THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau
NEW ZEALAND

SCIENCE
SCHOOL OF CHEMICAL SCIENCES

School of Chemical Sciences Summer Research Scholarship Projects 2018 - 2019

(Abstracts listed alphabetically in order below)

A/Prof David Barker projects

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1. Synthesis of biologically active lignan natural products
2. Understanding the biogenesis of H2S in yeast and its role cell signalling
3. Synthesis of novel polymeric materials as surface active antimicrobial agents

Distinguished Prof Margaret Brimble Research Group projects

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1. Total Synthesis of Bioactive Natural Products from Traditional Chinese Medicine
2. Asymmetric Synthesis of Spiroketals and Polyketides
3. New Chemical Reactions: Discovery and Mechanistic Studies
4. Drug Discovery: Towards New Clinical Agents to Address Antimicrobial Resistance

Peptide Lab Projects

5. Synthesis of Pentaminomycin A, an Anti-melanogenic Agent
6. Synthesis of New Generation Lipopeptide-based Antibiotics
7. Chemical Synthesis of a Conotoxin Derived from the Venom of Cone Snails
8. The Impact of AGEs in Alzheimer's Disease
9. TLR2 Activation: Modulating the Activity of Lipopeptide Constructs as Adjuvants for Vaccines
10. Synthesis of Pseudoxylallemycins, Antimicrobial Cyclic Tetrapeptides
11. Antibody-Drug Conjugates (ADCs)
12. Divergent Peptide Cyclisation with a Minimalist Linker

Prof Penny Brothers projects

1. Lighting up sugars – fluorescent probes for mono-saccharides
2. New dyes for electron and energy transfer
3. Modular fluorescent tags: clickable BODIPYs
4. Porphyrin compounds for new functional materials
5. Cobalt complexes for catalytic hydrogen production

Dr Rebecca Deed projects

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1. Wine chemical features linked to minerality in wines and the potential role of yeast

Professor Christian Hartinger projects

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1. Bioorganometallic Anticancer Chemotherapeutics: Preparation of Metal Complexes with Bioactive Ligands
2. Design of Multimodal Organometallic Anticancer Agents
3. Design and Applications of Organometallic Complexes for Catalysis
4. Bioanalytical Mode-of-Action Studies of Metal-based Anticancer Agents
5. Supramolecular structures and their use for targeted delivery of anticancer agents

Professor Paul Kilmartin projects

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1. Characterisation of beverage antioxidants using cyclic voltammetry
2. Antioxidant packaging produced using biodegradable polymers

Dr Erin Leitao projects

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1. Towards new bioerodible materials
2. Understanding the mechanism of copper-catalysed cross-coupling with main-group substrates
3. Catalytic routes to robust polytetrels

Dr Ivanhoe Leung projects

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1. Production and characterisation of putative mycobacterial Fe(II) and 2-oxoglutarate-dependent dioxygenases
2. Recombinant protein expression and purification
3. Mechanistic and mutagenesis studies of grape (*Vitis vinifera*) polyphenol oxidase

A/Prof Duncan McGillivray projects

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1. Development of a bacterial cell membrane analogue using the Langmuir trough
2. Exploring the molecular interaction of nanoplastics and proteins
3. Atmospheric pressure plasma reactions for surface functionalization

A/Prof Gordon Miskelly projects

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1. Chemical changes in fingermarks

A/Prof Siew-Young Quek projects

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1. The effect of drying methods on the physicochemical properties of microcapsules containing fish oil and carotenoids

Dr Jóhannes Reynisson projects

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1. Water and lipophilic solubility of thienopyridines anticancer compounds as calculated using density functional theory (DFT)
2. The physicochemical properties of genotoxic compounds as compared to known drugs
3. Molecular modelling of Heat shock protein 90 (HSP90) inhibitors to the binding pocket of the enzyme - an evaluation study.

Dr Viji Sarojini projects

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1. New Enzymes for Water Treatment
2. Anti-Biofilm Peptides for Water Disinfection
3. Antifreeze Peptides for Preserving Texture in Frozen Foods
4. Lipopeptides with Broad Spectrum Antimicrobial and Antibiofilm Activities
5. Cell Penetrating Peptide Nanoparticles for Drug Delivery
6. Antimicrobial Peptides against Food Spoiling Psychrophiles
7. *De novo* Designed Models of Protein -sheets

8. Synthesis of Antimicrobial Cyclic Tetrapeptides

A/Prof Jonathan Sperry projects

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1. New Chemical Technologies for the Depolymerisation of Lignin
2. Chemical Synthesis using Biomass-Derived Building Blocks
3. Novel Synthetic Methods for Indole Construction
4. Mechanochemical synthesis
5. Natural Indole-Inspired Therapeutics for Multidrug-Resistant Infections and Psychiatric Disease

Prof Jadranka Travas-Sejdic projects

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1. UV-crosslinkable, Highly Elastomeric Conducting Polymers

Dr Geoff Willmott projects

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1. Surfaces for Dynamic Microfluidics

Prof L. James Wright projects

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1. Metallabenzenes as building blocks for new materials
2. Water purification by catalytic oxidation of pollutants
3. CO-Releasing Molecules with Targeted Pharmacological Activity

A/Prof David Barker projects

1. Synthesis of biologically active lignan natural products

A/Prof David Barker
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Lignans are a class of compound which has become the a target of particular interest to researchers, owing to their numerous biological activities including anti-cancer and cytotoxic properties and have also shown an array of pharmacological activities, including antifungal, antibacterial, antioxidant and anti-proliferative properties. In this project we will explore our recently developed methods to prepare a range of classes of lignan natural products using a common, easily made intermediate. This compound can be converted to both THF lignans and also aryl-tetralin lignans, both classes have highly bioactive members including clinically used drug. The student undertaking this project will be involved in organic synthesis, purification and compound characterisation (NMR, MS, IR, etc). They should have a reasonable knowledge of synthetic chemistry.

2. Understanding the biogenesis of H2S in yeast and its role cell signalling

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Dr. Bruno Fedrizzi
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There is growing recognition that H2S is a “gasotransmitter’’ that plays critical roles in cellular signalling and hormonal regulation. In humans, H2S has come under intense recent scrutiny because of its importance in cardiovascular diseases, cellular energetics and apoptosis. Since gaseous transmitters diffuse rapidly and with fine temporal control, understanding their modes and sites of synthesis is critical to understanding their biology. Several enzymes produce H2S, but their roles and relative importance in H2S signalling are not yet clear. In this project students will work on the synthesis of novel H2S donors. These molecules are synthetic complexes that break down under cellular conditions to product H2S and are required to study the effect of H2S in the inter-species signaling. The student undertaking this project will be involved in organic synthesis, purification and compound characterisation (NMR, MS, IR, etc) and also complex analytical techniques such as GCMS and LCMS and they should have a reasonable knowledge of synthetic and/or analytical chemistry.

3. Synthesis of novel polymeric materials as surface active antimicrobial agents

A/Prof David Barker
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Prof Brent Copp
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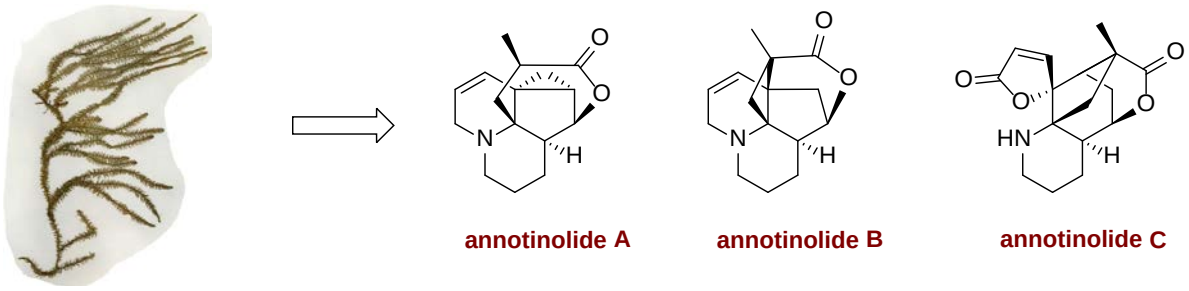
Due to the increase in bacterial resistance there is a need to develop new antibacterial agents, in particular in a hospital and medical environment. In this project we will synthesize novel antimicrobial polymers which not only kill bacteria upon contact but allow visualisation of the bacterial killing. The polymers will be designed so they can be used in a either a solution to be applied where desired or could be attached permanently to a surface to give an antibacterial surface. This project is conducted in collaboration with Prof Brent Copp. The student undertaking this project will be involved in organic synthesis, purification and compound characterisation (NMR, MS, IR, etc). They should have a reasonable knowledge of synthetic chemistry.

Distinguished Professor Margaret Brimble projects

1. Total Synthesis of Bioactive Natural Products from Traditional Chinese Medicine

Supervisors: Distinguished Professor Margaret Brimble, Dr Dan Furkert
Contact: Office: 301-729A, Ph: 923 7478, Email: d.furkert@auckland.ac.nz



Lycopodium annotinum Linn.

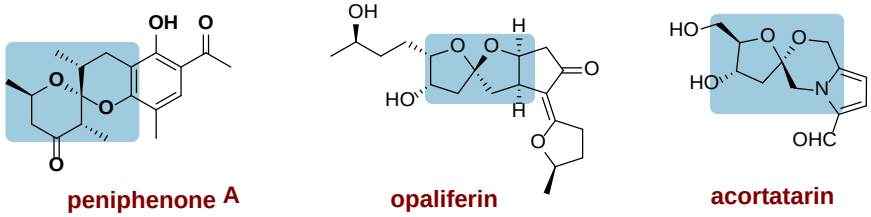
Our group has a strong interest in the total synthesis of complex and bioactive molecules, in both their asymmetric synthesis and potential applications in medicinal chemistry. **Annotinolides A-C** were isolated in 2016 from the moss *Lycopodium annotinum* Linn. (*above left*) in Shaanxi, China, and showed inhibitory activity against aggregation of αβ peptides, important in the progression of Alzheimer's disease. This is the first time lycopodium alkaloids have shown this type of biological activity, showing the relevance of traditional Chinese medicinal knowledge and making them high priority targets for synthesis. Our group is currently focusing on identification of strategies for construction of advanced intermediates containing the polycyclic scaffold of annotinolide C. Once effective ways to assemble these substructures on useful scales have been identified, with control of stereochemistry, the final goal is the asymmetric total synthesis of the natural product, annotinolide C.

New students will have a great opportunity in the exciting challenge of natural product synthesis, and gain an insight into the tactics and techniques of synthetic organic chemistry. Research areas will include developing synthetic routes towards natural product intermediates, methods to functionalise and couple these with other substructures, and investigating biological mechanisms through structure-activity relationships of derivatives against Alzheimer's disease.

2. Asymmetric Synthesis of Spiroketals and Polyketides

Supervisors: Distinguished Professor Margaret Brimble, Dr Dan Furkert
Contact: Office: 301-729A, Ph: 923 7478, Email: d.furkert@auckland.ac.nz

Synthesis of spiroketals and spiroketal-containing natural products is a longstanding interest of our group. These molecular scaffolds, consisting of two (or sometimes even three) rings joined at a quaternary carbon with two bonds to oxygen, are privileged scaffolds found in a wide range of natural products that demonstrate promising bioactivity against a variety of pathologies. Some examples of our current and previous targets are shown below (*spiroketals highlighted in blue boxes*).



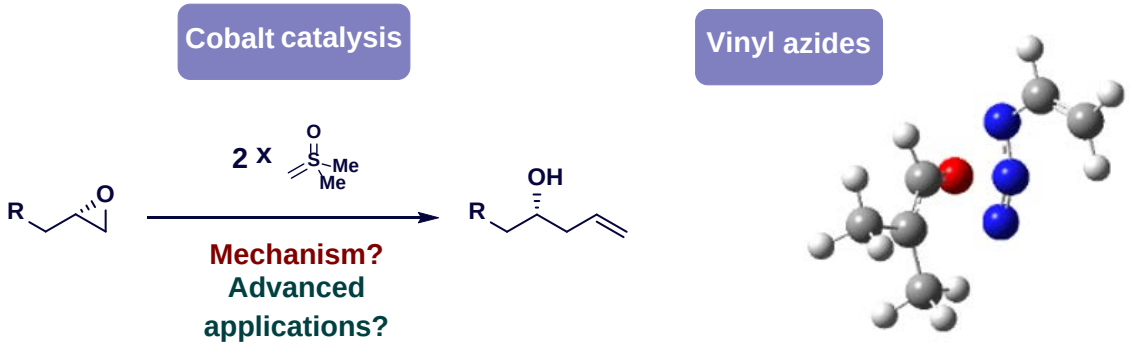
peniphenone A **opaliferin** **acortatarin**

This research area offers a great opportunity to apply your organic chemistry background to the synthesis of complex molecules, building on our group's particular expertise in spiroketal natural products. Projects will based on stereoselective multistep organic synthesis, aiming to successfully prepare structures found in recently-isolated natural products that can then be investigated for their activity in biological systems. New students will learn a wide variety of classic and state-of-the-art chemistry techniques for asymmetric synthesis including transition metal catalysis, C-H activation, pericyclic reactions, aldol and organometallic reactions.

3. New Chemical Reactions: Discovery and Mechanistic Studies

Supervisors: Distinguished Professor Margaret Brimble, Dr Dan Furkert
Contact: Office: 301-729A, Ph: 923 7478, Email: d.furkert@auckland.ac.nz

The discovery and development of new reactions offers opportunities to improve synthetic access to important materials, to readily and selectively access previously challenging structures and improve our fundamental understanding of chemical processes. New reactions recently uncovered by our group include an epoxide opening that proceeds *only* in the presence of a cobalt catalyst, to give products homologated by two carbon atoms (*below left*), and an unexpected [3+2] cycloaddition of *in situ* generated vinyl azide (*below right*), a little-used reagent with an intriguing history dating back to original work conducted in 1910.



We are currently pursuing the possibilities opened up by these new reactivity patterns. Exploration of the mechanistic basis for the observed results through both experiment, real-time data collection and computer calculation (*e.g.* transition state TS1 *above*) will enable allow optimization and wider application for rapid synthesis of previously inaccessible synthetic intermediates and functional groups. We also aim to assess the potential of rarely-reported vinyl azide itself in organic synthesis. This project offers an unusual and fast-moving chance for new students to discover new areas of chemistry, while expanding your organic synthesis and lateral thinking skills.

4. Drug Discovery: Towards New Clinical Agents to Address Antimicrobial Resistance

Supervisors: Distinguished Professor Margaret Brimble, Dr Dan Furkert
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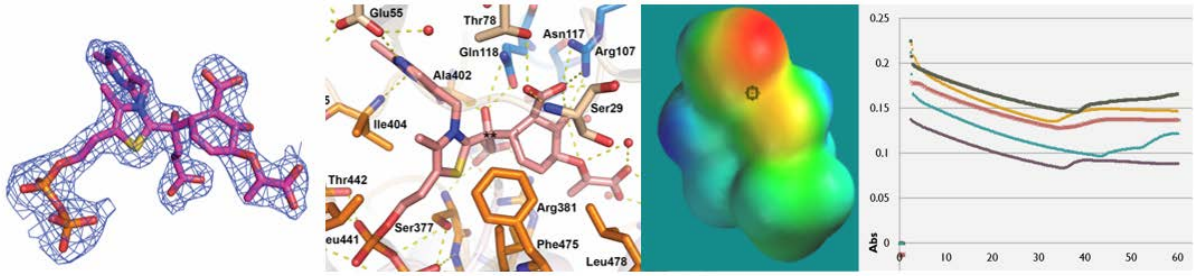
Growing incidence of antimicrobial resistance to clinically used antibiotic drugs is an immediate global health concern, as recently highlighted by the World Health Organisation (WHO), US and NZ governments. Academia and small biotech firms have an important role to play in generating novel compounds to address this resistance problem due to the low numbers of new pharma drug candidates currently entering the industrial development pipeline.



Our group is involved in several projects in medicinal chemistry, combining our skills in organic synthesis with the expertise of our collaborators in computer modelling, *X*-ray crystallogyraphy, enzyme reaction mechanisms, microbiology and pharmacology, to develop lead compounds against human pathogenic bacteria (*above*).

Our current work includes synthetic routes towards the rare aminoacid enduracididine (*3rd from left*) a component of teixobactin, an antimicrobial peptide recently isolated from soil bacteria with potent activity against MRSA and vancomycin-resistant *Enterococci* (VRE) and *C. difficile*. We are also pursuing the rational design of inhibitors of enzymes in the mitochondrial electron transport chain (ETC) in bacteria with the aim of identifying selective antibacterial agents against *M. tuberculosis* (Mtb) and other pathogen species dependent upon similar enzymes for ATP production.

5. Synthesis of Pentaminomycin A, an Anti-melanogenic Agent

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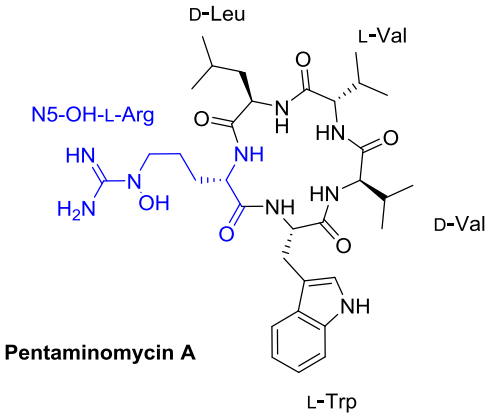

Melanogenesis is the process of melanin production that serves to protect skin against the damaging effects of ultraviolet radiation exposure. However, overproduction and accumulation of melanin in skin can lead to various dermatological disorders. Over the past years, the search for safe and effective anti-melanogenic agents has received considerable attention for medicinal and cosmetic applications. The initial rate-limiting steps of melanin biosynthesis are catalysed by tyrosinase, which is therefore an attractive target for the development of anti-melanogenic agents.

Pentaminomycin A, a naturally occurring hydroxyarginine-containing cyclic peptide derived from the cultures of *Streptomyces sp*. RK88-1441, has recently been shown to exhibit anti-melanogenesis activity by suppressing the expression of melanogenic enzymes including tyrosinase, tyrosinase-related protein-1 (TRP-1), and tyrosinase-related protein-2 (TRP-2), with no observed cytotoxicity. This research project aims to establish a comprehensive structure-activity relationship of pentaminomycin A in order to obtain analogues with improved anti-melanogenic properties. Solid-phase peptide synthesis (SPPS) techniques will be used in combination with standard organic synthesis techniques.

6. Synthesis of New Generation Lipopeptide-based Antibiotics

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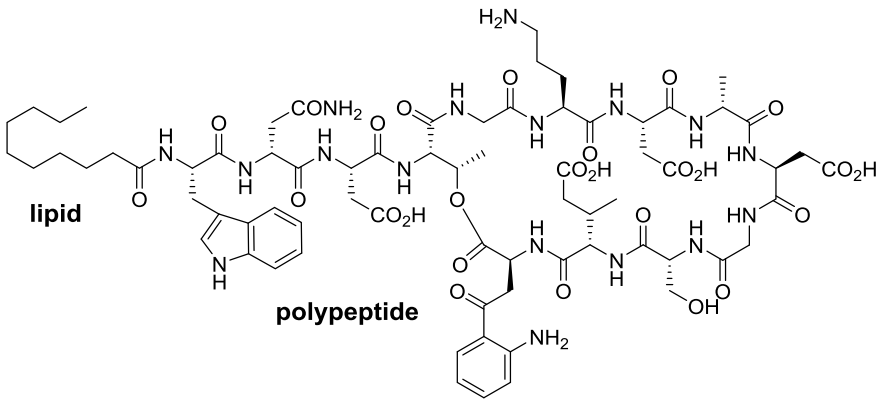

Antibiotic resistance has been recognised by the WHO as one of the greatest threats to humanity and infectious diseases rank as the second most common cause of death worldwide. This is further compounded by the observation that development of new structural classes of antibiotics has all but ceased in the past 40 years.

An emerging subset of peptide based antibiotics include cyclic peptides containing a lipid or fatty acid e.g. daptomycin. They have been shown to be clinically relevant and are used as the "last line of defence" against otherwise untreatable bacterial infections. The challenge remains, however, to efficiently produce new antibiotics based on a cyclic peptide scaffold incorporating the crucial lipid motif.

Using our newly devised method of installing a lipid onto a peptide (a thiol-ene reaction), this project aims to exploit and develop this chemistry to generate a chemical library of peptide based antibiotics, which will undergo biological testing against the most antibiotic resistant strains of bacteria. Successful candidates will be using organic synthesis techniques and modern methods of solid phase peptide synthesis.

http://brimble.chem.auckland.ac.nz/research-3/

7. Chemical Synthesis of a Conotoxin Derived from the Venom of Cone Snails

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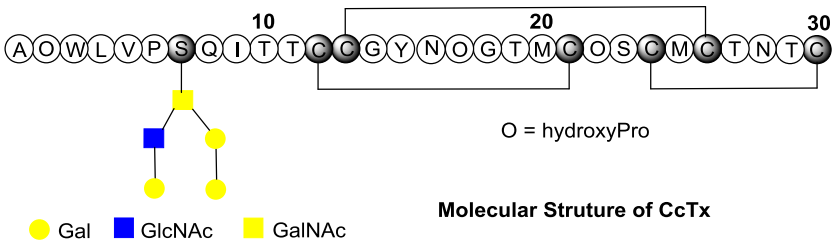

Cone snails have evolved a venomous harpoon able to paralyse prey with an arsenal of toxic compounds, such as conotoxins, which show great promise in the treatment of conditions such as pain and neuromuscular disorders. κA-conotoxins are a major component of the venom of several species of fish-hunting cone snail, but as a class of compounds have been less well studied due to their molecular complexity and post-translational modifications.

CcTx is a 30 residue glycopeptide that contains an intricate serine-linked pentasaccharide, 3 intramolecular disulphide bonds, several hydroxylated proline residues and a C-terminal alpha helix spanning residues ^{23}Ser-^{27}Thr. The unique pentasaccharide moiety, which contains several rare and unnatural L-sugars, probably plays a key role in its bioactivity.

This project will embark on a total synthesis of CcTx using glycosylation and peptide chemistry to assemble the fully functional molecule from individual amino acids. Candidates will become well versed in modern methods of glycopeptide chemistry.

http://brimble.chem.auckland.ac.nz/research-3/

8. The Impact of AGEs in Alzheimer's disease

Distinguished Prof Margaret Brimble, Dr Iman Kavianinia, A/Prof Nigel Birch
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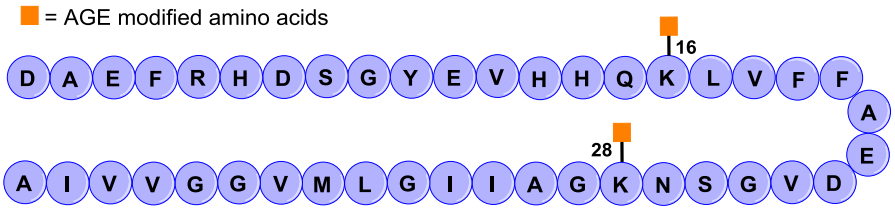

Alzheimer's disease (AD) is a complex neurodegenerative disorder that results in progressive cognitive impairment, loss of memory and changes in behaviour. In 2011, 34 million people worldwide were diagnosed with AD, and it is estimated that this figure will triple by 2050 due to an increasing ageing population. Despite vast research spanning more than a century, current treatments for AD are still limited to modest symptomatic relief and the precise causes of AD remain largely unknown.

Recently, new evidence has suggested that beta-amyloid (A-beta) peptides (a hallmark of AD) that have been irreversibly modified by sugar derivatives known as advanced glycation end products (AGEs) are more pathogenic than A-beta itself. However, the A-beta-AGE peptides used in these studies were prepared by the non-specific incubation of A-beta in glucose; this results in the formation of a complex mixture of A-beta-AGE peptides. Thus, the precise impact of individual AGEs on the biophysical properties of A-beta remains to be evaluated.

This project aims to prepare a small library of A-beta-AGE peptides, which will then undergo biological testing by Associate Professor Nigel Birch (SBS) and Professor Michael Dragunow (FMHS). Successful candidates will employ organic synthesis techniques to prepare AGE building blocks followed by incorporation of the AGE building blocks into the A-beta peptide using solid phase peptide synthesis.

http://brimble.chem.auckland.ac.nz/research-3/

9. TLR2 Activation: Modulating the Activity of Lipopeptide Constructs as Adjuvants for Vaccines

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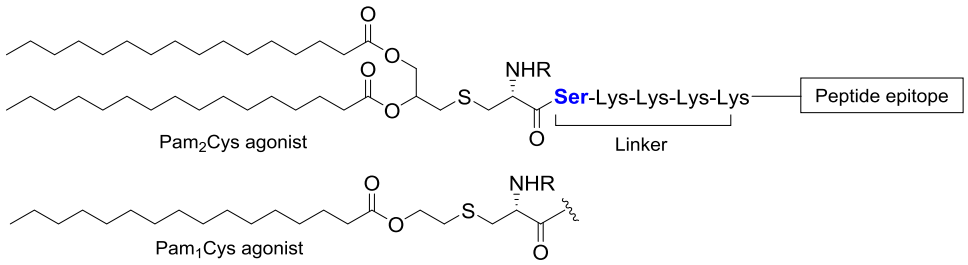

Toll-like receptor 2 (TLR2) is a highly conserved membrane pattern recognition receptor that has evolved to recognize Lipoprotein motifs expressed by foreign pathogens. On binding of an agonist motif the receptor is activated and, after internalisation of the foreign agent, then modulates the production of signalling factors that up-regulate an effective immune response to that pathogen.

It has been shown that activation of TLR2 can be attained with *S*-(2,3-bispalmitoyloxypropyl)cysteine-based (Pam2-Cys and Pam-1-Cys) lipid motifs present in the cell wall of Gram-positive bacteria. Thus, by creating a construct in which this lipid is linked to a suitable peptide epitope, the TLR2 receptor can be recruited into producing a highly targeted immune response that can then be directed against cancerous cells within a host.

The linker portion of the lipid-peptide construct epitope has conventionally been Ser-Lys-Lys-Lys-Lys but it is still not clear to what extent TLR2 activation is governed by this sequence. The project aims to investigate this question by exchanging the key Serine residue by other amino acids – both natural and unnatural – to evaluate the effect on receptor activation and through this to better modulate the immunogenic response. The relative activity of the library of analogues thus generated will be evaluated in the HEK-blue™ cell assay.

The skills to be trained to undertake this project will include organic synthesis, modern solid-phase peptide synthesis and purification.

http://brimble.chem.auckland.ac.nz/research-3/

10.Synthesis of Pseudoxylallemycins, Antimicrobial Cyclic Tetrapeptides

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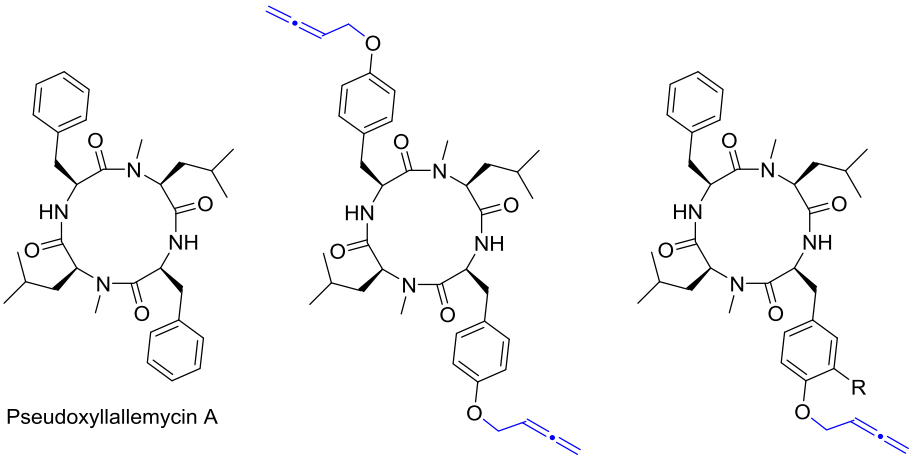

Multidrug antibiotic resistance poses an increasingly urgent threat to human health. Amongst antibiotic resistant species, Gram-negative bacteria in particular have become resistant to almost all available treatments. Whilst a number of antibiotics are currently being developed to target Gram-positive infections, only few are in progress for Gram-negative infections.

Recently, a family of four cyclic tetrapeptides, namely pseudoxylallemycins A-D, isolated from the termite-associated fungus *Pseudoxylaria* sp. X802 were found to exhibit Gram-negative antimicrobial activity (MICs of 12.5-25.0 µg/mL), cytotoxicity (HeLa cells, CC_{50} 10.3-49.5 µg/mL) and antiproliferative activity (HUVEC cells, GI_{50} 4.3-33.8 µg/mL; K-562 cells, GI_{50} 4.2-42.8 µg/mL).

Pseudoxylallemycins B-D contain unique allene moieties (highlighted in blue), which rarely occur in natural products. Using a combination of organic and peptide chemistry, this project aims to synthesise the natural products pseudoxylallemycins A-D and structurally related analogues, which will then be evaluated for antimicrobial activity in collaboration with Professor Greg Cook (University of Otago).

http://brimble.chem.auckland.ac.nz/research-3/

11. Antibody-Drug Conjugates (ADCs)

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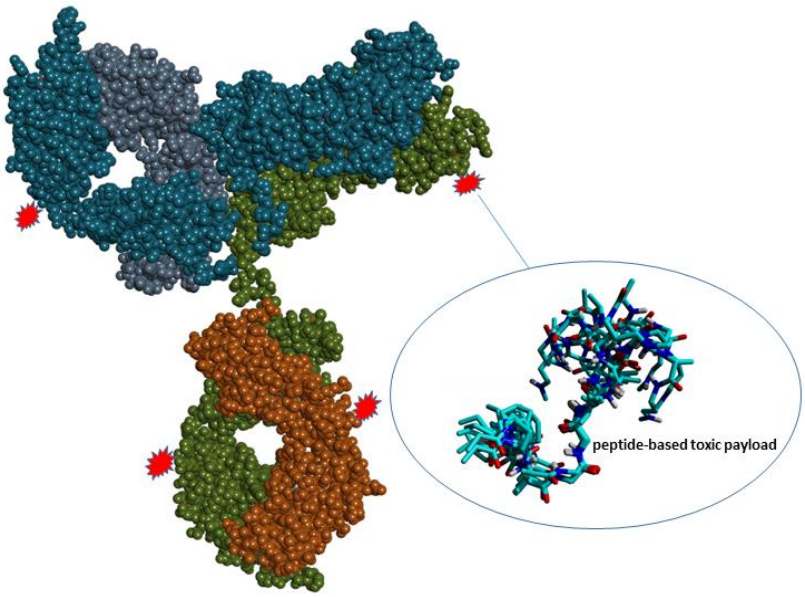

Antibody-drug conjugates (ADCs) are a clinically proven class of medicines used in the treatment of various cancers. Utilisation of the exquisite selectivity of antibody targeting to cancer epitopes coupled to delivery of highly potent small molecules is revolutionising modern oncology. Given the modular nature of the ADC design concept, the future potential of this field is truly vast, and will rely on the discovery of i) new antibody-antigen couples, ii) novel linker chemistries and iii) the discovery of highly potent cytotoxins for conjugation.

Critically, the availability of suitably potent, stable cytotoxic agents is considered rate-limiting for progress in this field. Cytotoxic peptide natural products provide a rich source of anticancer agents that can be readily appended to antibodies using amino acid-based conjugation technology.

This research project provides a unique opportunity to develop a novel class of cytotoxin with optimal properties for use in ADCs. The student undertaking this project will be involved in modern solid-phase peptide synthesis, HPLC purification and compound characterisation using related spectroscopic techniques.

12.Divergent Peptide Cyclisation with a Minimalist Linker

Distinguished Prof Margaret Brimble, Dr Iman Kavianinia, Dr Paul Harris
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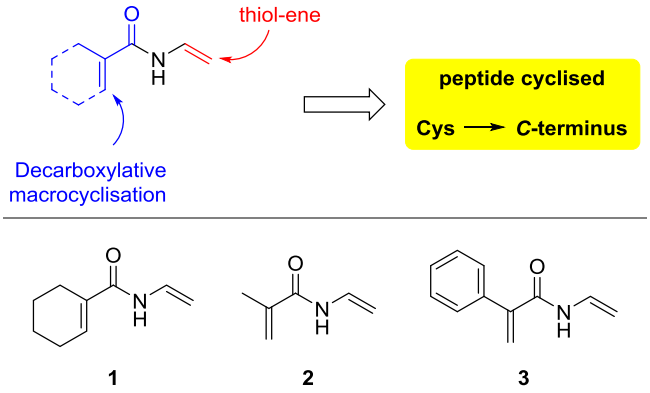

Cyclic peptides and depsipeptides are abundant in nature and possess a wide range of interesting biological activities, making them highly valuable molecules for drug development. Cyclisation of linear peptides can enhance both receptor binding, by reducing conformational freedom, and peptide stability towards physiochemical stress and enzymatic digestion.

Recently our research group reported the facile synthesis of *N*-vinylamides **1**–**3** via an unexpected and novel vinyl azide-enolate [3+2] cycloaddition. In this project we will exploit the bifunctional nature of compounds **1**–**3** for use in peptide cyclisation. The vinyl amide functionality can be used *via* a thiol-ene reaction to attach the linker to the sidechain of a cysteine residue. The α,β-unsaturated Michael acceptor can then be used to cyclise the peptide using recently reported decarboxylative macrocyclisation *via* photoredox catalysis.

The student working in this project will be trained in organic synthesis, purification, compound characterisation (NMR, MS, IR, etc) as well as solid-phase peptide synthesis. Students with interests in both organic and peptide chemistry are encouraged to apply.

Prof Penny Brothers projects

1. Lighting up sugars – fluorescent probes for mono-saccharides

Prof Penny Brothers, Dr David Ware
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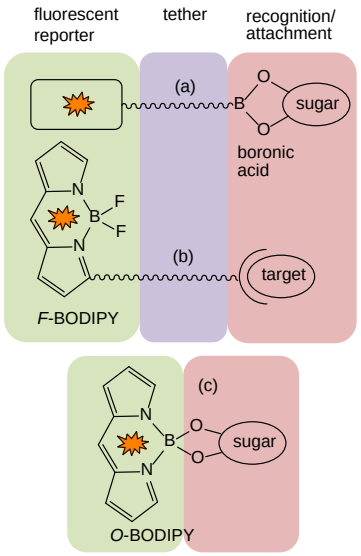

We have developed a method of attaching a fluorescent label directly to glucose. This allows for highly targeted, sensitive, fluorescent labelling of sugars which could be applied to the detection of specific sugar disease markers on cell surfaces, the labelling of saccharide capsules coating pathogenic bacteria, and the determination of polysaccharide fine structure in biology and materials science. The project will involve exploring the chemistry of the fluorescent BODIPY molecule and its chemistry with sugars, *focussing on monosaccharides*.

Activities: chemical synthesis and spectroscopy
Skills: Stage 2 or 3 organic or inorganic chemistry

2. New dyes for electron and energy transfer

Prof Penny Brothers, Dr David Ware
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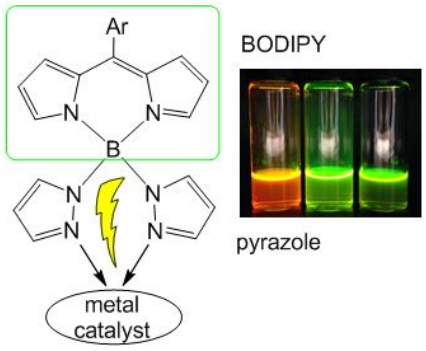

Many systems for light harvesting use a sensitiser dye which absorbs light energy and then either transfer the energy to a metal catalyst (e.g. hydrogen production from water) or transfer an electron to a semiconductor (e.g. dye sensitised solar cells). The key to an efficient process is a good connection between the sensitiser and the acceptor. We have been investigating the use of highly fluorescent BODIPY dyes as sensitisers and have developed new chemistry for introducing linking groups directly to the BODIPY boron. This project will investigate the synthesis of BODIPY pyrazole complexes and their use as sensitisers.

Activities: chemical synthesis and spectroscopy
Skills: Stage 2 or 3 organic or inorganic chemistry

3. Modular fluorescent tags: clickable BODIPYs

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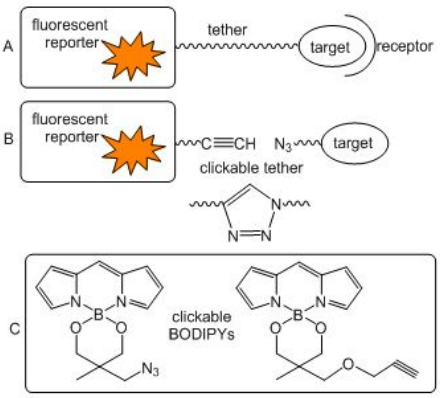

BODIPY dyes are widely used as fluorescent tags for key sites in biomolecules. Typically, a BODIPY is synthesised with a specially designed tether attached to a receptor target, which in turn recognises the biomolecule receptor (Figure A). A new BODIPY is designed for each receptor target, and they are sold for over $100 per mg. We have designed a scheme whereby "clickable" azide or alkyne functional groups are appended to BODIPY. When paired up with the complementary alkyne or azide-functionalised receptor target, this will create modular BODIPY/receptor target combinations which can be tailored to particular receptors (Figure B). We have already prepared prototype clickable BODIPYs (Figure C). This project will further develop these and investigate click reactions to suitable targets.

Activities: chemical synthesis and spectroscopy
Skills: Stage 2 or 3 organic or inorganic chemistry

4. Porphyrin compounds for new functional materials

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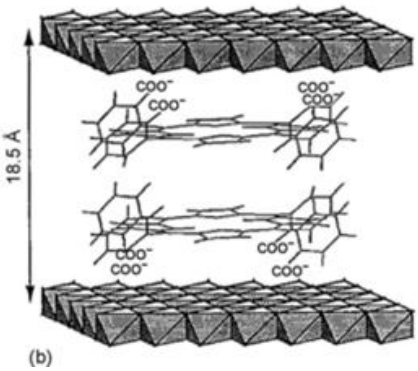

Poryphyrins are the pigment which gives heme its red colour. These planar, electron-rich molecules are good absorbers of light and can also bond to small gas molecules. In this project they are investigated as the active site in gas sensors, and for their ability to act as building blocks in new functional electronic materials. This project will explore the synthesis of a range of porphyrins designed for these applications.

Activities: chemical synthesis, surface chemistry, spectroscopy, electrochemistry
Skills: Stage 2 or 3 chemistry

5. Cobalt complexes for catalytic hydrogen production

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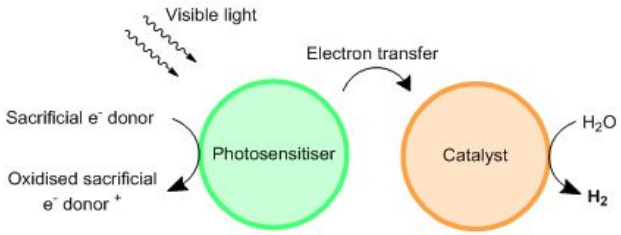

The efficient production of hydrogen from sustainable sources is an important goal in the search for new fuels. We have recently developed a cobalt-BODIPY dye complex which can be used for the photocatalytic production of hydrogen from water. This kind of technology is directed towards the use of sunlight to drive hydrogen production.

Activities: chemical synthesis, laser spectroscopy, electrochemistry
Skills: Stage 2 or 3 chemistry

Dr Rebecca Deed projects

1. Wine chemical features linked to minerality in wines and the potential role of yeast

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Minerality is a metaphorical sensory attribute which is frequently used by wine tasters when evaluating wine aroma, palate, and mouthfeel. Descriptors linked to minerality in wines range from wet stone, chalk, gunflint, freshness, and steely mineral; however, the mechanisms resulting in increased minerality in wines have not been fully elucidated. So far, a mineral component in wine has been shown independently to be linked to wine flavour neutrality, high concentrations of succinic acid (produced by yeast in low nitrogen musts), wine acids balanced by phenolic compounds, and the presence of certain volatile sulfur compounds (VSCs) including hydrogen sulfide. Since all of the mechanisms listed above are modulated by the yeast used in winemaking, this project aims to delve deeper into how yeast contribute directly and indirectly to wine minerality. The student undertaking this project will be involved in routine handling of *Saccharomyces cerevisiae* yeast, small-scale fermentation, complex analytical techniques such as GC-MS and LC-MS, and wine sensory evaluation. The student should have a reasonable knowledge of fermentation and analytical chemistry.

Prof Christian Hartinger projects

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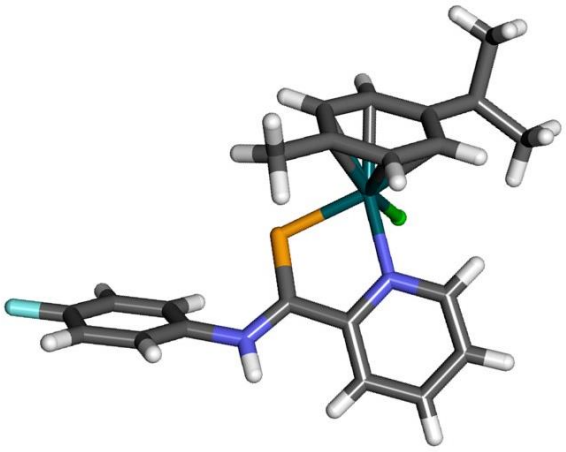
1. Bioorganometallic Anticancer Chemotherapeutics: Preparation of Metal Complexes with Bioactive Ligands

Medicinal bioinorganic chemistry is a relatively new but fervent area of research. It offers possibilities for the design and development of metal-based drugs for specific therapeutic needs that are not readily accessible to organic compounds. Currently, iron, ruthenium and osmium organometallic compounds have become the focus of interest and appear to be promising anticancer drug candidates. Some examples are at an advanced stage of preclinical development. Among the half-sandwich, piano-stool configured organometallic anticancer complexes, two most extensively studied approaches involve the coordination of ethylenediamine (en) and 1,3,5-triaza-7-phosphatricyclo[3.3.1.1] decane (pta) ligands to metal centres. *In vivo* studies on bifunctional RAPTA-C revealed excellent inhibition of metastasis growth. Monofunctional $[Ru(\eta^6\text{-arene})Ru(en)Cl]^+$ type complexes were found to have *in vitro* anticancer activity similar to that of cisplatin, one of the most widely used anticancer drugs in clinics.

Within this project a series of organometallic metal-arene compounds (metal = ruthenium and osmium) will be prepared to feature bioactive ligands. We are currently focusing on *O*,*O*-, *N*,*O*- and *S*,*N*-chelating ligands which are chosen based on their intrinsic biological properties. The compounds that we will prepare in this project, will be evaluated for potential anticancer activity by *in vitro* assays. Experiments on biologically-relevant metabolisation including hydrolysis, interactions with proteins and DNA model nucleobases will be carried out.



The student will be exposed to different levels of the drug development process and will gain extensive training in a range of synthetic procedures (both organic and inorganic synthesis) and separation/purification techniques. The prepared compounds will be characterised with state-of-the-art analytical methods (NMR, IR and UV/vis spectroscopy, electrospray ionisation mass spectrometry and X-ray diffraction analysis).

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2. Design of Multimodal Organometallic Anticancer Agents

Since the discovery of cisplatin, the design of most metallodrugs has been based on the paradigm that DNA is the target in tumour cells. Such agents however cannot explicitly discriminate between healthy and cancerous cells. More recently, this paradigm has shifted and a small body of research has been aimed at developing inhibitors of specific enzymatic targets via organometallic compounds. Late transition metals such as ruthenium and osmium are ideally suited for this purpose. Their (relatively slow) ligand exchange rates and versatile synthetic chemistry can be exploited to construct novel structural scaffolds (e.g. octahedral motifs) that are not generally accessible to purely organic small molecules, which are largely restricted to tetrahedral, planar, or linear geometries. This molecular complexity can be utilized for developing inhibitors of specific enzymatic targets by linking a metallopharmacophore to a ligand or to construct metal complexes that resemble the shape of substrates of such enzymes.

In tumours, a number of proteins are upregulated, often to satisfy the increased demand of rapidly dividing cancerous cells for nutrients. These alterations in tumours can be successfully targeted for rational design of anticancer agents with high selectivity. One of such targets are zinc-containing histone deacetylases (HDACs) which are considered important targets for anticancer chemotherapeutics but others will be considered as well. Connecting two or more pharmacophore will result in a compound that can bind to more than one target and thereby provide a means to overcome drug resistance through multi-modal activity.

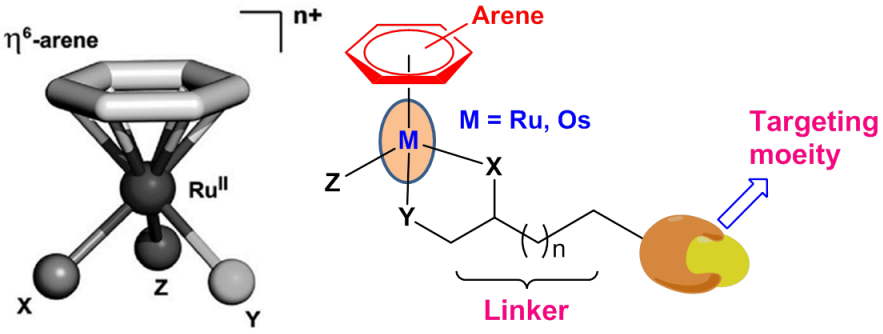

Figure. *General structures of half-sandwich, piano-stool metal(arene) complexes (left) and outline of the design strategy for multimodal organometallic anticancer agents (right).*

The student will be exposed to different levels of the drug development process and will gain extensive training in a range of synthetic procedures (both organic and inorganic synthesis) and separation/purification techniques. The prepared compounds will be characterised with state-of-the-art analytical methods (NMR, IR and UV/vis spectroscopy, electrospray ionisation mass spectrometry and X-ray diffraction analysis).

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Prof. James Wright
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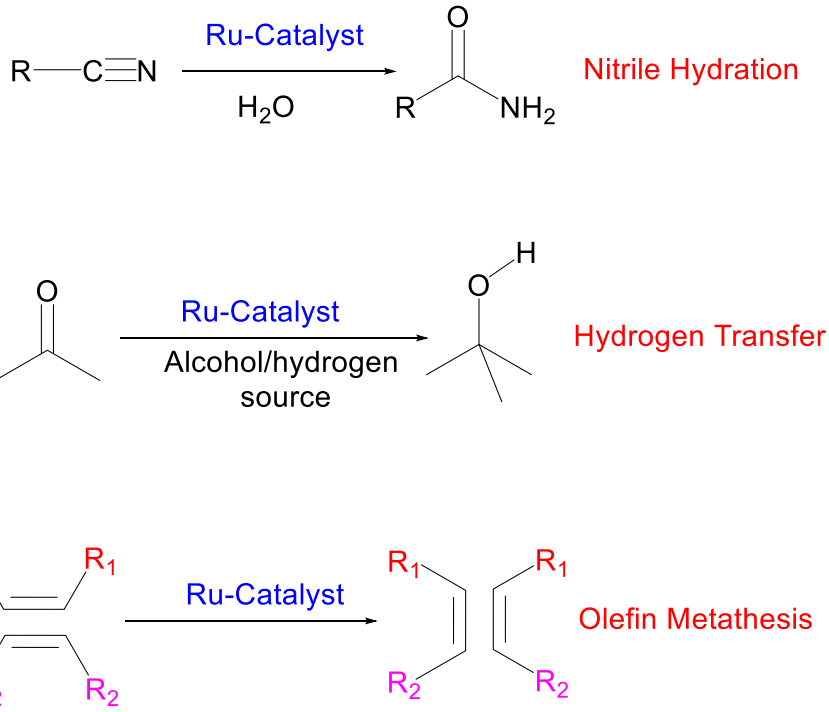
3. Design and Applications of Organometallic Complexes for Catalysis

The production of everyday products, such as pharmaceuticals, fertilisers and functional materials, is reliant on efficient chemical transformations to yield high amounts of the desired products at low cost and with minimal impact on the environment. Catalytic processes are often the only efficient option to prepare certain compounds. In recent years, we have designed and synthesised a large variety of ruthenium complexes featuring ligands with phosphorus, nitrogen, oxygen and sulfur donor atoms.

In this project we will explore the use of these and other closely related new ruthenium complexes as catalysts for a number of key reactions. These will range from the hydration of nitriles and transfer hydrogenation of ketones, to olefin metathesis. Each of these reactions has a very important role in the preparation of chemicals widely used in industry.



The student will gain extensive training in a range of synthetic procedures (both organic and inorganic synthesis) and analytical methods to characterize compounds and study their catalytic properties (TON, TOF). The methods employed will include NMR, IR and UV/vis spectroscopy, HPLC, GC and electrospray ionisation mass spectrometry.

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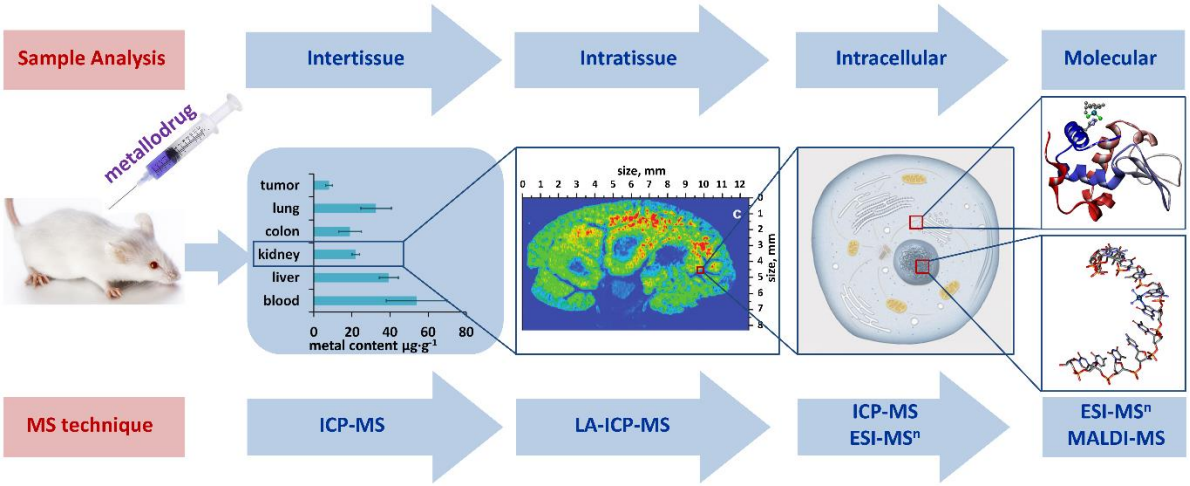
4. Bioanalytical Mode-of-Action Studies of Metal-based Anticancer Agents

DNA has been identified as the target of Pt-based anticancer agents in tumour cells. However, until anticancer drugs reach DNA, they may interact with many other biological molecules. Therefore, we extensively study the binding of metal-based anticancer agents with amino acids and with proteins. For this purpose, we use different analytical methods which include capillary electrophoresis, gel electrophoresis, X-ray diffraction, high performance liquid chromatography, NMR spectroscopy and mass spectrometry (Figure).



In this project, the student will be learn about different levels of the drug development process and will gain training in analytical methods such as NMR, X-ray diffraction, CE, HPLC and electrospray ionisation mass spectrometry. The project will involve studying the interactions of metal complexes designed as anticancer agents with biological binding partners. Studies with model proteins will be followed by experiments to elucidate the interaction with (serum) proteins. These studies will allow us identifying the influence of different structural components on the reactivity of metal complexes. This is important information to decide which compounds to put forward for further in depth preclinical studies as anticancer agents.

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5. Supramolecular structures and their use for targeted delivery of anticancer agents

The formation of flexible supramolecular architectures in nature is key to the function of many biomolecules.[1,2] Supramolecular structures arise from a defined number of building blocks that reversibly interact through weak forces (*e.g.* metal coordination, hydrogen bonding, and electrostatic interactions), rather than by covalent bonds.[1,3] Such systems have been used in catalysis, drug delivery, molecular imaging, as ion sensors, and as 'molecular containers' to sequester reactive species and environmental pollutants.[4] There is considerable interest in stimuli-responsive systems, indeed the 2016 Nobel Prize was awarded to Sauvage, Stoddart and Feringa for their work on synthetic molecular machines.[5]

In this project, we aim to develop and study well-defined heterobimetallic supramolecular structures. We will overcome the challenges encountered in creating stimuli-responsive architectures by engineering heterobimetallic supramolecular containers that we term supramolecular 'flowers', which are inspired by real flowers opening and closing under the stimulus of sunlight (Fig. 1). The design of these flowers will enable response to external stimuli, such as redox processes, light, or pH, by reversibly changing their structure in a controlled manner that is comparable to a flower blossoming (Fig. 1). We will examine the utility of the supramolecular flowers in key proof-of-principle applications, which include catalysis and the controlled release of guest molecules held within the closed flowers.

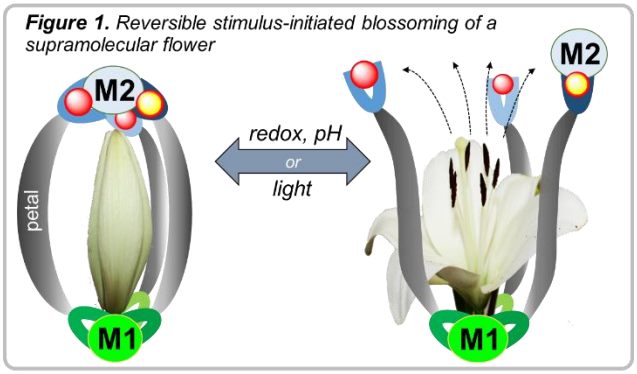

Figure 1. *Reversible stimulus-initiated blossoming of a supramolecular flower*

In this project, the student will learn about supramolecular chemistry and will be involved in the synthesis of molecular containers. The compounds will be characterised with analytical methods such as NMR, X-ray diffraction, CE, HPLC and electrospray ionisation mass spectrometry.

References

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[2] B. J. G. E. Pieters, M. B. van Eldijk, R. J. M. Nolte, J. Mecinovic *Chem. Soc. Rev.* **2016**, 45, 24-39.
[3] J.-M. Lehn *Science*. **2002**, 295, 2400-2403.
[4] B. Therrien, G. Süss-Fink, P. Govindaswamy, A. K. Renfrew, P. J. Dyson *Angew. Chem., Int. Ed. Engl.* **2008**, 120, 3833-3836.
[5] I. V. Kolesnichenko, E. V. Anslyn *Chem. Soc. Rev.* **2017**, 46, 2385-2390.

Prof Paul Kilmartin projects

1. Characterisation of beverage antioxidants using cyclic voltammetry.

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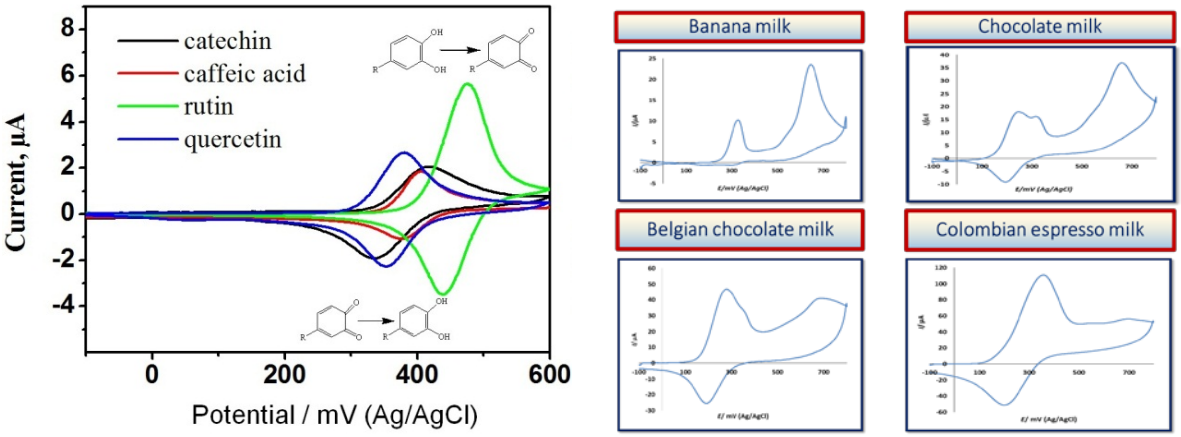
The antioxidants present in beverages can be quantified and information provided about their reducing strength using the electrochemical technique of cyclic voltammetry. This technique has been developed at the University of Auckland to profile wines, fruit juices, teas and coffees, and milk. In this project, the voltammetry procedure will be applied to the antioxidants present in a series of alcoholic beverages, including beer and fortified drinks. An examination of the most appropriate solvent for the measurement of the phenolic and other antioxidants present will be made, along with the electrode conditions needed to make a reliable quantification. Comparisons will be made with standard Food Science antioxidant assays, and a wide range of beverages of different strengths will be surveyed.



1. P.A. Kilmartin and C.F. Hsu, "Characterisation of polyphenols in green, oolong, and black teas, and in coffee, using cyclic voltammetry", *Food Chemistry* **82** (2003): 501-512.
2. O. Makhotkina and P.A. Kilmartin, "Uncovering the influence of antioxidants on polyphenol oxidation in wines using an electrochemical method: cyclic voltammetry", *Journal of Electroanalytical Chemistry* **633** (2009) 165-174.
3. M. Moteshakeri, J. Travas-Sejdic. A.R.J. Phillips and P.A. Kilmartin, "Rapid electroanalysis of uric acid and ascorbic acid using a Poly(3,4-ethylenedioxythiophene)-modified sensor with application t o milk", *Electrochimica Acta* **265** (2018) 184-193.
4. P.A Kilmartin, "Electrochemistry applied to the analysis of wine: A mini-review", *Electrochemistry Communications* **67** (2016) 39-42.

2. Antioxidant packaging produced using biodegradable polymers

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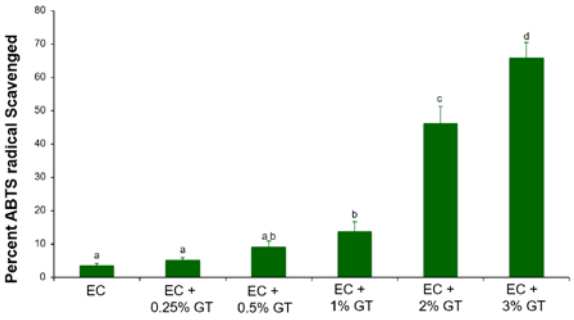
www.biocidetoolbox.com

A major research stream within the MBIE funded Biocide Toolbox programme is to produce and evaluate polymer blends. These consist of extracts from agricultural waste streams, specifically, grape tannins from Marlborough grape marc and from hop waste, inserted into various polymer materials. These are designed to develop active packaging solutions with New Zealand companies, for applications where antioxidant and biocidal properties are required to extend product shelf-life. In this project the target plastic will be biodegradable polylactic acid (PLA), with the inclusion of active natural tannin and/or essential oil containing additives. The mechanical performance of the films will be checked, and their application for active packaging evaluated through a range of antioxidant test procedures combined with leaching studies.



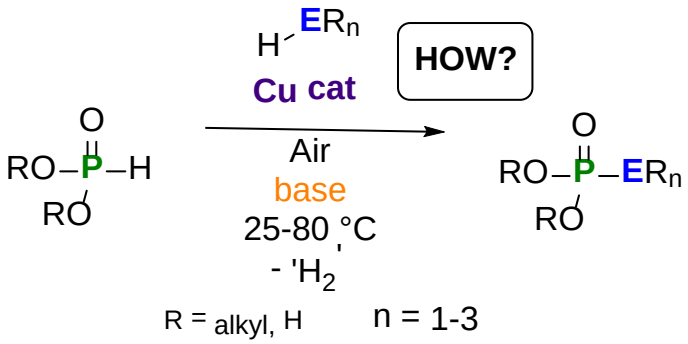
Grape tannins (GT) display high antioxidant activity in the ethyl cellulose (EC) blend

1. A.V. Nand, S. Swift, B. Uy and P.A. Kilmartin, "Eva luation of antioxidant and antimicrobial properties of biocompatible low density polyethylene/ polyaniline blends", *Journal of Food Engineering* **116** (2013) 422-429
2. K.J. Olejar, S. Ray, A. Ricci and P.A. Kilmartin, "Superior antioxidant polymer films created through the incorporation of grape tannins in ethyl cellulose", *Cellulose* **21** (2014) 4545-4556.
3. A. Ricci, K.J. Olejar, G.P. Parpinello, A.U. Mattioli, N. Teslic, P.A Kilmartin and A. Versari, "Antioxidant activity of commercial food grade tannins exemplified in a wine model", *Food Additives and Contaminants* **33** (2016) 1761-1774.
4. K.J. Olejar, C. Vandermeer, and P.A. Kilmartin, "Grape tannins: Structure, antioxidant and antimicrobial activity", *Tannins. Biochemistry, Food Sources and Nutritional Properties* (2016) C.A. Combs (Ed.), Nova Pub. 59-83.

Dr Erin Leitao projects

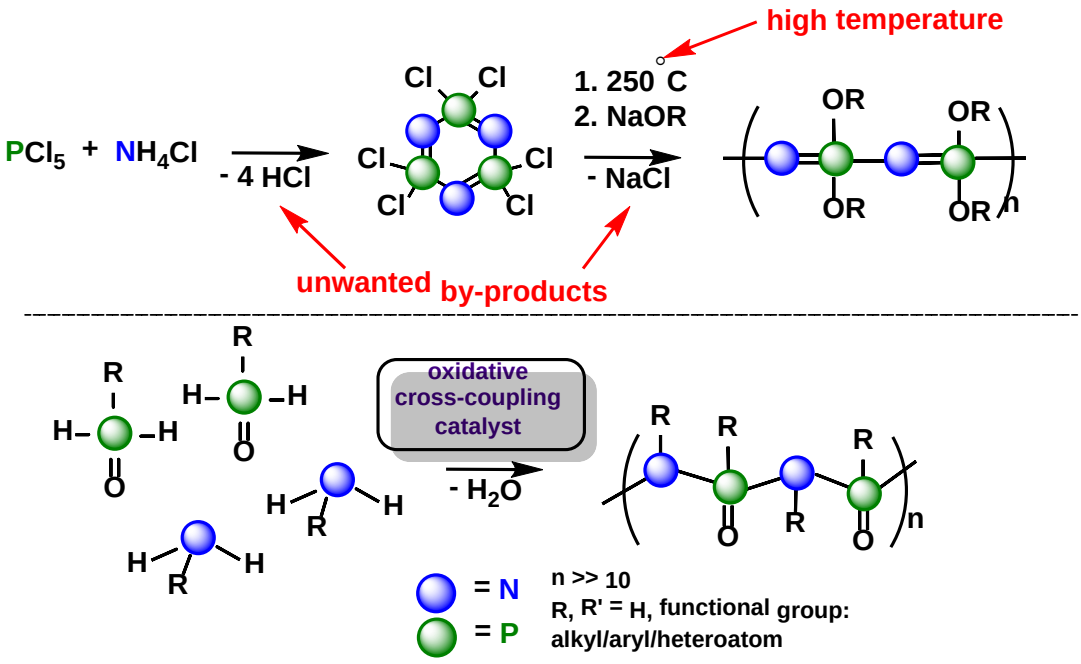
1. Understanding the mechanism of copper-catalysed cross-coupling with main-group substrates

Compounds containing P-E bonds (E = N, S, O, P) expand a wide range of applications such as flame retardants, pesticides, coenzymes, as well as several bioactive molecules. Since the recent seminal reports of copper-catalyzed oxidative cross-coupling to furnish hypophosphates (P-P), pyrophosphates (P-O-P) and phosphoramidates (P-N) from H-phosphonates ($(RO)_2P(O)H$), there has been some expansion in the reaction scope using this methodology (including P-S bond formation), however, the mechanism(s) of the catalysis remain elusive. The seemingly simple and readily available catalysts (CuX_2 or CuX, *e.g.* X= halide, OAc, OMe) and substrates used in the majority of the transformations make this reaction attractive to study mechanistically (see Figure). Not to mention the elimination of byproducts such as H_2O (observed in some cases) and high selectivity in the P-N bond forming reaction (very little P-P, P-O-P products observed under the reaction conditions). Preliminary data suggests a homogeneous catalyst is in operation and forms more readily from the Cu(II) salts. Techniques such as: stoichiometric reactions, control reactions (*e.g.* absence of Cu catalyst, absence of a reagent, changing the order of addition), solvent and temperature studies, attempted synthesis of postulated intermediates and use of model complexes/analogues, will reveal pertinent details concerning the rate-determining step, potential transition states, and intermediates. This project will involve specially designed experiments to gain insight into the mechanism, along with analysis and characterization using NMR spectroscopy and GC-MS.



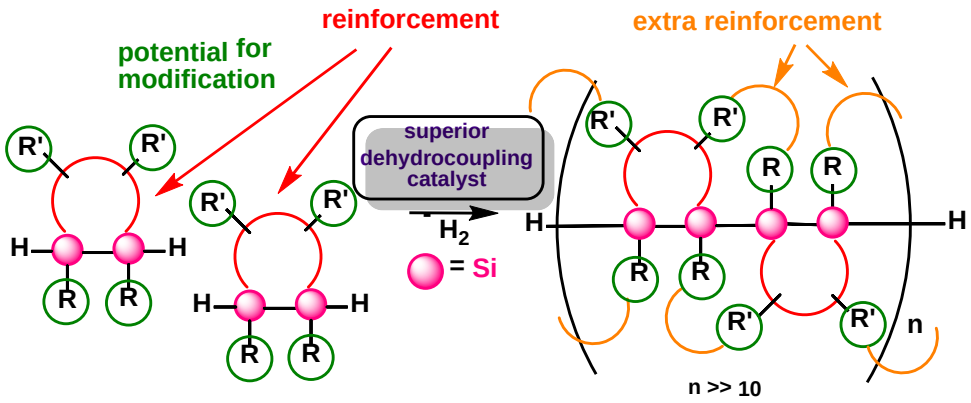
2. Towards new bioerodible materials

Recent research demonstrates that polyphosphazenes are attractive bioerodible polymers postulated to be useful in the construction of synthetic bone. Polyphosphazenes are made from the ring opening polymerization of hexachlorocyclotriphosphazene $(Cl_2P{=}N)_3$ at high temperatures followed by functionalization by replacing the Cl atoms (see top scheme below; *e.g.* with RO, NRH, etc.). This synthesis suffers from the use of high temperatures, toxic reagents and production of large amounts of unwanted by-products. Copper-catalyzed oxidative cross-coupling (see bottom scheme below) has recently been shown to be an effective way to make P-N bonds from H-phosphonates $((RO)_2P(O)H)$ and amines $(R'NH_2)$. Expansion of this method, as well as other methods, in an attempt to make phosphoramidate polymers will be explored. The project will involve inorganic synthesis using various Cu(I) and Cu(II) catalysts with analysis and characterization using NMR spectroscopy and GC-MS.



3. Catalytic routes to robust polytetrels

Polymers with a carbon backbone are ubiquitous. It is hard to go a day without coming in contact with one (polyethylene: *e.g. plastic bags, bottles, toys*; polypropylene: *e.g. dollar bills; thermal clothing*; polyisobutylene: *e.g. chewing gum, tires*). Polytetrels, polymers containing a Si-Si, Ge-Ge, or Sn-Sn backbone, are in their relative infancy in terms of commercialization, but are highly sought after, as strong electronic σ-conjugation is achieved upon linear E-E (E = Si, Ge or Sn) chain formation giving rise to properties with a wide-range of potential applications (*e.g. photoconductors/initiators, explosive detecting materials, molecular recognition and information storage, semi-conductors suitable for modern energy generation*). Despite the first synthesis of polysilanes (Si-Si backbone) reported by Kipping nearly 100 years ago, and the growing interest in the utility of these materials, access to a mild and controlled synthetic method amenable to the large scale production of defect free (well-defined), strong (high molecular weight), high silicon content (extensive σ-conjugation) and tunable polysilane is non-existent. Of the current methods available to synthesize polytetrels, catalysis is the most promising. Catalytic dehydrocoupling is attractive because dihydrogen (H_2) is the only by-product and there is literature precedence for the formation of long chains of E-E atoms with primary tetrel substrates. For example, to make robust polysilane (see Figure), secondary silane substrates will need to be employed which is a significant challenge as strained Si-Si bonds are subject to disproportionation via Si-Si bond cleavage (much weaker than C-C bonds) producing low molecular weight oligomers. Furthermore, bulky substituents on the monomers can cause steric congestion at the metal-centre of catalyst as the chain grows limiting the chain length. Creating of new polymer building blocks and/or investigation of catalysts will be explored. The project will involve inorganic synthesis and analysis using NMR spectroscopy and mass spectrometry.



Dr Ivanhoe Leung projects

1. **Production and characterisation of putative mycobacterial Fe(II) and 2-oxoglutarate-dependent dioxygenases**

Dr Ivanhoe Leung, School of Chemical Sciences

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The non-haem Fe(II) and 2-oxoglutarate (2OG)-dependent dioxygenases (hereafter 2OG oxygenase) belong to a family of structurally related enzymes that are ubiquitous in plants, micro-organisms and animals. 2OG oxygenases catalyse oxidation reactions by incorporating a single oxygen atom from molecular oxygen into their substrates. This is always coupled with 2OG oxidation into succinate and carbon dioxide

In humans, 2OG oxygenases are involved in a wide range of important biological functions, from biosyntheses (e.g. collagen biosynthesis and carnitine biosynthesis) to oxygen sensing to epigenetic regulations (e.g. nucleic acid demethylation). 2OG oxygenases are also found to play important functional roles in microorganisms and plants.

Mycobacterium tuberculosis is the bacteria that causes tuberculosis, a disease that still affects about 1 in 3 people in the world. Whilst existing treatments against *M. tuberculosis* is largely effective, there is an increasing concern about multi-drug resistant *M. tuberculosis*. The identification of new drug targets is important to combat this problem.

Interestingly, giving the importance of 2OG oxygenases in animals and humans, mycobacterial 2OG oxygenases have been poorly-characterised to date. A complete biochemical and functional characterisation of mycobacterial 2OG oxygenases would enable new drug targets to be identified and hence allow new tuberculosis treatments to be developed.

You will be part of a wider team that aims to identify and characterise mycobacterial 2OG oxygenases. You will apply bioinformatics tools (e.g. BLAST) to identify potential mycobacterial 2OG oxygenases, use molecular biology techniques to produce mycobacterial 2OG oxygenases, and, if time allows, characterise the purified recombinant proteins using different biophysical techniques such as fluorescence spectroscopy.

There is no formal prerequisites to this summer scholarship, although an understanding of basic molecular biology and an enthusiasm in enzymology will be helpful. The work will be highly relevant to CHEM 350 and CHEM 390 in Stage 3. Training and supervision in molecular biology and enzymology will be given throughout the summer period. Please contact me by email if you require any more information.

References:

M. S. Islam, T. M. Leissing, R. Chowdhury, R. J. Hopkinson and C. J. Schofield, 2-Oxoglutarate-dependent oxygenases. *Annu. Rev. Biochem.*, **2018**, DOI: /10.1146/annurev-biochem-061516-044724

Research group website: http://leungresearchgroup.wordpress.fos.auckland.ac.nz/

2. Recombinant protein expression and purification

Dr Ivanhoe Leung, School of Chemical Sciences

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Our research group is interested in the applications of biophysical techniques to study proteins and enzymes that are important for (1) human health and disease, and (2) New Zealand's agricultural industry.

A key step for any biophysical studies of proteins and enzymes involves the production and purification of recombinant proteins. In this project, you will be responsible for molecular cloning, conduct protein expression trials, optimise protein purification procedure and use biophysical tools including mass spectrometry and nuclear magnetic resonance spectroscopy to characterise the recombinant protein that you made.

There is no formal prerequisites to this summer scholarship, although an understanding of basic molecular biology and an enthusiasm in enzymology will be helpful. The work will be highly relevant to CHEM 350 and CHEM 390 in Stage 3. Training and supervision in molecular biology and enzymology will be given throughout the summer period. Please contact me by email if you require any more information.

Example of recent work from my group (including contribution from summer student):

Huang, R.; Ayine-Tora, D. M.; Muhammad Rosdi, M. N.; Li, Y.; Reynisson, J.; Leung, I. K. H. Virtual screening and biophysical studies lead to HSP90 inhibitors. *Bioorg. Med. Chem. Lett.* **2017**, *27*, 277–281.

Research group website: http://leungresearchgroup.wordpress.fos.auckland.ac.nz/

3. Mechanistic and mutagenesis studies of grape (*Vitis vinifera*) polyphenol oxidase

Dr Ivanhoe Leung, School of Chemical Sciences

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Polyphenol oxidases (PPOs) are type 3 di-copper enzymes that are widely found in both prokaryotes and eukaryotes. There are two main types of PPOs, including tyrosinase and catechol oxidase. Tyrosinase catalyses the oxidation of both monophenols and *ortho*-diphenols, whilst catechol oxidase only catalyses the oxidation of *ortho*-diphenols.

A number of structural and mechanistic studies were conducted in the last decade in order to understand the substrate selectivity of tyrosinase and catechol oxidase. Two proposals have emerged: One suggests the presence of a bulky 'blocker' residue above CuA may restrict PPO's monophenolase activity, whilst the other suggests that the amino acid residues that govern the entry of the substrate(s) to the active site are more important for selectivity. To date, the differences in substrate selectivity between these two closely related enzymes are still not fully understood.

By using grape (*Vitis vinifera*) PPO as a model system, we hope to understand the structural and mechanistic basis of PPO substrate selectivity. This summer scholarship will form an integral part of this project, which will include the design and production of mutant PPO, and *in vitro* kinetic characterisation of different substrates using biophysical techniques.

There is no formal prerequisites to this summer scholarship, although an understanding of basic molecular biology and an enthusiasm in enzymology will be helpful. The work will be highly relevant to CHEM 350 and CHEM 390 in Stage 3. Training and supervision in molecular biology and enzymology will be given throughout the summer period. Please contact me by email if you require any more information.

References:

M. Goldfeder, M. Kanteev, S. Isaschar-Ovdat, N. Adir, A. Fishman, Determination of tyrosinase substrate-binding modes reveals mechanistic differences between type-3 copper proteins, *Nat. Commun.* **2014**, *5*, 4505.

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Research group website: http://leungresearchgroup.wordpress.fos.auckland.ac.nz/

A/Prof Duncan McGillivray projects

1. Development of a bacterial cell membrane analogue using the Langmuir trough

A/Prof Duncan McGillivray - d.mcgillivray@auckland.ac.nz
A/Prof Jane Allison - j.allison@auckland.ac.nz
Dr Chris Seal - c.seal@auckland.ac.nz

Lipoteichoic acid is a major constituent of the cell wall of Gram positive bacteria that is known to be bound by anti-microbial peptides such as polymyxins, a current last resort antibiotic. However, little is known about its effect on the cell membrane and its interaction with other components, such as membrane proteins.

You will help us to develop a synthetic outer membrane system to investigate these effects as well as provide quantitative experimental data to calibrate molecular dynamics simulations. This will be done using the Langmuir trough, which offers a robust method for generating a monolayer by physically compressing a suspended layer of molecules – in this case, membrane lipids.

2. Exploring the molecular interaction of nanoplastics and proteins

A/Prof Duncan McGillivray - d.mcgillivray@auckland.ac.nz
Dr Chris Seal - c.seal@auckland.ac.nz

There is no question that the quantity of waste plastic, particularly in marine environments, is a rapidly growing international concern. Photo-oxidation, biodegradation, and physical weathering of these plastics can reduce their size to below 100 nm (i.e., nanoplastics). The toxic actions of nanoplastics have been demonstrated by many researchers and it is thought that the origin of these adverse effects arises from dysfunctioning of biological molecules which results from this interaction.

Nanoplastics in living organisms encountering proteins and cell membranes (collectively biological macromolecules), modify the chemical nature of both the nanoparticles and the proteins. However, there is little literature discussing the molecular interaction between nanoplastics and biological macromolecules.

This project aims to improve understanding of this problem by using physicochemical characterisation (spectroscopy and light scattering) of a model system (polystyrene nanoparticles and a model protein and cell membrane).

3. Atmospheric pressure plasma reactions for surface functionalization

A/Prof Duncan McGillivray - d.mcgillivray@auckland.ac.nz
Dr Chris Seal - c.seal@auckland.ac.nz

Surface functionalisation using atmospheric pressure plasma (plasma enhanced chemical vapour deposition) is a process that is becoming more commonly integrated into current manufacturing processes. Unlike vacuum plasmas, the ability to generate a plasma at atmospheric pressures provides a relatively low cost, easy to use process with rapid deposition rates. The use of these

plasmas allows for a surface to be both physically and chemically modified that in turn creates desirable surface properties.

The aim of this project will be to create functional surfaces using atmospheric plasma modification and to characterise these surfaces using techniques such as Xray-photoelectron spectroscopy (XPS), scanning electron microscopy (SEM) and in-situ ellipsometry measurements.

A/Prof Gordon Miskelly projects

1. Chemical changes in fingermarks

A/Prof Gordon Miskelly – g.miskelly@auckland.ac.nz

Once fingermarks are deposited on a surface they can start to be altered. Processes that may occur include the evaporation of volatile components including water, penetration of components into the underlying substrate, and oxidation by gases such as ozone.

This project will investigate some of these chemical changes and the impact they have on fingermark enhancement.

A/Prof Siew-Young Quek projects

1. **The effect of drying methods on the physicochemical properties of microcapsules containing fish oil and carotenoids**

A/Prof Siew Young Quek

Room 302-869

Email: sy.quek@auckland.ac.nz

Microencapsulation through monodisperse droplet drying (MDSD) is able to control droplet size and size distribution, thereby generating uniform, controllable, and reproducible small droplets. The desirable particle size can highly enhance the delivery efficacy of the functional ingredients or bioactive compounds or the release kinetics during digestion. Through a comparison with two commonly used drying methods - spray drying (SD), and freeze drying (FD), the project aims to examine the differences between the physiochemical properties of this newly applied drying method (MDSD) and the other two common drying methods (SD and FD).

Fish oil (with high content of EPA and DHA) and carotenoids (β-carotene and lutein) will be firstly emulsified with whey protein isolate and OSA starch. The emulsions are then dried by mono-disperse droplet spray drying (MDSD), spray drying (SD), and freeze drying (FD) to produce high DHA/EPA oil powders containing carotenoids. The physicochemical properties of microcapsules will be determined including moisture content, density, solubility, microencapsulation efficiency, retention of bioactive compounds, glass transition temperature, and morphology. The key factors influencing powder stability will be studied.

Applicant is expected to have experience working in lab environment and is able to follow lab safety procedures well. Applicant should be interest on the topic and is committed to learn relevant research skill

Dr Jóhannes Reynisson projects

1. Water and lipophilic solubility of thienopyridines anticancer compounds as calculated using density functional theory (DFT)

Dr Jóhannes Reynisson – j.reynisson@auckland.ac.nz
A/Prof David Barker – d.barker@auckland.ac.nz

The thienopyridines is a novel class of highly potent anticancer compounds. Limited aqueous solubility is the main issue hampering their further development. In this project quantum chemical calculations will be used to derive the solubility profile of these compounds and correlated with their anticancer potency.

2. The physicochemical properties of genotoxic compounds as compared to known drugs

Dr Jóhannes Reynisson – j.reynisson@auckland.ac.nz
Dr Chris Seal – c.seal@auckland.ac.nz
A/Prof Duncan McGillivray – d.mcgillivray@auckland.ac.nz

In this project a compound collection with molecules known to be mutagenic / genotoxic, i.e. Ames and Comet positive, will be collected. The physicochemical parameters of these will be derived and compared to those of known drugs. The aim is to establish whether a unique property profile exists for DNA damaging agents as compared to clinically used drugs.

3. Molecular modelling of Heat shock protein 90 (HSP90) inhibitors to the binding pocket of the enzyme. An evaluation study

Dr Jóhannes Reynisson – j.reynisson@auckland.ac.nz

Molecular modelling is a very useful tool in drug design. In order to test the robustness of the scoring functions used in docking a host of known inhibitors of the anticancer target HSP90 will be benchmarked against their experimental counterparts.

Dr Viji Sarojini projects

1. New Enzymes for Water Treatment

School of Chemical Sciences (Centre for Green Chemical Science)

Dr Viji Sarojini – v.sarojini@auckland.ac.nz
Prof James Wright – lj.wright@auckland.ac.nz

In developing as well as in industrialized nations, a growing number of contaminants are entering the aqueous environment from human activity. Organic herbicides/pesticides for controlling weeds, insects and fungi in agriculture comprise the largest group of xenobiotic compounds deliberately introduced into the environment. These compounds, and their metabolites end up in drinking water at concentrations exceeding the 0.1µg/L threshold of pesticide residues in drinking water. This translates into an immediate need for effective, low-cost, robust water treatment methods to remediate waters without further stressing the environment or endangering human health.

This project aims to undertake the basic research to develop biodegradable peptide-based scavenger enzymes for water remediation applications. The summer student working in this project will be trained in Molecular Modelling, Solid Phase Peptide Synthesis, HPLC purification and residue scavenging techniques relevant to the project.

2. Anti-Biofilm Peptides for Water Disinfection

School of Chemical Sciences (Centre for Green Chemical Science)

Dr Viji Sarojini – v.sarojini@auckland.ac.nz
Prof James Wright – lj.wright@auckland.ac.nz

Billions of people lack access to safe drinking water and millions die annually from diseases transmitted through the consumption of unsafe water. Waterborne infectious agents causing such diseases include bacteria, fungi, protozoa and viruses. Viruses are of particular concern and account for half of the emerging pathogens in recent times. The main water disinfectant used worldwide, free chlorine, is ineffective in controlling certain waterborne pathogens, particularly *Mycobacterium avium*, ubiquitous in biofilms found in water distribution systems. Growing of biofilms within ageing water distribution systems is a significant challenge facing infrastructure providers across the world.

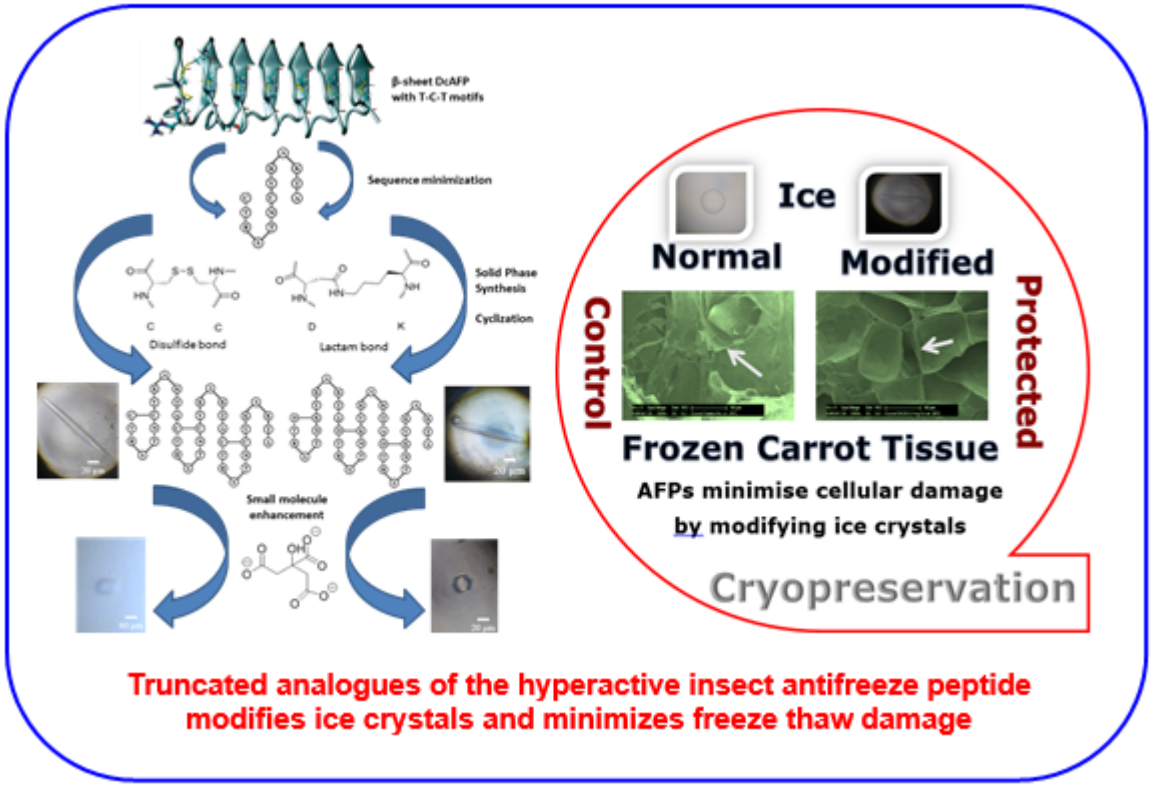
Using our previous experience in developing antimicrobial peptides for biofilm control, this project aims to develop antimicrobial peptides with potency and selectivity towards *Mycobacterium avium* biofilms found in water distribution systems. The summer student working in this project will be trained in Solid Phase Peptide Synthesis, HPLC purification and microbiology techniques relevant to the project.

3. Antifreeze Peptides for Preserving Texture in Frozen Foods

Dr Viji Sarojini – v.sarojini@auckland.ac.nz

Antifreeze proteins (AFPs) enable organisms like polar fish to survive the freezing temperatures of their natural habitat. As well as being cryoprotective, AFPs have the ability to influence the size, morphology and aggregation of ice crystals which can be used in food technology, where the growth of ice crystals in frozen foods is of primary concern. AFPs expressed in yeast have been used in the ice-cream industry for creating a smooth texture and preserving ice crystal size distribution until consumption. However, infusing large protein molecules into fruits and vegetables is not a viable option and there are no analogous commercial products in the frozen fruit and berry industries. In this project we aim to develop tailor-made analogues of natural AFPs for fundamental mechanistic studies as well as potential applications in the frozen food industry. Ice crystal morphology studies and texture analysis of frozen fruits using the synthetic peptides will be done in collaboration with the Food Science group at UoA.

This interdisciplinary project applies cutting edge peptide research to the needs of the frozen fruit industry which plays a major role in New Zealand's economy. The summer student working in this project will be trained in Solid Phase Peptide Synthesis, HPLC purification and food science techniques relevant to the project.



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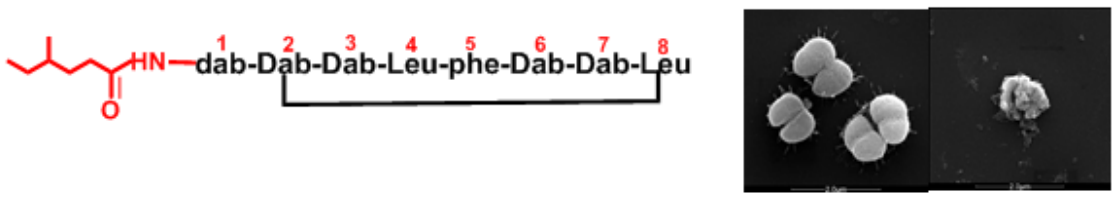
2. Kong, H.Z.C., Hamid, N. Liu, T. and **Sarojini, V.** Effect of Antifreeze Peptide Pre-treatment on Ice Crystal Size, Drip Loss, Texture, and Volatile Compounds of Frozen Carrots. *J. Agric. Food Chem*. (**2016)** 64, 4327−4335.

4. Lipopeptides with Broad Spectrum Antimicrobial and Antibiofilm Activities

Dr Viji Sarojini – v.sarojini@auckland.ac.nz

According to the World Health Organisation, the rapid emergence of multidrug resistant 'superbug' bacteria has created an urgent need to develop novel classes of antimicrobial agents. Unfortunately, over the last 30 years, no major types of antibiotics have been developed. Cationic antimicrobial peptides (CAPs) are promising therapeutics to address the challenge of bacterial resistance. The near success of MSI-78 (pexiganan acetate) and MX-226 or CPI-226 (Omiganan) in reaching the clinic, provide us with the enthusiasm to overcome the current roadblocks of CAPs (e.g. proteoclytic susceptibility) to achieve clinical implementation of AMPs. To this end, we have developed several linear and cyclic lipopeptides with nonprotein amino acids which have shown low micromolar activity against bacterial pathogens and the ability to lyse bacterial membranes.

This project will develop stereoisomers of our potent lipopeptides through chemical synthesis and investigate their potency and mechanism of action. The summer student working in this project will be trained in Synthetic Organic Chemistry, Solid Phase Peptide Synthesis, HPLC purification and spectroscopic techniques such as NMR and Circular Dichroism.



Lipopeptide sequence and cell morphology of *S. aureus* before (left) and after treatment

References

1. De Zoysa, G. H., & **Sarojini, V**. Feasibility Study Exploring the Potential of Novel Battacin Lipopeptides as Antimicrobial Coatings. *ACS Applied Materials & Interfaces*, (**2017**) *9*(2), 1373-1383. doi:10.1021/acsami.6b15859

2. De Zoysa, G.H., Cameron, A., Hegde, V. V., Raghothama, S. and **Sarojini, V.** Antimicrobial Peptides with Potential for Biofilm Eradication: Synthesis and Structure Activity Relationship Studies of Battacin Peptides. *Journal of Medicinal Chemistry* (**2015**) 58, 625−639

5. Cell Penetrating Peptide Nanoparticles for Drug Delivery

Dr Viji Sarojini – v.sarojini@auckland.ac.nz
Prof Jadranka Travas-Sejdic – j.travas-sejdic@auckland.ac.nz

Increase in the number of new therapeutics that fails to reach the clinic due to poor delivery has made novel drug delivery systems an important consideration in therapeutic development. Cell penetrating peptides (CPP) are promising tools for delivering biologically active molecules like oligonucleotides and proteins into cells. The carrier-biomolecule (cargo) interactions are dictated by the sequence of the CPP. Mechanism of cellular drug internalization by CPPs is not well understood.

This project aims to develop short synthetic peptides derived from the *trans*-activating regulatory protein (TAT) of the human immunodeficiency virus (HIV) which is the first known CPP ever. The TAT sequence will be synthesized by Solid Phase Peptide synthesis and conjugated to short oligonucleotide chains. It is expected that the peptide-oligonucleotide complex will form stable nanoparticles facilitating the entry of the drug into the cell through the plasma membrane. Morphological features of the CPP-oligonucleotide complex will be investigated by scanning electron microscopy (SEM) and light scattering measurements in collaboration with Prof Jadranka Travas-Sejdic. This project also involves collaboration with the Auckland Cancer Society Research Centre.

The summer student working in this project will be trained in Solid Phase Peptide Synthesis, HPLC purification and spectroscopic techniques such as NMR and Circular Dichroism and nanoparticle synthesis and analyses.

General scheme of peptide drug conjugate system

Reference

1. Dissanayake, S., Denny, W. A., Gamage, S., & **Sarojini, V**. Recent developments in anticancer drug delivery using cell penetrating and tumor targeting peptides. *Journal of Controlled Release*. (**2017**) 250, 62–76 doi:10.1016/j.jconrel.2017.02.006

6. Antimicrobial Peptides against Food Spoiling Psychrophiles

Dr Viji Sarojini – v.sarojini@auckland.ac.nz
A/Prof Siew-Young Quek – sy.quek@auckland.ac.nz

Psychrophilic bacteria are cold-adapted organisms, found widely over the earth's surface due to the vast number of habitats in which they can grow. Psychrophilic bacteria have also been found to grow in refrigerators, which is of great concern to the food industry. In particular, meat products have been found to be affected and spoiled by psychrophilic growth. An important psychrophile is the species *Clostridium estertheticum*, which has been found to cause blown pack meat spoilage in chilled vacuum-packed meat products. As New Zealand has a prominent meat industry, in particular of beef and lamb exports, targeting psychrophilic species such as *C. estertheticum* would be economically beneficial.

This project will explore the potential of naturally produced antimicrobial peptides of the ice fish *Chionodraco hamatus* to inhibit the growth of *Clostridium estertheticum* in meat products. Promising peptide analogues will be used in combination with food packaging technologies in collaboration with A/P Quek, Director of the Food Science Programme.

The summer student working in this project will be trained in Solid Phase Peptide Synthesis, HPLC purification, anti-bacterial and anti-biofilm assays, microscopy techniques as well as spectroscopic techniques such as NMR and Circular Dichroism.

References

1. Danilo Ercolini, Federica Russo, Antonella Nasi,Pasquale Ferranti and Francesco Villani. Mesophilic and Psychrotrophic Bacteria from Meat and Their Spoilage Potential In Vitro and in Beef. *Appl Environ Microbiol.* (**2009**) 75(7): 1990–2001.

7. *De novo* Designed Models of Protein β-sheets

Dr Viji Sarojini – v.sarojini@auckland.ac.nz
Prof Juliet Gerrard – j.gerrard@auckland.ac.nz

The remarkable biological functions exhibited by proteins depend on the ability of the flexible peptide chains to fold into well-ordered and compact structures that originate with distinct secondary structural elements like alpha-helices and beta-sheets discovered by Linus Pauling half a century ago. Thus, the *de novo* design of protein secondary structures is an important step towards understanding the biological functions of proteins in living cells. Amongst the protein secondary structural elements, beta-sheets (aggregates of beta hairpins) are particularly interesting, since they ensure not only

protein function but also mis-function as in the case of amyloid plaque formation in Alzheimer's disease.

This project aims to understand the factors that modulate the formation and stability of beta-sheets which are not well understood. Survey of the various peptidic and non-peptidic structures that promote chain reversals in proteins will be followed by the incorporation of selected structures in short synthetic peptides by Solid Phase Peptide Synthesis techniques. The ability of the peptides to fold into the desired beta-hairpin fold as well as its propensity to aggregate into higher order structures will be investigated using multi-dimensional NMR and circular dichroism (CD). The summer student working in this project will be trained in Synthetic Organic Chemistry, Solid Phase Peptide Synthesis, HPLC, NMR and CD.

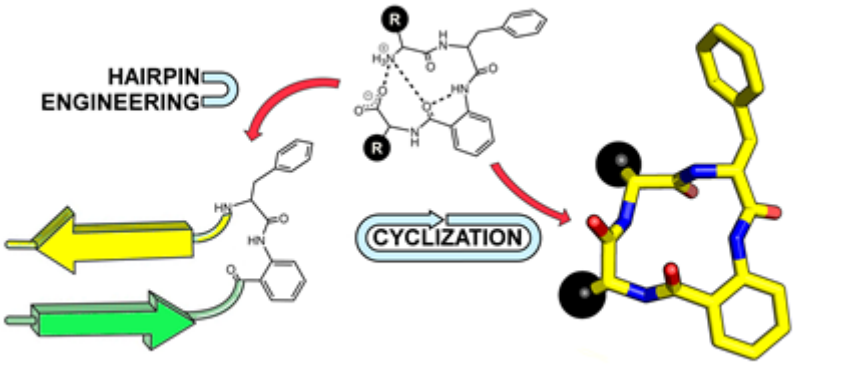
8. Synthesis of Antimicrobial Cyclic Tetrapeptides

Dr Viji Sarojini – v.sarojini@auckland.ac.nz
Dr Heru De Zoysa - heru.de-zoysa@auckland.ac.nz

Cyclic tetrapeptides (CTPs) are an important class of natural products that exhibit a wide spectrum of biological activities and are therefore attractive candidates in the development of pharmaceuticals. They generally contain turn-inducing non-protein amino acids such as alpha-amino-isobutyric acid (Aib), D amino acids and beta amino acids such as 2-aminobenzoic acid (Abz). CTPs are important models to study beta-turns. Their constrained structure provides the necessary stability against degrading proteases and also help to enhance target selectivity.

This project explores the synthetic methodology and biological activity analyses of naturally occurring and designed cyclic tetrapeptides incorporating the novel D-Phe-2-Abz turn recently reported from the group. A combination of Organic Chemistry and Fmoc-Solid Phase Peptide Synthesis will be used to achieve the synthesis of novel cyclic tetrapeptides with biological activities, particularly antimicrobial activity. Secondary structure of the synthetic CTPs will be investigated using multi-dimensional NMR and circular dichroism (CD).

The summer student working in this project will be trained in Synthetic Organic Chemistry, Solid Phase Peptide Synthesis, HPLC, NMR, CD and bioassays relevant to the project.



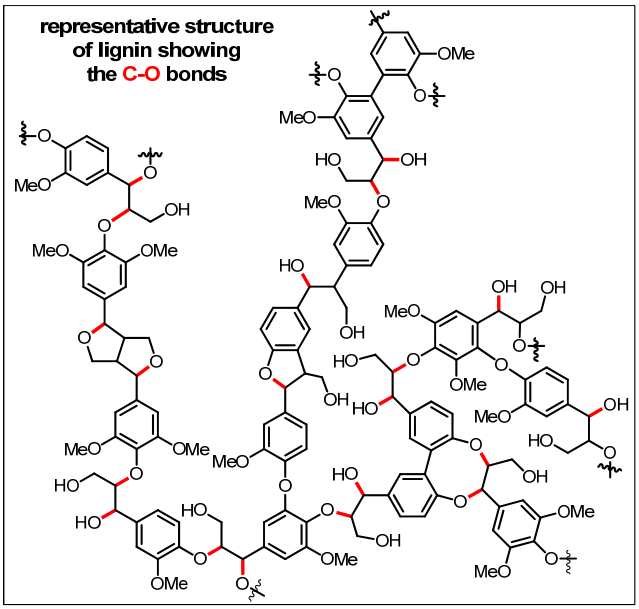
Linear and Cyclic Tetrapeptides as β-Hairpin Nucleators

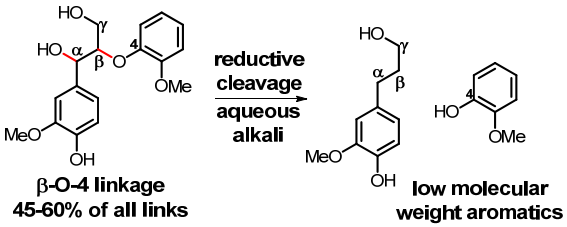
Associate Professor Jonathan Sperry

Room 727A. Ph. Extn: 88269, E-mail:j.sperry@auckland.ac.nz

1. New Chemical Technologies for the Depolymerisation of Lignin

Fossil fuels are the carbon feedstock that modern society relies upon for the production of fuels and fine chemicals. Besides the environmental impact from their extraction and processing, fossil fuels are a finite resource for which there are currently no sustainable alternatives. Biomass is the only renewable carbon feedstock that could potentially replace fossil fuels and the efficient conversion of biomass into fuels and fine chemicals on a global scale is one of the great scientific challenges of the 21st century. Lignocellulosic biomass (dry plant matter) is the most abundant renewable carbon resource on earth, with an annual growth in the region of 200 billion tonnes. The separation of lignocellulosic biomass (wood pulping) produces the cellulosic fraction and the lignin fraction. The cellulosic fraction is amenable to chemical and enzymatic degradation techniques and its conversion into useful monomers is relatively well advanced. On the other hand, the large-scale potential of lignin is mostly limited to use as a low value fuel in pulp mills. As an aromatic biopolymer, lignin is an ideal candidate to meet future demand for aromatic commodity chemicals (phenols, benzene, xylenes, BTX etc) and other marketable aromatic products. This project will investigate novel reductive methods for the depolymerisation of lignin, specifically targeting the β-O-4 linkage that comprises up to 60% of the lignin linkages.





Associate Professor Jonathan Sperry

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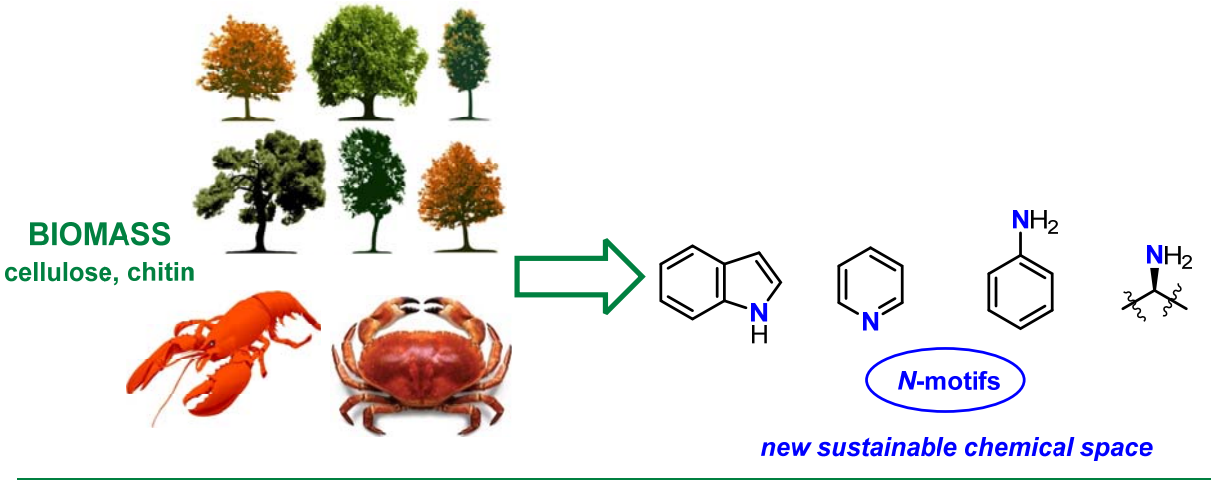
2. Chemical Synthesis using Biomass-Derived Building Blocks

The global chemistry community must reduce its reliance on fossil fuels and employ molecules derived from biorenewable sources in the production of society enhancing chemicals. This project will investigate the synthesis of fine chemicals, such as natural products and pharmaceutical intermediates, from building blocks derived from renewable biomass (cellulose and chitin).



Associate Professor Jonathan Sperry

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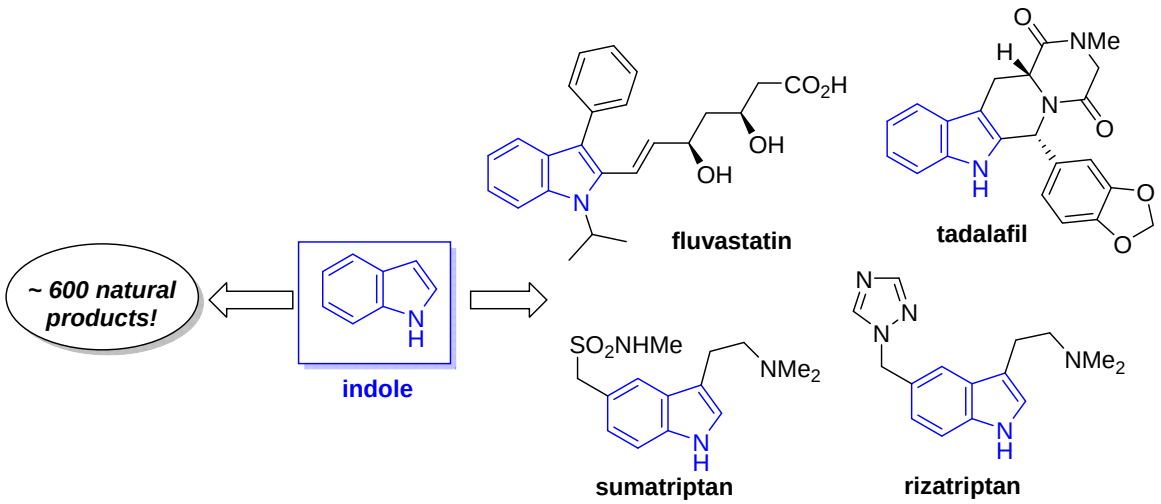
3. Novel Synthetic Methods for Indole Construction

The indole ring system represents one of the most abundant and important heterocycles in nature, with over 600 natural products possessing this ring system. Additionally, drugs containing the indole heterocycle below accounted for nearly US$8 billion in sales annually. In keeping with their importance, the development of new routes towards indoles is a central theme and ongoing challenge in contemporary organic synthesis.[1] This project aims to develop a novel indole synthesis using some intriguing transition metal chemistry recently reported by our research group.[2]



1. Inman, M.; Moody, C. J. *Chem. Sci*. **2013**, *4*, 29.
2. Wang, C.; Sperry, J. *Chem. Commun*. **2013**, *49*, 4349.

Associate Professor Jonathan Sperry

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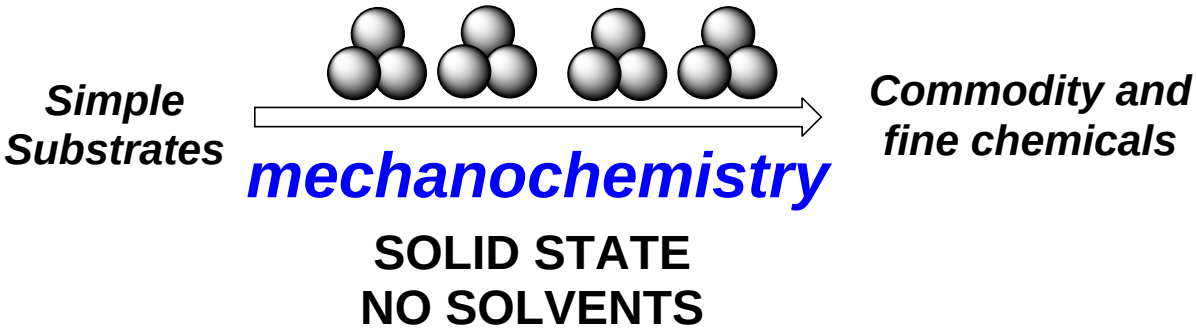
4. Mechanochemical Synthesis

Solvent waste from the chemical industry is an enormous financial and environmental burden and the greatest opportunity for positive financial and environmental impact within the chemical industry comes from waste minimizing improvements to existing, traditional chemical production processes. One potential solution to this issue is to synthesise valuable compounds in the solid state using mechanochemistry, an unexplored technique in chemical synthesis. In this project, the mechanochemical synthesis of medicinally important heterocycles and pharmaceutical motifs will be developed, with the aim to eliminate solvent from these processes.



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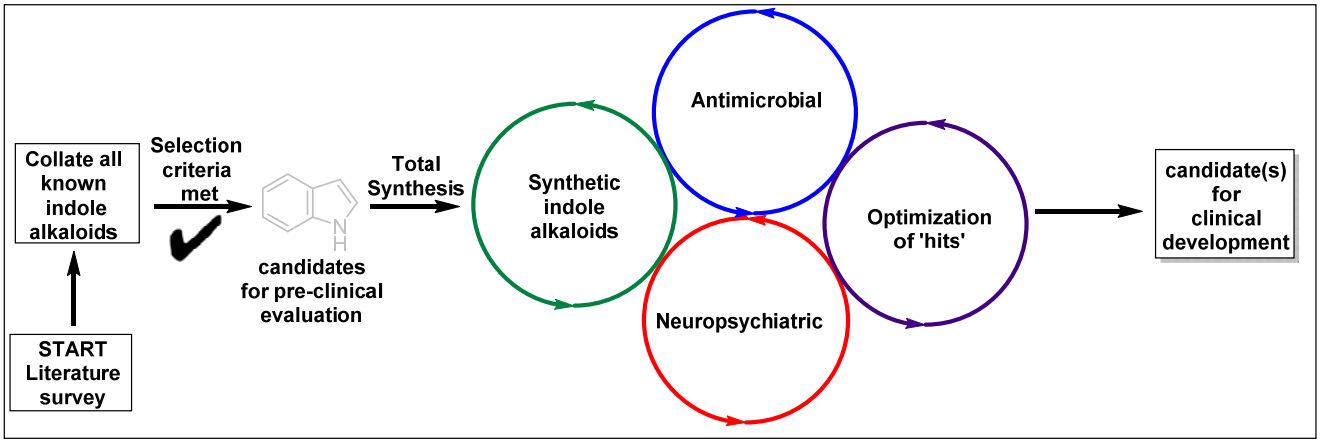
5. Natural Indole-Inspired Therapeutics for Multidrug-Resistant Infections and Psychiatric Disease

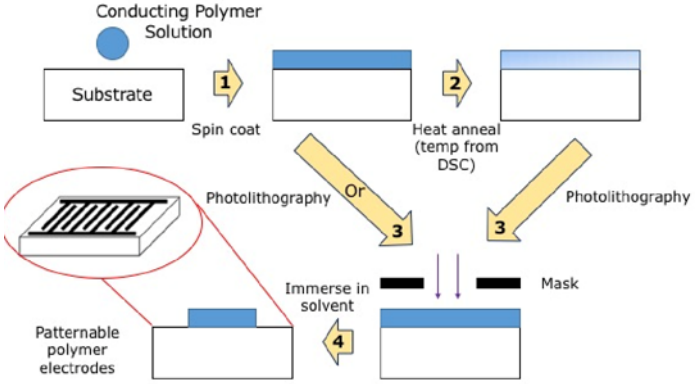
Natural products (secondary metabolites) contain a level of structural and chemical diversity that is unsurpassed by man-made libraries. Natural products are not vital for the growth or reproduction of the host organism, but serve as defence molecules that aid long-term survival. Natural products are produced by organisms after millions of years of evolution, having undergone several rounds of 'natural optimisation' to interact efficiently with biological macromolecules. As such, natural products are inherently biologically active and constitute the greatest source of drugs; from the 1940s to the end of 2014, around half of all small molecule drug approvals can be classified as a natural product, derived from a natural product or a natural product mimic. The 2015 Nobel prize in Physiology or Medicine was awarded for the discovery of the avermectins and artemisinin, natural products that have transformed the treatment of parasitic disease. Despite this, over the past ~20 years pharmaceutical companies have scaled back their natural product drug discovery programmes in favour of combinatorial synthesis, generating huge man-made libraries that can be assessed quickly by high-throughput screening. It is of no coincidence that a reduction in new drug approvals was subsequently recorded and it is widely accepted that this change in tactic has been of limited success. As a result, natural products are undergoing resurgence in what has been termed a New Golden Age of natural products drug discovery. Tens of thousands of natural products derived from an enormous amount of terrestrial and marine sources are known. This research project will focus on natural products that contain the **indole heterocycle.** This class of natural products have a rich history and many are used as pharmaceuticals, playing a huge role in human health. The exquisite biological activity of these indole alkaloids subsequently led to the indole heterocycle being deemed a 'privileged scaffold' in drug discovery, which led to many synthetic pharmaceuticals incorporating this motif. Based on this evidence, **the vast pool of indole alkaloids present in the natural world is an excellent source of new drug candidates.** The overarching aim of this research project is to advance a natural product or natural product-inspired molecule(s) into clinical development in the antimicrobial or neuropsychiatric areas.



Prof Jadranka Travas-Sejdic projects

1. UV-crosslinkable, Highly Elastomeric Conducting Polymers

Prof Jadranka Travas-Sejdic – j.travas-sejdic@auckland.ac.nz
Paul Baek – pbae002@aucklanduni.ac.nz



The rapidly growing field of stretchable bioelectronics includes examples of wearable and implantable devices and sensors for biomedical applications. Such growth demands scalable production of bioelectronics, which calls for exciting new development in low-cost, solution processable, biomimetic polymers with electrical properties. In this work, we report molecular engineering of conjugated polymers to impart biomimetic properties such as elasticity, self-healing and softness - properties that are not inherent in conjugated polymers – for aforementioned applications.

The student involved in this project will partake in characterising the novel conducting polymer materials and fabrication of stretchable electrodes using a wide range of techniques: UV-Vis, NMR, FTIR, AFM, SEM, and much more. This project will present a great opportunity to understand the process of research as well as a wide range of characterisation techniques used in research.

Dr Geoff Willmott projects

Surfaces for Dynamic Microfluidics

Supervisor: Dr Geoff Willmott (g.willmott@auckland.ac.nz)

The impact of nanotechnologies and microfluidic devices on society is becoming more and more significant. In these fields, materials behave differently from bulk materials, and devices operate in different ways to similar large-scale devices. One important reason for this is the high ratio of surface area to volume at small length scales. Often, surfaces form an interface between a solid and a moving fluid.

Experimental projects are available in which solid surfaces are chemically altered in order to control their interactions with adjacent, moving fluids at small length scales. High-speed photography is an important tool for characterizing the flows, for example in capillary uptake, or by following the paths of tracer particles. Examples of surfaces that may be functionalized include (i) spherical beads, which may be asymmetrically coated to create 'Janus' microparticles that self-assemble into interesting structures, (ii) capillary tubes, which are relevant to development of microfluidic devices, and (iii) substrates used on a quartz crystal microbalance. Suitable for chemistry students with good quantitative skills.

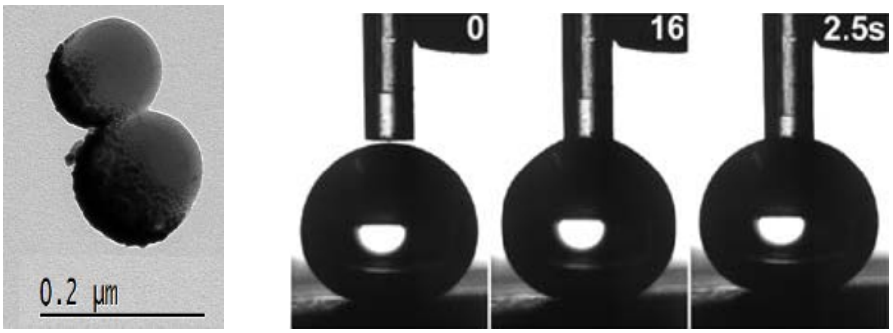


Figure: Left, Janus beads prepared by thermal evaporation of gold onto glass. Right, high speed sequence showing a water drop interacting with a PTFE capillary (time labelled in ms for the first two frames).

Prof James Wright projects

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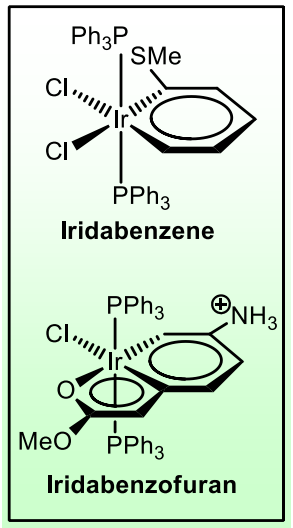
1. Metallabenzenes as building blocks for new materials



Metallabenzenes are compounds in which one of the CH groups of benzene has been formally replaced by a transition metal with its ancillary ligands. The first example of a metallabenzene, an osmabenzene, was synthesised at the University Auckland. We are interested in exploring the syntheses, reactivity and bonding of this intriguing new class of compounds and have an active research programme in this area. Summer Scholarship projects will involve the investigation of routes to functionalised metallabenzenes that will serve as precursors for the fabrication of new materials. Particular targets are conducting polymers that contain the metallabenzene unit as part of the polymer backbone and two-dimensional sheets that are comprised of fused-ring metallabenzenes that can be viewed as nascent metallagraphenes. The projects will enable experience to be gained in a broad range of areas including synthesis, spectroscopy (especially NMR, IR, ESMS), and X-ray crystallography.

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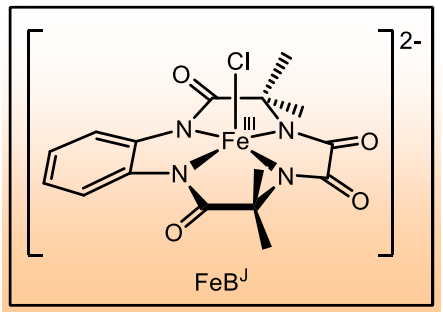
2. Water purification by catalytic oxidation of pollutants

Oxidation chemistry plays a central role in many key processes including fine chemical and commodity chemical manufacture, bleaching, waste remediation and disinfection. The use of the environmentally benign oxidant hydrogen peroxide in these processes is very attractive, but it reacts very slowly with most organic compounds under ambient conditions. Appropriate oxidation catalysts are therefore needed. In a joint Green Chemistry programme with Carnegie Mellon University in the USA, we are investigating the applications of a series of new iron complexes (TAMLs) that efficiently catalyse hydrogen peroxide oxidations. The Summer Scholarship project involves studies of these iron compounds as catalytic oxidants in a new solid state technology we have developed for the oxidative destruction of dilute organic pollutants in water. Oxidative removal occurs without contamination of the water with hydrogen peroxide, catalyst or base. The project will enable experience to be gained in a broad range of areas including synthesis, spectroscopy and analysis (especially using NMR, IR, UV-vis, ESMS and HPLC).



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3. CO-Releasing Molecules with Targeted Pharmacological Activity

It has recently been established that carbon monoxide (CO) plays a key role as a gaseous messenger in the human body. At very low concentrations, CO has been shown to elicit protection and beneficial outcomes against inflammation, apoptosis (including cancer cells), cell proliferation, and oxygen reperfusion damage. Accordingly, there is rapidly growing interest in the potential therapeutic applications of CO. Since administration of CO gas through inhalation is not feasible because of its lack of selectivity and high general toxicity, there is a strong research drive to develop water soluble transition metal (TM) compounds that can bind CO and release it inside the body in a controlled way. Current CO-releasing molecules (CORMs) of this type release CO either by hydrolytic or photolytic processes. There is a clear need for the development of CORMs that are selectively activated by certain tissue types. We are currently developing special ligands for metal carbonyl complexes that will show this tissue selectivity and only release CO in target tissues such as those found in solid tumours or in the heart after cardiac arrest. The project will involve the synthesis of selected examples of these special ligands, the formation of metal carbonyl complexes of these ligands and the study of CO release from these. The project will enable experience to be gained in a broad range of areas including synthesis, spectroscopy and analysis (especially using NMR, IR, UV-vis, ESMS and HPLC).