CBMS research booklet
2016
Research in the Department of Chemistry and Biomolecular Sciences

Macquarie University’s Department of Chemistry and Biomolecular Sciences (CBMS) is integrating chemical and biomolecular sciences to achieve a sustainable environment, understand health and disease, and advance new molecular technologies.

CBMS has experienced, motivated research-active staff with a unique research culture comprising a combination of chemistry and biomolecular sciences and this booklet describes those research interests. The booklet introduces the Department and helps identify research interests. Clearly, the outlines here are very brief and general, so please contact staff offering projects that are of interest to you.

Members of the Research Committee are always available to assist students, postdocs and visiting researchers in finding a suitable project amongst CBMS research activities.

Members of the CBMS Research Committee
Professor Nicki Packer (Research Director)
Professor Ian Paulsen
Professor Peter Karuso
A/Prof Mark Molloy

29 February 2016
# Table of contents

Dr Morten Andersen – Analytical Glycobiology and Glycoimmunology ................................................................. 4
Dr Louise Brown – Biophysics Group - Structural Biology ......................................................................................... 6
Professor Paul A. Haynes – Plant and Environmental Proteomics ............................................................................ 8
Dr Ian Jamie – Chemical Ecology, Atmospheric Chemistry, and Chemistry Education ......................................... 10
Assoc Professor Joanne Jamie – Bio-Organic and Medicinal Chemistry and Science Outreach ......................... 12
Dr Paul Jaschke – Synthetic Biology ......................................................................................................................... 14
Professor Peter Karuso – Chemical Biology ................................................................................................................ 16
Dr Fei Liu – Organic and Biological Chemistry/Chemical Biology ........................................................................ 18
Assoc Professor Bridget Mabbutt – Protein Structure ................................................................................................. 20
Dr Christopher McRae – Analytical and Environmental Chemistry ............................................................................ 22
Professor Barbara Messerle – Organometallics and Catalysis ................................................................................... 24
Assoc Professor Mark P Molloy – Biomedical Proteomics ......................................................................................... 26
Professor Helena Nevalainen – Molecular Biotechnology .......................................................................................... 28
Professor Nicki Packer – Glycomics@MQ Group ........................................................................................................ 30
Professor Ian Paulsen – Microbial Genomics ........................................................................................................... 32
Dr Andrew Piggott – Next-generation Antibiotics .................................................................................................... 34
Professor Shoba Ranganathan – Bioinformatics and Computational Biosciences ................................................. 36
Dr Anwar Sunna – Molecular Biotechnology ........................................................................................................... 38
Dr Sasha Tetu – Environmental and Applied Microbiology ...................................................................................... 40
Assoc Professor Andrew Try – Organic Synthesis of Functional New Materials .................................................... 42
Professor Robert Willows – Biochemistry: From Protein Composition to Enzyme Structure and Function .......... 44
Dr Danny Wong – Biological, Environmental and Medical Analytical Chemistry ................................................... 46
We conduct research in structural glycobiology with the aim to advance our understanding of how complex carbohydrates (glycans) affect the function of key proteins in complex biological systems including inflammation, innate immunity, cancer and pathogen-host interactions [1]. We develop and utilise state-of-the-art mass spectrometry-based technologies for the accurate molecular mapping of glycoproteins (glycomics [2] and glycoproteomics [3]) and use molecular and cellular assays to investigate the structure/function relationships of glycosylated proteins in the context of human diseases [4]. The following are examples of available MRES research projects. You will be working closely with PhD students and postdocs in our small but very dynamic research team.

Feel free to come and discuss potential projects.

GLYCOIMMUNOLOGY: EXPOSURE OF GLYCOEPITOPES DURING CELL DEATH

Glycoproteins are directed to specific locations within healthy cells and they carry important chemical information in their terminal epitopes for cell communication [5]. During cell death apoptotic and necrotic cells expose previously hidden glycoepitopes on their surfaces, which may be recognized locally by immune-related lectins and initiate an immune response. Surprisingly little biochemical knowledge has been established of the glycosylation signatures associated with cell death, the proteins carrying these immune-centric glycoepitopes and their involvement in the immune response. In this study we seek to investigate these overlooked aspects using our LC-MS/MS technologies in glycomics [2] and glycoproteomics [3] and lectin cytochemistry to map the exact molecular changes in protein glycosylation during the transition of healthy viable human cells into various death pathways. Advancing our understanding of the molecular mechanisms in cell death is instrumental to delineate many pathologies in particular immunological and inflammatory diseases.
NOVEL HUMAN GLYCOEPITOPES IN INFLAMMATION AND CANCER

We recently discovered a new class of asparagine-linked glycoproteins displaying truncated glycoepitopes in inflamed tissues [6, 7]. We identified that a subset of these, the very short chitobiose core type epitopes (i.e. GlcNAc-Asn and Fuc-GlcNAc-Asn), were abundantly present on intact and fully functional proteins derived from human immune cells [8]. This project will follow up on these exciting findings and investigate for the wider presence of such unusual glycoepitopes in a range of human immune and cancer cells using three approaches: 1) western blotting using GlcNAc-specific antibodies and lectins, 2) glycoproteomics mapping [9] and the parallel analysis of glycoproteomics data already stored in public repositories using the Byonic search engine and 3) curation of the PDB repository to search for 3D structures of chitobiose glycoproteins. It is expected that this work will provide a better understanding of the protein and cellular distribution of these truncated glycoepitopes and yield clues to their involvement in inflammation and cancer.

Selected publications
(see publicationslist.org/m.thaysen-andersen for more)

BIOPHYSICS GROUP - STRUCTURAL BIOLOGY

Many key physiological processes are controlled at a molecular level by large multi-protein complexes. These complexes are often prone to disease-producing mutations. Research in the lab focuses on ‘pushing the limits’ of structural techniques to reveal structure and movement in several large dynamic protein complexes, including:

(i) The Troponin complex – the ‘ON’ switch for muscle contraction,

(ii) The metamorphic CLIC ion channel family

Due to the large size and the dynamic nature of these two protein complexes, their structures are often difficult to determine by conventional biophysical methods. The focus of our group is to therefore use ‘reporter-probe’ based spectroscopic methods to study these challenging protein systems. We use site-directed labeling methods to attach small fluorescent or magnetic chemical labels to targeted regions of interest on the protein complex (Fig. 1). This enables the structure and dynamics of the proteins to be revealed using spectroscopic techniques including Electron Paramagnetic Resonance (EPR), Nuclear Magnetic Resonance (NMR) and Fluorescence Spectroscopy.

We are also exploring new labeling technologies – namely Nanodiamonds as biological probes. Nanodiamonds are promising labels for tracking and imaging of proteins down to the single molecule level.

THE CONTROL OF MUSCLE CONTRACTION BY THE TROPONIN COMPLEX

There are many debilitating and even fatal cardiovascular and skeletal diseases that arise from defects in muscle proteins. This project aims to understand the molecular basis for some of these disorders in the large muscle protein complex called ‘Troponin’. There are now more than 60 mutations in Troponin linked to heart disease (Fig. 1). However, understanding how these often single point mutations can result in the disease state is still experimentally challenging due to the large size and dynamic nature of the complex. In this project, we are using novel EPR and NMR methods to construct a dynamic molecular movie of Troponin function to better understand why mutations lead to disease states.

STRUCTURE OF THE METAMORPHIC CHLORIDE INTRACELLULAR ION CHANNELS - CLICS

Chloride ion channels are involved in diverse physiological processes and channel malfunction can lead to severe diseases. This project examines the structure and conformational changes of a unique chloride ion channel, called ‘CLIC’ (Chloride Intracellular Ion Channel). CLIC proteins
are highly unusual in that they can reversibly transit between a soluble and active membrane channel form (Fig 3). We use x-ray crystallography, EPR, fluorescence spectroscopy and electron microscopy methods to ‘track the view the structural gymnastics CLICs undergo as they interact with membranes to form ion channels.

Figure 3: Insertion of CLIC into the membrane bilayer. Structural studies, using site directed mutagenesis and single probe studies, will help us understand this unusual ion channel family (from ref. 5)

**NANODIAMONDS AS BIOLOGICAL PROBES**

Nanodiamonds (< 100nm) have emerged from primarily an industrial and mechanical applications base, to potentially underpinning sophisticated new technologies in quantum science and biology. In addition to their unique chemical and physical stability, they can have colour centres whose properties make them attractive bio-labels for imaging and tracking. The bright and stable photoluminescence, as well as the straightforward surface functionalisation for targeting to biological structures, has allowed us to begin to probe cellular processes down to the single-molecule scale; one of the primary goals of biomedical science and, ultimately, therapeutics. We are exploring applications ranging from using nanodiamonds as superior biological markers to, potentially, developing novel bottom-up approaches for the fabrication of hybrid quantum devices that would bridge across the bio/solid-state interface.

Projects in our lab would suit students keen to work at the interface of biology, chemistry and physics with backgrounds in any of the following: molecular biology, biochemistry, protein chemistry, physical chemistry (spectroscopy), organic chemistry, nanotechnology, synthetic biology or computational chemistry.

**Recent selected publications**


See [biophysicsmq.wordpress.com](http://biophysicsmq.wordpress.com) for more information
PLANT AND ENVIRONMENTAL PROTEOMICS

Research in our laboratory focuses on plant and environmental proteomics. We aim to understand what happens at the molecular level when an organism is exposed to changes in its external environment. We work in different systems, including plants and animals. We have two mass spectrometers in our laboratory, and we are constantly refining the analysis approach we use, in terms of both protein chemistry and bioinformatics. In recent years we have published a number of studies on the effects of temperature stress on rice cells and seedlings, and drought stress on rice plants. We are currently working on a project involving analysis of temperature stress on grape cells and drought stress on grape vines as part of a field experiment trial, in collaboration with colleagues at the University of Nevada, Reno. We also work on marine organisms, and have published studies on the effects of heavy metal contamination on Sydney rock Oysters, and are following this up with a study of how marine amphipods are affected by heavy metal contaminated sediments.

ANALYSIS OF TEMPERATURE AND DROUGHT STRESS IN PLANTS

The figure to the right is a heat map generated from label-free quantitative shotgun proteomic analysis of rice cells exposed to five different temperatures. The cluster on the right corresponds to cells subjected to 3 days at 44°C, and is clearly the most different to the others. This is a summary of the identification and quantification of more than 2500 proteins, generated from more than two million spectra of raw mass spectrometric data. We also developed our own software to enable quantification of those proteins which are differentially expressed between different environmental conditions.

Drought stress affects plants severely and is a real problem in the face of future climate change. The figure to the right shows rice plants from a previous study involving analysis of drought signalling. We were able to show using split-rooted pots that the molecular signal for drought stress is communicated from droughted roots to well-watered roots, but not the other way around.
ANALYSIS OF STRESS RESPONSE IN OYSTERS

We have performed several studies in recent years on analysis of environmental stress responses in oysters. This has included oysters exposed to heavy metal stress, modelling the impact of pollution, and oysters exposed to acidic conditions modelling the impact of future climate change upon our oceans. We are currently investigating bio markers of disease stress in oysters, focusing on two diseases of importance to the Australian oyster industry – QX disease and Winter Mortality.

ANALYSIS OF EXTERNAL STRESSES ON RAT BRAINS

We have a long-standing collaboration with researchers in the Department of Psychology at Macquarie, examining protein expression in the brains of rats exposed to environmental stresses, including addictive drugs, and high sugar and high caffeine diets. This work has generated considerable public interest because we have shown that the impact of high sugar diet on protein expression in rat brains is very similar to the impact of drugs of addiction.

ANALYSIS OF ANCIENT PROTEINS

We have recently begun a collaborative project with researchers in the Department of Ancient History at Macquarie, aiming to identify any proteins still preserved in tissue samples from Egyptian mummies. We have access to a range of skin and muscle tissue samples already, and we are planning to gain access to stomach content samples in the near future. Identifying proteins from these tissues will provide important molecular level evidence in support of archaeological information.

Selected publications


cbms.mq.edu.au/academics/phaynes.html
Chemicals that are found in trace quantities in the atmosphere can play significant roles in processes that directly and indirectly affect the quality of our life. Chemicals are used by plants and animals in growth, development, reproduction and defence. We are interested in understanding the sources, reactions and effects that these species have.

Understanding the way in which students learn and teachers teach will allow us to develop better teaching and learning methods.

The research programs described here are examples of what might be investigated. Other projects can be accommodated if they fall within the general theme of the group’s activities.

ATTRACTANT AND PHEROMONE COMPOUNDS OF ECONOMICALLY IMPORTANT INSECTS AND THEIR ENVIRONMENT (with Joanne Jamie, CBMS and Phil Taylor, Biology)

*Bactrocera* fruit flies – a genus of more than 500 species – include some of the world’s most devastating insect pests of horticulture. Air-borne pheromones are used by these insects to communicate, and in synthetic form also have potential as tools for control. Attractant compounds are used to monitor and control fruit fly populations. We are also interested in how fruit flies react to odours produced by bacteria, as some bacteria are pathogens, some are symbionts, and some are key elements of nutrition. How do *Bactrocera* fruit flies avoid harmful bacteria and locate beneficial bacteria? Natural enemies of fruit flies, such as predators and parasites, have a significant impact on the lives of fruit flies but little is known about how these flies might counter such threats. One mechanism is through detection and adaptive response to chemical cues (‘kairomones’) either emitted directly from enemies or deposited as enemies move through the environment.

Projects in these areas may focus on one or more category of compounds, and may encompass synthesis of novel and known compounds, qualitative and quantitative analysis of pheromones or odour emissions (e.g., by GC-MS), and studies of behavioural responses of *Bactrocera* fruit flies to these compounds. Activities may include travel for the collection of emissions and assays to test for biological activity (e.g., GC-coupled electroantennogram, wind tunnel, field trials).

EMISSIONS OF ORGANIC COMPOUNDS FROM PLANTS

Vegetation emits significant quantities of Volatile Organic Compounds. These emissions may be correlated with internal chemistry of the plants, and give clues on such things as the presence of useful compounds, stage of plant development and the maturation state of fruit. The relatively new technique of Solid-Phase Microextraction (SPME) offers a route to convenient *in situ* sampling. SPME combines in one-step sampling and preconcentration, prior to GC or GC-MS analysis. Our research activity aims at developing methods of *in situ* SPME-GC analysis, and to develop a database of VOC emissions from Australian native vegetation. We are also interested in the ways that plants and animals use VOCs for signalling and deception purposes.
INDOOR AND OUTDOOR AIR QUALITY: GREENHOUSE GASES, VOLATILE ORGANIC COMPOUNDS AND SECONDARY ORGANIC AEROSOLS (with CSIRO Energy Technology, North Ryde)

Identifying and quantifying the sources of volatile organic compounds (VOCs) is important as these compounds are involved in complex chemical and physical transformations that result in effects such as smog and aerosol formation, and changes in the oxidative capacity of the atmosphere. Large volumes of VOCs are emitted from plants (biogenic VOCs) and from human activities (anthropogenic VOCs). We have a range of projects concerned with identifying and quantifying VOCs and their sources and looking at the chemical composition of aerosols formed from these compounds. Of interest at the moment is the fate of carbon sequestering amines fugitively emitted to the atmosphere.

MATHS ANXIETY IN CHEMISTRY STUDENTS, CHEMICAL MISCONCEPTIONS AND CONSTRUCTIVISM

Maths anxiety is the situation where, to greater or lesser extent, panic, helplessness, paralysis, and mental disorganization. This may mean that the student stops him- or herself from starting on a task, even if capable of doing it. Students may be caught in a cycle of maths avoidance when, in the past, the student has suffered a bad experience relating to maths. It is of interest to measure the extent of maths anxiety amongst the student cohort, and to develop mechanisms for identifying these people early in their studies, so that appropriate support for them can be provided. “Constructivism” refers to the theory that the process of learning is not one of simple acceptance and remembrance of facts, but one where the learner must incorporate them into an already constructed world-view. It is necessary for teachers to understand the ways in which students incorporate knowledge into these existing knowledge frameworks, which may include preconceptions and/or misconceptions. Misconceptions in chemistry are extremely persistent and are likely to still be present in tertiary level students, right through to those studying for their Ph.D.’s. It is important that teachers are aware of the range of preconceptions and misconceptions that students bring with them, and put in place appropriate teaching methods that adequately address these issues.

Selected publications

4. S.J. White, I.M. Jamie and D.E. Angove, "Chemical characterisation of semi-volatile and aerosol compounds from the photooxidation of toluene and NOx", Atmospheric Environment, 83 (2014) 237-244

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BIO-ORGANIC AND MEDICINAL CHEMISTRY AND SCIENCE OUTREACH

Current research is focussed on studies aimed at understanding medicinally important human enzymes and developing potent inhibitors of them; collaborative partnerships with Indigenous communities for documentation, biological screening and isolation of bioactive compounds from traditional medicines; and studies on isolation and synthesis of fruit fly attractants and analysis of their effectiveness. Projects on development of educational resources for a science engagement program and/or evaluation of the effectiveness of the program, are also available.

KYNURENINE PATHWAY (Willows and Smith, CBMS; Guillemin and Lovejoy, Faculty of Medicine and Health Sciences)

The kynurenine pathway (KP) is the major metabolic route for tryptophan catabolism in mammals. It begins with the oxidative ring cleavage of the essential amino acid L-tryptophan and leads to NAD+ biosynthesis. Changes in KP activity leads to changes in control of the immune system, inflammatory state and neuronal function, making KP enzymes attractive targets for related diseases.

Indoleamine 2,3-dioxygenase 1 (IDO1) catalyses the first and rate limiting step of the KP. Under a variety of pathological conditions, IDO is over-expressed. This leads to increased levels of the neurotoxic metabolites that have been linked to neurological disorders, including AIDS dementia complex, cerebral malaria and Alzheimer’s disease. Additionally, various tumour cells are known to express IDO and IDO inhibition has been shown to be an anti-cancer immunotherapeutic strategy. Kynurenine-3-monoxygenase (KMO) catalyses the oxidation of L-kynurenine to L-3-hydroxykynurenine. KMO over-expression and the metabolites that it influences are linked to various neurodegenerative diseases including Huntington’s, Alzheimer’s and Parkinson’s diseases. Thus, IDO1 and KMO are important drug targets. Research projects on investigating IDO’s and KMO’s active site and the design, synthesis and biological testing of IDO and KMO inhibitors are available. These studies will assist in the development of potent and selective inhibitors. IDO projects can be customised to combine synthesis, biological testing, molecular modelling and mutant studies or can be focussed on a particular aspect based on interest.

FRUIT FLY ATTRACTANT AND PHEROMONE COMPOUNDS (Ian Jamie, CBMS and Phil Taylor, Biology)

Bactrocera fruit flies include some of the world’s most devastating insect pests of horticulture. Air-borne pheromones are used by these insects to communicate, and in synthetic form also have potential as tools for control. Attractant compounds are used to monitor and control fruit fly populations. We are interested in understanding the structure activity relationship (SAR) of attractants to fruit flies. We are also interested in how fruit flies react to odours produced by bacteria, as some bacteria are pathogens, some are symbionts, and some are key elements of nutrition. Natural enemies of fruit flies, such as predators and parasites, have a significant impact on the lives of fruit flies but little is known about how these flies might counter such threats. One mechanism is through detection and adaptive response to chemical cues (‘kairomones’) either emitted directly from enemies or deposited as enemies move through the environment.
Projects in these areas may focus on one or more category of compounds, and may encompass synthesis of novel and known compounds, qualitative and quantitative analysis of pheromones or odour emissions (e.g., by GC-MS), and studies of behavioural responses of Bactrocera fruit flies to these compounds. Activities may include travel for the collection of emissions and assays to test for biological activity (e.g., GC-coupled electroantennogram, wind tunnel, field trials).

ETHNOPHARMACOLOGICAL STUDY OF MEDICINAL PLANTS (Vemulpad, Ranganathan)

Research projects aimed at working with Indigenous people to isolate and identify novel bioactive compounds from traditional Indigenous medicines are available. Approximately 25% of all pharmaceutical products worldwide have originated from traditional medicinal knowledge and the study of this knowledge is of key importance in the discovery of new drugs. Plants that have been used traditionally by Indigenous people to treat conditions of a microbial origin are the main focus of our research. Through research partnerships we have established with elder custodians of traditional knowledge, we have identified a range of medicinal plants with strong antimicrobial activities. Various projects are available. This includes working with Indigenous communities and undertaking assays, chromatographic methods and spectroscopic studies to elucidate the compounds responsible for the flora’s medicinal properties. Projects may also incorporate developing bioinformatics databases to integrate, visualise and analyse both firsthand and public domain traditional medical plant data in order to preserve the traditional knowledge of Indigenous people and provide information that can be used for their cultural and educational purposes and/or development of community healthcare products.

NATIONAL INDIGENOUS SCIENCE EDUCATION PROGRAM (Ian Jamie, Vemulpad)

Using science as a tool for developing student engagement, the National Indigenous Science Education Program (NISEP) allows secondary students from low SES regions, especially Indigenous youth, to succeed in their secondary education and to make the transition to tertiary education. NISEP is a consortium of Australian universities, high schools and science and Indigenous outreach organisations. NISEP has tangible positive educational outcomes for participants and there is demand for its implementation more widely across higher education institutions. Given this demand, it is essential to have science engagement activities of the highest calibre and to identify the critical components of NISEP’s success. Projects will be available to develop effective engagement resources and activities and to build an evidence base for the effectiveness of NISEP.

Selected publications


cbms.mq.edu.au/academics/jjamer.html
SYNTHETIC BIOLOGY

Genetically engineered microbes and viruses have the potential to transform chemical production, therapeutics development, and our entire economy to be more efficient and sustainable. A barrier to realising this vision is the fact that all genetic engineering design choices are currently driven by a fear of breaking the system in unanticipated ways. For example, the totally synthetic Mycoplasma genome created by Craig Venter’s group contained few changes from the natural sequence. There is currently a disconnect between the explosive growth in our ability to write synthetic DNA of any sequence we desire, and our ability to rationally design functional genetic systems.

The Jaschke lab uses bacteriophage, viruses that infect bacteria, as model systems to learn how to design and build synthetic genomes. We aim to redesign natural genomes to be modular and easier to understand and reuse while maintaining the original functionality of their natural ancestors. Bacteriophages are ideal models because they can be thought of as self-contained genetic ‘programs’ that run within a constant cellular ‘operating system’ that, like computer software, can be debugged if not working as designed. Bacteriophages also share many lifecycle characteristics of self-replicating cellular systems, such as DNA replication and temporal regulation of gene expression.

Our group draws on a wide range of cutting edge techniques from synthetic biology such as synthetic DNA design, standardisation, and manipulation to produce novel bacteriophage genomes. We study the new viruses that we create using both traditional techniques from microbiology such as plate-based plaque assays (pictured above, right), but are also developing, in collaboration with groups in the United States, novel microfluidic approaches to scaling down and automating phage lifecycle measurements.

PROJECT 1: DEEP CHARACTERISATION OF A HIGHLY ENGINEERED BACTERIOPHAGE

The phage øX174 has been part of many firsts in science, from being the first DNA genome sequenced in 1977 (Nature 1977, 265: 687-695), to the first synthetic genome ‘booted up’ by Craig Venter in 2003 (PNAS 2003, 100: 15440-5), to the first bacteriophage genome accessioned by MoMA1. The genome of øX174 is interesting from many perspectives, but one feature that has puzzled and intrigued scientists over the years is the fact that many of its genes are overlapped with each other. This creates a genome with highly compressed information analogous to what happens when music gets compressed into an MP3 file. Several years ago the genome of øX174 was redesigned to fully decompress (separate) all the overlapped genes from each other. The resulting virus was shown to be functional but not studied any further2. The decompressed øX174 phage will be analysed using microbiological methods to determine viral lifecycle characteristics, while molecular techniques will be used to determine how RNA and protein expression is altered from the naturally occurring wild-type øX174 phage.
PROJECT 2: REFINING THE GENOME OF A HIGHLY ENGINEERED BACTERIOPHAGE USING EVOLUTION

This project will aim to improve lifecycle characteristics, such as growth rate, of the fully decompressed synthetic øX174 genome. Our approach will be to use evolution to refine the genome through iterative rounds of natural selection followed by sequencing and analysis to understand how the observed genome changes result in a faster growth phenotype. Evolution is a unique property of biological systems that sets them apart from the raw material of other engineering fields (Nature 2005, 438: 449-453). Synthetic biology has yet to fully recognize the utility of evolution in shaping engineered genomes. This project will complement recent work from our group that has shown that a øX174 genome containing hundreds of silent point mutations can be improved through an evolutionary process3.

PROJECT 3: ENGINEERING START CODON FLEXIBILITY WITHIN NATURAL AND SYNTHETIC BACTERIOPHAGE GENOMES

The vast majority of all known genes, across all known species, use the three DNA letters ATG as their first (start) codon. Recently in an experimental survey of all 64 possible codons it was found that there may be as many as 15 codons, that under certain conditions, will function as the start codon for a gene4. This project will explore the possibility of recoding all the genes of an organism to use non-canonical start codons. This work will aim to reveal the total functional start codon sequence space available for bioengineering. In this project, both the wild type øX174 genome as well as the fully decompressed øX174 genome will have the start codon for each known gene swapped out for a series of non-canonical codons shown to have activity. Genomes will be constructed and evaluated in high-throughput screens to identify codon combinations that result in viable phage. Results of this work will contribute to our understanding of how natural genomes are 'designed' by natural selection as well as lead to better understanding of additional ways to tune protein expression from artificial genetic systems.

Selected publications

jaschke-lab.science
CHEMICAL BIOLOGY

Our research interests lie in the application of small molecules to biological systems, which involves new and exciting multidisciplinary approaches incorporating molecular biology, organic synthesis, analytical chemistry, NMR spectroscopy, computational chemistry and biochemistry to solving medicinally relevant problems. We are particularly interested in marine natural products and fluorescent molecules, their biological activity, biosynthesis and most importantly, their modes of action as drugs and uses in biotechnology.

NATURAL PRODUCTS CHEMISTRY

The search for bioactive compounds from marine organisms is still a relatively new field, however, the biodiversity of the marine environment far exceeds that of its terrestrial counterpart so the oceans represent an enormous resource for new biologically active compounds (biodiversity = chemical diversity) and in a recent NCI study, marine animals were 10× more likely to contain anticancer activity than plants, animals or microorganisms. In this project, we use bioassay directed isolation to discover new compounds from marine sponges with antibiotic, herbicidal and anticancer activity. In this area, I can offer a number of projects that range from collection and isolation to the structure elucidation of new natural products from marine animals, medicinal plants and the discovery of new fluorophores. Please see me for details on isolation/structure elucidation projects.

BIOMIMETIC SYNTHESIS OF NATURAL PRODUCTS

Our group published the total synthesis of a compact and highly active natural product called “ageladine A”. This is the first member of a new group of alkaloids called pyridoimidazoles. By using the putative biosynthetic pathway (biogenesis) of the natural product, we were able to design a very short synthesis (3 steps) by recognising that Nature probably uses a Pictet-Spengler reaction to cyclise two amino-acid derivatives to form the ageladine A skeleton. The synthesis was highlighted in C&E News. We have since extended the synthesis to a one-pot reaction which makes it attractive to industry and patented this process for making analogues. This project involves exploring the chemical space around ageladine A in search of compounds with more potent anticancer activity. This search is supported by collaborators at ANU and the CNRS, Roscoff. Specifically, the project involves using the Pictet-Spengler reaction to make ageladine A and analogues of ageladine A and testing these for kinase and antiangiogenic activity. We also have projects on the biomimetic synthesis of other natural products such as the oroidin alkaloids, mopines, glossularins and others. Please come see me if you are interested in total synthesis.

ANALYTICAL CHEMISTRY

Recent discoveries in my group have resulted in the commercialisation of a fluorescent natural product from a fungus and we have discovered other new highly-fluorescent natural products from marine sponges, microbes and plants. We are also interested in other fluorescent probes for use in biotechnology such as analogues of the fluorescent (anticancer) marine natural product ageladine A and epicocconone as well as latent fluorophores such as sulforhodamine trimethyl lock and difluoromethyl derivatised fluorescein diacetate, which could be used to detect lipase activity inside live cells or in 2D gel blots. We have recently synthesised and patented an analogue of the chromophore inside the Green Fluorescent Protein (GFP) that display dual emission. That is if fluoresces two different colours depending on the local environment. Such fluorophores are very rare and sought after for ratiometric analytical assays. This is your chance to get in on some real commercially-relevant research.
FLUORESCENCE ASSAY FOR MMP ENZYMES

Matrix Metalloprotease Assays are useful analytical tools for the measurement of antiangiogenic activity and marketed by Anaspec, Invitrogen and others. These assays work by measuring the rate of hydrolysis of a coumarin-labelled peptide, producing a blue-fluorescence readout. There are a number of issues with this technique such as the requirement for expensive labelled peptides and interference from cellular autofluorescence. This project aims at developing a new analytical method to assay the activity of MMP enzymes using their actual substrates (cheap and readily available soluble collagen for example). The assay is based on our recent finding that the hydrolysis of protein results in a net gain of charge and that fluorescent dyes that are sensitive to charge can be used to amplify this signal and follow protein hydrolysis in real time on real substrates like in this graph of the digestion of bovine serum albumin by the protease trypsin.

REVERSE CHEMICAL PROTEOMICS

Molecular Biology has a lot to offer to chemistry, especially in the area of synthetic biology and understanding the role and function of small molecules in biological systems. We (Drs Piggott, Liu and Jamie) are interested in understanding the role of natural products in biology. This involves many aspects but one where molecular biology can play an important role is in the genetic manipulation of bacteriophages (T7 phage) and yeast (Saccharomyces cerevisiae) to display foreign proteins on their surface as part of a cDNA or genomic library. Such “libraries” would be very useful for the unbiased and rapid identification of proteins that bind to small molecules. Every protein identified links a phenotype to the genome and identifies that protein as a druggable target. This project will allow you to use your molecular biology and biochemistry skills toward a new frontier in drug design and development.

STRAIGHT SYNTHESIS

We have a number of projects that are just organic synthesis aimed at making fluorescent compounds useful in biotechnology and natural products. Please inquire.

SELECTED PUBLICATIONS

ORGANIC AND BIOLOGICAL CHEMISTRY/CHEMICAL BIOLOGY

The interest of this group is on design and discovery of reactions and mechanisms in chemical and biological systems. New reactions and mechanisms are fundamental to our ability to discover new chemical space and construct novel tools to ask and answer questions important to life sciences. Reaction and synthesis development, coupled with modern biochemical/biological techniques, is envisioned to be the driving force for not only refined understanding of chemical reactivity but also creative discovery in modern biology.

ASYMMETRIC ORGANO-CATALYSIS: ENZYME-INSPIRED CHEMICAL COOPERATIVITY DESIGN

Asymmetric organocatalysis has seen tremendous growth in the past decade and is now standard operation in chemical, pharmaceutical, and materials industries worldwide (Nature 2012, 489, 278). Continuing on the theme of developing green and sustainable catalytic methods, this area of research currently focuses on new catalytic strategies that are highly proficient with enzyme-like control of both reaction rate and enantioselectivity. Such proficiency control has been one of the most difficult problems in organocatalysis and will require new mechanistic insight in reaction design. Furthermore, the ability to control more than one catalytic cycle at a time is a new exciting direction in organocatalysis of complex chemical systems (Angew. Chem. Int. Ed. 2007, 46, 1570).

Our group has pioneered in new catalytic mechanism design for achieving proficient asymmetric organocatalysis in carbon-carbon bond forming reactions. In particular, we reported the first trifunctional, enantioselective organocatalytic system for the Morita-Baylis-Hillman (MBH, Scheme 1) reaction with regulation (Advanced Synthesis & Catalysis 2009, 331. Highlighted by Synfacts, 009,447). Cooperative counteranion regulation is built into the catalytic cycle for high enantioselectivity with concurrent rate enhancement. We continue to elucidate the mechanistic details behind this unusual catalysis by using a combination of techniques such as kinetics, NMR spectroscopy, mass spectrometry, and computational chemistry. The key question here is to understand the proton transfer steps in these multifunctional enantioselective reactions with complex rate-determining factors (Scheme 2). Such proton-transfer characteristics in this multi-step organocatalytic mimics of this natural system. As smallest and simplest catalyst, in-depth amino transfer reactions and organocatalytic systems are critical to finding ultimately be tunability of our catalytic systems metal centers (Highlighted by JOC 2007). These hybrid catalytic systems with multiple catalytic centers will be used in domino reactions.
ISOZYME SPECIFICITY: TARGETING CONFORMATIONAL FLEXIBILITY IN DRUG DISCOVERY

Enzymes are major drug targets, and their conformational flexibility is known to be a major factor in designing drug leads with isozyme specificity (Nature Review Drug Discovery, 2003, 527). This is exemplified by the discovery of Gleevec as the first CML drug that specifically induces a particular conformational state of the Ber-Abl kinase domain, which is the molecular driver behind chronic myelogenous leukemia (CML). Protein flexibility is difficult to predict or model thus presenting considerable challenges in rational drug design. Our group has used a semi-targeted approach, using natural products as leads, to access derivatives that can induce specific conformational change in the protein target for achieving isozyme specific recognition. In particular, we are using nucleotide mimics such as the K252 family and balanol to construct libraries of compounds using a fragment based approach (Journal of Organic Chemistry 2009, 254; Organic Letter 2007, 195). Subsite targeting motifs and conformational tuners are assembled using diversity-oriented synthesis. Activity- and binding- based SAR profiles are then established to guide the next cycle of library synthesis to improve specificity and potency.

ACTIVITY-BASED PROTEOMICS: FINDING THE MOLECULAR SIGNATURE OF CANCER

The long history of research in covalent modification of enzymes serves as a rich source for developing activity probes for functional proteomics (Annu. Rev. Biochem., 1984, 53, 493-535). We have developed highly specific labeling techniques for tagging protein active sites (Journal of the American Chemical Society 2004, 7754. Highlighted by the Chemistry & Engineering News of the American Chemical Society). These techniques have allowed analysis of protein function and their mechanistic role in a complex environment. One of the most important applications of ABPs is in drug discovery (Curr. Opin. Chem. Biol., 2011, 57). In addition, this approach has been successfully used to clarify molecular mechanisms that drive disease onset and progression (Mol. Cell. Proteomics, 2008, 1887-2006).

Our group, in collaboration with the Australian Proteomics Analysis Activity Activity-based proteomics Facility is investigating the role of signaling enzymes in cancer by designing and synthesizing activity probes for membrane signaling enzymes (Proteomics, 2011, 2683). The elucidation of signaling networks and mechanisms responsible for cancer progression will lead to identification of more effective drug targets.

Selected recent publications

PROTEIN STRUCTURE

The structure and form of any protein shapes its unique function, as well as driving its interactions with biological partners. Structural biology and structural genomics are vibrant research activities worldwide, providing detailed molecular maps of large biomolecules and even larger protein complexes. Today, 3D structures of proteins and protein complexes are being solved as part of projects ranging across medicine, biochemistry and nanomaterial design.

Our Protein Structure group offers significant expertise in recombinant expression, protein engineering, structure methods, and protein reactivity. Our work is very collaborative; current collaborators include New Zealand researchers, as well as fellow members of the Biomolecular Frontiers Centre at Macquarie.

SYNTHETIC BIOLOGY- FABRICATION OF RING-SHAPED NANOTUBULES

The self assembly of proteins occurs naturally in the cell, forming well-defined structures and supramolecular assemblies. These biological structures are now attracting attention in nanotechnology, which aims to exploit ‘bottom-up’ construction to develop novel molecular scaffolds.

Our team is one of the world’s few labs studying structures of the Lsm family of RNA-binding proteins, implicated in autoimmune disease and some cancer types [1-3]. This project takes a new direction, in which we use the remarkable self-assembling property of Lsm proteins as building blocks to control-build artificial protein rings and tubules in the 5-10 nm range. These relatively large rings expand the repertoire and complexity of molecular forms available, and our ultimate aim is to fabricate new RNA sensing materials or delivery capsules.

You will engineer recombinant Lsm proteins into ordered ring assemblies, chemically modify them into molecular conjugates, and utilize biophysical techniques (chromatography, electron microscopy, AFM, etc) to examine how they organise. This project has attracted US funding, in partnership with the Biomolecular Interactions Centre, University of Canterbury (NZ).
GENOMIC ISLANDS AND PATHOGENICITY IN ACINETOBACTER BAUMANNII (with Ian Paulsen)

Acinetobacter baumannii is poses a serious global health threat due its emerging multidrug resistant forms. Genome sequencing of A. baumannii isolates, including Australian strains, is revealing their extraordinary genetic plasticity [4].

We have pursued structural genomics [5] to discover some of the highly novel proteins found within genomic islands of Australian strains. Of the proteins for which we have obtained crystal structures, several are ready for functional testing prior to publication. They appear to be enzymes involved in biosynthesis of cell wall polysaccharide.

Recombinant enzymes will be screened for specific functions (e.g. saccharide binding) and/or relevant bioassays will be conducted on original bacterial strains. Alternatively, you can be involved in learning crystallisation techniques to grow and optimise high-quality protein crystals in conjunction with relevant cofactors and substrates. More highly refined structures will provide atomistic detail to the catalytic mechanism of these new proteins, a necessary step for developing new antibiotics.

STRUCTURE/FUNCTION RELATIONSHIPS OF MEDICALLY-IMPORTANT PROTEINS (with ASAM)

Researchers Ian Blair and Roger Chung have recently transferred their research teams to the neurobiology division of ASAM. We are instigating new projects to investigate structure/function links for several proteins of relevance to their research into neurological disorders. Projects will cover RNA-binding systems, as well as proteins with amyloid propensities. You will be learning how to prepare and probe the structure of proteins in both laboratory and cellular contexts.

Selected publications


cbms.mq.edu.au/~proteins
ANALYTICAL AND ENVIRONMENTAL CHEMISTRY

Research in the Analytical Geochemistry laboratory focuses on both the development of new analytical methodology and instrumentation, and their application to the understanding of environmental and geochemical problems. The problems we address are often extremely diverse, employing almost the complete gambit of analytical instrumentation; all modes of chromatography, flow injection analysis, mass spectrometry, NMR and FTIR spectroscopy, and thermal analysis. The skills you gain in this field of research will vastly improve your employability in the Australian chemical and biochemical job market. The following projects are just a few examples of projects available.

RESCUING ALUMINA FROM HUMIC SUBSTANCES

Alumina is made from bauxite at refineries in the Northern Territory, Queensland and Western Australia. Around two and a half tonnes of bauxite are needed to produce one tonne of alumina. Australia is the world’s leading producer of alumina, producing 30% of global output. More than 90% of the world’s alumina production is used to make aluminium.

The majority of the world’s alumina is produced in a process known as the “Bayer Process” wherein ground bauxite is mixed with concentrated NaOH to form a slurry. The amphoteric nature of alumina (Al₂O₃) means it dissolves out of the bauxite (forming aluminate) and leaving behind the other components of bauxite (Fe₂O₃, TiO₂ & SiO₂). The dissolved aluminate is filtered, cooled and “seeded” with crystals of aluminium hydroxide to precipitate alumina hydrate from the supersaturated aluminate liquor. The precipitated hydrate is filtered off, washed and passed through rotating calcinating kilns operating at high temperatures to produce the white powder known as alumina. The problem is, natural organic material (humic substances) in the bauxite interfere with the precipitation step, preventing recrystallisation and resulting in an estimated production loss of 20% per annum. In context, this equates to a loss of $2.94 billion export dollars at current alumina prices. This project will involve the structural characterisation of the humic substances isolated from Bayer Liquor with a view to developing a strategy for their removal.

DEVELOPMENT OF A SOLID PHASE, SILANE BASED REDUCING AGENT

Silanes are established reducing agents. Indeed, we developed a novel silane based reagent, n-butylsilane [3], which enabled the complete and specific reduction of carboxylic acid, alcohol, aldehyde, and ketone functions to their hydrocarbon backbone in high yield, and in a one-pot reaction. A feat has yet to be replicated or improved on by any other reducing agent. We have used this reagent extensively in our studies of humic substances, however in that role the reagent has one major flaw. A by-product of the reduction is the formation of butyl siloxanes. Whilst these by-products are readily identified during chromatographic/mass spectrometric analysis, their presence could potentially be masking important analytes. Thus the ideal situation would be for these siloxane by-products to be eliminated from the reaction products altogether. The immobilisation of the reducing agent on a solid support would allow the ready removal of the siloxane byproducts by simple filtration. The aim of this project is thus the immobilisation of an n-butyl silane analogue on a solid support and to test the effectiveness of this novel solid phase reducing agent.

STUDYING THE EFFECT OF LOW POWER MICROWAVE ENERGY ON GAS CHROMATOGRAPHIC
A molecule’s rotational energy can be changed by exposure to microwave energy. The degree of the effect is dependent on the molecule’s dipole. In gas chromatography (GC), movement through the system can only occur while the molecule is in the gas phase. Microwave energy can be used to excite certain classes of compound over others providing a separation parameter not otherwise available in GC separations. The application of microwave energy for the purpose of adjusting chromatographic behaviour is entirely novel with the potential to greatly enhance the analytical potential of GC. As such, your aim for this project will be to study and quantify the effect of microwave energy on GC separations using and refining a heavily modified gas chromatograph fitted with a 1000W microwave generator.

Selected publications

1. McIntyre, C. P; Wressnig, A. M; McRae, C. R. “Fish gut content analysis by thermocatalysis with tetramethylammonium hydroxide (TMAH) and gas chromatography–mass spectrometry (GC–MS)” *Journal of Analytical and Applied Pyrolysis*, 2007, 80 (1), 6-15.


cbms.mq.edu.au/~geochem
ORGANOMETALLICS AND CATALYSIS

Organometallic catalysts are important in reducing the energy used and waste produced of chemical processes by improving the reaction efficiency. We develop novel monometallic and multimetallic transition metal catalysts as well as new methodologies for catalysis. We target key organic transformations, in particular the synthesis of heterocycles and amines.

MULTIMETALLIC CATALYSTS FOR ENHANCED REACTIVITY

Homogeneous catalytic processes can benefit from cooperative effects between adjacent active centres mimicking enzymatic capabilities. Bimetallic complexes are important as homogeneous catalysts as the immobilization of two metal centres in close proximity can lead to cooperative effects between the metal centres, so that the resulting catalysts have exceptional efficiency and selectivity. We have shown a direct correlation between bimetallic catalyst structure and catalyst efficiency.

We develop new scaffolds and catalysts for promoting the synthesis of heterocycles and are also interested in understanding how these cooperative effects work (in collaboration with Prof S.A. Macgregor, UK).

CATALYSING MULTISTEP REACTIONS

The synthesis of pharmaceuticals relies on the stepwise formation of multiple bonds. Promoting multistep reactions in a single reaction vessel is highly desirable as it reduces the energy required and number of by-products formed. We are developing mono-metallic as well as multimetallic catalysts that mediate two or more sequential reaction steps. These reactions provide efficient routes to the synthesis of oxygen and nitrogen containing heterocycles.
CATALYSTS ON SURFACES (with Prof Justin Gooding, UNSW)

The separation of homogeneous catalysts from products or substrates continues to be a challenge. To overcome this, we are attaching catalysts already developed by our group onto a variety of robust structures and surfaces. The new anchored catalyst systems can be readily separated from reaction mixtures. This will not only allow easy catalyst/product separation, but will also provide a greater control over the nature of catalyst reactivity. The supports themselves can use the electrochemical properties of the catalysts to promote reactivity, or induce high enantioselectivity in asymmetric transformations.

Selected publications


BIOMEDICAL PROTEOMICS

Proteomics is the large-scale analysis of proteins present in biological matrices including cells, tissues and fluids. My research uses proteomic technologies (mostly mass spectrometry) to investigate dysregulated proteins functions that often underlie human disease. As the proteome is highly dynamic our research involves comparisons of samples to measure changes in protein levels over timecourses. One of my main interests is in translational cancer biology which involves collaboration with clinicians to analyse patient specimens to better understand and treat disease. For example, we are interested in discovering protein biomarkers relevant to cancer progression, patient response to treatment and in understanding how cell signaling networks are altered in cancers. To facilitate these studies we need to optimize sample handling procedures and analysis methods using quantitative mass spectrometry. Examples of studies we perform include: regulation of protein post-translational modifications, protein-protein interactions, quantitation of protein biomarkers in cells and fluids, examining protein expression responses to drugs and gene knock-downs. My research utilises the state-of-the-art equipment located within the Australian Proteome Analysis Facility (APAF) and the Biomolecular Frontiers Research Centre. The projects below are examples and can be tailored for PhD or MRes students.

PHOSPHOPROTEOMICS REVEALS HIDDEN SIGNALING ACTIVITIES IN CANCERS

Cells use protein phosphorylation as rapid switches to control intracellular signaling and gene expression. In cancer, the mutation of various kinases causes signaling dysregulation leading to aberrant cellular proliferation. This project seeks to investigate the phosphoproteome of various cancers (colon, melanoma, etc) to delineate hidden signaling networks. This knowledge may lead to improved targeting of drug inhibitors to control signaling pathways. We modulate signaling pathways by use of inhibitors or genetic disruption, then profile the phosphoproteome using advanced mass spectrometry.

Two current projects are examining the role of oncogenic BRAF and Protein kinase CK2 in various cancers. Students will learn techniques including mammalian cell culture, protein/peptide biochemistry, chromatography, quantitative protein mass spectrometry and bioinformatic data analysis.
THERMAL SHIFT PROTEOMICS IDENTIFIES DRUG/NATURAL PRODUCT PROTEIN TARGETS

It is well known that ligand bound protein complexes have greater resistant to melting than unbound proteins. This characteristic can be exploited to identify soluble protein binders to new drugs and natural products and to determine off-target effects. By using mass spectrometry as the detection method analyses can be carried out in vivo, in a large-scale unbiased manner to detect such proteins. Through collaborations we have a number of drug molecules where the thermal shift profiling can be applied. This is a “hot” new technique in proteomics and drug discovery and would be of interest to students with interest in medicinal chemistry and medical science.


MICROSAMPLING AND THERAPEUTIC DRUG MONITORING

Only a small volume of blood or plasma is required for mass spectrometry detection of chemotherapeutic drugs. We are investigating novel approaches to introduce microliter volumes to the mass spectrometer to detect drug levels in patients, enabling therapeutic drug monitoring to ensure appropriate patient dosing. The project suits students with interests in bioanalytical chemistry.


Selected publications


3. Lin, C-H., Chik, J., Packer, NH., Molloy, MP. Multi-dimensional fractionation is a requirement for quantitation of Golgi-resident glycosylation enzymes from cultured human cells. J. Proteome Res. 2015, 14, 747-55.


web.science.mq.edu.au/directory/listing/person.htm?id=mmolloy

cbms.mq.edu.au/academics/mmolloy.html
MOLECULAR BIOTECHNOLOGY

Filamentous fungi are the world-champions of protein secretion and loving it! On the flipside, fungi can also cause infections and disease either alone or by interaction with other microorganisms. Research projects available within the group contribute to the development of new technologies for the production of industrially and medically important gene products and understanding protein secretion in the fungal cell factories. Also, understanding the molecular mechanisms underlying fungal pathogenesis is addressed with a view of developing new approaches for treating fungal diseases. In addition to research with fungi, we are exploring the capabilities of a eukaryotic protist in the context of making single cell food in collaboration with an industrial partner.

Our research uses a variety of contemporary molecular technologies applied to eukaryotic microorganisms. We use molecular tools for high level gene expression and knockout studies, and create and analyse genomic and proteomic data to understand cell metabolism, protein secretion and fungal pathogenesis. We make recombinant enzymes for industrial uses and develop synthetic biology methods for microbial strain improvement with a view of making things in a totally new way. This involves internal and external collaboration.

If you are interested in working with eukaryotic microorganisms on the topic areas discussed above, please come and talk to us so we can put together a project according to your interests. Our research organisms are:

- **Trichoderma reesei**  Industrial producer of recombinant gene products
- **Scedosporium aurantiacum**  A fungus found in the lungs of patients suffering from cystic fibrosis
- **Euglena gracilis**  A protist using light for making single cell food
Selected publications


chem.mq.edu.au/academics/hnevalainen.html
GLYCOMICS@MQ GROUP

Glycomics is defined as an integrated systems approach to study structure-function relationships of complex carbohydrates (or glycans). These glycans are estimated to be attached to at least 50% of the proteins of the mammalian genome and are found in all eukaryotes and many prokaryotes. Their capacity for heterogeneity confers their ability to “fine-tune” the function of the protein.

They are usually expressed on the surface of the cell and are therefore the first molecules involved in cell-cell contact. They are thus integral to the function of many crucial cellular processes such as:

- Cell growth and development
- Tumour growth and metastasis
- Blood coagulation
- Immune recognition/response
- Cell-cell communication
- Microbial pathogenesis
- Fertility

The analysis of these post-translational modifications requires specific sample preparation, mass spectrometric and bioinformatic techniques which our lab is applying to a range of glycobiological questions.

GLYCOSYLATION AND CANCER

Aberrant glycosylation has been implicated in many diseases due to changes associated with biological function and protein folding. Several studies have now clearly established the glycosylation changes associated in cancer. Alteration of the cell surface glycosylation can lead to enhanced tumour progression and invasion. Identification of relevant glycosylation changes in proteins could facilitate novel glycan based biomarkers for diagnostic and prognostic indicators of cancer.

DIFFERENTIATING TISSUE TYPES BY IMAGING MASS SPECTROMETRY OF GLYCANS

Recent developments in targeting protein distribution in tissue sections by spatial proteomics imaging have paved the way for retrospective in situ mass spectrometry (MS) analyses of formalin-fixed clinical tissue samples. We are using enzymatic mediated release and measurement of N-linked glycans from sections of formalin-fixed tissue to allow analyses of tissue-specific N-glycosylation profiles that can differentiate a tumour from other tissue types.
DEVELOPMENT OF ADVANCED MASS SPECTROMETRY TECHNIQUES TO CHARACTERISE GLYCOCONJUGATES

There currently are three main mass spectrometric analytical approaches to the analysis of protein glycosylation which are at various levels of technological development: Glycomics (the global structural analysis of N- and O-glycans attached to proteins); glycoprotein (glycan structure and site analysis of a single protein); and glycoproteomics (glycan structure and site analysis of complex mixtures of glycoproteins).

GLYCOINFORMATICS

As has been the case in proteomics and genomics, an essential requirement for glycomics and glycoproteomics to progress out of our relatively small community into the greater scientific sphere is the development of informatics tools to interpret and store diverse experimental glycan data and enable public accessibility. Ultimately the analytical data must relate to the function of these glycans and their glycoconjugates. UniCarbKB (www.unicarbKB.org) is an initiative that is providing an online information storage and search platform for glycoproteomics research.

INNATE PROTECTION AGAINST PATHOGENS BY GLYCANs IN BODILY FLUIDS

One of the key initial processes involved in pathogen infection is the attachment to host cell receptors, typically glycans (sugars) conjugated to proteins or lipids on epithelial cell surfaces. We have shown that the host provides an ingenious innate defence mechanism that uses the glycoproteins in their secreted fluids to competitively bind to the bacterial pathogens to prevent infection. Our research shows that bacteria bind differentially to glycan moieties on secreted glycoproteins from human tears, milk, saliva and sweat, potentially providing decoys for selective adhesion and clearance of pathogens as the secretory fluids wash the epithelial cell surface.

NANOPARTICLE LABELLING FOR BIOMEDICAL IMAGING

Despite significant advancement in the methodology used to conjugate, incorporate and visualize fluorescent molecules at the cellular and tissue levels, biomedical imaging predominantly relies on the limitations of established fluorescent molecules. These fluorescent dyes and conjugates are highly susceptible to photobleaching and compete with cellular autofluorescence, making biomedical imaging unreliable, difficult and time consuming in many cases. In addition, some proteins have low copy numbers and/or poor antibody recognition, further making detection and imaging difficult. We are developing better methods for imaging with labelled with fluorescent nanodiamonds or lanthanide chelates. These tags have increased signal and photostability and can also discriminate against tissue/cell autofluorescence.

Selected publications


chem.mq.edu.au/academics/npacker.html
MICROBIAL GENOMICS

The research interests of my group are focused on applying high throughput genomic approaches to understand bacteria. Potential projects include:

USING PSEUDOMONAS BACTERIA TO PROTECT PLANTS FROM DISEASE

Australia is home to a number of serious plant diseases, which, if left unchecked, could devastate our multibillion dollar agricultural industry. In modern agriculture, diseases are typically controlled mainly through the use of agrochemicals, which are expensive and environmentally damaging. We are currently investigating a group of natural plant-associated bacteria that are able to act as biocontrol organisms suppressing infections from a range of important fungal, bacterial, viral and insect pests. This well-funded project will apply a combination of next-generation transcriptomic and proteomic technologies, as well as innovative genome-wide transposon mutagenesis methods to identify the key genes and gene clusters involved in biocontrol mediated by Pseudomonas bacteria.

FACTORS INFLUENCING THE SUCCESS OF THE PATHOGEN ACINETOBACTER BAUMANNII

The hospital intensive care unit should be a place of healing and care for the most vulnerable. Nonetheless, several microbial pathogens continue to plague this environment, causing serious infections in the immunocompromised patients that pose ever more challenging problems for clinicians. Acinetobacter baumannii has recently emerged as one of the most problematic hospital-acquired pathogens worldwide due to its highly drug-resistant nature. This project aims to define the key mechanisms of drug resistance operating in clinical A. baumannii isolates using a combination of cutting-edge next-generation transcriptomics and proteomics, and essential resistance genes identified by saturation mutagenesis methods. An alternative project in collaboration with A/Prof. Bridget Mabbutt uses structural and functional genomics to characterize laterally-acquired genes in A. baumannii that might help it flourish in clinical settings.

Molecular ecology of an ancient symbiosis between sponges and bacteria

Marine sponges are crucial members of marine ecosystems that are often overlooked despite being a dominant and ubiquitous component of the sea bed. Research involving sponges is linked to various scientific aspects from environmental and evolutionary studies to biotechnological and medical applications, with anti-cancer drugs and anti-HIV products derived from sponges. A large proportion of species contains sponge-specific photosynthetic symbionts related to free-living cyanobacteria, which are abundant and key primary producers of marine environments. This project aims to elucidate the molecular basis of the stable symbiosis of these two modern day "fossils", using a combination of traditional and next-generation genomics and transcriptomics.

GENOMICS AND ECOLOGY OF MARINE CYANOBACTERIA IN AUSTRALIAN WATERS

Tiny single-celled marine cyanobacteria constitute up to two thirds of all marine productivity. As the base of the marine food-web, the activity of these organisms impacts on all marine life. Using a rapid molecular diagnostic we will perform the first survey of the environmental distribution of marine Synechococcus cyanobacteria along ecosystem gradients of the Australian Coast. Representative isolates will be selected for further study to identify key genes and proteins involved in adaptation to tropical and temperate habitats.

This is a multidisciplinary project that will combine elements of fieldwork with the latest generation molecular techniques to understand the spatial and seasonal distribution of locally adapted 'ecotypes'. Understanding the environmental factors that affect the abundance and activity of these organisms is fundamental to predicting the impacts of climate change on our local marine resources.
COAL: PROKARYOTIC PIONEERS (with CSIRO)

Using natural gas, rather than coal for electricity generation provides a means of reducing CO2 emissions and combating climate change. In coal seams where moisture and sufficient nutrition is available, natural gas is produced from microbial activity. To date, we have identified the types of microbes that inhabit coal, but have not identified those microbial pioneers whose metabolic degradation of the coal, not only underpins the microbial community but also facilitates the production of natural gas. Using culturing, sequencing and bioinformatics techniques and an established coal-degrading microbial consortia, the project aims to identify these early pioneers and how they degrade coal.

LIFE IN A GLUEY STICKY MESS (with Packer, Super Science team)

The thick mucus that forms in the lungs of cystic fibrosis (CF) patients provides a breeding ground for chronic bacterial infection. *Pseudomonas aeruginosa*, an opportunistic human pathogen is one of the main and most successful colonisers in CF lungs. As a part of the multidisciplinary ARC Super Science project, this study will be aimed at identifying specific adaptations developed by *P. aeruginosa* during chronic CF infections, including its ability to form biofilms. Whole genome transcriptomic analysis using RNA-Seq to sequence the entire bacterial transcriptome will be applied to identify genes important for adaptation and virulence in CF lung mucus.

Selected publications


chem.mq.edu.au/academics/ipaulsen.html
NEXT-GENERATION ANTIBIOTICS

The widespread use and misuse of antibiotics, both clinically and agriculturally, has led to a dramatic increase in the prevalence of antibiotic-resistant strains of pathogenic bacteria, particularly in hospitals. New resistance mechanisms are transferring rapidly between different species of bacteria, imparting broad-spectrum antibiotic resistance to an ever-increasing microbial population. If this disturbing trend continues, deaths from previously treatable bacterial infections will soon return to levels experienced in the early 20th century, before the dawn of the antibiotic era.

Our group works at the exciting and challenging interface between chemistry and biology to identify, isolate, characterise and develop next-generation antibiotics that are effective against these deadly superbugs. Projects are available spanning a range of areas, from natural products chemistry and organic synthesis, to chemical biology and chemical proteomics. Please see the descriptions below for two specific project examples, or feel free to contact me to discuss other possible projects.

MICROBIAL BIODISCOVERY1–5

Natural products have long been a mainstay of the pharmaceutical industry, with almost 70% of the FDA approved antibiotics either derived from, or inspired by, natural products. These figures are not surprising when you consider that natural products have evolved through millions of years of natural selection in biological systems to interact with biological systems. The technology for pursuing natural products has matured considerably over the last three decades, making it possible to investigate the chemistry and biology of structurally novel and diverse metabolites present at sub-milligram levels in complex extracts.

In this project, you will use the latest HPLC, LCMS and NMR techniques to isolate, elucidate and characterise potent and/or selective new antibiotics from a range of unique microorganisms provided by our collaborators at Microbial Screening Technologies in Sydney. You will assay these new antibiotics against a range of clinically important microorganisms, both in-house and in collaboration with leading national and international infectious disease researchers. The cellular targets and modes of action of these antibiotics will also be investigated in collaboration with other group members (see following project).
PHAGE DISPLAY

The substantial costs associated with getting a new drug to market mean that early prioritisation of leads is essential. The most significant challenge facing modern antibiotic chemotherapy is the impact of multidrug resistance, so a key factor in the prioritisation equation must be "mode of action". New antibiotic scaffolds that operate by the same compromised pathways as known antibiotics are clearly less attractive than those that operate by entirely new uncompromised pathways. The prioritisation of natural product antibiotics presents significant challenges as their cellular targets and modes of action are generally not known. Inevitably, these molecules end up being published as basic science or simply abandoned, squandering countless invaluable antibiotic drug leads.

In this project, you will use T7 phage display to identify the cellular targets of both new and historic (abandoned) antibiotic natural products, allowing their modes of action to be determined and facilitating their prioritisation and development as chemotherapeutic agents. This multidisciplinary project draws on a range of techniques from chemistry and biology, including organic synthesis, molecular biology and biochemistry. Projects are also available to construct new bacterial T7 phage display libraries from a range of clinically important pathogens and other model organisms. Please contact me for further details!

Selected publications


cbms.mq.edu.au/~apiggott
BIOINFORMATICS AND COMPUTATIONAL BIOSCIENCES

Our research area is Bioinformatics, which is the application of computational approaches to understand how biological systems function. Bioinformatics addresses key problems in biomolecular, biomedical and chemical sciences, using computational approaches. Our group focusses on comparative genome sequence analysis, computational structural biology and biodiversity analysis.

ALTERNATIVE SPlicing AND HUMAN DISEASES

Alternative pre-mRNA splicing is an important mechanism for controlling gene expression in higher eukaryotes. A single gene produces several functionally diverse proteins by alternative usage of exons or introns within pre-mRNA transcripts. These gene products can be specific to tissue, developmental stage, and disease state. We have pioneered the use of graph theory for genome-wide analysis of alternative splicing in the fruitfly, chicken compared to mouse and human (1) and more recently, the cow.

The major alternative splicing events involved in human diseases are shown below, in the splicing graph formalism:

1. exon skipping (cassette exon) and 2. intron retention.

Why are some exons skipped and some introns ignored? A detailed genome-wide analysis of the information content of the regions surrounding the splice sites for all “normal” exons and “disease-related” alternatively spliced exons could provide the answer.

SECRETOME DATABASE OF HELMINTH PARASITES

Excretory-secretory (ES) proteins are an important class of proteins in many organisms, spanning from bacteria to human beings, and are potential drug targets for several diseases. ES proteins constitute the secretome of any organism and are particularly relevant for parasitic organisms. Helminth parasites are responsible for a range of neglected tropical diseases, such as ancylostomatosis, necatoriasis, lymphatic filariasis, onchocerciasis, ascariasis and strongyloidiasis in humans and others can cause massive production or economic losses to farmers as well as to animal and plant industries.

Recent transcriptomic and proteomic analysis (2) has shown that parasites adopt non-classical pathways to generate ES products. To identify novel genes for parasite intervention, the secretome of helminth parasites needs to be compiled. This project is aimed at developing a searchable helminth parasite secretome database with experimentally identified ES proteins.
MAPPING DISEASE GENE MUTATIONS TO PROTEIN STRUCTURE FOR GENOME-PHENOME CORRELATIONS

Mapping disease mutations to the structure of the protein can help in understanding the functional consequences of these mutations and thus indirectly, the finer aspects of the pathology and clinical manifestations of the disease, including phenotypic severity as a function of the genotype. Recently, we studied mutations in the gene \textit{(MAN2B1)} encoding lysosomal \(\alpha\)-D-mannosidase, causing improper coding and resulting in dysfunctional or non-functional protein and resulting in the disease \(\alpha\)-mannosidosis.

We would like to extend this approach to other human diseases, using data from OMIM, OMIA and PDB databases, to predict regions prone to disease-causing mutations, known as mutational hotspots.

CORRELATING AUSTRALIAN ABORIGINAL PLANT HABITATS WITH THE STRUCTURE AND PROPERTIES OF THEIR BIOACTIVE COMPOUNDS

Australia covers a diverse range of habitats, from alpine heaths to tropical rainforests, and is recognised as a megadiverse country. Due to the great age and consequent low levels of fertility of the continent and its extremely variable weather patterns and long-term geographic isolation, much of Australia’s biota is unique and diverse. It is known that the beneficial medicinal effects of plant materials typically result from the combinations of bioactives present in the plant. We have integrated Australian Aboriginal customary medicinal plant knowledge into a database, CMKb (4). The database stores information related to taxonomy, phytochemistry, biogeography, biological activities of customary medicinal plant species as well as images of individual species.

This project aims to organise Australian aboriginal medicinal plants based on their habitats and then correlate the location attributes to the bioactives identified.

Selected publications

2. E. Chacko, S. Ranganathan “Comprehensive splicing graph analysis of alternative splicing patterns in chicken, compared to human and mouse” BMC Genomics, 2009, 10, Suppl 1, S5.

cbms.mq.edu.au/~ranganathan
MOLECULAR BIOTECHNOLOGY

The research interest in my laboratory is protein biochemistry and application of biotechnological relevant proteins. Currently we are focusing on immobilization of industrial enzymes and proteins to different inorganic solid matrices. The immobilization is mediated through affinity of synthetic peptides and selected through phage display screening. A second aspect of our research is development of cell-free biocatalytic modules for biotechnology and enzyme-based processes by incorporating the principles of *in vitro* synthetic biology.

NEW GENERATION OF PROTEASE RESISTANT SYNTHETIC PEPTIDE LINKERS

Most of the methods available for immobilising proteins onto solid supports traditionally have relied on non-specific adsorption or on the reaction of naturally occurring chemical groups within proteins with appropriate reactive groups on the matrix. In both cases, the corresponding proteins are attached to the surface in a random orientation that may cause the reduction or loss of the protein’s biological activity. We have developed synthetic peptide linkers with high binding affinity to a large range of commercially available and inexpensive silica-containing materials. This project is aimed at producing a new generation of protease resistant peptides for immobilization of proteins in industrial–scale applications using combinatorial display technologies like phage-display and cell surface display. The industrial host organisms for this application is *Trichoderma reesei*, a filamentous fungus used extensively by industry for the production for autologous and heterologous proteins.

![Diagrammatic representation of enzyme recycling using peptide linker technology and solid matrix immobilization. Lower panel represents a real time assay performed at 60ºC.](image-url)
DEVELOPMENT OF CELL-FREE BIOCATALYTIC MODULES

The aim of this research project is to incorporate the principles of in vitro synthetic biology to design cell-free biocatalytic modules. This principle is based on the development of stable building blocks (individual immobilized enzymes) with defined functions and catalytic properties. Assembly of both natural and non-natural pathways for special applications is achieved by combination of all pathway enzymes (basic building blocks) into complex biocatalytic modules. This “mix & match” approach combines several aspects of enzyme engineering and enzyme immobilization. The result is increasing engineering flexibility and decreasing dependence on cells and physiological constrains.

FIG. 2 Cell-free biocatalytic modules for biomanufacturing

Selected publications


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**ENVIRONMENTAL AND APPLIED MICROBIOLOGY**

The field of Microbiology is currently undergoing an exciting period of rapid development, driven largely by the ‘omics’ revolution. We now have the tools and capabilities to explore how microorganisms respond to, and influence their environment on both a local and global scale. Our lab applies a wide range of molecular techniques to address a range of questions relating to applied and environmental microbiology. A main focus of recent work has been examining how marine microbes respond to a wide range of different stressors. This work involves transcriptomic, genomic and metagenomic analyses. A second key area of research focus is microbial community analyses. Using the latest molecular microbial ecology tools we have examined the microbial communities associated with humans, animals and aquatic environments to learn about how microorganisms contribute to health and disease in hosts, and improve our understanding of the vital ecosystem services that microbes provide.

**HOW DO COMMON CHEMICAL POLLUTANTS AFFECT KEY PHOTOSYNTHETIC MARINE BACTERIA?**  
(Dr Deepa Varkey, Dr Sophie Mazard, Dr Martin Ostrowski)

Environmental pollution threatens the sustainability of the world’s oceans. However, we still do not understand how pollution affects primary producers at the base of oceanic food chains. Current approaches to understand and monitor the impact of chemical pollution on the marine environment are inadequate considering the severity of environmental degradation.

Transcriptomic techniques can monitor expression across thousands of genes simultaneously, generating an overview of the molecular, cellular and physiological mechanisms that constitute an organism’s adaptive stress response. Delving into the details of such stress responses has the potential to tease apart the mode of action of chemical stressors, detect and quantify sub-lethal stress exposure levels and identify genetic markers for general or specific toxicant exposure. This Australian Research Council funded project will use RNA-Seq transcriptomics to investigate how common chemical pollutants (herbicides, plastic leachates and crude oil) affect key marine photosynthetic bacteria *Synechococcus* and *Prochlorococcus*.

**Figure 1.** Hierarchical tree showing a cluster of genes in *Synechococcus* sp. WH102 for which transcript levels tended to increase on exposure to multiple stress conditions. The colour bar indicates the fold change (log2 ratio) between control and experimental conditions. These genes may be candidates for transcriptional monitoring of general stress responses in this strain.
HOW WILL ANTHROPOGENIC IMPACTS ON THE MARINE ENVIRONMENT INFLUENCE MICROBIAL COMMUNITIES? (Dr Deepa Varkey, Dr Liam Elbourne, Prof Ian Paulsen)

Genome, metagenome and transcriptome analyses of key marine photosynthetic bacteria have indicated that there is significant variation in both gene repertoires and expression patterns within subgroups of these organisms. Horizontal gene transfer and other genome shaping processes are thought to have provided the basis for adaptive changes, resulting in strains which are better able to tolerate certain environmental stressors. This project will use microcosm experiments to determine how the microbial community composition shifts on exposure to selected environmentally relevant pollutants. This will help elucidate how microbial population composition may shift in marine regions which are exposed to high levels of environmental toxicants as a result of human activities.

Figure 2. Two strains of Synechococcus, one which resides in coastal regions (A) and one which is found in the open ocean (B) were found to show very different responses to chemical toxicants (Full figure legend in publication 1).

Selected publications
ORGANIC SYNTHESIS OF FUNCTIONAL NEW MATERIALS

The properties of a material are a function of its molecular components. The properties of a molecule are, in turn, dependent upon the type and orientation of its functional groups. Organic synthesis provides us with a way of programming the type and orientation of functional groups on a given organic framework and therefore the basis for designing new materials.

Several projects are available within each of the three broad areas outlined below and examples of other research areas of interest include the design of new colorimetric/fluorescent sensors, the development of chiral stationary phases for the resolution of enantiomers, the development of non-chromatographic methods to resolve Tröger’s base enantiomers, and synthesis of artificial light-harvesting systems. Dr. Try is available for a discussion on any aspect of the projects. All of the research areas are interdisciplinary in nature and involve organic synthesis and access to a wide range of modern instrumentation for characterisation of new materials.

CHIRALITY TRANSCRIPTION OF RIGID MOLECULAR SCAFFOLDS TO HYBRID SILICAS (with Ecole Nationale Supérieure de Chimie de Montpellier, France)

We are interested in utilising a series of related molecular frameworks, in the synthesis of chiral hybrid silicas. As can be seen from the X-ray crystals structures shown below, we have control over the shape of frameworks, and we also have control over the type and placement of a variety of functionality available on the aromatic rings.

We aim to use this control to prepare a range of hybrid silicas of the type shown in the SEM images on the right, which were prepared by our collaborators in Montpellier; the helicity of the fibre-like bundles was always right-handed for the materials obtained from (R,R)-1,2-diaminocyclohexane and left-handed when the (S,S)- enantiomer was used as the organic framework. The resultant hybrid materials are expected to find application in the areas of heterogeneous asymmetric catalyst design and chiral chromatographic separation.

SYNTHESIS AND CHARACTERISATION OF NEW FLUORESCENT BORON COMPLEXES

Research in the area of novel organic fluorescent dyes continues to develop due to their various applications. Despite the immense interest and research in the area there is still much more to be done to produce the ideal fluorophore. The ideal fluorescent dye should be chemically and photo physically stable, exhibit excellent photo physical properties and be easily tunable to emit in different regions of the visible-NIR spectrum. Boron complexes are known to have high quantum yields, large absorption coefficients, long excited life times and good chemical stability.
In this project a new series of ligands and their boron complexes will be designed, synthesised and characterised. The figure to the left shows the solid state fluorescence of a recently prepared series of compounds, under irradiation at 365 nm light.

The image highlights the tunability available within this family of compounds.

CHIRAL LIQUID CRYSTALS (with Kent State University, USA)

Liquid crystalline crystals can be regarded as a fourth state of matter. A liquid crystalline phase (mesophase) is one the disordered isotropic (liquid) state, but exists only for molecules possessing a certain set of parameters. Chiral liquid crystals are a subclass of these compounds. These molecules display desirable properties that are exploited in display devices such as watches, clock radios, calculators and laptop computer screens.

Three important features present in liquid crystalline molecules are the incorporation of a polarisable group (as this helps to orient the molecules in a given direction in the presence of an applied electric/magnetic field), a rigid region (typically an aromatic ring) and the presence of one or more flexible chains. In this area we are interested in incorporating long alkyl chains linked to novel chiral scaffolds by a variety of functional groups.

Structure- property studies will then be carried out using Differential Scanning Calorimetry (DSC) and polarised-light microscopy in order to determine, and ultimately predict, how variations in properties of the bulk liquid crystalline phase result from a series of subtle electronic and orientational changes to the structure of the scaffolds of the individual molecules.

Selected publications


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BIOCHEMISTRY: FROM PROTEIN COMPOSITION TO ENZYME STRUCTURE AND FUNCTION

Proteins are the main functional components of life, with functions including storage of nitrogen, structural rigidity, transport, signaling, binding, and enzymatic catalysis. The projects offered in my lab span the broad area of protein biochemistry including: proteomic analysis of cereals, enzyme functional analysis, structural studies of molecular machines, regulation of pigment biosynthesis and protein-protein interaction studies.

BIOSYNTHESIS OF CHLOROPHYLLS

Chlorophyll is a dangerous molecule as it is a potent photosensitizer and producer of reactive oxygen species. The organisms which make chlorophyll go to great lengths to ensure that it or its coloured precursors don’t accumulate to reek oxidative devastation on the cell. The projects on offer aim to understand the mechanism by which chlorophyll is made by enzymes in the pathway and identify the regulatory mechanisms for chlorophyll synthesis.

PURIFICATION OF A REGULATORY KINASE

Characterisation of a kinase that phosphorylates the GENOMES UNCOUPLED 4 protein in plants or algae. This project builds on our recent paper in FEBS Letters and our recently published crystal structure which both show the algal and plant GUN4 differs significantly from the cyanobacterial GUN4.

MAGNESIUM CHELATASE COMPLEXES (with ANSTO)

We have all five magnesium chelatase subunits expressed and are able to reconstitute the large protein complexes in vitro. The stoichiometry of the subunits is variable as some subunits act as substrates with corresponding substrate like properties. X-ray and neutron scattering at ANSTO and the Australian Synchrotron allow us to probe the mechanism of assembly of these complexes as shown in the figure.

We also use synthetic biology techniques to examine the assembly of the complex in vivo by controlling expression of each subunit and monitor the magnesium protoporphyrin formation.

SYNTHETIC BIOLOGY: CHLOROPHYLL SYNTHESIS IN E. COLI

The 2013-2015 iGEM teams have cloned all of the known genes involved in chlorophyll biosynthesis from a eukaryotic organism, Chlamydomonas reinhardtii, into E. coli. Some of these genes have been assembled into operons. This project will assemble the different operons into super operons to test the effectiveness of chlorophyll biosynthesis in an organism that normally does not make chlorophyll. Optimisation of expression and testing of individual operons will allow for evaluation of how chlorophyll synthesis may be regulated in the absence of other potentially competing regulatory factors.
ANALYSIS OF HALOMICRONEMA: A CHLOROPHYLL F CONTAINING ORGANISM ISOLATED FROM STROMATOLITES

We have a complete genome sequence of this organism and have extensive proteomic data which indicate light dependent changes in protein expression.

There are numerous projects available on this novel organism, ranging from genomic analysis to light quality regulation of photosynthetic genes and structural studies of phycobilisomes (see articles 2, 7, 9, 11). One particularly interesting project is in identifying the light regulatory mechanisms for gene synthesis in this organism.

PROTEOMICS OF CEREALS PROTEOMICS OF CEREALS

The cereal research is associated with Grain Growers Pty Ltd looking at proteomics of barley and wheat grains. We are interested in determining the extent to which environmental and genetic variation determines protein composition in wheat, rice and barley. The protein profile between varieties grown at the same location and varieties grown at different locations is being determined. Initial trial scale analyses have found numerous differences between the varieties of barley grain grown at the same time and location. The reason for these variations may shed light on how cereals cope with environmental factors such as nutrient availability, drought, salinity and temperature as well as biological stresses. In addition, many cereal proteins have distinct impacts on quality; taste and performance in baking and malting are key examples.

Understanding these factors are very important for optimizing quality in the food industry.

Selected publications

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BIOLOGICAL, ENVIRONMENTAL AND MEDICAL ANALYTICAL CHEMISTRY
Dr Wong and his research group are particularly interested in the development and applications of (i) electrochemical sensors and/or (ii) electroanalytical techniques to biological, environmental or medical analyses. The following projects offer an opportunity to students with interest in some of these areas. As such, almost all of our research projects are interdisciplinary and they couple electroanalytical chemistry to a diverse area including immunology, biochemistry, neuroscience, medical science, biotechnology, polymer chemistry, environmental science, method validation and quality assurance. Each of these projects will engage students in acquiring hands-on experience in a range of analytical techniques. **There is also opportunity to tailor make a project of mutual interest as well.**

NEW ELECTROCHEMICAL MICROSENSOR DESIGN FOR BIOLOGICAL, MEDICAL AND PSYCHOLOGICAL DIAGNOSTICS
Dr Wong's electroanalytical chemistry laboratory is internationally recognised for designing structurally small electrochemical sensors. Indeed, increasing biological, medical and psychological diagnostics are relying on electroanalytical techniques because of their unique capability in performing real-time measurements. In Dr Wong's laboratory, electrodes with small physical dimensions (≤1 µm in tip diameter) are routinely manufactured by pyrolysing hydrocarbon gases inside and outside pulled capillaries. The carbon produced is then deposited at the tip and on the shank of the capillaries. In recent years, we have perfected the technique to produce a large carbon surface area to obtain amplified detection signal. We are particularly interested in exploiting these electrodes in detecting neurotransmitters in mammalian brain systems. Such a study enables a better understanding of the central neural pathways that stimulate dopamine neurons to burst fire in various neural processes. In this project, we aim at employing sensors with physical dimensions down to 1 µm that are then chemically modified to enhance their sensitivity and selectivity towards detection of dopamine released in targeted regions in the brain. Such a study will aid in identifying the chemical pathways involved in mediating dopamine neuron burst firing and forebrain dopamine release in the central nervous system. This project provides an excellent opportunity for students to gain research experience in both a chemistry laboratory and a medically oriented laboratory.
A VERSATILE MOLECULAR ARCHITECTURE FOR AN ELECTROCHEMICAL IMMUNOSENSOR OR AN ELECTROCHEMICAL DNA BIOSENSOR

In this research area, we are keen to fabricate and characterise biological sensors based on the principles of immunology and DNA hybridisation. In the former, the interactions between an antibody and an antigen are known to be very specific chemical reactions. Such a specific molecular recognition of antigens by antibodies has been exploited in immunoassays to develop highly selective detection methods in many clinical analyses and medical diagnostics as well as for environmental monitoring. Similarly, in the latter, owing to specific recognitions, a DNA probe will only hybridise with its complementary DNA target. Many detection tools used in forensic identifications, medical diagnoses, drug discovery are based on DNA hybridisation. Electrochemical detection is particularly well suited for immunoassays and DNA hybridisation detection owing to its ease and sensitivity. Currently, a lot of work is being focused on the development of rapid, simple, sensitive, automated, and on-site electrochemical immunoassays. In this project, we are interested in fabricating a simple electrochemical immunosensor using a range of chemical and biological reagents. Compared to other methodologies used, our design has a distinct capability in aligning an antibody or a DNA probe in an optimum orientation for interaction with an antigen analyte or a DNA target, respectively. This is a significant factor in maximising the detection sensitivity of the immunosensor. We will also explore the application of nanoparticles or graphene to the development of an immunosensor or a DNA biosensor to further enhance their sensitivity. In immunosensor development, we will apply it to the detection of a real-life analyte (e.g. cortisol, tumour marker), while the DNA biosensor will be used to study the interaction between DNA and selected drugs of medical significance. Graduates with familiarity in analytical techniques are of demand in the current employment market. Note that a background in biology is not required but willingness to acquire new bioanalytical skills will be essential.

PROBING ENVIRONMENTAL CHEMISTRY USING ELECTROANALYTICAL TECHNIQUES ELECTRO-REMEDIAITION OF POLLUTED TEXTILE EFFLUENTS

Azo dyes are commonly used in the textile and carpet dyeing industries. Very often, enormous quantities of dye containing wastewaters are being released into effluent streams. Such dyes are harmful to aquatic fauna and flora as well as humans. In this project, electrochemical removal and/or treatment of azo dyes in textile effluents will be explored. This will be achieved using the conducting polymer, polypyrrole, or its derivatives. A distinct advantage of this method is that dye molecules are entrapped in the polymer film for removal, rather than being chemically treated that generates even more harmful products as exhibited by many other treatment methods. Apart from electrochemistry, students will also engage in polymer chemistry, materials chemistry and environmental chemistry in this project.

These projects will provide an opportunity for students to gain experience with a range of analytical techniques, as well as that in method validation and quality assurance. Graduates equipped with all these skills are always of demand in the current employment.
Research in the
Department of Chemistry and Biomolecular Sciences

Analytical Glycobiology and Glycoimmunology
Biophysics Group – Structural Biology
Plant and Environmental Proteomics
Chemical Ecology, Atmospheric Chemistry and Chemistry Education
Bio-Organic and Medicinal Chemistry and Science Outreach
Synthetic Biology
Chemical Biology
Organic Biological Chemistry/Chemical Biology
Protein Structure
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