactions are best. When drug/nanocarbon interactions are moderate to weak these materials could be applied as slow drug release materials. Where interactions are medium to strong, these nanocarbons can be used to form the building block of sensitive and selective sensors designed to quantify the presence of the drug. When interactions are strong and irreversible, these can be used to purify waste water contaminated by the analyte.
Our research focuses on applying NMR spectroscopy to shed light on important chemical problems, often in the areas of inorganic and organometallic chemistry. NMR spectroscopy is probably the most powerful technique available to the chemist and the Mark Wainwright Analytical Centre is bristling with shiny, state-of-the-art instruments eagerly awaiting YOU to run experiments that push the boundaries!

Increasingly, our experimental work is greatly enriched by using computational chemistry techniques. This is a superb way to get up close and personal with your molecules without all the risk assessments!

a) Short-lived metal complexes and reactive intermediates

Petrol. Put it in your car and burn it till we run out yeah? Well hopefully actually! For the last three decades, chemists across the globe have working on ways of converting relatively unreactive alkanes found in petroleum into useful compounds. A process known as C-H activation the core of these conversions, and we are studying the key short lived intermediates in this chemistry, which have an intact alkane molecule bound to a metal, to aid design of new catalysts.

These reactive intermediates are generated by hitting precursor complexes with laser light while they are in the NMR spectrometer. Low temperatures are used to stabilise the intermediates, permitting their characterization. With this strategy, we have observed several types of alkane complex\(^\text{1,2,3}\) including the recent JACS cover opposite\(^\text{1}\) and even complexes where xenon acts as a ligand.\(^\text{4}\)

*Designing new exotic molecules: Computational investigations of alkane and noble gas complexes*

We are increasingly employing computational methods (DFT, *ab initio*) to aid the understanding of these fascinating compounds. Current projects are aimed at answering questions such as: How does the alkane bind to the metal centre? Can we make more stable alkane complexes? Can we observe complexes with ligands that even more weakly than alkanes and xenon using NMR?


(b) Organic reactive intermediates
We are now applying our novel photochemical NMR techniques to extract structural information about reactive organic molecules that have tantalised organic chemists as to the nature of their structures and bonding such as carbenes, cycloalkynes and nitrenium ions. These molecules are highly reactive due to unstable electronic configurations or because they are highly strained. The field of organic photochemistry is vast and there are many compounds that are waiting to be tackled!

(c) Anti-cancer drug-DNA interactions (in collaboration with A/Prof Larry Wakelin, School of Medical Sciences and Dr Don Thomas, NMR Facility)

DNA presents one of the most logical and practical targets for anti cancer therapeutics. We are investigating the binding of several bis-intercalating molecules that show promise as anti-cancer drugs. The solution structures the DNA-ligand adducts are obtained via a suite of 2D NMR techniques coupled with NOE-constrained molecular dynamics simulations employing AMBER forcefield. Our recent results have lead to a re-evaluation of how these bis-intercalators interact with DNA.

The project involves a traditional fusion of NMR spectroscopy and molecular modelling, primarily at the molecular mechanics level. The project can be tailored to focus on NMR studies, molecular modelling or a balanced amount of both. We have a number of drugs synthesised that are ready for investigation.

(d) In silico studies of catalytic reductions (with A/Prof S. Colbran)

Building on the exciting empirical results from A/Prof Colbran’s group, we are modelling catalytic cycles of reductions of key small molecules such as CO₂. Using density functional theory (DFT) allows us to get at the gritty of the mechanism of the catalysis and inform rational design of the next generation of catalysts. Lab coat not required!
The use of weak, non-covalent interactions to form functional self-assembled architectures is core to our research interests, with a focus on metal-ligand bonds to direct the assembly of large multifunctional molecules, and light as a tool for chemical control.

a) **Confined and Controlled Chemistry**

Nature exerts spectacular control over the chemistry of biological systems by compartmentalising processes, and by the ability to strictly control the local environments where reactions occur. The ability to conduct synthetic chemistry within well-defined and controllable nanospaces offers the potential for similar control by synthetic chemists. This project aims to develop self-assembled polymersomes (synthetic vesicles) which can act as “nanoreactors” with responsive groups confined exclusively within their interiors.

b) **Photoswitchable Systems**

Light is a contactless, fast and convenient tool for chemists to deliver information to chemical systems, offering molecular-level control with the flick of a switch. However, for the most general applications a means of transforming light into chemical signals is required. Molecules called “photoacids” offer an appealing method by photoisomerising between non-acidic and acidic forms, allowing acidity to be switched OFF and ON with light. Projects will focus on the use of visible light to control the catalytic functions of small molecules and molecular recognition by self-assembled nanostructures.

c) **Metallosupramolecular Chemistry**
The use of metal-ligand bonds to direct the assembly of large molecular architectures has developed into a major area of supramolecular chemistry with metal complexes acting generally as simple structural elements. We aim to expand the use of metals in this class of structures to exploit the rich chemistry of transition metals for electronic and luminescent applications.

Selected References:


ASSOC. PROF. STEVE COLBRAN
Level 2, Dalton Building (F12)
T: 9385 4737  E:  s.colbran@unsw.edu.au
Transitional Metal Chemistry and Catalysis

- **Synthesis.** My group makes new, 'never-seen-before', metal-containing molecules: exciting stuff!
- **Spectroscopy and electrochemistry.** We zap the new molecules with light and electricity — because extreme conditions create highly reactive species.
- **Reactivity and catalysis.** Highly reactive species exhibit unmatched, extraordinary, chemical properties — we hunt for useful, important, reactions and energy-efficient catalyses.

It would be great to work with Honours students on the following projects:

(a) A bio-inspired sustainable approach to chemical reduction

In recent breakthrough research, we've proved that cleverly designed organo transition metal–organo-hydride conjugates are exceptionally effective catalysts for energy efficient chemical reductions of unsaturated substrates under benign conditions (in air at ambient temperature and pressure). In the following research projects, you'll use our conceptually new approach to chemical reduction to make chiral drug precursors or to produce methanol sustainably from carbon dioxide.

**Saving the world: Advanced transition metal–organohydride catalysts for CO₂ to methanol conversion (with Professor Les Field, School of Chemistry)**

In this research project you'll investigate sophisticated conjugates of transition metal complexes and multifunctional organo-hydride ligands — ligands that can store and donate hydride ion — as catalysts for reduction of carbon dioxide beyond the two-electron level. In particular, you'll target catalysts for the selective, energy-efficient electro- conversion of CO₂ to methanol, a widely sought alternative fuel. In this research, you'll also be assisted by the deep experience of Prof. Field and his research team in the chemistry of highly reactive organo-transition metal complexes that bind and activate CO₂.

**Making drugs better, more efficiently: Chiral transition metal–organohydride catalysts for efficient asymmetric reduction (with Dr Graham Ball, School of Chemistry)**

In this research, you'll advance and apply our new catalytic methodology for chemical reduction to the asymmetric hydrogenations of prochiral unsaturated organic substrates, including imine, carbonyl and alkene precursors to chiral drugs suggested by a commercial partner. There is scope to undertake DFT studies on the new catalytic processes — supervised by the redoubtable Dr. Ball.

(b) Chemistry and applications of a new large-ring macrocycle: bis(phenanthroline-pyrrole)

Large-ring oligo(pyridyl-pyrrole) macrocycles are used as discotic materials for liquid crystal displays, as dyes and photosensitizers, and as ligands for macrocyclic encapsulation of lanthanide or actinide ions. We’ve invented the world’s shortest and most convenient preparation of a large-ring rigid macrocycle, namely the bis(phenanthroline-pyrrole), $H_2L_{MC}$. We make $H_2L_{MC}$ on a large (multi-gram) scale by stirring commercial reagents in ethanol overnight.

Better TVs: Magnetic discotic materials for liquid crystalline displays (with Associate Professor John Stride, School of Chemistry)

Discotic liquid crystals are formed from molecules with flexible alkyl substituents bound to a planar, rigid and π-electron-rich core. Direct (one-pot) transesterification and ester-to-amide conversions will be used to afford derivatives of $H_2L_{MC}$ with varying (long) alkyl chain lengths. The liquid crystallinity and opto-electronic properties of these novel materials will be investigated. You’ll also investigate complexation with metal ions to form metallomesogens, which should exhibit useful electrical- and/or magnetic-switching between mesophases.

Into the unknown: The unexplored chemistry and applications of $H_2L_{MC}$ and its metal complexes

We created $H_2L_{MC}$ late in 2012. So far we’ve only skimmed the surface of the chemistry of $H_2L_{MC}$. The discoveries are remarkable. Two examples. $H_2L_{MC}$ is not only highly fluorescent, it’s an amazingly potent photosensitizer that photo-dehydrochlorinates chlorinated solvents — so, is it a catalyst for clean up of environmental chlorohydrocarbon contamination? $H_2L_{MC}$ is also a superb ligand that produces incredible metal complexes: e.g., the fluorescence and magnetism of the unique $\text{Eu(III)}_2(\mu$-$\text{OH})$ dimer shown is exquisitely sensitive to its surroundings suggesting diverse applications for the complex ranging from nano-electronics to intra-cellular imaging. A rich and diverse chemistry awaits discovery and development.

(c) Other projects

Other projects involving transition metal chemistry, spectroscopy and/or (spectro)electrochemistry are available. Projects will be tailored to you and your abilities and interests. Please feel free to come and chat about possible research projects.
Our research interests span the organometallic and hydride chemistries of the p- and f-block, with a view to developing syntheses for rare low oxidation state metal complexes and heavy metal hydrides. These species may be kinetically stabilised by bulky, sterically hindered ligands. Our research is driven by scientific curiosity, with a view to downstream applications in areas as diverse as H₂ storage, metal film deposition and catalysis. Students receive training in the manipulation and characterisation of ultra-air sensitive compounds with an emphasis on NMR and IR spectroscopies, and crystallography.

**a) New paths to low oxidation state aluminium and silicon**

The principal oxidation states of light group 13 and 14 metals are +3 and +4 respectively. The preparation of low oxidation state species, e.g. Al(I) and Si(II), represents a significant synthetic challenge. These species exhibit bonding that frequently challenges accepted bonding theories. Examples include multiple bonding between non-2nd period elements, mixed oxidation state cluster complexes, and so-called umpolung (polarity inversion) reactivity.

Current routes to low oxidation state group 13 and 14 species utilize extremes of temperature and pressure to prejudice redox equilibria, or a strong non-stoichiometric reducing agent such as potassium. These are hazardous, non-selective and expensive to reproduce. In this project you will prepare several hydride complexes of aluminium and silicon and use these as gateways to low oxidation state species via catalytic, chemical and photochemical dehydrogenation (see above).

**b) Catalysis using frustrated 3rd period Lewis pairs**

Frustrated Lewis pairs (FLPs) contain a sterically hindered Lewis acid and base that cannot form an adduct due to steric buttressing. This leads to high, potentially catalytic, reactivity with small molecules like H₂ and cyclic ethers, albeit with low turnover. We have unparalleled expertise in the design of sterically hindered ligands and their application to the stabilisation of frail chemical functions (see projects a and c). In this project you will develop sterically frustrated aluminium Lewis acids and silicon Lewis bases and apply them to the FLP hydrogenation of sterically hindered imines (see image).
(c) Heavy group 13 hydrides

We have an interest in the preparation of 5th and 6th period hydride complexes. These are unstable due to the size mismatch of the hydrogen 1s orbital with the heavy metal valence orbitals. Australia has vast mineral deposits of aluminium, gallium, indium and thallium ores, many of which essential for the fabrication of microelectronics. Hydride compounds offer promise in this regard as they are typically volatile, available in high purity, exhibit low deposition temperatures and do so without the deleterious inclusion of carbonaceous material. They are ideal for the development of single source precursors.

The hydride chemistry of thallium is currently non-existent and that of indium is nascent. In this project you will prepare low oxidation state compounds of indium and thallium supported by stabilising ligands as precursor materials for the oxidative addition of dihydrogen or low polarity Si-H and B-H bonds (see above). Particular emphasis will be placed on in situ monitoring of oxidative addition reactions using multinuclear NMR spectroscopy.

(d) Low oxidation state lanthanides

The principal lanthanide oxidation state is +3. Once considered the domain of Eu (4f^7), Sm (4f^6) and Yb (4f^14), the +2 oxidation state has been extended to La, Nd, Dy and Tm over the past decade. Of these, only thulium(II) iodide, TmI₂ (4f^13), can be prepared using conventional lab techniques. Given the numerous synthetic applications of samarium(II) iodide in one electron reduction syntheses (>2000 published synthetic applications), TmI₂ has great promise as a potent organic reducing agent.

In this project you will investigate ligand systems for the stabilisation of Tm(II) and study the reactivity of thulium diiodide with a range of substrates, including N-aryl imines, CO, CO₂, azobenzenes, and cyclic and acyclic oligoolefins (see above).

DR. ALEX DONALD
Mass spectrometry is a core enabling technology that is used in many emerging and existing scientific fields. The sustained expansion of mass spectrometry is driving the demand for mass spectrometrists in many research fields and industries. ARC Discovery Early Career Research Award fellow Alex Donald’s lab is developing and applying experimental methodologies in mass spectrometry with a focus on problems in catalysis, biology, and separation science. We are looking for students who are interested in developing a valuable mass spectrometry skill set.

(a) Strike while the iron is hot – Structure and reactivity of complexes that mimic C-H bond activating enzymes (in collaboration with Prof. S. Blanksby and Dr. A. Trevitt, U. Wollongong, and Prof. R. O’Hair, U. Melbourne)

Billions of years of evolution have led to an impressive and diverse array of enzymes that catalyse a wide range of reactions of industrial importance that are challenging to perform in the laboratory. For such reactions, nature has selected iron, which has the advantage that it is highly abundant, inexpensive, and environmentally benign. In this project an elegant series of novel Fe-oxo complexes that mimic the active sites of enzymes will be generated and characterized in the gas phase, where the effects of solvent, ligand architecture, and metal oxidation state can be carefully controlled, using laser ion spectroscopy and ion-molecule reactions. More broadly, this work will pave the way for using ultraviolet laser action spectroscopy to characterize the structure of inorganic complexes. In this project, you will gain experience in mass spectrometry, laser spectroscopy, and computational chemistry. The iron-oxide complexes have already been synthesized and are ready for analysis.

(b) Novel methodologies in chemical separations and desalination

We currently have projects that focus on developing a novel methodology for separating the components of solutions by taking advantage of the unique properties of micron and sub-micron charged droplets. A major goal is to improve the energy efficiency of current separation processes, e.g., distillation methods and seawater desalination. This is important because current technologies that are used for chemical separations and seawater desalination (e.g. reverse osmosis, thermal distillation) are energy intensive and expensive to operate. This is also important because the proportion of the global population that lives in countries that are water stressed is predicted to rise from one-third to over two-thirds within 20 years, which makes water scarcity one of the greatest challenges of this century.

We also aim to adapt our separation methods to purify ionic liquids (with Dr. Jason Harper), which is a new class of solvents that show promise for use in green chemistry. This is important because ionic
liquids are challenging to efficiently purify, which is hindering the wider-scale adoption of ionic liquids. You will be using a range of mass spectrometers and electrochemical methods in these projects.

(c) Analytical mass spectrometry projects

A major goal in science is to develop the capacity to comprehensively identify and quantitate all proteins in complex biological mixtures to rapidly facilitate biological and therapeutic discoveries. Because of the complexity, wide dynamic range, and impressive molecular diversity of biological systems, this is an immense challenge. A number of projects are available that broadly focus on developing and applying novel methodologies in mass spectrometry to address this challenge.

**Novel ionization source for improved mass spectrometry performance**

Electrospray ionization is a Nobel Prize winning technology that has resulted in the widespread use of mass spectrometry as an important analytical tool in many research areas and industry. One strategy to improve the performance of electrospray ionization is to generate smaller initial droplets during the spray process. However, current electrospray emitters utilize capillaries that clog upon attempts to further improve performance by reducing droplet sizes, which significantly reduces the sensitivity and tolerance to impurities of electrospray ionization mass spectrometry than if smaller droplets could be formed. I have recently developed a novel electrospray ionization emitter in order to solve this problem. In this project, you will improve and characterize the analytical performance of this electrospray ionization emitter in biological mass spectrometry experiments.

**Supercharging in electrospray ionization mass spectrometry**

A significant barrier to the wide-scale adoption of the top-down characterization of large molecules, such as proteins, by mass spectrometry is that it is challenging to finely control the charging of proteins in electrospray ionization. Supercharging agents are small molecules that are added to electrospray solutions to increase the number of charges that ionize peptides and proteins in electrospray ionization mass spectrometry. An honours student in my lab has recently discovered a new class of supercharging reagents that perform significantly better than all other supercharging reagents that have been reported. We are currently developing new reagents that can be used to enhance our control over the ionization of biomolecules in electrospray ionization in order to improve the identification and quantitation of biomolecules using mass spectrometry.
My research group undertakes research in synthetic organometallic chemistry, directed towards the application of transition metals in organic chemistry. We are particularly interested in the development of new organometallic catalysts that are able to activate small molecules (such as N₂, CO₂, etc), functionalize organic hydrocarbons to make value-added products, and perform specific organic transformations. We are also developing organometallic polymers for application in areas such as molecular electronics.

a) The Organometallic Chemistry of Carbon Dioxide

Carbon dioxide reacts with many organometallic compounds to give products in which the CO₂ is incorporated into the metal complex. A greater understanding of the ways in which CO₂ binds and reacts with metal compounds may provide new ways to trap and capture CO₂ and new alternate uses for this wasted and environmentally dangerous compound.

Our previous work has focused on the stoichiometric insertion of CO₂ into metal-hydride and metal-carbon bonds, to give metal formates and acetates, respectively. There have been many reports in the literature of catalytic activation of CO₂ to yield formic acid (by hydrogenation), acrylates (by reaction with ethylene), and carbonates (by reaction with epoxides). We are interested in exploring the ability of novel iron(II) and ruthenium(II) complexes that we have prepared in the lab to catalytically activate CO₂.

\[
\text{CO}_2 + \text{H}_2 + \text{Et}_3\text{N} + \text{ROH} \xrightarrow{\text{cat.}} \text{HCOOR}
\]

(b) Organometallic Polymers

Organometallic compounds containing complexed metals linked by bridging groups have many potential applications in materials science. We are particularly interested in the use of alkyne groups as the bridging unit, and are developing new methods for forming metal-acetylide bonds. Acetylide-bridged organometallic complexes show interesting electrochemical behaviour, and communication between the two metal centres is often observed.
Alternative Bridging Groups for Organometallic Polymers

The majority of alkyne-bridged organometallic polymers use linear aromatic spacer units, such as diethynylbenzene, as the bridge between metal centres. Non-aromatic bridges such as 1,12-diethynyl-p-carborane (C_{6}H_{12}B_{10}) have been described “3D aromatic systems”. We are interested in the effect of non-aromatic bridges, as well as non-linear aromatic bridges such as 1,3-diethynylbenzene, on the chemical and electrochemical behaviour of organometallic polymers.

The Chemistry of Ruthenaindene Complexes

We recently discovered a straightforward route for the synthesis of ruthenaindene complexes, a class of complexes in which a ruthenium centre is intimately imbedded in an aromatic framework. We are interested in exploring the chemistry of these complexes, and probing the effect of aromatic ring substituents on the chemistry of the ruthenium metal centre.

(c) The Chemistry of “CP_{3}” Complexes

We have recently developed a new type of polydentate ligand for transition metals, which binds to metal centres using three phosphorus donors and an anionic carbon donor. To date, we have only explored the chemistry of this ligand on ruthenium(II). We anticipate that this ligand will form complexes a wide range of transition metals, and are particularly interested in investigating the synthesis and catalytic properties of new rhodium and iridium complexes.
Biosensors, Nanomaterial, and Nanomedicine

The research group that I lead, which is also part of the Australian Centre for NanoMedicine, specializes in using self assembled monolayer or other surface modification technique to provide surfaces with unique functionality. The surfaces are the base upon which we build functional devices from nanoscale component including polymer, protein, nanoparticles, and porous material. The three major programs in which these surfaces are applied are, biomaterials, biosensor, and drug delivery. The multidisciplinary nature of our research means we need people with interest in medicinal chemistry, surface chemistry, polymer chemistry, nanotechnology or analytical chemistry. All new members of the group will be looked after by a post-doctoral researcher as well as Prof. Gooding. Specific projects are:

Mesoporous silica as biochemically controlled drug delivery nano-carrier

Mesoporous silica nanoparticles (MSN) are one of the most promising nanocarriers for delivery with around 500 nm in diameter with pores in the range of 2-10 nm in which the drugs can be loaded. We are exploring strategies that use the biochemistry located near the pathology to control the release of the therapeutic (see scheme). At present focus on the upregulation of protease enzymes, which are stimuli found in cancers. Hence these stimuli responsive particles will only release their drug payload where and when required. Other stimuli such as pH and other enzyme could also be incorporated into the system design to increase its specificity. In this project you will synthesize the particles, modify them and monitor the release of the drug upon the presence of the enzyme and in vitro analysis.

Development of porous silicon biosensor for enzyme detection by naked eyes (in collaboration with Dr. Peter Reece)

Porous silicon (PSi) is material produce from silicon wafer by electrochemical etching to form uniform nanoscales pores. The porosity of the material can be controlled to produce 1D periodic structures known as photonic crystals. These nanostructured pores could be tuned to create a material that reflects light in the visible region of electromagnetic spectrum, making it an exciting biosensor device. In this project, we will design an enzyme responsive polymeric material and anchor it inside a porous silicon photonic crystal (PSi). As such, PSI will act as both a nanoreactor (enzymatic reaction) and a transducer (in the form of visible light detectable by naked eyes), making it an ideal biosensor platform. In this work, you will learn polymer chemistry, photonic crystal-polymer hybrid material, and testing its sensing capabilities.

Enzyme-responsive hydrogels for improved tumour modelling (in collaboration with Dr Sharon Sagnella and Prof Katharina Gaus, Australian Centre for Nanomedicine).
Our current understanding of cancerous tumours is heavily based in vivo experiments in animals or in experiments on tissue culture plates. To date, few techniques that can satisfactorily recreate the tumour environment in vitro in 3-Dimensions. Such models would allow biologists to better understand the effect of spatial organisation of biomolecules on cell behaviour. Of particular interest are molecules that trigger cancer cell metastasis, or invasion, to other parts of the body. In our lab we are developing materials that can recreate the 3D tumour environment, made from polymers that provide a matrix for cells to attach to (see figure). In the proposed project, the polymers will be modified to include a peptide (protein-based) crosslink that stabilises the structure. Such protein-based regions are susceptible to degradation by specific types of enzymes (proteases) released by cancer cells when they invade surrounding tissue. The new materials developed in this project will be used by our collaborators to discover what triggers cells to invade, and to test new drugs that hinder invasion.

Detection of Biomolecules using Au nanoparticle dimers

A typical nanoparticle based biosensors consists biomolecule that can specifically bind to the target molecule and the nanoparticle plays the role of a signal transducer. The signal transduction is achieved by exploiting a change in the optical response of the nanoparticle. Gold nanoparticles are attractive for this application, as gold nanoparticles of different sizes and shapes can be synthesized in a straightforward manner. The optical properties of gold nanoparticles are dependent on its size, shape and the dielectric environment surrounding the nanoparticle. In this project, we propose the synthesis of functionalized gold dimers which can specifically disassemble in the presence of the target analyte. A typical functionalization scheme involves the use of biomolecules (such as cyclodextrins) which can undergo degradation in the presence of target molecule. The experimental techniques in the project include the synthesis and functionalization of Au nanoparticles. The nanoparticle dimers will be characterized using various microscopy and spectroscopy methods.
Our research is focussed on understanding how organic processes happen and what affects reaction outcomes. Particularly this encompasses examining how structural features in both the reagents themselves and the solvent used can change how a reaction proceeds. This knowledge can then be applied to a range of fields, including bioorganic, synthetic, analytical and environmental chemistry. Being particularly interdisciplinary, there is extensive opportunity for collaboration and this is currently underway in the areas of catalysis, reaction kinetics, synthesis and molecular dynamics simulations.

a) **Non-planar aromatic hydrocarbons: different reactivity based on structure**  
(in collaboration with Prof. Lawrence Scott, Boston College, USA)

Aromatic hydrocarbons are meant to be planar – right? Yet the synthesis of carbon nanotubes and related structures relies on the reactivity of curved aromatic systems. This project focuses on the different reactivities of these systems relative to ‘normal’ aromatics and how it might be controlled and exploited. It will predominantly involve synthesis and reactivity of systems, such as those shown below, with the opportunity for some kinetic studies to interpret the reactivity. Ultimately, understanding exploiting these differences will allow the rational synthesis of these geodesic polyarenes.

\[ X = \text{halogen, OMe, CN, NO}_2 \]

b) **Catalysis using \(N\)-heterocyclic carbenes: understanding structure/activity relationships**  
(in collaboration with Assoc. Prof. Marcus Cole, University of New South Wales)

\(N\)-Heterocyclic carbenes, have significant roles in organo- and organometallic catalysis, however some carbenes are effective for some processes but not for others and the origin of this is not well understood. This project aims to relate structure and
chemical properties of carbenes to catalytic efficacy, along with observing any solvent effects – this requires a series of chosen carbenes that vary in one way only (steric bulk, electronics, heteroatoms). Along with making the precursors to the carbenes, this project involves the opportunity to utilise various characterisation techniques and to undertake evaluation of catalytic systems; the latter can vary from simple screening of catalysts through to detailed kinetic analyses. The ultimate goal is to be able to rationally choose an NHC catalyst for a given process.

c) Ionic liquid effects on organic reactions: getting the reaction outcomes you want (in collaboration with Dr Anna Croft, University of Nottingham, UK; Dr Ron Haines, University of New South Wales; and Dr James Hook, Mark Wainwright Analytical Centre)

Ionic liquids are salts that melt below 100°C. They have potential as replacements for volatile organic solvents but outcomes of reactions in ionic liquids are often unexpectedly different to those in traditional molecular solvents. The focus of this project is to extend the understanding of ionic liquid solvent effects we have already developed and to use this knowledge to demonstrate that ionic liquids can be used to control reaction outcome. The project would involve using NMR spectroscopy to monitor reactions and kinetic analyses of these results, along with synthetic organic and analytical chemistry. The project can be readily tailored for students with more interest in the physical and analytical aspects, with the opportunity to develop new methods for following reaction progress and undertaking molecular dynamics simulations, or to more synthetic aspects, by focusing on increasing reaction yield and optimising isolation. That is, to get the reaction outcome you want!

d) Solvent-solute interactions in ionic liquids: can we design better solvents? (in collaboration with Dr Leigh Aldous, University of New South Wales; and Dr Anna Croft, University of Nottingham, UK)

We have previously made use of molecular dynamics simulations to understand interactions between a solute and components of an ionic liquid; this can be used to explain why benzene is so soluble in ionic liquids and why certain reactions proceed faster on moving to ionic solvents. This project aims to extend this and to model - both with simple compounds and simulations – which ionic liquid would be better solvents for a given solute. In order to do this both physical measurements of solubility and molecular dynamics would be undertaken to highlight key solute-solvent interactions. The outcome would be a better understanding of what interactions are required to confer good solubility giving us the opportunity to 'design' appropriate properties into ionic liquids – and these could then be made!
Research in the Hunter group focuses on the design and synthesis of functional molecules. We have a particular interest in using organofluorine chemistry to optimise molecules' properties: selectively incorporating fluorine atoms into molecules can be valuable in a variety of applications, including medicinal chemistry [see projects (a)–(c) below], fluorescent imaging [see project (d)] and catalysis [see project (e)]. Our research is interdisciplinary in nature, and we collaborate extensively to analyse the properties of the molecules that we create.

(a) **Anti-cancer integrin ligands (in collaboration with Dr Eddy Pasquier, Children’s Cancer Institute Australia)**

Integrins are cell-surface receptors that mediate a variety of processes related to cell adhesion: for example, $\alpha_v\beta_3$ integrin is involved in angiogenesis, and is therefore a target for the treatment of solid tumors. In this project, we are aiming to block this receptor by synthesising fluorinated peptides that have precisely-controlled 3D shapes. This project will involve the experimental techniques of solid-phase peptide synthesis, NMR, and Matrigel angiogenesis assays.

(b) **Anti-microbial cyclic peptides (in collaboration with Prof. Kiaran Kirk, Research School of Biology, Australian National University)**

We are investigating natural cyclic peptides that have promising anti-bacterial and anti-malarial properties. We are creating fluorinated analogues of these molecules, in order “fine-tune” their conformations and thereby maximise their potency. This project principally involves synthetic organic chemistry, HPLC and NMR.

(c) **Towards a treatment for stroke (in collaboration with Dr Nicole Jones, School of Medical Sciences, UNSW)**

In this project, we are investigating natural plant-derived compounds that have been shown to exhibit neuroprotective activity. The idea is to make systematic modifications to these lead compounds, in order to find analogues with optimal activity. The long-term aim is to develop a drug that limits brain damage after a stroke. This project will involve synthetic chemistry and cell-based assays.
(d) Light-harvesting dyes for use in biomedical imaging (in collaboration with Prof. Ewa Goldys, Department of Physics and Astronomy, Macquarie University)

Light-harvesting dye molecules can be attached to fluorescent nanoparticles, in order to enhance the signal strength in medical imaging. However, common dye molecules suffer from low stability due to rapid photobleaching. In this project, we are making fluorinated versions of such dye molecules that are designed to be more robust and better suited to imaging applications.

(e) Fluorinated organocatalysts

Modern synthetic chemists have an obligation to minimise energy consumption and waste. One way to achieve this is to develop more efficient catalysts. In this project, we are investigating fluorinated amino acids as next-generation organocatalysts that give valuable products in high yield and with high enantioselectivity.
The concept that distinguishes chemistry from other sciences is to understand, and then predict and control, how one set of connected atoms (a molecule) evolves into another. Whether the simple bond cleavage of a diatomic molecule, or the complexity of a biological reaction, the identification of key intermediates and transition state structures defines the current paradigm of the chemical reaction. We use laser-based techniques to initiate and control reactions, making and probing transient intermediates along the way.

a) Weird chemistry – reactions that just don’t go where they should. (Collaborators: A/Prof Meredith Jordan, Sydney Univ., Dr David Osborn, Sandia National Labs, CA, USA)

Since the 1930’s, the concept of a transition state (TS) has formed the bedrock of chemical reaction theory. When the activation energy is very near the TS energy, the reaction becomes very slow and other unsuspected processes become competitive, even dominant. Over the past few years we have identified new chemical pathways to products that should not occur. We have hypothesized and then found new mechanisms in atmospheric chemistry to explain where organic acids come from. We are exploring why molecules like to break as many bonds as the photon energy will allow.

There are two sub-projects on offer for 2014. Both use state-of-the-art laser systems, and unique spectrometers that have been manufactured specially for our laboratory.

Photo-tautomerisation in the atmosphere

In 2012 we published a paper in Science hypothesizing that photo-tautomerization is the origin of 30 Mtonnes of organic acids that have been measured but not explained in the atmosphere. In 2013 we found the first experimental evidence. This project is to discover how widespread photo-tautomerization is and to explore the impact via collaboration with atmospheric modelers.

Triple fragmentation

One photon breaking two or three bonds is actually much more common than previously realized and frequently misunderstood in the literature. We have developed a new theory of triple fragmentation, but there are scarcely any experimental data to test it on. This project is to perform experiments on one or more photochemical reactions, and refine the model as needed.

(b) Radicals in the atmosphere and combustion (Collaborator: Prof Tim Schmidt)
Free radicals are key intermediates in all complex chemical reactions. The chemistry of the Bunsen burner requires a minimum of 50 chemical reactions, 49 of which involve radicals. OH attack is the first step in the “processing” of nearly all atmospheric compounds. Processing can reduce the molecular weight, leading eventually to fully oxidized products (CO$_2$ and H$_2$O) or increase the MW, thereby reducing the volatility and leading to harmful aerosol formation. The processing of either biogenic emissions (e.g. terpenes) or anthropogenic emissions (e.g. toluenes) is largely unknown.

We have developed laser-based techniques and built custom instruments to create and isolate a wide variety of radicals. Different types of laser spectroscopy are used to probe their structure. There are several sub-projects on offer for 2014:

*Radicals from OH attack on atmospheric species*

OH can attack unsaturated hydrocarbons in two different ways: abstracting H to form H$_2$O and a radical, or adding across a π-bond to form an OH-adducted radical. The OH-adducted radicals have been scarcely measured in the literature. In this project you will investigate either a typical biogenic compound (e.g. α-pinene) or anthropogenic compound (e.g. cyclohexene) and react it with OH. The ensuing OH-adducted or abstracted radical will be isolated in vacuum and probed using laser spectroscopy to determine where the OH adds or attacks and the isomeric and electronic structure of the radical product. This will provide firm evidence for the first step in atmospheric processing of these compounds.

*H-atom addition/loss from common fuels and biofuels*

Hydrogen atoms can be lost or gained by aromatic fuels, in both cases making radicals. In this project you will choose such a fuel, use a custom-built reactor to make it gain or lose H. The resulting radical, the first intermediate in combustion, will be mass selected and probed by laser spectroscopy.

All projects above can be tailored to have a significant computation chemistry component, or tailored to be almost exclusively experimental in nature.

(c) *Science Education* (Collaborators: Profs Mark Buntine, Curtin Univ. (Chemistry), Manju Sharma, Sydney Univ. (Physics), Karen Burke da Silva, Flinders Univ. (Biology), and many more)

I have a long-standing interest in how students learn in the laboratory and have directed a national program on laboratory education for 12 years. There are a variety of Honours projects on offer, including research involving both higher education (university) and secondary education (school) sectors, that would suit a science student from any discipline with an interest in education (e.g. interested in becoming a teacher).
The main focus of the research undertaken in my group is the discovery and development of novel bioactive molecules. Naturally produced chemicals are of fundamental importance in biological systems. Such chemicals are used to mediate interactions across all levels of biological hierarchy. Very often such diverse molecules are produced only in minute quantities. New or innovative organic syntheses not only provide access to sufficient quantities of these molecules but also their analogues. The access to various structurally-related analogues allows full assessment of their biological activity and mode of action, and offers opportunities to develop new therapeutic leads. The research is multidisciplinary research involves a combination of synthetic organic chemistry, molecular modelling and biological screening, and involves extensive collaboration with various groups from within the University and outside industry partners.

(a) NOVEL ANTI-MICROBIAL PEPTIDE MIMICS
(in collaboration with Prof. David Black, UNSW)
Peptide mimics are small peptide-like molecules designed to improve upon the properties of existing peptides by specific structural variations. The emergence of multidrug resistance to current antibiotics highlights the need for new antimicrobial agents for the treatment of infectious disease. We have developed a novel class of peptide mimics from N-acylisatins which inhibit the regulatory quorum sensing communication pathways of bacteria, which represents a non-growth inhibition strategy that is less likely to result in the development of drug resistance. Recently, we extended this methodology to the preparation of more complex systems such as dendrimers with the aim of developing a more efficient drug delivery system.

(b) EXPLOITATION OF BACTERIAL TRANSCRIPTION INITIATION AS A TARGET FOR NEW ANTI-MICROBIALS
(in collaboration with A/Prof. Renate Griffith, UNSW and A/Prof. Peter Lewis, University of Newcastle)
The enzyme RNA polymerase (RNAP) that transcribes DNA into RNA is highly conserved across bacterial species. However, the factors that regulate the activity of RNAP are target-specific. Therefore, the unique interaction of sigma factors with RNAP in bacteria represents an ideal target for the development of small molecules that can specifically inhibit this interaction. We are rationally designing and synthesizing compounds that target these essential protein-protein interactions. These small molecules would represent lead compounds for the development of new antibiotics.

Lead bis-indole compound mapped onto the pharmacophore
(c) SYNTHESIS OF NOVEL FLAVONES AND ISOFlavONES

(in collaboration with Prof. David Black, UNSW)
Flavones and isoflavones are two structurally related large and diverse groups of natural compounds with broad spectra of biological activities including antioxidant, anti-cancer, antiviral and anti-inflammatory properties. They are recognized as “privileged” medicinal chemistry molecular frameworks because they are commonly found in biologically active compounds that show drug-like characteristics. Recently we have focused upon novel biflavonoid systems such as the natural product dependensin and its analogues which show potent anti-malarial activity. We have also synthesised a series of novel azaflavone and azaisoflavone analogues in which the ring oxygen atoms are replaced by nitrogen atoms.

(d) DEVELOPMENT OF NOVEL ANTICANCER AGENTS

(in collaboration with Prof. Glenn Marshall and Dr Belamy Cheung, Children’s Cancer Institute Australia for Medical Research)

Design and Synthesis of RARβ-selective ligands
Retinoids have therapeutic activity against many cancers, particularly neuroblastoma, and their anticancer activity is mediated by the nuclear retinoic acid receptor beta (RARβ). We are employing structure-based virtual screening to identify RARβ small molecule ligand candidates. Our aim is to synthesize these leads and optimize their activity as potent RARβ-selective ligands.

Design and Synthesis of SAHA synergists
Histone deacetylase (HDAC) inhibitors, such as suberoylanilide hydroxamic acid (SAHA, Vorinostat), are a class of cytostatic agents that inhibit the growth of tumours. A pilot screen of the WEHI compound library has identified 24 compounds that could act synergistically with SAHA to overcome HDAC inhibitor resistance. Our aim is to synthesize analogues of the lead compounds in order to generate novel anticancer agents.

(e) SYNTHESIS OF NOVEL INDOLES AND RELATED HETEROCYCLES

(in collaboration with Prof. David Black, UNSW)
Heterocyclic chemistry is the field responsible for generating the overwhelming majority of pharmaceutical agents and drugs in use today. It is becoming increasingly important as a source of distinctly new molecular structural types, to overcome the rising problems of resistance of biological organisms to the heavily used current drugs. Our research is focused on the deliberate design and synthesis of new structural types, rather than known natural products. Our current major emphasis is on the chemistry of activated indoles which can generate numerous innovative molecules such as "molecular baskets" and structures related to biologically-important natural products.
We have a diverse array of projects involving organic synthesis, molecular and cancer biology, and biochemistry. Our synthesis projects start from a natural product template, and our goal is to design analogues of the natural product. We then test these molecules in cell growth assays, biochemical assays, and cell-based assays in order to determine their activity and potency. Once we understand their biological target, we then design new analogues to improve their selectivity, solubility and efficiency.

a) **Synthesis of novel ribosomal inhibitors: Sanguinamide B**

Sanguinamide B is a unique natural product that was isolated from a sea slug. We have made a number of derivatives of this natural product and found that it targets the ribosome, where proteins are made. Protein synthesis is critical for cells to survive, thus, inhibiting this process is one good mechanism to stop cancer cells from growing. In this project, we are making new molecules that are based on the structure of our most active compound. Upon completion of their synthesis, we will test them in ribosomal-based assays to investigate their activity. Experimental techniques will include synthetic organic chemistry, NMR, LCMS, translational assays, cell death and cell growth assays.

b) **Synthesis and mechanism studies of Urukthapelstatin A**

Urukthapelstatin A is a natural product that has shown extremely potent activity at inhibiting cell growth. Our goal is to investigate it as a potential anti-cancer therapy. We have just developed a successful route for making the natural product. This project would involve making this molecule and several derivatives, and investigating their mechanism of action. Experimental techniques will include synthetic organic chemistry, NMR, LCMS, DNA binding assays, cell growth and death assays, and perhaps other new assays based on the biological results.

c) **Mechanism studies of new heat shock protein inhibitors in metastasis**

Cancer cells migrate to various sites in the body in a process called metastasis, and metastasis involves several pathways that are regulated by the molecular chaperone Hsp90. This project will evaluate how derivatives of the Hsp90 inhibitor Sansalvamide A affect cell migration pathways involved in metastasis. Experimental techniques will involve cell proliferation assays, protein expression studies, flow cytometry and microscopy (images to the right show cells treated with a Sansalvamide A derivative).
d) **Synthesis and mechanism studies of new heat shock protein inhibitors**

Heat shock proteins are in charge of folding and maintaining over 200 other proteins in the cell. They are essential for protecting these proteins from stress-related damage. In cancer cells, these proteins are up-regulated and they protect the cells from dying. Blocking the function of heat shock proteins allows cells to die, which is a good thing in cancer cells.

We have developed several unique inhibitors of heat shock protein 90 (hsp90), one of which is compound 1. However, compound 1 is not very soluble, and therefore drug delivery is a significant problem. This project would involve making soluble derivatives of compound 1 (i.e. like compound 4). We would then test these compounds and examine their ability to kill cells effectively, inhibit hsp90, stop migration of cancer cells, and induce degradation of proteins critical for cancer growth. You would learn how to do synthesis, analysis of compound structures using NMR, LCMS, HRMS, and TLC, as well as run biological assays on your compounds.

e) **Synthesis and mechanism studies using nanoparticles**

Heat shock proteins are in charge of folding and maintaining over 200 proteins in the cell. They are essential for protecting these proteins from stress-related damage. In cancer cells, these proteins are up-regulated and protect the cells from dying. Blocking the function of heat shock proteins allows the cells to die, which is a good thing in cancer cells.

We have developed several unique inhibitors of heat shock protein 90 (hsp90), but they are poorly soluble. Therefore, drug delivery is a significant problem. This project would involve making compound 1 with a tag on it so it can be coupled to a polymer. We would then test these compounds for their ability to kill cells effectively, inhibit hsp90, stop migration of cancer cells, and induce degradation of proteins critical for cancer growth. You would learn how to do synthesis, analysis of compound structures using NMR, LCMS, HRMS, and TLC, make polymers, and participate in the biological studies.
Enhancing the economic viability and energy efficiency of chemical transformations is of fundamental importance in the fine chemicals industry. Organometallic catalysts are an increasingly important means of providing new and more efficient routes for chemical processes, and the development of novel transition metal catalysts for organic transformations is a key part of devising new routes for the synthesis of fine chemicals. Our research projects aim to achieve highly efficient multistep transformations, using a variety of approaches based on transition metal complexes as catalysts.

The research involves the synthesis of catalysts, which require new organic scaffolds, ligands and metal complexes, as well as the investigation of catalytic routes, molecular structure and dynamics using NMR spectroscopy and X-ray crystallography. Where we create new catalysts bound to surfaces, we also utilize surface chemistry techniques such as XPS.

Multimetallic Complexes for Multistep processes
The aim of this project is to develop novel multimetallic catalysts held on scaffolds that promote multistep or tandem processes in a single reaction vessel (1). The synthesis of complex organic molecules relies on the formation of multiple new bonds, and the challenge in these projects is to develop multimetallic catalysts that mediate two or more sequential reactions. The multimetallic complexes that will be made will contain ligands and complexes that we understand well, attached to scaffolds that direct the relative orientation of the metal centres (e.g. 2). The closer the metal centres are to each other, the more effectively they promote the multistep processes. Homogeneous catalytic processes can benefit from cooperative effects between adjacent active centres, mimicking enzymatic capabilities. We are also interested in understanding how these cooperative effects work.

Catalysts on Surfaces (with Prof Justin Gooding, UNSW)
Although homogeneous catalysts are highly efficient, the separation of homogeneous catalysts from products or substrates continues to be a challenge in the chemicals industry. New approaches to selectivity and reactivity are also important. This research project involves attaching catalysts already developed by our group onto a variety of structures and surfaces. This will not only allow easy catalyst/product separation, but will also provide a greater control over the nature of catalyst reactivity. The supports themselves can use the electrochemical properties of the catalysts to promote reactivity, or induce high enantioselectivity in asymmetric transformations. The surfaces and supports under investigation in this project include glassy carbon electrodes and glassy carbon nano-beads (3).

Target Catalysed Transformations – Making Biologically active Molecules
The ultimate goal of our projects is to use our new catalysts for promoting important organic transformations. Our projects involve following the catalytic reaction processes and establishing relative reactivity and selectivity of the catalysts.

**Single step Reactions**

*The formation of C-N, C-O and C-S bonds:* The synthesis of N, S containing heterocycles is of fundamental importance in the synthesis of biologically active compounds. An atom efficient approach to the synthesis of heterocycles involves the direct addition of N, O or S to unsaturated C-C bonds (Scheme 1). Our catalysts are particularly efficient for the synthesis of new N-heterocycles and O-heterocycles.

*The reduction of Imines and Alkenes:* The reduction of imines is an important route to the synthesis of amines. We have developed highly efficient catalysts for the reduction of imines both via hydrogenation and hydrosilation. By designing chiral catalysts, we aim to achieve the enantioselective synthesis of amines which is of particular importance in the synthesis of pharmaceuticals.

**Tandem Reactions**

The synthesis of complex organic molecules relies on the formation of multiple new bonds. These projects investigate the most efficient catalysts for promoting multiple step reactions in one pot. Efficient approaches to the synthesis of molecules containing amines, and O- and N-containing heterocycles are our primary goals. These routes can involve C-X bond forming reactions followed by C-C bond forming reactions, or C=X reduction reactions (e.g. Scheme 2).

**References**


My research interests lie in organic synthesis, with a particular emphasis on the synthesis of naturally occurring compounds that have profound biological activities. Working on a total synthesis is a significant challenge, but provides excellent training. In addition to the new chemistry you will carry out, you will develop skills in planning, retrosynthetic analysis, determining mechanisms, and structure elucidation. There are always new projects being developed and I would be happy to discuss them with you.

(a) **Total Synthesis of Biologically Active Natural Products**

The development of efficient syntheses of biologically active natural products is a major activity of the Morris group, with current targets including coproverdine and embellistatin. The focus is on:

- developing new strategies for the synthesis of natural products that are of biological significance,
- generating new methodologies for the preparation of molecules in an efficient, reliable manner, and
- examining the biological properties of these natural products.

![Chemical structures of coproverdine and embellistatin](image)

(b) **Generation of Natural Product-like Chemical Libraries using the Diels-Alder Reaction**

Fused and bridged bicyclic structures are common among biologically active natural products and semisynthetic derivatives. Noteworthy examples include Taxol (1) and Zocor (2). From a synthesis point of view such structures do not lend themselves to library synthesis, however the corresponding heterocyclic structures are more tractable. The goal is to synthesize a collection of bridged heterobicycles inspired by the potential for these rings to act as surrogates for carbocycles by using a straightforward, versatile Diels-Alder strategy. The libraries will be investigated by biological assays.

![Chemical structures of Taxol and Zocor](image)
(c) Axially Chiral Biaryls – An Important Scaffold for Drug Discovery and Catalyst Design

The axially chiral biaryl motif is a common structural component in a large number of naturally occurring and synthetic materials. Biaryl compounds can be used as scaffolds in drug discovery, chiral auxiliaries and catalysts for asymmetric synthesis. This project is focused on developing new strategies for the synthesis of biaryl-containing structures.

(d) Anti-leukaemia activity of metabolically stable sphingosine analogues (in collaboration with Dr Anthony Don, Lowy Cancer Centre)

FTY720 (Fingolimod) is a promising new immunosuppressant that is currently in Phase III clinical trials for the treatment of multiple sclerosis, after showing considerable promise in Phase II studies. FTY720 is a synthetic analogue of the endogenous lipid sphingosine. Recent work has shown that FTY720 is highly effective at inhibiting proliferation and inducing cell death in patient derived multiple myeloma, chronic myelogenous leukaemia (CML), chronic lymphocytic leukaemia (CLL) and BCR/ABL positive acute lymphoblastic leukaemia (ALL) cells. Furthermore, the FTY720 analogues AAL(R) and AAL(S) have also been investigated by Don and co-workers and it has been found that these analogues show very similar potency on cultured leukaemic cell lines, as well as childhood ALL cells derived from several different patients. It has recently been found that AAL(R) is a superior substrate for SphK2 compared to FTY720, and is therefore much more rapidly phosphorylated by cultured cells or whole blood. This project is concerned with the discovery and development of therapeutic agents based on the AAL(S) scaffold.

(e) Identification and Modification of Chemical Compounds for Hepatitis C Virus Polymerase Inhibition (in collaboration with Assoc Prof Peter White, BABS, UNSW)

HCV is a very significant global problem with approximately 3% of the world's population infected and the rate of new cases increasing rapidly. The majority (~70%) of all infections become persistent and lead to various clinical outcomes ranging from an asymptomatic carrier state to chronic active hepatitis and hepatocellular carcinoma. There is no vaccine for HCV and current treatments have variable response rates, high incidence of side effects and are not widely available; less than 12% of the Australian HCV infected population has been treated. Moreover, many potentially useful antiviral polymerase inhibitors for HCV have been discontinued through toxicity issues with only very few making it to phase II clinical trials. Recent high throughput screening has identified several new hits that show promise in the inhibition of hepatitis C virus polymerase. Current efforts are focused on the optimisation of these hits.
My research group investigates how molecules interact with light, and the consequences, with applications ranging from studying radicals and ions of astrophysical and atmospheric interest, to renewable energy. Our principal tools are femtosecond and nanosecond lasers, with sophisticated detection schemes, vacuum chambers and mass spectrometers.

a) Photochemical Upconversion for Improved Solar Energy Conversion

Light from the sun reaches us as a continuous spectrum. To generate a photovoltage in a solar cell, we usually neglect part of the spectrum with photon energies below the band. Such a strategy limits the energy conversion efficiency of solar cells to about 33% (UNSW Si cells have reached 25%). Photochemical upconversion (PUC) can be harnessed to convert long wavelength into shorter wavelength light, increasing the photocurrent of the device.

Recently, we have applied PUC to amorphous silicon, organic polymer and dye-sensitized solar cells. But, efficiencies are still too low for application. To concentrate the absorption of light and increase upconversion efficiencies, we are currently exploring a range of nanostructured architectures incorporating biomimetic light harvesting materials.

(b) New Materials for Luminescence Solar Concentration (with A/Prof. Pall Thordarson)

One strategy to slash the cost of solar energy is to use a small area of solar cell and a large solar collector. However, usually such systems rely on geometric concentration of sunlight using mirrors. Such systems are expensive and cumbersome, and cannot concentrated diffuse light. The luminescence solar concentrator is promising way to do this using passive molecules.

When light falls on a slab of material containing fluorophores, light is absorbed but re-emitted isotropically. About 75% of this light is trapped in the slab by total internal reflection, and guided towards solar cells on the edge of the slab. Until now, such systems have been plagued by reabsorption effects. We will couple fluorescent dyes to light-absorbing nanomaterials to separate the roles of absorption and emission, and reduce reabsorption. Further improvements have been shown by us to be possible by clever design of the orientation of transition dipole moments.
(c) Laser Spectroscopy of Isolated Radicals and Ions (with Prof. Scott Kable)

The new Molecular Photonics Laboratory houses sophisticated lasers and equipment with which we can discover new transient chemical species of importance in the gas phase chemistries of our atmosphere and the interstellar medium.

Atmospheric Radicals
One of the greatest scientific challenges of our time is to understand the complex chemistry of the atmosphere. Plants and human activity are responsible for $>1000$ Tg ($10^{12}$ kg) of volatile organic compounds being emitted into the atmosphere each year. These molecules are processed into less volatile compounds which then find their way into secondary organic aerosols, which are a major natural impactor on public health and climate. In this project, we will develop laser-based spectroscopic methods to detect and characterize intermediates formed on the way from the plant to the aerosol particle.

Interstellar Molecules and Ions
As stars die, they eject complex organic molecules into the interstellar medium, where they live out millennia before being incorporated into new stars and planetary systems. These organic molecules are the seeds of life, but, as yet, we do not know the chemical make up of the interstellar medium from which planetary systems are formed.

Using a star as a lamp, we can peer into this medium using telescopes by observing molecular absorption spectra. However, despite there being hundreds of nibbles taken out of the visible stellar spectra of stars occluded by diffuse clouds, only a few molecules have been unambiguously detected by their visible spectra. The unidentified features are known as the diffuse interstellar bands, and are the longest standing mystery in astrophysical spectroscopy.

In this project, we will develop techniques to capture the spectra of isolated, never-seen-before aromatic cations which the leading candidates for carrying the DIBs, and (hopefully) solve this long standing problem.

(d) Advanced Spectroscopy for Complex Functional Materials (with Dr Dane McCamey, School of Physics)

Complex functional materials are employed in a range of applications, the development of which is motivated by the future technological needs of society. Organic solar cells, organic light emitting diodes and organic electronics all employ materials characterized by a complex relationship between morphology and function which can only be elucidated by advanced spectroscopic techniques.

Combining lasers and magnetic resonance, we will develop and apply new advanced spectroscopic techniques to complex functional materials, revealing the dynamical behaviour of charge carriers and excited states.
My group investigates how we can improve current energy-related devices and develop the next generation of devices, as is essential for our technology-driven lives. We explore how atomic arrangement (crystal structure) inside materials influences their physical properties. Then we use chemical methods to tune the crystal structure to improve the desired property, whether it is to provide more power, better performance, or use materials with a lower environmental cost. This research encompasses exploratory synthesis, crystal structure determination using synchrotron X-ray and neutron scattering, physical property measurements of components and in situ structure and property characterisation of real-life devices constructed in my group.

a) Towards the next generation of batteries: Sodium-ion batteries

Lithium-ion batteries are ubiquitous in our daily lives, e.g. mobile phones and laptop computers, but their limitations have restricted wide-scale use in applications requiring higher power, e.g. electric vehicles and energy storage of renewable energy. This project will target new battery chemistries, in particular sodium-ion batteries, by developing and characterising new electrode and electrolyte materials. We will work to develop a reliable and affordable room-temperature sodium-ion battery to provide sufficient power for large-scale energy storage from intermittent renewable power sources. Students will work on one of the following parts of a battery and test their component in idealized batteries.

Positive electrode materials

These electrodes provide the source of the sodium-ions and represent the largest cost and energy limitations for lithium-ion batteries. Here, sodium-containing transition metal oxides, phosphates or sulfates will be synthesized and characterized to determine the relationship between crystal structure and battery performance.

Electrolytes

Sodium-ion conducting ceramics or glassy-ceramics are known to be excellent electrolytes at high temperatures (>300°C). This project works towards making materials with sufficient sodium-ion conduction at room temperature.
**Negative electrode materials**

Negative electrodes are the least investigated component in a sodium-ion battery and the compounds used for lithium-ion batteries show poor performance in sodium-ion batteries. By developing new negative electrodes and understanding their limitations towards reversible sodium insertion/extraction we will be enable the next generation of devices.

(b) **In situ structural-electrochemical characterisation of lithium-ion battery materials**

Understanding the relationship between crystal structure and electrochemical performance of electrodes in a battery allows us to propose and implement changes in the rational design of materials that maximize performance. We approach this problem by directly characterizing electrode structural evolution and correlating it simultaneously to battery electrochemistry, an *in situ* approach. The project will involve selecting a known set of electrode materials and conducting *in situ* experiments, where a battery is used and re-charged while both electrochemical and structural data is collected - cycling batteries on X-ray or neutron diffractometers. Then systematic chemical modifications will be made to the electrodes, such as doping or controlling particle size distribution or morphology, to determine what makes the best performing electrodes.

(c) **Improving solid-state electrolytes by understanding their formation characteristics and phase evolution**

Safety is an important aspect of high power batteries. Using a solid-state electrolyte has significant advantages to the highly flammable liquid electrolytes that are commercially available. Unfortunately the ionic conductivities of solid-state compounds are generally lower than the liquid counterparts, especially under ambient conditions. At the other extreme, solid oxide fuels cells often operate at approximately 1000°C as the operating temperatures are essentially determined by the ionic conductivity of the electrolyte. In both examples, electrolyte ionic conductivity is a critical hurdle in preventing further development and use of these technologies. The ionic conductivity is directly related to the crystal structures adopted by the electrolytes and how they evolve with temperature. In this project lithium-ion and oxide-ion conducting materials will be synthesized and their ionic conductivities characterized. Importantly, variable temperature time-resolved neutron powder diffraction will be used to study the formation (from starting reagents) of these ionic conductors under varied conditions. This will shed light on the formation processes and optimal conditions required for synthesis.
My group focuses on making and understanding new materials
Our key areas of interest are related to the major challenges facing us today: energy, water and sustainability
We make use of cutting-edge techniques to obtain a detailed understanding of hierarchical emergent properties and complexity, that build upon the basic interactions between molecules

It would be great to work with Honours students on the following projects:

(a) Metal organic frameworks (MOFs): coordination chemistry of the 21st century

Over the last 15-20 years, inorganic chemistry has taken on board a number of new concepts and approaches that have reinvigorated the subject toward materials that are central to many current technological advances – one area which shows particular promise is polymeric coordination compounds or MOFs. These topologically beautiful materials display intimate long range ordering and immense compositional flexibility with structural rigidity; they are ideal hosts for a range of molecular guests.¹

A solution to carbon emissions? Tailored metal organic frameworks for CO₂ capture or H₂ storage

This research project is specifically targeted towards the very real challenge of CO₂ emissions. It is now widely accepted in scientific circles that the rapid rise in CO₂ emissions associated with industrial scale consumption of fossil fuels is altering long-term climate patterns. In order to maintain our current standard of living we need to moderate our emissions either by capturing and re-cycling the carbon or by avoiding it altogether. As many MOFs are highly porous, they make excellent host materials for small molecules such as CO₂ or H₂; by tuning their properties MOFs can become efficient storage vessels, effectively trapping CO₂ emissions or delivering H₂ in a viable format as an alternative fuel.

New magnetic materials: fundamental insights

Magnetic materials have revolutionised the way in which store information, they have been a navigational aid for centuries and are pretty useful at securing notes to the fridge door. It is therefore fascinating that we still do not fully understand the behaviour of such materials, especially when dimensionality is constrained. MOFs can have single chains (1D) or sheets (2D) of metal ions embedded into a non-magnetic matrix, making them ideal materials in which to study the effects of magnetic quantum confinement.

¹ For further details, see reference [1].
(b) **Organic electronics: new materials, new technologies**

Organic alternatives to many conventional technological materials offer solutions to some important issues; (i) they are low density materials and so are attractive in realm of incorporation into portable devices; (ii) organic materials are readily processable from the solution phase, providing a low cost, low energy alternative to solid oxides and ceramics; (iii) end of life processing of organics is far less arduous than that of many inorganic materials, providing a more environmentally sustainable solution.

**Room temperature organic ferroelectrics as non-volatile memories?**

Ferroelectric materials have the intrinsic property of undergoing a change in polarisation in applied electric fields; mostly inorganic in nature, they are of great interest for applications such as sensors, communications and non-volatile data storage technologies. Organic ferroelectric materials are an emerging class of ferroelectrics that share the technologically attractive response to electric fields, but have greater flexibility in material processing, offering lightweight and solution deposable alternatives to traditional ferroelectrics. Recent advances in such materials have greatly increased the potential to deliver truly low-density, wholly organic ferroelectric devices that are fully interfaced to organic, flexible, easily processed electronic circuitry.¹ This project aims to synthesise new ferroelectric materials based upon the recognised modalities of mixed-stack and hydrogen-bonded systems.

**Donor-Acceptor stacks: heterojunction photovoltaics to molecular magnets**

The intermolecular interactions between efficient electron donors and acceptors (A) yield optically active charge transfer materials that can act as organic semiconductors, photovoltaics, ferroelectrics and light emitting diodes, whilst complete electron transfers can result in bulk magnetic materials. We aim to investigate the interactions of relatively simple D…A mixed-stacks whilst modifying the peripheral functional groups that are known to contribute to molecular packing. In this way, self-healing semi-conducting liquid crystalline materials can be produced that show remarkable anisotropy, enabling uniaxial conduction under greater load. With the wide range of suitable D and A molecules available, these materials have tremendous promise in their capacity to be tuned for specific applications, whether it be for emission in the visible spectrum (OLEDs) or broad-range absorption (OPVs); being relatively small molecules, they are also suited to computational studies that have been found to be highly informative in terms of the electronic interactions and π-π stacking interactions.²

(c) **Other projects**

Other projects involving materials-based chemistry, nanotechnology, crystallography and spectroscopy are available and can be tailored to your interests. Feel free to come and discuss possible research projects.

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Combining the latest advances in synthetic and physical organic chemistry with advanced characterisation tools such as atomic force microscopy (AFM), the work of ARC Future Fellow A/Prof. Pall (Palli) Thordarson is aimed at i) understand better complex self-assembly processes and ii) create functional nanomaterials by self-assembly for application ranging from catalysis to drug delivery and tissue engineering.

a) Light-driven chromophore-protein hybrids

At the core of this work is the idea that light can be used to control protein function by forming hybrids between synthetic chromophores and redox active proteins. These systems are then self-assembled either on surfaces or in large polymer-based vesicles to create enzymatic cascades for applications such as proton pumping to control reactions in confined spaces. Additionally, this work will deepen our understanding of light-driven process in nature (photosynthesis) and industry (solar cells).

(b) Understanding self-assembly in water – From nanoscale fibres and vesicles to macroscopic gels (collaboration with Prof. Michael James, ANSTO and Dr. Chris Marques, BABS, UNSW).

Self-assembled systems in water is what makes life – think cell membranes, organelles and the extra cellular matrix between cells! Our work is focused on the kinetics of self-assembly in water using a combination of spectroscopic, scattering and microscopic methods such as AFM. This work should allow us to predict better a priori the properties of these systems and hence enhance their utility in a range of areas including display technologies, drug delivery and regenerative medicine.

c) Nanomedicine: Smart soft nanomaterials for medical applications (collaboration with Prof. Maria Mariaditis, Children’s Cancer Institute Australia, Prof. Peter Gunning, Medicine, UNSW and Dr. Keith McLean, CSIRO).
This work is aimed at designing and synthesising peptide-based smart soft nanomaterials for application in medicine ranging from drug delivery and 3D-cell culture models to regenerative medicine and stem cell therapy. In collaboration with medical researcher both inside and outside UNSW, we are targeting systems such as brain cancers and muscular dystrophy.

d) Novel donor-acceptor dyes for applications in solar energy research (collaboration with Algae Enterprises Ltd, Dr. Murad Tayebjee, Photovoltaics, UNSW and Dr. Justin Hodgkiss, Victoria U. Wellington).

In this project we focus on the synthesis of aromatic dyes such as perylenes and linear acenes (benzene, naphthalene, anthracene, tetracene, pentacene…). We tailor the design of these molecules with the photophysical properties desired (e.g. emission at a particular wavelength). The photophysical properties of these molecules are then measurement to optimise further their properties for applications in cutting-edge solar energy research such as solar concentrators, upconversion and singlet-fission. Ultimately, the aim of this work is to generate new materials for industry to address the ever-growing need for renewable energy.

Selected Publications:

Clean, renewable energy has enormous implications for the future prosperity of humankind. As creatures, living better and longer has been our instinctive pursuit, and advanced biomedical technology is therefore always highly demanded. Electron transfer is one of the most fundamental processes in both the energy and life systems. Research in our lab addresses these problems by using electrochemical technology, nanotechnology and biotechnology. Our research areas include solar water splitting, batteries, bionics, biosensors and drug delivery.

(a). Hydrogen Fuel Generation From Solar Water Splitting

Hydrogen generated from water and sunlight, similar to the process that known in nature as “photosynthesis”, can provide a sustainable and clean fuel supply for human use. To make usable hydrogen fuel from solar splitting of water, efficiency is the key. We have made a breakthrough discovery that water can be relatively easily photooxidized in ionic liquids. This has opened new pathways for solar water splitting with high efficiency. This project aims to develop a photoelectrochemical system that uses sunlight to split water into hydrogen and oxygen with significantly improved efficiency. The project will involve fabrication of a number of novel water splitting devices, advanced photocatalysts and electrolytes.

(b). Nanostructured Carbon Electrodes for Efficient Energy Conversion and Storage (in collaboration with CSIRO & Zenogen Ltd)

Electrocatalysts are the key for direct conversion and storage of electrical energy obtained from intermittent renewable energy resources such as solar and wind, into chemical energy in the form of chemical bonds, e.g. hydrogen molecules and lithium in batteries. We are interested in discovering novel nanocarbon-based electrocatalysts (e.g. nanotubes, nanoribbons and graphene), because they are abundant, tuneable in structures and properties, and environmentally friendly. This project will design and fabricate novel nanocarbon-based composites for use in electrochemical energy devices such as water electrolysis, fuel cells, and Li-air batteries.
(c). Versatile Ionic Liquids Microarray and Microreactors

Ionic liquids (ILs) are attractive “green” (environmentally friendly) solvents and have a number of unique chemical and physical properties, such as negligible vapour pressure (they will never evaporate), wide electrochemical window, thermal stability, and wide range of solubilities. Microcontact printing is a simple, elegant technique which can be used to create patterns of micron-sized features on gold surfaces over relatively large areas by utilizing alkanethiolates and the strong gold-sulfur interaction. This project will combine these two technologies to fabricate gold chips printed with large arrays of IL microdroplets which will then be applied as gas sensors and “wall-less” microreactors.

(d). Controlled Drug Delivery Using Graphene-Wrapped MSN

Mesoporous silica nanoparticles (MSN) have stable mesoporous structures, large surface areas, tunable pore sizes and volumes, and their surfaces can be tailored via numerous chemical methods to introduce various functionalities. These properties make MSN ideal candidates for controlled delivery for drugs, proteins, genes as well as biocides in vitro or in vivo. Using MSN in CDD includes drug loading, open end sealing as well as drug release. Among these steps, the latter two are the most challenging and attract most of the research interest in this area. In this project, a unique “Rock-Paper-Scissors” approach will be developed to seal MSN using paper-like graphene nanosheets to wrap MSN and to release loaded drugs under stimuli such as heat, light and pH change.

(e). Bionic Eyes and Ears - Neural Prostheses (in collaboration with A/Prof Gregg Suaning, School of Biomedical Engineering, UNSW, and Cochlear Ltd)

Neural prostheses are a series of devices that can substitute a motor, sensory or cognitive modality that might have been damaged as a result of an injury or a disease. The design of next-generation high-resolution and site-specific neural prostheses requires greater numbers of microelectrode array. However for a fixed charge, reduction in electrode size increases charge density. If charge density exceeds the reversible charge injection limit, undesirable and irreversible electrochemical reactions occur which damage both stimulating electrodes and neural tissues. In this project, we’ll develop an effective way to increase the surface roughness and charge injection limit of electrodes, and maintain low impedance of the microelectrodes.