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Welcome from Head of School and BABS Honours Coordinator

This handbook provides a guide for students considering undertaking Honours or a Master of Philosophy in the School of Biotechnology and Biomolecular Sciences (BABS) at the University of NSW during 2015.

The biomolecular sciences encompass the disciplines of chemistry, biochemistry, molecular biology and cell biology, and include the specialist areas of genetics, genomics, bioinformatics, proteomics and chemical biology. Biotechnology underpins much of the research.

Researchers in BABS are aligned into four discipline areas:

- Environmental Microbiology
- Infectious Disease
- Molecular Medicine
- Systems and Cellular Biology

The School’s research includes human bacterial pathogens, hepatitis viruses, tissue engineering, cancer, cell biology, genetics, bioinformatics, extremophiles and functional genomics. Many of our staff have international reputations for research and have established collaborative links with industry and other research institutions in Australia and overseas. BABS also hosts a number of important research centres that conduct pioneering research and provide the highest level of technological expertise and services in their respective fields.

Apart from imparting skills in scientific research, another aim of the BABS Honours program is to equip students with additional skills in information technology, scientific communication and critical thinking, which will not only increase confidence but also make graduates more employable in the increasingly competitive workplace.

Honours is an intensive year that is immensely rewarding intellectually, sometimes perhaps only in hindsight. Our staff will do everything they can to ensure such reward is achieved by all Honours and MPhil (BABS) students, and to make each student’s experience as enjoyable and scientifically stimulating as possible.

We invite you to become a part of our research efforts and initiatives by undertaking Honours or a Master of Philosophy in the School of BABS.
Why do Honours in BABS?

The BABS BSc (Hons) Degree provides an opportunity for students to experience hands-on scientific research. Honours students become part of a research team within one of the research labs in the School, and complete a supervised research project and thesis during the year-long program. The course is designed to provide advanced training and knowledge in one of the following areas:

- Biotechnology
- Genetics
- Microbiology
- Molecular and Cell Biology

Honours may lead to the student enrolling in a higher degree by research; however, that is not the only purpose of the Degree. Honours graduates acquire greater competence and confidence in the practice of relevant methods achieved by the end of their third undergraduate year. These attributes are well recognised by employers and greatly increase the possibilities of gainful employment in industry, agriculture, hospitals or research organisations.

BABS Honours students have a great range of opportunities, including:

- development of critical thinking skills
- extensive use of a variety of information and communication technologies
- a range of computer software for oral and written presentations
- training in online database manipulation and data analysis
- industrial research collaboration and commercialisation of science nationally and internationally

A key benefit of the Honours year is that it provides for a different type of learning experience. It proceeds at the pace of the individual student, with suitable supervisory oversight providing relevant training in an informal, relaxed atmosphere. Honours is also an opportunity for the student to undertake measured and reflective decision making about their future scientific career.
Who is eligible for Honours?

Admission to Honours is competitive, and depends on academic merit as well as the availability of an approved supervisor. Consideration of academic merit is focused on performance in third level Science subjects and overall WAM, and students must meet all requirements of their undergraduate degree (stages 1 to 3) before being considered eligible.

- Students with an average overall WAM of 65 or lower and/or an average of 65 or lower in third-level Science courses will usually not be accepted.

- Students who have achieved an average overall WAM of 65 or higher and an average of 65 or higher in third-level Science courses may be admitted if an approved supervisor is available.

A current BABS undergraduate student’s major will normally determine their Honours enrolment category, but there is some flexibility depending on the student’s interests and availability of supervisors. As of 2015, BABS Honours categories have been streamlined from 6 to 4 categories: Biotechnology, Genetics, Microbiology and Molecular & Cell Biology.

Students in dual programs who may still be completing retired majors (Biochemistry, Medical Microbiology and Immunology, Molecular Biology), will no longer be able to enrol into the corresponding category for Honours. Their category will be determined by the Honours research project selected.

UNSW Medical Science students (3991 Program) and graduates from other Australian or overseas universities are welcome to apply for the BABS Honours program. Their selected research project will determine the Honours category in which they enrol.

Components of the Honours Program

The major component of Honours is a research project carried out under the supervision of a BABS staff member or an approved external supervisor, culminating in a thesis. There are, however, other aspects of the program that make the Honours year in BABS especially attractive.

BABS Honours orientation course

Orientation for BABS Honours students comprises a series of tutorials and seminars held during the first week of the semester. Attendance is compulsory. During this time, students will be fully occupied with workshop activities and will be discouraged from attempting research work.

Research plan seminar

This is a 10-minute seminar that is held in March (August for mid-year entry). Other students and staff will attend and in consultation with your supervisor, you will develop and present a plan of your research for the year: Why? How? When? Your supervisor will provide you with feedback on your research plan after your seminar.

Literature review

The literature review is an important component of the continuous assessment for all Honours projects. It comprises a major assignment of approximately 3,000 words (not more than 4,000 words) on your project topic, selected in consultation with your project supervisor. The aims of this review are for students to become familiar with the UNSW library and all its resources, and to develop a critical approach in assessing published literature in the area relevant to your research project.
Final research seminar
Towards the end of their project, students will present a 15-20 minute seminar to the School on the outcomes of their research. This is worth 10% of the final mark.

Research project thesis
This is the major component of the Honours year and accounts for 90% of the final mark. A written practice thesis is due for lodgement in August (February for mid-year entry); the student's final report will then be submitted as a thesis in October (May for mid-year entry). The final thesis mark is a combination of the written thesis, thesis interview, and overall lab aptitude throughout the Honours year.

How are Honours students assessed?

<table>
<thead>
<tr>
<th>Activity</th>
<th>Means of Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Literature Review</td>
<td>Supervisor feedback#</td>
</tr>
<tr>
<td>Practice Thesis</td>
<td>Supervisor plus 2 academic staff</td>
</tr>
<tr>
<td>(written &amp; oral)</td>
<td></td>
</tr>
<tr>
<td>Final Seminar†</td>
<td>School academic staff will attend and grade as many seminars as possible</td>
</tr>
<tr>
<td>Final thesis‡</td>
<td>Supervisor plus 2 academic staff</td>
</tr>
<tr>
<td>Thesis interview.§</td>
<td>Supervisor plus 2 academic staff</td>
</tr>
<tr>
<td>Lab aptitude¶</td>
<td>Lab books and supervisor report</td>
</tr>
</tbody>
</table>

* The literature review (A=highest; E=lowest) and practice thesis (Satisfactory/ Unsatisfactory) receive qualitative scores, as these activities will be assessed quantitatively in the final thesis. The purpose of these two assessment tasks is to train students to write a better final thesis. Feedback will be provided for both these tasks. This qualitative assessment is not expected to contribute to the final assessment of the student.

# The student must complete the literature review even though it is not formally assessed. If the literature review is not completed the final thesis will receive 0 marks for the Introduction section.

† The final seminar will occur within parallel sessions that mimic the structure of a scientific meeting. Final seminars are attended by Honours students, supervisors and School academics.

‡ Detailed guidelines for the number of marks awarded for each section will be provided to the assessors by the Honours Convening Committee to ensure uniformity of marking for all students.

§ Students will be interviewed by their Assessment Committee to evaluate the extent of the student's knowledge and to confirm that the student is fully in possession of the contents of their thesis. Students are graded by their committee based on their interview, and includes their ability to articulate verbally the significance of their findings, an understanding of the methods they employed, an ability to answer questions, and a background understanding of the field of study.

¶ Students will be assessed based on their overall Honours year; attitude and diligence in the lab shown, initiative demonstrated, and general performance. Students will be graded based on their laboratory notebooks and a report form submitted by their supervisor.
How to apply for Honours in BABS

Honours projects and supervisors

Information on available Honours supervisors and projects can be found in this booklet or on the BABS website. A total of five potential supervisors and projects must be selected and ranked in order of preference, as each supervisor has a limited capacity to take on new students. After selecting their five choices, applicants should complete the relevant Honours application form/s (see below). Applicants will be allocated to supervisors based on academic merit and available resources. At least three choices must be from within BABS; a maximum of two choices may be external supervisors/projects.

It is essential to spend time with prospective supervisors to discuss the details of their projects before submitting your preferences. Once you have decided which supervisors you wish to contact for further discussion, email is the preferred method of contact. Please ensure that you:

(a) identify which research project you are interested in and why
(b) indicate which semester you intend on commencing Honours (Semester 1 or 2)
(c) advise your availability times for a face-to-face interview
(d) attach a copy of your CV and academic transcript

Internal Applicants

Existing UNSW students should submit a BABS Honours Application Form (end of this booklet) to the BSB Student Office, Room G27 Biological Sciences Building, together with a CV, brief list of interests and academic transcript. The application form is also available at the BSB Student Office, and online at: http://www.babs.unsw.edu.au/future_students/how-apply-honours-mphil-babs

External Applicants

Local students applying from an institution other than UNSW need to complete the BABS Honours Application Form AS WELL AS a UNSW External Student Application Form: https://www.unsw.edu.au/sites/default/files/documents/HonoursWeb1.pdf

International students need to follow the steps on the UNSW International Office ‘How to Apply’ page: http://www.international.unsw.edu.au/study/applying/ (Note that you are applying for Honours only).

Application dates

Application forms are due at the beginning of November for Semester 1 commencement, and the beginning of June for Semester 2. External student application forms are due early December for Semester 1 commencement and early May for Semester 2. Exact dates can be found on the application form at the end of this booklet.

Please note that applications for Honours will be accepted only when five supervisor and project preferences are listed on the application form

Honours inquiries

BABS Student Advisor
BSB Student Office, Room G27 Biological Sciences Building
Ph: 9385 8047
Email: BABStudent@unsw.edu.au
BABS Honours application process timeline

1. **Start Timeline**
   - August/September or earlier

2. Review available projects in the BABS Honours/Mphil Booklet or the Research Projects section of the BABS website

3. Arrange to meet with at least 5 potential supervisors
   - Rank Honours project preference list from 1 - 5

4. **Internal Applicants:**
   - Submit BABS Honours application form to the BSB Student Office (Room C27, Biological Sciences Building)

5. **External Applicants:**
   - Submit BABS Honours application form to the BSB Student Office AND
   - **Domestic students:** submit UNSW Honours application form
   - **International students:** Apply online via the UNSW International Office

6. Science Faculty assesses applicants to determine if Undergraduate Stage 1 - 3 requirements have been met

7. Applicants approved by Faculty of Science are assessed by the School to determine if WAM requirements met

8. Applicants who have met WAM requirements allocated to supervisors and projects

9. Offers/Declines sent to student email accounts

10. Mid/Late December

11. Early June to Mid/late July

12. Early June to mid-July

13. Mid July
Master of Philosophy (BABS) – Alternative to Honours

The MPhil (BABS) combines research training with a substantial coursework component. Students undertaking this masters degree will experience modern and sophisticated laboratory techniques that apply to a wide range of biotechnology and molecular biology fields.

Students are required to complete three semesters of supervised research, with the outcomes of the project reported in a thesis, which is examined. Three subjects of coursework must also be completed, one core course and two electives (see options below).

Difference between Honours and MPhil (BABS)

The entry requirements for an MPhil (BABS) are the same as for Honours, but students should consider the MPhil (BABS) as an alternative to Honours.

- An Honours Degree at UNSW comprises 3 years of undergraduate coursework with an additional year of supervised research, and qualifies for HECS.
- The MPhil is an internationally recognised research degree that sits somewhere between a BSc and a PhD. The MPhil (BABS) is designed to be completed over 3 semesters, or 1.5 years. As the MPhil (BABS) is classified as a research degree, it does not qualify for HECS.

Components of the MPhil (BABS)

Research component

Prospective students need to identify a preferred supervisor and research project from this booklet. They then need to approach the supervisor to request to be taken on as an MPhil (BABS) student.

Coursework component

Students are required to complete one core course and two electives over the three semesters of the program.

Electives

Research Techniques (BABS7180)

Electives

Within BABS:
Advanced Topics in Biotechnology and Biomolecular Sciences (BABS8010)
Environmental Biotechnology (BABS7081)
Bioinformatics Methods and Applications (BINF9010)
Relevant third year course (with permission from PG Coordinator and supervisor)

From other postgraduate programs:
Biocompatibility (BIOM9332)
Cellular and Tissue Engineering (BIOM9333)
Chemistry and Physics of Synthetic and Biological Polymers (BIOM9432)
Chromatography (CHEM7114)
Chromatography/Mass Spectrometry (CHEM7116)
Water Treatment (CVEN9856)
Advanced Food Chemistry (FOOD1697)
Food Microbiology (FOOD2627)
Nutrition (FOOD3567)
Safety Risk Management: Physical Hazards (AVIA9201)
Biomass Energy Sources (SOLA9011)
Entry requirements

Local applicants are required to have a relevant 3-year undergraduate degree with >65 (credit) average. Overseas applicants require a first class degree or a 4-year degree in a relevant discipline.

Acceptance into the MPhil (BABS) is contingent upon satisfying the usual UNSW admission/academic requirements as well as being accepted by an approved BABS supervisor.

Career options

The MPhil (BABS) program is a high level qualification that will stand by itself or qualify graduates to enter a higher degree research program. Graduates will be qualified to take up employment in government, industry, education and research organisations in areas of biopharmaceuticals and vaccines, enzyme biotransformations, food and beverage fermentation, environmental management and pollution control.
How to apply for an MPhil (BABS)

All applications for a Master of Philosophy at UNSW Australia are processed by the Graduate Research School: www.grs.unsw.edu.au

All applications for an MPhil (BABS) must be made online: https://apply.unsw.edu.au/portal/dt

On that website you will find details of all documentation that you will need to provide as part of your application, including proof of contact with the proposed supervisor (please note that contacting and negotiating with prospective supervisors is the responsibility of the applicant).

Please note it is essential that applicants have an academic supervisor in place prior to submitting an application for an MPhil (BABS)

Information on available research projects and approved supervisors is contained in this booklet and available on the BABS website. Once you have decided which supervisor/s you wish to discuss your choice with, please note that email is the preferred method of contact. Please ensure that you:

(a) identify which research project you are interested in and why
(b) indicate which semester you intend on commencing the MPhil (BABS) (Semester 1 or 2)
(c) advise your availability times for a face-to-face interview
(d) attach a copy of your CV and academic transcript

International students should also indicate that they have appropriate visa status, and that they have funding available to cover living expenses as well as UNSW Australia’s tuition fees.

Further information

The BABS website provides further information about this Degree:
http://www.babs.unsw.edu.au/future_students/future-master-philosophy-babs-students

MPhil (BABS) inquiries:

BABS Postgraduate Administration
BABS School Office, Room 229 Biological Sciences Building
Ph: 9385 2029
Email: babs-pg@unsw.edu.au
Research Projects: Environmental Microbiology Group

The members of this research group form one of the strongest gatherings of world-class microbiologists and biotechnologists in Australia, which has for decades been recognised for its internationally competitive advantage in this research area. This group addresses globally relevant research themes.

Current research areas for this group include:

- global ecosystems health
- environmental microbial evolution and genomics
- microbial ecology of Antarctic soils
- bioremediation and bacterial biofilms
- biological oceanography
- bioastronautics
- bioprospecting for drug discovery and design
Dr Brendan Burns, Senior Lecturer

Room 344, Level 3
Biological Sciences Building
Ph: 9385 3659
brendan.burns@unsw.edu.au
http://www.babs.unsw.edu.au/staff_academic/dr-brendan-burns

Research focus: Environmental microbiology (microbial diversity, adaptation, evolution, ecosystem function) and astrobiology (early life and human health)
Suitable for students who have majored in Microbiology or Biotechnology and excelled in MICR3071 and BIOT3081

Project 1: Stromatolites and the origins of life

Stromatolites represent a model for studying the origins and evolution life on our planet. They are geobiological structures composed of complex and diverse microbial communities. The study of micro-organisms associated with these formations may also be applied to the search for extra-terrestrial life, particularly with the discovery of unique bio-signatures. This project is part of research undertaken at the UNSW Australian Centre for Astrobiology and at NASA in the United States. Novel microorganisms (bacteria and archaea) are being investigated for their mechanisms of osmotolerance, cell-cell signalling, gene transfer, and other unique physiologies that allow adaptation to extreme habitats and permit the formation and persistence of these evolutionarily significant systems.

We have access to unique field sites on the coast of Western Australia (and other locations throughout the world through our collaborators), and work closely with the WA Department of Environment and Conservation to ensure these unique ecosystems are carefully monitored in the face of threats such as climate change. This research program combines biogeochemical field measurements, laboratory analytical methods, and recent advances in functional genomics. In particular, there is the opportunity to employ next-generation sequencing methods, including 454 tagged and shotgun pyrosequencing. Students will use these and other modern microbial and molecular biology techniques.

Project 2: Bioastronautics: The influence of microgravity on cellular function

Technological and scientific advances in astronautics have enabled us to explore outer space, including numerous planetary missions and construction, maintenance and use of space stations. Astronauts are exposed to a number of environmental factors; in particular, the absence of gravity. The transition from a terrestrial to a space environment has an impact on human physiology, causing adaptive or pathological changes. Understanding the effects of such microgravity (weightlessness) on human physiology will assist in the health and safety of astronauts. As life’s basic processes are conducted at the cellular level, the effect of microgravity on a variety of cell types are able to be analysed. Via collaborators at NASA, we have access to samples that have been flown aboard the last three space shuttle missions and compared to ground controls.

A comparative differential expression profile can be generated using proteomic and genomic approaches. In addition, morphological adaptations to microgravity conditions can be examined using scanning electron microscopy. We can then further examine specific proteins that link to particular functional pathways in a cell altered under microgravity conditions.

We also aim to determine if microgravity alters the wound healing potential, cell cycle arrest and cell differentiation status of post-flight cultures compared to ground controls. Once these changes are identified, they can be correlated to observed health problems encountered in microgravity conditions. Depending on ability, students in this program may get the opportunity to participate in NASA’s prestigious Summer Academy Program in the US.
To learn more about the research focus, please contact Professor Rick Cavicchioli.

*Professor Rick Cavicchioli*

Room 309, Level 3  
Biological Sciences Building  
Ph: 9385 3516  
r.cavicchioli@unsw.edu.au  
https://research.unsw.edu.au/people/professor-ricardo-cavicchioli

**Research focus:** Environmental microbial genomics, extremophiles and global ecosystems health

Suitable for students who have majored in Microbiology, Molecular Biology, Bioinformatics, Genetics, Biochemistry or Biotechnology

If you are interested in Antarctic research – research relevant to the environment and health of the planet – then read on.

The group studies Antarctic microbes and the research involves both lab work, and field work in Antarctica and on the high seas of the Southern Ocean. Research is orientated at discovering which microbes live in Antarctica and how they grow and survive.

Your Antarctic research in the group could address:

- what types of microbes are present, and how diverse and unique are they?
- how do microbes adapt, and what enables them to function effectively in the cold?
- what processes do the microbes perform, and how does this affect ecosystem function?
- what interactions occur within communities, and how does this affect ecosystem function?
- how does gene exchange influence speciation, and what enables dominance to arise?
- how did the organisms evolve from a marine environment to the various lake environments?
- how will the microbes and the ecosystems they control be affected by human activities including climate change?
- how can microbes and their cellular products (e.g. enzymes) be used for biotechnological applications?

Honours/Masters and undergraduate projects can be based in microbial ecology, microbial physiology, microbial genetics, genomics/proteomics, metagenomics/metaproteomics, microbial evolution, bioinformatics, biochemistry/biophysics or enzymology.

Specific opportunities exist to work alongside Dr Tim Williams, who has unique expertise in meta/proteomics and microbial physiology/ecology, and Dr Susanne Erdmann who is an EMBO Fellow studying viruses and virus defence systems of Antarctic haloarchaea.

All students will be linked to established members of the group, and projects will aligned to those of existing PhD students and research staff.

**Selected articles:**

Dr Suhelen Egan, ARC Future Fellow

Room 303, Level 3
Biological Sciences Building
Ph: 9385 8569
s.egan@unsw.edu.au
http://www.babs.unsw.edu.au/staff_research/dr-suhelen-egan

**Research focus:** Microbial ecology and interactions; antimicrobial discovery
Suitable for students who have majored in Microbiology, Biotechnology or Molecular Biology

**Project 1: Discovery of novel bioactive compounds from marine host-associated bacteria**

The bacterial symbionts of marine eukaryotes (seaweeds, sponges, corals etc.) are proving to be an excellent, yet understudied, source of new metabolites that hold potential as next generation antibiotics. This project will use both traditional culturing and modern culture-independent (functional metagenomics) methods to discover new biologically active metabolites from bacteria and the genes involved in their production. Students will have the opportunity to learn a range of skills including antimicrobial bioassays (against nematode, fungal and/or bacterial targets), molecular biology (e.g. PCR, DNA sequencing, cloning) and natural product chemistry (e.g. chemical extraction and separation technologies) methods. For further reading see Penesyan et al, 2012, Marine Drugs, 11:40; or Egan et al, 2008, Current Opinion in Microbiology, 11:219.

**Project 2: Deciphering the mechanism of microbial disease progression in marine habitat-forming macroalgae**

It is proposed that with increases in anthropogenic stressors of coastal systems (pollution/climate change) there comes an increase in the prevalence of disease caused by opportunistic pathogens. Here we are using genomic and gene expression analysis together with site-directed mutagenesis to identify and characterise potential virulence mechanisms in model macroalgal disease systems. We also perform environmental surveys to assessing prevalence of pathogens and determine how the natural microbial community shifts under disease conditions. This project is in collaboration with A/Prof. Torsten Thomas.
For further reading see Egan et al, 2014, Environmental Microbiology, 16: 925.

**Project 3: The ecological role of antibiotic-producing bacteria**

Antibiotics from natural sources are an essential part of modern medicine, however their function in the environment is poorly understood. In this project we perform manipulation experiments (both at UNSW and at Sydney Institute for Marine Science (SIMS)) combined with a range of -omic technologies (e.g. deep sequencing of phylogenetic marker genes, genomics, transcriptomics etc) to define how antibiotic-producing bacteria from marine macroalgae determine ecological interactions. This project addresses the fundamental question of the impact of antibiotics in natural systems and the role of antibiotic-producing bacteria in safeguarding important habitat-forming macroalgae against environmental stress. For further reading see Egan et al, 2013, FEMS Microbiology Reviews, 37:462.
Dr Belinda Ferrari, Senior Lecturer

Room s132 Lab s118, Level 1
Samuels Building
Ph: 9385 2032
b.ferrari@unsw.edu.au
http://www.babs.unsw.edu.au/staff_academic/dr-belinda-ferrari

Research focus: Application of single-cell technologies to investigate microbial ecology of Antarctic and sub-Antarctic soils
Suitable for students who have majored in Microbiology or Biotechnology and excelled in MICR3071, BABS3021 or BIOT3081

Project 1: Residual toxicity of petroleum hydrocarbons in Antarctic and sub-Antarctic soils
Fuel contamination poses significant environmental risk to Antarctic and sub-Antarctic regions. Key to cleaning up contaminated sites in cold regions is an understanding of how petroleum products degrade over time to less toxic residual products. This study will evaluate the toxicity of fuels on microbes as they degrade with a focus on areas currently undergoing soil remediation at Macquarie Island and Casey Station. This project will form part of a larger project aimed at identifying safe levels of contamination where no environmental risk remains, and will provide rigorous, scientifically based targets for cleaning up contaminated sites in Antarctic and sub-Antarctic regions.

Project 2: Microbial ecology of frost boils on Browning Peninsula, Antarctica
Browning Peninsula is a pristine site close to Casey Station in eastern Antarctica. It has an ice-free and barren landscape consisting of permafrost soils separated by frost boils. These frost boils, or polygons, are between 2-10 metres in diameter (see diagram) and we have recently found that they have a strong influence on the local bacterial community. In this project we will investigate what environmental factors influence the extant microbial diversity, and at the same time gain insight into major functions being carried out by microbes in these poor nutrient soils. As the majority of bacteria and fungi have not yet been cultured in the laboratory, we hope to uncover a unique system for further exploration.

Project 3: Characterisation of the newly named bacterial division: Saccharibacteria
Saccharibacteria is a new Division of bacteria that are yet to be cultured in the laboratory. It is a highly ubiquitous phylum with 16S rRNA gene sequences reported in soils, sediments, wastewater and animals, as well as a host of clinical environments and the association with several human diseases. In this project we will use novel cultivation methods and next generation sequencing technologies to understand what bacterial species are commonly associated with Saccharibacteria in soil and sludge. In doing so, we hope to uncover a syntrophic relationship between the bacterial species we suspect are in close association with Saccharibacteria that we can exploit for successful cultivation of a member of this Division in the laboratory.
Numerous archaeal genomes have been sequenced in recent years, some of which include plasmids. These elements range in size from small and phenotypically cryptic to large megaplasmids, at times classified as minichromosomes as they carry genes essential to their host. Many plasmids carry genes that ensure their inheritance by daughter cells at cell division, which is important for the survival of the plasmid within a population of cells in the absence of selection. One such method is plasmid partitioning – the movement of plasmids to the poles of the cell prior to cell division. Partitioning systems typically consist of a cis-acting centromere-like DNA site and two trans-acting proteins, one ATPase protein and one that binds with the centromere-like site.

**Project: Investigation of putative plasmid partitioning systems in haloarchaea**

We have identified and cloned some putative partitioning systems from haloarchaea into plasmid vectors, and are currently conducting assays to establish whether the presence of these systems assists in retention of the vector within the cell population. This project will involve conducting site-directed mutagenesis to create non-functional partitioning systems, and performing further plasmid maintenance assays to compare the segregational stability of wild-type plasmids in a population compared with those carrying a non-functional partitioning system. This will demonstrate for the first time the plasmid maintenance function of an archaeal plasmid partitioning system.

Further work may include overexpression of the partitioning proteins for further studies and the construction of parA/parB–GFP fusions for later microscopy analysis. This research will contribute to our understanding of microbial evolution and assist in the creation of more stable vector systems in archaea.
Project 1: Bioremediation of contaminated groundwater
The global pandemic of cancers and degenerative diseases is increasingly being linked to soil, water and air pollution. Sydney, like all major cities around the world, is home to sites polluted with chlorinated compounds (Botany Bay, Sydney Harbour, Homebush Bay). We have developed three bacterial cultures for bioaugmentation of polluted groundwater, and diagnostic monitoring tools for assessing microbial activity in groundwater. In collaboration with our home-grown biotech company Micronovo Pty Ltd and our extensive network of industry partners, we are further developing and testing cutting-edge tools for the Australian remediation market.

Project 2: Biogas production
Biogas production is key to meeting the energy needs of Australians into the future. Biogas (methane) can be generated by microbes from renewable resources such as food waste and algal feed-stocks or from non-renewable resources such as coal. Biogenic methane production is a complex process carried out by bacteria and archaea involving interspecies electron transfer. The Manefield group has recently discovered that biogenic methane production can be greatly enhanced in the presence of organic semiconductors that facilitate interspecies electron transfer. This discovery has recently been patented as we continue to explore the mechanism and broad utility of the technology.

Project 3: Wastewater treatment
Wastewater treatment through application of activated sludge processes is the most successful wastewater treatment technology globally. Despite this, relatively little is known about the process of activated sludge floc formation. The Manefield group explores the role of colonisation of particulate organic matter in the life cycle of activated sludge, incorporating the influence of bacterial intercellular signalling (quorum sensing) and redox active metabolites.
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Research focus: Protein biotechnology
Suitable for students who have majored in Biotechnology, Biochemistry or Microbiology

Project 1: Lipase-mediated production of biodiesel using coconut oil

Lipase-mediated biodiesel production is becoming industrially accepted because of its capacity to handle lower-quality feed oils and produce a cleaner fuel product for downstream processing. This project will aim to produce a recombinant lipase for biodiesel production that has the capacity to be immobilised onto a nanoparticle surface for re-use. The enzyme will be evaluated against commercial enzymes for its capacity to produce biodiesels with a range of starting substrates.

Project 2: Recombinant reductive dehalogenases

Reductive dehalogenases are enzymes involved in the reductive dechlorination of polychlorinated hydrocarbons, such as hexachlorobenzene. Microbial processes to degrade hexachlorobenzene and other chlorinated hydrocarbons have been described, however the anaerobic processes in particular are relatively slow, because of low cell densities, slow growth rates and low substrate concentrations. This project will aim to identify a candidate reductive dehalogenase, followed by generating and evaluating a recombinant version of the enzyme.

Project 3: Microorganism Resistance to Antimicrobial Nanosilver: Stimulation of Intracellular Reactive Oxygen Species (ROS) (with Dr. Cindy Gunawan, School of Chemical Engineering)

Antimicrobial nanosilver, one of the earliest and most developed products of nanotechnology has found extensive applications in consumer products, ranging from wound dressings and antibacterial textiles to water and air purification systems – and even some baby products. Nanosilver has proven efficacy against bacteria, yeast, fungi, algae and viruses. Recently, we found that the antimicrobial activity of nanosilver is non-universal and that some bacteria appear to adapt quite rapidly to its presence (Gunawan et al., 2013; featured in The Age and Science Alert).

The project seeks to elucidate the origins and routes of the cellular ROS-mediated nanosilver toxicity (Gunawan et al., 2009; 2013), identifying the nature of ROS stimulation by the leached soluble silver and the undissolved silver particulates. The project will involve exposure of laboratory strain Bacillus subtilis to the overall presence of nanosilver (leached species and undissolved particulates), compared to that of exposed to the leached species-only. The generated intracellular ROS from the two systems will be detected via live cell ROS staining, while also monitoring their toxic impacts. The project is carried out in a collaboration between BABS and the UNSW School of Chemical Engineering.
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Research focus: Investigations into the diversity of life for the application of drug discovery and design
Suitable for students who have majored in Microbiology, Medical Microbiology & Immunology, Biotechnology or Molecular Biology

Our research looks at merging the potential of microbial evolution and chemical diversity for applications in environmental health and drug discovery. The work is divided into several programs linked by the underlying theory that diversity of life on Earth is the basis for the evolution of natural products and other biotechnologies. Measurement of biological diversity and detection of previously unknown organisms is essential to the process of drug discovery and successive drug design. Our projects expose students to the latest in cutting-edge molecular, cellular and analytical technologies that are prerequisites for employment or future research in the biomedical and environmental sciences.

Project 1: Genetics of marine toxin biosynthesis
A number of sophisticated but poorly understood mechanisms are involved in the production of microbial neurotoxins. These alkaloids are responsible for amnesic or paralytic shellfish poisoning, and are synthesised via a complicated multi-enzyme pathway. The isolation and characterisation of the genes involved in the synthesis of these compounds from microbes is the first step in understanding the environmental signals that trigger toxin production and how we can use these enzymes to produce novel neuroactive drugs. This project includes study of the blue-ringed octopus, marine sponges and marine algae.

Project 2: Discovery and molecular engineering of novel antibiotics
Using natural products as a blueprint, we are able to construct new pharmaceuticals with altered activity and specificity. In particular, the pathways for non-ribosomal peptides are being used as the basis for potential combinatorial biosynthesis, and the range of possible new drugs is practically limitless. We are applying this proprietary technology to the design and production of new antibiotics, immunosuppressants and antiviral compounds. This work is also closely coupled to the search for novel microorganisms and their natural products using Australian and Chinese traditional medicines as a defined basis for bioactivity. Other microbes and their natural products, as well as the mechanism for their production, are being studied from a range of the Earth's habitats, including volcanoes, Antarctica, hypersaline bays and stromatolites, uranium mines and mineral springs.

Project 3: Prokaryote-eukaryote symbiosis
This research involves studying symbiosis in a variety of systems, including farming crops/microorganisms. The objective is to determine the usefulness of some cyanobacteria and mycorrhizal fungi in assisting crops to tolerate saline conditions. Research into bioamelioration of soil salinity in Australia could lead to increases in the areas of cropping land previously lost due to poor management practices. This program of research will involve a range of microbial culturing and genetic screening techniques for the selection of stable and advantageous symbiotic relationships. An extension of this work (combined with Project 1) is the evolution of algal metabolism, including photosynthesis and toxin production.

Honours students will be given mentoring in experimental research and scientific communication. Travel to attend national scientific conferences will be encouraged and supported. Students in these projects may also qualify to be part of the Australian Centre for Astrobiology. Further information can be obtained from Professor Neilan.
The interaction of microorganisms with their environment and with higher organisms is central to many biological topics, including environmental health, the evolution of complex biological systems and the genetic diversity of life. We explore the microbial world with high-throughput DNA sequencing techniques and we use bioinformatics to make predictions about functional and ecological properties of microbial communities. Ultimately, we perform directed molecular experiments to support our predictions and establish a clear link between microbial function, diversity and evolution. The laboratory is currently focusing on four main areas, for which many exciting Honours projects are available:

**Project 1: Bacteria-sponge symbiosis**

Marine sponges survive by eating bacteria from the seawater, but at the same time they also harbour bacterial symbionts that they don’t digest. We have recently discovered that the genomes of bacterial symbionts of sponges encode for proteins that are similar to eukaryotic proteins (Fan et al. *PNAS USA* 2012). These bacterial proteins appear to control phagocytosis and cytoskeletal formation in eukaryotic cells (Nguyen et al. *Molecular Ecology* 2013; picture on left shows how gfp-labelled bacteria accumulate in the food vacuoles of eukaryotic cells). We hypothesise that bacterial symbionts use these proteins to control their symbiosis with the sponge host and test this with a range of evolutionary, microscopic and molecular approaches.

**Project 2: Effect of charcoal on microbial processes in agricultural soil**

Charcoal is an emerging additive to agricultural soil and several studies have shown that it can increase plant yield and reduce greenhouse gas emission from soil. How charcoal exerts its positive effect is largely unknown, but there is evidence that microorganisms have developed specific interactions with charcoal (picture on the left shows bacteria on the surface of charcoal). In this project, we use high-throughput DNA sequencing and advanced visualisation techniques to characterise microbial interactions on charcoal and determine how they change nutrient cycling and utilisation in soil. This project is undertaken with a commercial partner and its outcomes will help to develop charcoal as a new tool for sustainable and improved agriculture.

**Project 3: Microbial disease of marine seaweeds**

Marine seaweeds suffer from microbial infections and diseases in much the same way as humans do. Importantly, in recent years it has been recognised that microbial diseases of seaweeds increase with climate change and environmental pollution. We have now identified several bacterial pathogens that can cause bleaching diseases in red and brown seaweeds (Egan et al. *Enviro. Microbiol.* 2014; picture on the left shows bacteria-induced bleaching of a red alga). To better understand and potentially manage these diseases, we perform environmental surveys of pathogens as well as molecular analysis of virulence mechanisms and correlate our findings with environmental parameters. This project is performed in collaboration with Dr Suhelen Egan.

**Project 4: Evolution of surface-associated communities**

Microorganisms on surfaces often live in high-cell densities and are embedded in a biofilm matrix (picture on left shows a biofilm on a seaweed surface). We have recently studied the genetic composition of such biofilm communities and found that they possess a high number of mobile genetic elements (Burke et al. *PNAS USA* 2011) and that they can evolve very rapidly (McElroy et al. *PNAS USA* 2014). In this project we use high-throughput DNA sequencing and bioinformatics to described the evolutionary changes and dynamics of laboratory-based and natural microbial communities. This fundamental project provides a new insight into the evolution of bacteria and how this generates the enormous genetic diversity that we see in the microbial world.
Research Projects: Infectious Disease Group

The BABS Infectious Disease research group is committed to a broad range of research and teaching activities in Sydney and around the world. This group's research focuses on vital health issues.

Current research areas for this group include:

- tracking the evolution of pandemic norovirus responsible for acute gastroenteritis
- mathematical, computational and statistical models of infectious disease evolution
- molecular evolution of bacterial pathogens
- understanding how the hepatitis C virus evades host immune responses
- investigating the role of mucus-associated bacteria in gastrointestinal disease
- whether viruses such as human papillomavirus and Epstein-Barr virus are implicated in human cancer
Infectious diseases caused by pathogenic bacteria are a major threat to human health. Our group takes a multi-disciplinary approach to study pathogenic bacteria. We use "omics" (genomics, transcriptomics and proteomics) approaches to address how pathogens arise and cause disease, how they evolve and adapt – and how to identify these pathogens.

Projects on *Bordetella pertussis*

Pertussis, commonly known as whooping cough, is an acute respiratory disease caused by *B. pertussis*. Despite widespread vaccination, pertussis remains a public health burden. Australia has just experienced a prolonged pertussis epidemic with nearly 40,000 cases at its peak in 2011.

**Project 1: Proteomics of epidemic B. pertussis**

The resurgence of pertussis has been partly attributed to the adaptation of *B. pertussis*, but little is known of the proteomic changes of the epidemic *B. pertussis* strains. The aim of this project is to elucidate key changes at the proteomic levels that may have contributed to the adaptation of the epidemic strains circulating in Australia. The project involves western blot, proteomics and bioinformatics analysis.

**Project 2: Development of an internationally standardised typing scheme for B. pertussis**

There are over 500 *B. pertussis* genomes publicly available, including more than 120 recently circulating *B. pertussis* isolates. The genome data have been extracted to reveal genome-wide SNPs, which can be used to provide the best resolution to genotype *B. pertussis* isolates. The aim of this study is to establish a minimum set of SNPs for molecular epidemiology of global *B. pertussis* as an internationally standardised molecular typing scheme. The project involves genome analysis, SNP typing and bioinformatics analysis.

Projects on *Salmonella enterica* serovar Typhimurium

*S. Typhimurium* represents up to 50% of human and 20-25% of bovine and chicken isolates in Australia. Current epidemiology of *S. Typhimurium* is largely based on phage typing. There are 209 definitive phage types (DTs). DT108/DT170 has been increasing over the years, and became the most frequent phage type in 2004.

**Project 1: Genotype variation and molecular typing of S. Typhimurium epidemic phage type DT108/DT170**

Currently, a method of choice in Australia for epidemiological typing of *S. Typhimurium* is molecular variable number of tandem repeats (MLVA), and this has been standardised across public health laboratories nationally. MLVA has been very useful for investigating outbreaks. However, 80% of DT108/DT170 strains isolated from unrelated cases in NSW belonged to the five most frequent phage types which can be misleading, particularly during outbreak investigation. Thus, better molecular markers are required to differentiate between these DT108/DT170 isolates. We aim to use genome data that are more discriminatory than MLVA for outbreak detection and long-term epidemiology to develop a molecular typing system. The project involves genome sequencing, SNP typing, and bioinformatics analysis.

**Recent publications**

- Genomic diversity and adaptation of *Salmonella enterica* serovar Typhimurium from analysis of six genomes of different phage types. *BMC Genomics*. 2013 14:718.
Our research focuses on the role of microorganisms in the etiology of gastrointestinal disease. We seek to understand the importance of the gastric microbiota, including the pathogen *Helicobacter pylori*, intestinal microbiota and host genetic polymorphisms in Crohn's Disease (CD) and ulcerative colitis (UC), both forms of Inflammatory Bowel Disease (IBD). A further research area is the role of *Helicobacter pylori* and host genetic polymorphisms in genes associated with the immune response and gastric cancer development. A range of cutting-edge technologies, including high-throughput sequencing, real-time PCR, nuclear magnetic resonance, mass spectrometry, proteomics, electron microscopy, confocal microscopy as well as more basic techniques such as cell culture, ELISA, Western blotting PCR and 2D gel electrophoresis are employed in the projects.

**Projects on IBD:** IBD is a chronic relapsing idiopathic inflammatory disease of the gastrointestinal tract, whose cause remains unclear. It is hypothesised that an initiator, believed to be either gastrointestinal microorganisms or their by-products, in association with a disruption of the gastrointestinal epithelium, stimulates and subsequently drives a dysregulated immune response in genetically predisposed individuals. Using high-throughput sequencing we have investigated the importance of dysbiosis (change in the balance) of intestinal microbiota in IBD by comparing newly diagnosed patients with controls. This has identified specific bacterial groups that appear to be associated with the initiation of inflammation in children with newly diagnosed CD. We are also examining the role of a number of emergent pathogens, including Campylobacter species in gastroenteritis and IBD and have fully sequenced the genomes of 7 *C. concisus* strains. This identified major differences in the genetic content of strains isolated from chronic disease compared with acute gastroenteritis and healthy controls. Importantly, we detected a plasmid to be present in chronic strains but not in acute gastroenteritis strains or in a healthy control, suggesting that this plasmid may be responsible for the heterogeneity in the invasive potential of *C. concisus*.

- **Project 1:** To identify emerging Campylobacter species in faecal samples from patients with gastroenteritis using PCR, RT-PCR and culture and to assess the presence of virulence factors associated with disease.
- **Project 2:** To determine the effect of environmental factors on strains of Campylobacter species, including *Campylobacter concisus* in patients with different gastrointestinal disease outcomes.
- **Project 3:** To determine the effect of specific mutations in *C. concisus* virulence factors on the ability of *C. concisus* to attach to and invade intestinal cells.

**Projects on Helicobacter pylori:** Helicobacter *pylori* has been causally linked to the development of gastritis, peptic ulcer disease (PUD) and gastric cancer (GC). Although 50% of the world’s population is infected with *H. pylori*, only a small percentage develops PUD (10-15%), GC (1-3%) and B cell MALT lymphoma (<1%). These outcomes suggest that factors other than bacterial infection (environmental risk and host genetic susceptibility) may contribute to more serious disease outcomes. We are interested in the role of host genetic polymorphisms in genes involved in cell signalling pathways, including Toll-like receptors.

- **Project 4:** To investigate the association between genetic polymorphisms in genes encoding Toll-like receptors and gastric cancer.

**Project 5:** To determine the importance of a range of novel *H. pylori* virulence factors in the outcome of *H. pylori*-related disease in subjects from Malaysia and Singapore.

**References:**
We are interested in understanding evolution in host-pathogen and other biological systems by developing mathematical models and statistical methods for analysing data. These projects would suit enthusiastic biology students with some experience in computer programming and an interest in developing skills in bioinformatics or mathematical biology, or alternatively, students with a background in mathematics, physics, statistics or computer science, and an interest in evolutionary biology or infectious diseases.

**Project 1: Molecular evolution of viruses**

Many viruses are known to mutate at a very fast rate of around 0.5 to 1 mutations per genome per replication. This fascinating observation has important implications for the spread and control of viral diseases. Why are these rates so high? It is sometimes argued that high mutation rates are selected due to the challenge presented by the fast-changing environment of the virus, in particular, the immune response of hosts. Others have questioned this argument, suggest instead that there is a biochemical trade-off between replication efficiency and accuracy. Since there is strong selection for viruses to replicate fast, their accuracy must be low and their mutation rates must therefore be high. This project aims to understand the process of viral mutation from an evolutionary perspective using mathematical and computational models.


**Project 2: Modelling the dynamics of drug-resistant strains of bacteria**

The evolution of antibiotic resistance poses a challenge to efforts to control bacterial infections in human and other populations. The emergence of multiple drug-resistant strains of bacteria makes the situation worse. Some strains of *Mycobacterium tuberculosis*, the cause of tuberculosis, are extensively drug-resistant (XDR-TB); they are resistant to two of the front-line drugs and also to one or more of the second-line drugs. The epidemiological consequences of XDR-TB and other multi-drug-resistant bacteria are largely unknown. Although drug-resistant bacteria outcompete sensitive bacteria in the presence of the antibiotics in question, they are also believed to bear a fitness cost. This fitness cost may be reduced through compensatory mutations. In this project, you will mathematically model the population level outcomes of the evolution of multiple drug resistance. The project may also involve developing computer simulation models.

References:
In collaboration with Emeritus Professor Jim Lawson from the Faculty of Medicine, my lab has established an impressive bank of cancer and normal breast and prostate specimens. We have demonstrated the presence of three viruses, HPV, MMTV and EBV, in Australian breast and prostate cancer specimens. Our results indicate that HPV, perhaps in collaboration with EBV, has a causal role in initiating carcinogenesis in these tissues, in a similar way to cervical cancer and head and neck tumours. We have also identified MMTV in human breast cancer, but not normal breast tissue, indicating that MMTV may also have a role in human breast cancer.

**Project 1 & 2: Examining the role of viruses in breast and prostate cancer**

The projects involve screening clinical samples (fixed and fresh/frozen) and cancer cell lines for the presence of viruses using various protein and molecular biology techniques, including immunohistochemistry, DNA purification, PCR and in situ PCR.

**References:**

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Research focus: Molecular virology
Suitable for students who have majored in Medical Microbiology & Immunology and have excelled in MICR3061

The Molecular Microbiology Laboratory (Lab 263) is located in state-of-the-art facilities. Research in this multi-disciplined group encompasses molecular virology, antiviral drug discovery, viral evolution and paleovirology.

Project 1: Norovirus replication and epidemiology

Norovirus is the major cause of outbreak gastroenteritis worldwide and causes around 220,000 deaths each year. Major pandemics of norovirus gastroenteritis occur every ~3 years and six pandemics have occurred since 1996. These pandemics are associated with novel noroviruses from a single genotype (GII.4) which escape herd immunity though both antigenic drift and shift. Our group is part of international and national networks that trace and track pandemic noroviruses globally, and we first identified and characterised 2 of the 6 pandemic viruses; Hunter 2004 and Sydney 2012. We have developed a number of norovirus molecular detection tools over the last few years for epidemiological studies. The aim of this project is to conduct a detailed molecular epidemiological and evolutionary analysis of Australian noroviruses. The project will determine if outbreaks are associated with the emergence of novel virus variants or recombinant (hybrid) viruses.

Project 2: Antiviral Research: Development of small compound viral polymerase inhibitors

In Australia 250,000 people are infected with Hepatitis C virus (HCV) and 10,000 new cases are reported each year. The majority (~70%) of infections become chronic and can lead to liver failure, liver cancer and death. In the field of virology, there is an extremely active hunt for antiviral agents to treat and prevent HCV infections. In fact, there is a revolution in the HCV field with new antiviral therapies becoming available that can cure 95% of infected patients. HCV and norovirus both have positive-sense RNA genomes that replicate in the cytoplasm of the infected cell via minus-strand RNA intermediates. One target for drug development is the viral RNA-dependent RNA polymerase (RdRp) because of its key role in replication and the lack of a homologous enzyme in humans. Using our established methodology we have produced highly purified, soluble and active recombinant RdRps from a range of HCV and norovirus genotypes and strains, using Escherichia coli expression systems. Through our previous antiviral work using high throughput screening we have identified two small antiviral polymerase inhibitors to HCV and four for norovirus. The aim of the antiviral program is to further characterise these six inhibitors for their range of antiviral activity and to determine their binding pocket on the viral polymerase. Their ability to inhibit viruses in cell culture will also be assessed.

Project 3: Paleovirology

The study of ancient viruses has been termed ‘paleovirology’. The aim of this project is to resurrect ancient viruses, or “zombie viruses” that could be used as biocontrol agents for the control of insects that carry human pathogens such as Dengue virus and Western Nile virus. The genomes of animals and insects contain traces of past viral infections through the integration of viral genetic material into the host genome, termed ‘endogenous viral elements’ (EVEs). These viral fossils can be used to look at viruses that existed millions of years ago. Around 1% of the human genome is comprised of EVEs, the vast majority are retroviruses that naturally insert their genomes into the host genome as part of their life cycle. For other viruses, germ line integration is extremely rare, but has been documented in many organisms. The most surprising viral fossils originate from RNA viruses. The genome of the Aedes mosquito contains numerous sequences exhibiting similarity to viruses of the Flaviviridae family, which comprise RNA viruses. Using the A. aegyptii genome we have identified 58 such fragments and pieced them back together to create nearly the entire genome of an extinct virus. A second newer and more intact partial flaviviral genome has been identified on a single EVE in the A. albopictus genome. This mosquito has not been sequenced, but we have the A. albopictus cell line C6/36. The aim is to determine if we can find the remaining portion of this ancient flavivirus within the DNA of its host. Given the full genome, reverse genetics can generate RNA that is capable of infecting cells, resulting in the production of viral particles.
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Research focus: Role of oral and intestinal bacteria in chronic inflammatory diseases and cancer
Suitable for students who have majored in Medical Microbiology & Immunology or Microbiology

Research areas include Inflammatory Bowel Disease (IBD), mucus-associated bacteria, *Campylobacter* species, enterohepatic *Helicobacter* species, chronic inflammation and cancer, mucosal immunology, and immune regulatory effects of probiotics and other natural products.

**Project 1: The impact of the zonula occludens toxin produced by *Campylobacter concisus* on the gut mucosal immune system and the intestinal barrier**

*Campylobacter concisus* is an oral bacterium that is associated with inflammatory Bowel Disease and diarrheal disease. We previously found that some strains of *C. concisus* have acquired the zonula occludens toxin gene from a bacterial phage. We are currently examining the effects of the *C. concisus* zonula occludens toxin on the gut immune system and intestinal epithelial barrier function. Two Honours projects are available under this research topic. Techniques used in these projects include cell culture, confocal microscopy, flow cytometry, western-blotting, protein sequencing, ELISA, small animal handling and bacterial cultivation.

**Project 2: The role of *Campylobacter* species in demyelinating diseases**

We are currently investigating the role of a number of virulence factors produced by *Campylobacter* species in initiating demyelinating diseases including multiple sclerosis (MS) and chronic inflammatory demyelinating polyneuropathy (CIDP). Both diseases are chronic progressive neurological disorders caused by the immune system attacking the myelin sheath of the nerve. This project is to examine the presence of specific antibodies and T cells to a number of *Campylobacter* proteins in patients with MS and CIDP. Techniques used in this project include cell culture, ELISA, western-blotting and immune staining.

**Project 3: *Campylobacter concisus* and *Campylobacter ureolyticus* prophage**

We previously identified *C. concisus* prophage CON-phi2, which contains a number of potential virulence genes. More recently, we found that a prophage in *Campylobacter ureolyticus* has a structure that is similar to CON-phi2. Both *C. concisus* and *C. ureolyticus* have previously been shown to be associated with inflammatory bowel disease and diarrheal disease. This project investigates the prophage genetic diversities, the pathogenic role of prophage proteins and phage induction. Techniques used in this project include bacterial cultivation, cell culture, ELISA, western-blotting, confocal microscopy and electron microscopy.
Research Projects: Molecular Medicine Group

Molecular Medicine within BABS has a unique strength in combining fundamental biological and biomolecular sciences with a strong applied biotechnology and medical focus. The School facilitates collaborative research efforts across discipline boundaries for fundamental discoveries, generation of commercial opportunities and clinical research. Molecular medicine represents a significant proportion of research output from BABS within the medical area.

Specific research themes include:

- cancer chemotherapeutic agents
- role of transcription factors in development and disease
- immunological bioinformatics
- neurobiology and neuroscience
- novel chemotherapeutics for the treatment of some cancers
- protein biotechnology
- non-coding RNAs in controlling gene expression
- biomaterials for wound repair and regenerative medicine
Project: Antioxidants – gamma-glutamylcysteine

GGC is the immediate precursor to the tripeptide glutathione, which is considered the "master" antioxidant for all aerobic organisms. Many human disorders and diseases such as Alzheimer’s, Parkinson’s – and ageing itself – are related to the body’s inability to maintain sufficient levels of glutathione within its cells.

It is widely thought in the scientific community that any treatment that can replenish glutathione levels in cells would offer broad therapeutic benefits. For many instances of chronic glutathione depletion, the problem lies with damaged regulatory control of the enzyme responsible for synthesising GGC (GGC synthetase) from glutamate and cysteine. That is, GGC becomes a limiting substrate for the final synthesis reaction catalysed by glutathione synthetase (condenses GGC with glycine to form glutathione).

There are only a few natural sources of GGC, with garlic, egg white and the whey fraction of milk having the highest amounts. High purity GGC has not been commercially available in sufficient quantities for widespread testing of its therapeutic potential. In 2006, my research group developed a biocatalytic process for GGC manufacture which we patent protected and licensed. The company is now manufacturing and commencing to sell GGC for cosmetic and dietary supplement applications in the US, where GGC has "GRAS" (generally regarded as safe) status. As the next step towards demonstrating therapeutic benefits, it is now planned to undertake human clinical bioavailability trials here at UNSW, which will hopefully confirm that orally administered GGC can increase glutathione levels in white blood cells.

This project will explore the ability for the thiol antioxidant, gamma glutamylcysteine (GGC) to protect human cell lines against oxidative insults. The objective of the project is to continue our exploration of the therapeutic potential of GGC using human cell line models for glutathione depletion. Providing the data/results are suitably complete, it is intended to publish any significant findings.
Project: Investigations of the functions of murine isotopes using engineered monoclonal antibodies

We recently described a new model of human antibody isotype function that emphasises the importance of the timing of class switching. The development of the model was based on an analysis of somatic point mutations in VDJ rearrangements that were associated with different constant region genes.

This analysis exploits the fact that different levels of mutations in VDJ genes of different isotypes can be used to infer the timing of class switching. It also allows the inference of the relative antigen-binding affinities of different isotypes. We are now exploring antibody isotypes in the mouse, for it is essential to determine whether or not antibody isotypes in this important model organism serve corresponding functions to the human isotypes.

The C57BL/6 strain of mouse, which is very widely used in medical research, lacks the IgG2a isotype. Instead it produces the variant IgG2c isotype. IgG2a and IgG2c are assumed to have the same functions, but this has not been formally demonstrated. We have observed dramatic differences in the mean levels of mutation in VDJ genes associated with the two isotypes, and this suggests that their functions are different. In order to clarify their function, we need to produce monoclonal antibodies of each isotype, with identical antigen specificity.

This honours project will involve the engineering of monoclonal antibodies. A mouse IgG2a expression vector will be used to generate antibodies of known specificity, using VDJ genes from an IgG1 antibody. The vector will then be engineered to permit the generation of IgG2c antibodies. Vectors will be transfected into CHO or 293 cells and expressed transiently in serum-free medium. The binding properties of purified mAbs will then be determined. The project is particularly suited to a student with strong interests in biotechnology.
For nearly 25 years, I’ve worked in and closely with the poultry industry and am currently collaborating with the largest poultry meat producer in Australia. Research has ranged from the study of fundamental aspects of bacteria of human foodborne disease/public health significance, notably *Salmonella* and *Campylobacter*, through to ecologically informed strategies for management/intervention in primary production and processing, to the development and evaluation of diagnostics for detection and enumeration of these pathogens. This has also led to development of collaborative relationships with a range of commercial diagnostics companies, enabling development and evaluation of diagnostics for other foodborne pathogens.

We have also established a program of research around development of vaccines against human and veterinary pathogens and, downstream, the use of IgY for diagnostics and therapeutics.

Over time, my research students have also worked on an extensive range of foodborne pathogens, including *Bacillus cereus*, *Clostridium botulinum*, *Cronobacter*, *Escherichia coli*, *Listeria* spp., *Staphylococcus aureus*, and *Vibrio* spp.

The following research project is indicative, but other projects may be negotiated, based on the interests of students and/or industry partners.

**Project: The biology and ecology of poultry-associated enteropathogens**

Recently, we have been examining survivability of strains of *Salmonella Typhimurium* DT135a, a serovar associated with significant levels of human disease and with poultry. This project continues that work, with this and other serovars prevalent in poultry.

References:
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Research focus: Transcriptional regulation and cellular reprogramming
Suitable for students who have majored in Molecular Biology, Genetics, Biochemistry or Biotechnology

We study how transcription factors control cell fate and how the breakdown of this process leads to disease. We apply this knowledge with the ultimate aim of reprogramming cells to treat cancer, blood diseases and metabolic disorders. Currently, our research team includes 3 Postdoctoral Fellows, 6 PhD students, 2 Honours student and a laboratory manager. Two or more Honours positions will be available for 2015.

Project 1: Engineering the next generation of artificial transcription factors
The ability to artificially regulate gene expression offers immense promise for the treatment of human diseases. In this project, we will apply knowledge of how natural transcription factors regulate their target genes to engineer a new generation of more potent artificial factors.

Project 2: Understanding the molecular events of tumour metastasis
Tumour metastasis is associated with the development of late stage cancer and poor prognosis. In this project, we will study the molecules controlling cellular proliferation, apoptosis and adhesion to identify potential therapeutic targets.

Project 3: Controlling obesity: transcriptional regulation of adipogenesis
Obesity is currently one of the Western world’s greatest medical challenges. In this project, we will investigate the transcriptional control of adipogenesis by identifying the signaling cascades and downstream target genes controlling fat cell development.

Project 4: Regulating globin expression: a potential therapy for sickle cell anaemia and thalassaemia
Sickle cell anaemia and thalassaemia are debilitating blood diseases that arise due to mutations in adult globin genes. In this project, we will investigate the signaling cascades and networks involved in developmental regulation of globin gene expression, with an ultimate aim of reactivating the foetal globin genes.

Techniques:
All projects offer the opportunity to learn a wide variety of molecular biology techniques, including Chromatin immunoprecipitation (ChIP), Western blotting, gel shifts, subcloning and bacterial transformation, site directed mutagenesis, PCR and real-time PCR, microarrays and next-generation technologies, tissue culture, transient and stable transfections of mammalian cells, reporter gene assays and flow cytometry.

Recent publications:
- ‘Regions outside the DNA-binding domain are critical for proper in vivo specificity of an archetypal zinc finger transcription factor’, Nucleic Acids Res., 2014, 42(1):276-89
The Bio/Polymer Research Group has an international reputation in the synthesis and characterisation of novel biopolymers and their natural-synthetic hybrids. While ‘fundamental’ research is pursued, such as the effects of microgravity on cancer cells, the BRG strengths are in applied research. In particular, the BRG has a focus on the innovative design and development of devices for medical and environmental applications. In the BRG, Honours students work alongside postgraduate students in similar project areas, with additional postdoctoral support. Applicants should demonstrate critical and lateral thinking skills and an enthusiasm for research, fun and football (preferably Man Utd!).

Project 1: Novel conduits for nerve repair
We are currently developing novel biomaterials to promote the growth of nerve cells and subsequently using these biomaterials to fabricate innovative devices that support the regeneration of nervous tissue, both in the patient and in the lab! This neural engineering project will use state-of-the-art electrospinning to produce nerve conduits and assess cell responses to these devices.

Project 2: Electrospun wound scaffolding nano-materials
Electrospinning can be used to fabricate nanofibrous materials with controlled dimensions that promote cell adhesion, proliferation and differentiation. This cutting-edge technique is one of the foundations for Tissue Engineering. The project will use the new world-class electro-spinning instrument at the UNSW Fibre Spinning Facility to produce a novel device to support ulcerating wounds.

Project 3: Sustainable packaging
We have a novel idea for cost-effective disposable packaging to replace conventional thermoplastics without the relatively high costs normally associated with bioplastics. A niche market has been identified and the research will initiate this novel, applied research project. Students will gain valuable skills in research design and planning, critical evaluation of data and communication skills as well as technical skills including material design, fabrication and characterisation including cell culture and proteomics.
Our research focuses on studying human brain transcriptome using next-generation sequencing, in particular, RNA-Seq technique. We are interested in region-specific gene expression profiles in a healthy human brain as well as perturbation of the transcriptome as a result of neurodegeneration in multiple system atrophy (MSA).

**Project 1: Investigation of long intervening non-coding RNA (lincRNA) expression patterns in the human brain**

lincRNAs are a recently discovered subclass of non-coding RNAs. LincRNAs are expressed across the mammalian genome and contribute to the pervasive transcription phenomenon. They display a tissue-specific mode of expression and are present abundantly in the brain. The role of lincRNAs is thought to be in gene regulation, and in the brain it has been proposed that non-coding RNAs may play a role in regulating axon myelination in white matter (WM) and glial cell differentiation. We have recently detected a number of lincRNAs that show WM-specific expression. The project involves validation of expression patterns for selected lincRNAs using RT-PCR, qPCR analysis as well as analysis of RNA secondary structure and transcriptional factor binding motifs.

**Project 2: Determination of transcriptomic markers of the human brain ageing**

There is currently no widely accepted biomarker for ageing. Attention is now turning to developing molecular fingerprints for ageing, much in the same way as for cancer-related paradigms. Since ageing is likely a polygenic phenomenon, transcriptome profiling can help to identify transcripts contributing to longer life and define genes contributing positively or adversely to the ageing process. The aim of this project is to identify differentially expressed transcripts in peripheral blood of healthy individuals representing two age groups of 50 and 90 years old, respectively. The project will comprise differential gene expression analysis and comparative analysis between transcriptome profiles and genotypes of the investigated individuals using bioinformatics tools well established in our laboratory. No prior experience in bioinformatics is required.

**Project 3: Determination of the molecular mechanism of alpha-synuclein aggregation in multiple system atrophy**

Multiple system atrophy (MSA) is a distinct member of the group of neurodegenerative diseases called α-synucleinopathies, whereby the fibrillar protein α-synuclein aggregates in oligodendroglia. Although well-defined clinically, the molecular pathophysiology of MSA has been barely investigated. We recently completed comparative analysis of MSA transcriptome profiles and identified a number of genes that might be utilised as molecular markers of early stages of MSA. The project focuses on further analysis of these MSA-specific genes using RT-PCR, qPCR, western blotting and RNA interference.

**References**

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Research focus: Identifying novel chemotherapeutics for the treatment of cancer
Suitable for students who have majored in Biochemistry, Molecular Biology or Genetics

With the ageing of the baby-boomers, the incidence of age-related diseases such as cardiovascular disease and cancer will increase, and with them the need for better targeted therapies. Our group is interested in identifying novel chemotherapeutics for the treatment of cancer. This can be extremely costly, both in terms of time and expenditure, from the initial identification of a drug, through the laboratory testing and finally the animal and human trials. What might be preferable is to find drugs that are already approved for use in humans and repurpose them for cancer treatment. We have been working on two sets of drugs that fall into the "old for new" category.

**Project 1: Antipsychotic drugs and their effect on some cancers**
The first is the class of drugs called antipsychotics, which are used to treat patients with schizophrenia. Large-scale analysis of patient cohorts from around the world has revealed that those suffering schizophrenia have a lower incidence of some cancers compared with the general population. When we investigated further, we found that this may be due, in part, to the long-term use of the antipsychotic drugs that these patients take. These drugs are very effective in killing some cancer types, including those that are very recalcitrant to treatment – such as lung cancer and the brain tumour glioblastoma multiforme (less than 5% patient survival 1 year after diagnosis). This project involves investigating the mechanism by which these drugs kill cancer cells.

**Project 2: Statins and their effect on some cancers**
The second type of "old for new" drugs are those that are classed as statins. These drugs are widely used to reduce elevated cholesterol levels in those at risk of cardiac disease. However, it has been found that these drugs can also inhibit the growth of cancer cells. We have studied various breast cancer cells that respond differentially to treatment with statins – some are resistant while others are sensitive. Determining the mechanism for this differential response will allow us to ultimately identify those patients who would be good candidates for treatment with statins.
The Morris lab is interested in understanding the role of non-coding RNAs (ncRNAs) in modulating epigenetic and transcriptional states in human cells and developing techniques, based on knowledge of this emerging molecular pathway (see figure) to control gene transcription. We utilise HIV-1, cancer, and cystic fibrosis as our model systems to investigate the role of non-coding RNAs in human disease.

**Figure: ncRNA-mediated epigenetic and transcriptional regulation in human cells.**
Endogenous *cis* and *trans* expressed antisense lncRNAs can direct epigenetic remodelling complexes to target loci, resulting in heterochromatinisation of the target site and transcriptional gene silencing. This same pathway can be usurped by small antisense RNAs whereby Argonaute 1 (AGO1), DNA Methyltransferase 3a (MT3a), Enhancer of Zeste 2 (EZH2), and Histone Deacetylase (HDAC1) are localised by the action of the small antisense RNA to homology containing target loci, resulting in transcriptional gene silencing.

**Project 1: Transcriptional modulation of HIV-1**
ncRNA-directed transcription suppression or activation of HIV-1
The mechanisms of action whereby ncRNAs control viral replication are being studied.

**Project 2: Discovery and characterisation of endogenous long non-coding RNAs (lncRNAs) involved in gene regulation and disease**
Antisense lncRNAs and their interactions with various proteins (see figure) are being explored as well as the structural aspects of the protein/lncRNA interaction. Such studies may result in a new class of therapeutics to target the activation of epigenetically silenced tumour suppressor genes in human cancers.

**Project 3: Transcriptional and epigenetic modulation of the cystic fibrosis transconductance regulator protein (CFTR)**
Endogenous CFTR regulatory lncRNAs are being studied in order to discern the ability to target these transcripts to activate CFTR expression as a means to treat cystic fibrosis.

**Project 4: Determine the endogenous mechanistic function of bidirectional and pseudogene promoters and determine how these elements are differentially controlled in human cells**
Human genomes are littered with bidirectional promoters and sense/antisense transcription. How these elements function and are controlled remains largely unknown.

**Project 5: Basic mechanisms of ncRNA regulation in human cells and the role of ncRNAs in natural selection and driving the nucleotide content of the genome**

**Project 6: The role of exosomes in cell-to-cell transmission of signaling lncRNAs**
We have found several conserved classes of exosome-packaged lncRNAs that appear to package and spread to neighbouring cells. Interrogating their packaging and function is ongoing.
The overall aim of the lab is to develop more effective cancer chemotherapeutic agents based on cisplatin and bleomycin. These drugs are widely used in clinical applications: cisplatin is used to treat testicular and ovarian cancer; bleomycin is used to treat germ cell tumours, certain types of lymphoma, and squamous cell carcinomas. Both compounds are thought to act by damaging DNA inside tumour cells. Cisplatin preferentially targets G-rich DNA sequences, while bleomycin targets GT and GC DNA sequences. There are several hypotheses concerning the precise cellular DNA target(s) for cisplatin and bleomycin.

- **Telomeres**: Human telomeres contain thousands of tandemly repeated copies of the G-rich sequence, (GGGTTA)n. Since the telomeric repeat contains a GGG repeat sequence, it is expected to be a major target site for cisplatin adduct formation. The formation of cisplatin lesions at the telomeric regions of chromosomes would be expected to severely inhibit DNA replication and hence, cell division. Since the telomeric repeat contains a GT repeat sequence, it is also expected to be a major target site for bleomycin cleavage.

- **Guanine-rich promoter sequences**: A large number of human promoters contain G-rich regions (CpG islands) with GC and GT DNA sequences. Cisplatin or bleomycin damage in these regions would severely alter gene expression and lead to cell death. As well as inhibiting DNA replication, transcription would also be inhibited but its extent would vary from gene to gene. This could give rise to different levels of cell killing, dependent on the gene expression profile of the individual cell.

- **Effect of chromatin structure**: The more open nature of chromatin in transcribed genes can lead to more cisplatin and bleomycin damage in these regions. We have previously shown that nucleosome cores inhibit the ability of cisplatin to damage DNA. Bleomycin preferentially cleaves chromatin in the linker region of the nucleosome.

- **Twenty or more consecutive guanine bases**: There are at least 50 sites in the human genome that have 20 or more consecutive guanines. These sites would expected to be major sites of cisplatin adduct formation. We have initiated experiments to look at the interaction of these long runs of consecutive Cs with cisplatin (in plasmid constructs), in order to investigate the properties of these unusual DNA sequences.

There are two main aims of this project. First, by constructing plasmid clones containing various genomic elements (e.g. telomeric DNA sequences, promoter DNA sequences and consecutive guanine sequences) the relative targeting of these sequences by cisplatin and bleomycin can be assessed. Second, by utilising genome-wide DNA sequencing of human cells treated with cisplatin or bleomycin, we will pinpoint the precise DNA sequences targeted by cisplatin and bleomycin in human cells. In this latter aim, we will utilise the immense power of Illumina next-generation DNA sequencing techniques to determine the precise targets of cisplatin and bleomycin in the human genome, in a systematic and unbiased way.
Neurons are born as small spheres only a few micrometres in diameter, but grow into enormous cells with protrusions that can be several metres long in large animals. As they grow, they establish hundreds of contacts with other neurons to form a very precise network of connections. The whole process is important for the proper functioning of our brains. In our laboratory we work on molecules that are found at the surface of neurons. These molecules, called cell adhesion molecules, help neurons to analyse and navigate their environment during neuronal development, and to establish and maintain contacts with other neurons in a mature brain. Genetic alterations in cell adhesion molecules inflict mental disorders and/or mental retardation in humans, such as L1 and Down Syndromes, bipolar disorders, and schizophrenia. Our lab uses cutting-edge techniques of modern biochemistry, molecular biology and biophysics to understand why genetic alterations in adhesion molecules lead to such disorders, and whether we can develop novel diagnostic markers and therapeutic tools for early detection and treatment of such disorders.

Project 1: Mechanisms of neuronal development

As neurons grow, they have to pass through several developmental stages and develop an elaborate "tree" of protrusions, called neurites. Cell adhesion molecules are found at the cell surface of neurons, especially at the growing tips of neurites (the image shows the distribution of a cell adhesion molecule L1 in two neurons at different developmental stages). Students will use modern microscopy and biochemical methods to analyse how activation or inhibition of cell surface adhesion molecules influences growth and branching of neurites, which are the processes required for establishment of neuronal networks in the brain.

Reference:

Project 2: Molecular mechanisms of learning and memory

Mature neurons in the brain are connected to other neurons to form complex neuronal networks. Contacts between neurons are called synapses, and each neuron forms hundreds of contacts with other neurons (the confocal fluorescence image on the left shows a neuron labelled to visualise contacts with other neurons. Each individual red spot represents a synapse). Synapses are formed during learning, and play an important role in memory formation. Students will use proteomics tools combined with methods of molecular biology, neurobiology and biophysics to analyse how the macromolecular complexes formed by adhesion molecules at synapses facilitate learning and memory. A particular focus will be on cell adhesion molecules affected in psychiatric and mental disorders.

References:
Research Projects: Systems and Cellular Biology Group

The Systems and Cellular Biology (SCB) group undertakes research in the biology of eukaryotes. Members of the group are responsible for the establishment and running of two major centres in the School; the Ramaciotti Centre for Gene Function Analysis offering expertise in next-generation sequencing and microarray technology, and the NSW Systems Biology Initiative building capabilities and expertise in bioinformatics for genomics and proteomics.

Current research areas for this group include:

- cholesterol and sterols
- mitochondrial metabolism
- genetics of neurodevelopmental disorders
- sex chromosome structure and evolution
- evolutionary genetics
- protein-protein interaction networks and systems biology
- cellular metabolism of cholesterol, obesity and diabetes
**Professor Bill Ballard**

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**Research focus:** Selective forces influencing evolution of DNA; mitochondria as a model to study biochemical and bioenergetic link between genotype and phenotype  
Suitable for students who have majored in Genetics and/or Biochemistry

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**Project 1: Influence of diet on Parkinsonism**  
While drugs to treat the symptoms of Parkinsonism have been prescribed for decades, an unmet need remains for innovative strategies that either halt or reverse progression. Indeed, the management of Parkinsonism lags behind other major diseases of our society, such as cardiovascular disease. We employ parkin mutant Drosophila and human fibroblast cells to test the influence of the protein:carbohydrate ratio on mitochondrial functions, as we have shown this ratio influences mitochondrial functions in Drosophila and mice. We target mitochondrial function because there is strong corroborative evidence that the disease is linked to organelle dysfunction.

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**Project 2: Inheritance of mitochondrial DNA (mtDNA)**  
The central role of animal mtDNA in molecular ecology, and in medicine, has highlighted its critical importance in life sciences. Mutations in mtDNA are often used to infer genetic relationships and have been associated with the expression of human diseases. A surprising gap in our knowledge base is a mechanistic understanding of the processes involved in mtDNA inheritance. We aim to put currently accepted models of mtDNA inheritance to stringent tests. This project examines the exact mechanism of inheritance of mitochondrial genes to enhance biological interpretations and our understanding of the heritability of specific diseases.

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**Project 3: Animals that eat less live longer – up to a point**  
This is a view that has become a central theme in gerontology. However, recent studies have suggested that specific nutrients (proteins and certain amino acids) are responsible for increasing longevity. This project will investigate the role of different diets in the ageing of Drosophila females. The project will expose flies to diets with a range of Protein: Carbohydrate ratios and then examine mitochondrial functioning, using state-of-the-art equipment, in flies known to harbour different mutations.

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**Project 4: Genetic variation in the dingo**

This project employs population genetics and comparative genomics to investigate questions concerning the evolutionary history and population genetics of the dingo. The dingo is Australia’s top-level carnivore and has been present on the landscape for over 5,000 years. Despite constant public attention and media spotlight our basic understanding of the genetics and biology of the emblematic Australian icon is startlingly inadequate. Even at the most fundamental level it is not known whether the dingo is a single large genetically homogeneous population or whether local variation exists. This project builds upon a large database of Dingo samples already collected and in the laboratory and we collaborate extensively with the Bargo Dingo Sanctuary.
Cholesterol is an important and versatile molecule that has become a byword for heart disease risk. In fact, the cells in our body actually need cholesterol. However, too much can kill them and contribute to various diseases, including atherosclerosis and cancer. Our bodies have therefore engineered an elaborate system for keeping the cholesterol content of our cells tightly controlled: the overall goal of our research is to understand more about how our cells control cholesterol levels.

**Project 1: New factors in achieving cholesterol balance in cells**

An imbalance of cholesterol in certain cell types plays a role in several diseases. Therefore, knowing precisely how cells regulate their cholesterol levels is central to understanding the development of these diseases, and to identify possible new treatments. The statin class of drugs, worth >$30 billion a year, have been effective in treating heart disease, but are not without their side effects. Statins inhibit a very early step in cholesterol synthesis, and little attention has been paid to later steps in the pathway. This project investigates the regulation of novel control points later in cholesterol synthesis, which have been largely overlooked.

**Project 2: Cholesterol and cancer**

The link between cholesterol and heart disease is well established. Now, new evidence is forging an intriguing link between cholesterol and cancer. A high-fat diet is a well-known but poorly understood risk factor for prostate cancer, which may involve increased levels of cholesterol in the blood. Our lab recently discovered a connection between a major player involved in maintaining cholesterol balance in animal cells and a key proliferative pathway that is overactive in many cancers, including prostate cancer. This project investigates novel ways to decrease cellular cholesterol levels in prostate cancer cells, which may inform the development of new anti-cancer therapies.

Methods to be employed for both projects include mammalian cell culture, recombinant DNA techniques, fluorescence microscopy, real-time PCR, gene transfection, metabolic labelling, use of luciferase reporter assays, SDS-PAGE and Western blotting.

**Suggested references (available on request)**

Project 1: Molecular mimicry in host-pathogen interactions

Many viruses hijack host cellular machinery through the molecular mimicry of host Short Linear Motifs (SLiMs). It is likely that pathogenic bacteria may employ similar strategies. This project will apply state-of-the-art SLiM prediction tools developed in our lab to published datasets of host-pathogen protein-protein interactions. This will help us understand how pathogens mess with their hosts—and how to stop them!

Project 2: Mining cancer genomics for disease mutations that disrupt protein function

SLiMs tend to be involved in low affinity interactions and have a small number of amino acid residues that are required for function. These attributes make them potential sites of mutations that slightly disrupt cellular function, sometimes only in specific genetic backgrounds or environments. This project will combine methods for proteome-wide SLiM prediction with human genomics data and genetic variants associated with disease. This will focus on mutations in cancers, which affect many of the same pathways targeted by molecular mimicry in viruses.

Project 3: Yeast as a model for protein interaction dynamics

In addition to giving us bread and beer, the yeast *Saccharomyces cerevisiae* is an awesome eukaryotic model organism. This project will compare protein-protein interactions in humans and yeast to learn how both organisms exploit SLiMs and post-translational modifications to dynamically control the complex inner workings of their cells.

References:

Obesity contributes to the pathogenesis of numerous metabolic diseases, including cancer and diabetes. My laboratory is focused on identifying the key metabolic alterations that contribute to the development of obesity-related disorders and testing whether targeting cellular metabolism represents a viable therapeutic approach to treat these diseases.

**Project 1: Targeting glucose transporters in endometrial cancer**

We have recently discovered that the glucose transporter GLUT6 is highly up-regulated in human endometrial tumours compared to normal endometrium (unpublished). We have determined that blocking GLUT6 expression is sufficient to kill endometrial cancer cells in culture. These data indicate that GLUT6 may represent a possible drug target for the treatment of endometrial cancer. However, very little is known about the functional role of GLUT6. This project will investigate how GLUT6 expression regulates glucose transport and metabolism in malignant cells.

**Project 2: Evaluating the effects of diet on liver cancer incidence and tumour burden**

Obesity is highly linked to the prevalence of liver cancer in men. It was recently shown that male mice fed a diet rich in fat and sugar also have increased liver cancer incidence and tumour burden. These data identify a critical role for dietary nutrients in liver cancer initiation or progression; however, it remains unclear how dietary fats or sugars promote liver cancer. Based on unpublished preliminary data, we hypothesise that sugar intake (but not fat) is the main driver of liver cancer progression. This project will investigate how altering the metabolism of dietary sugar affects liver cancer initiation and progression in mice.

**Project 3: To determine the metabolic consequences of blocking sugar conversion to fat in the liver**

Excess dietary sugar is converted to fat. This process occurs primarily in liver tissue and requires the enzymes acetyl-CoA carboxylase 1 (ACCI) and ACC2. As such, it is widely thought that the inhibition of ACC activity will reduce fat storage in these tissues. Curiously, we have recently determined that genetic inhibition of both ACC1 and ACC2 in the liver of mice causes an accumulation of liver fat (Pubmed ID 24944901). This result is completely unexpected and indicates that ACC enzymes have a novel role in the regulation of liver fat storage. This project will test the hypothesis that ACC gene deletion causes an accumulation of the substrate acetyl-CoA that leads to the inhibition of enzymes involved in fat oxidation.

**Project 4: Increasing energy expenditure for the treatment of obesity and insulin resistance**

We have recently performed a chemical library screen and identified molecules that increase cellular energy expenditure (Pubmed ID 24634817). This project will test whether these molecules can protect against fat accumulation and insulin resistance in cultured cells, flies and mice.
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Research focus: Genetics of neurodevelopmental disorders, human brain transcriptome dynamics in normal and disease states
Suitable for students who have majored in Molecular Biology, Biotechnology or Bioinformatics

Project 1: The role of the neuronal splicing factor A2BP1/RBFOX1 in Autism Spectrum Disorders (ASD)

ASD are among the most heritable neuropsychiatric conditions, and at the same time genetically very heterogeneous, with hundreds of genetic loci implicated in the disease (Voineagu 2012). Given the genetic heterogeneity of ASD, a challenging yet fundamental question is whether the wide variety of genetic changes ultimately dysregulate a common set of molecular pathways, amenable as therapeutic targets. We recently demonstrated that despite genetic heterogeneity, shared abnormalities of gene expression could be detected in postmortem brain tissue from ASD cases (Voineagu et al. 2011). A key finding of this study was that the neuronal splicing factor A2BP1 (Ataxin-2 binding protein 1) was downregulated in a large subset of ASD brains. While A2BP1 has been previously implicated in ASD, the mechanisms of its transcriptional dysregulation and the functional consequences of altered A2BP1-dependent splicing in ASD remain unknown. This project aims to (a) identify the genetic and epigenetic causes of A2BP1 transcriptional dysregulation in ASD brain, (b) elucidate A2BP1-dependent alternative splicing targets in the human brain, and (c) investigate the cellular and transcriptional consequences of A2BP1 dysfunction.

Project 2: Genomic diversity in the human brain: the functional role of expandable DNA repeats

Although genetic variation can potentially occur anywhere in the genome, certain genomic regions are particularly susceptible to genetic changes. These regions are called hotspots of genomic instability, and are frequently underlined by repeated DNA sequences. One class of hotspots of genomic instability particularly relevant to brain function consists of expandable DNA repeats. These are tandem DNA repeats, most often trinucleotide repeats (TNRs) such as (CGG)n, (CAG)n, (GAA)n, which have an intrinsic propensity to increase in length during germline transmission. TNR expansions cause more than 30 neuro-psychiatric disorders, including Huntington’s disease, Fragile X syndrome and Friedreich’s ataxia (Mirkin 2007A). A surprising characteristic of human disorders caused by TNRs is that they affect primarily the brain (Mirkin 2007), although the mutation is present in all tissues, suggesting that the human brain is particularly vulnerable to this type of genetic variation. Somatic TNR expansions have been documented in the human brain at some of the TNR disease loci (Telenius et al. 1994; McMurray 2010). However, the human genome contains over 30,000 TNRs (Kozlowski et al. 2010) and whether somatic TNR expansions occur in the brain on a genome-wide scale is currently unknown. This project aims to identify somatic TNR instability events in the normal human brain and assess their effect on gene expression.

Recent publications by our Honours students:

More detailed information on projects and ongoing research is available on the lab website: http://voineagulab.unsw.edu.au
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Research focus: Sex chromosome structure, function, regulation and evolution
Suitable for students who have majored in Molecular Biology

We work on unusual model species that are uniquely placed in the vertebrate phylogeny to unravel mysteries surrounding the evolution of sex chromosomes and their epigenetic regulation.

Project 1: Evolution of mammal sex chromosomes
In order to understand the intricacies of X and Y chromosome evolution, we investigate Y chromosome gene content and structure in our model marsupial, the tammar wallaby (Macropus eugenii). Using gene-specific and whole Y chromosome probes to screen BAC libraries, we have identified novel genes on the wallaby Y. Many of these genes are also conserved on the Y in other Australian (Tasmanian devil) and American (opossum) marsupials, but lost from the Y in placental mammals. This project will focus on characterising genes on the Tasmanian Devil Y chromosome, not only helping to understand mammal Y chromosomes, but also the X.

Project 2: Marsupial X chromosome inactivation
X chromosome inactivation (XCI) is arguably the most spectacular example of epigenetic regulation in mammalian genomes. In the somatic cells of female placental mammals, a characteristic signature of epigenetic modifications accumulates on, and transcriptionally silences, one of the two X chromosomes. In marsupial mammals, it remains unclear which modifications are associated with the inactive X. However, protein immunofluorescence and CHiP-seq are revealing some surprising differences between the marsupial and placental mammal XCI systems. This project will further examine epigenetic regulation of the marsupial X chromosome, resulting in a better understanding of how silencing of the X evolved in humans.

Project 3: Monotreme and bird dosage compensation
Dosage compensation is required to balance gene expression from the X chromosome between males (which only have one X) and females (with two Xs). Necessity of dosage compensation would be expected in the platypus because of their complex sex chromosome system in which males have five Xs and five Ys, and females have five pairs of Xs. However, it appears that some genes on the sex chromosomes are not dosage-compensated between males and females, whereas others display varying degrees of compensation via transcriptional inhibition. Interestingly, the platypus sex chromosomes share considerable homology with the chicken Z chromosome (especially X5), but not the human X chromosome. Dosage compensation of genes on the chicken Z chromosome has also been shown to be incomplete, but it is unknown if this is via locus-specific transcriptional inhibition, as for the platypus, or an overall change in transcription from the Z. This project focuses on understanding the mechanisms of dosage compensation in the non-traditional model vertebrates, which will help untangle some of the mysteries surrounding the evolution of this complex epigenetic phenomenon.
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Research focus: How are the interactions of proteins controlled?
Suitable for students who like proteins and have majored in Biochemistry or Molecular Biology

Almost all proteins interact with other proteins to deliver their function inside the cell. One of the most fundamental questions of life is how are these interactions actually controlled? We have recently shown that eukaryotic cells use the addition and removal of methyl groups to control protein-protein interactions. This post-translational modification appears to be a widespread regulatory mechanism. In some cases, there is interplay between many different modifications on single proteins, such as methylation, phosphorylation and acetylation. There is evidence that the combinations of modifications may be a protein ‘interaction code’, where different combinations control the specificity of protein-protein interactions. Interaction codes have only been found for five proteins to date; we believe there are many more to be discovered.

Our experiments are done in the context of protein interaction networks. To study protein-protein interactions, we use two-hybrid techniques (that involve a lot of molecular biology techniques), protein separation and analysis methods (including mass spectrometry) as well as sophisticated bioinformatics. We welcome students who want to do wet-lab biochemistry/molecular biology projects, especially students who like proteins. We also welcome students who like to think big!

**Project 1: Searching for the protein interaction code**

We have recently developed a new system (the conditional two-hybrid system) to test whether interactions of proteins are modulated by modifications such as methylation and phosphorylation (Erce et al. 2013). We are now starting to look at ‘hub proteins’, those with many interaction partners but only 1 or 2 interaction interfaces, to see whether the cell uses combinations of protein modifications to control the specificity of interactions. This project will investigate one or more hub proteins for the presence of an interaction code. This will be a lot of fun.


**Project 2: Searching for new Protein Methylation Enzymes**

We have recently discovered two new methyltransferases – these are the enzymes that add methyl groups on to proteins (e.g. Couttas et al. 2012). We have a number of other proteins that also have sequence homology to methyltransferases; we need to explore these to understand whether these might also be new methyltransferases. If we can confirm these as new methyltransferases, we then have the task of naming the new enzyme something! Also a lot of fun.

We work on two areas: the cellular dynamics of lipid droplets, adipocyte development, obesity and diabetes; and cholesterol trafficking in eukaryotic cells and its role in neurodegenerative disorders.

Human obesity is, in essence, the accumulation of lipid droplets, which are storage granules of fat. We have identified many mutants that affect the size and number of lipid droplets, and have also uncovered a role for a human disease gene – seipin – in lipid droplet formation. Our recent data suggest that seipin may regulate the metabolism of fatty acids and phospholipids. Our current aim is to determine the molecular function of seipin, and how it regulates lipid droplet morphology and adipocyte development.

Aberrant distribution of cholesterol causes neurodegenerative diseases such as Alzheimer’s disease. We have identified novel proteins that regulate cholesterol transport from late endosomes and lysosomes. We now aim to identify additional regulators of cellular cholesterol distribution, and to understand how these proteins may regulate heart and brain function.

**Project 1: Oxysterol binding proteins, intracellular cholesterol trafficking and neurological diseases**

Selected References:

**Project 2: Seipin, lipid droplets, adipose tissue development and human obesity**

Selected References:
External Supervisors

Research projects are also available with the following external supervisors, who are located in institutions affiliated with the School of BABS. Students are requested to contact external supervisors directly for further information on projects they may have available for 2015.

Please note that it is School policy that a BABS academic be assigned as a primary co-supervisor in all cases.

Dr Till Böcking  
Centre for Vascular Research, UNSW School of Medical Sciences  
Email: till.boecking@unsw.edu.au  
Tel: +612 9385 8131  
Research area: Mechanisms of molecular motors; imaging of cellular processes; single molecule biophysics.

Dr Andrew Burgess  
Kinghorn Cancer Centre, Garvan Institute of Medical Research  
Email: a.burgess@garvan.org.au  
Tel: +612 9355 5777  
Research area: Cancer cell biology; cell and nuclear division

Dr Antony Cooper  
Garvan Institute of Medical Research  
Email: a.cooper@garvan.org.au  
Tel: +612 9295 8100  
Research area: Identifying molecular mechanisms and therapeutic approaches for Parkinson's Disease & other neurodegenerative diseases. Non-coding RNAs, mitochondrial dysfunction, pathogenic proteins, molecular stresses.

Dr Jennifer Cropley  
St Vincent’s Clinical School, UNSW Faculty of Medicine  
Email: j.cropley@unsw.edu.au  
Tel: +612 9295 8619  
Research area: Epigenetics, Environmental epigenetics, Epigenetic inheritance.

Professor Peter Croucher  
Garvan Institute of Medical Research  
Email: p.croucher@garvan.org.au  
Tel: +612 9295 8100  
Research area: Cellular and molecular mechanisms responsible for physiological and pathological regulation of the skeleton

A/Professor Sally Dunwoodie  
Victor Chang Cardiac Research Institute  
Email: s.dunwoodie@victorchang.edu.au  
Tel: +612 9295 8613  
Research area: Molecular mechanisms of mammalian embryonic development
Dr Dan Hesselson
Diabetes and Metabolism Division, Garvan Institute of Medical Research
Email: d.hesselson@garvan.org.au
Tel: +612 9295 8258
Research area: Parkinson's Disease; functional genomics; in vivo drug discovery

Dr Lawrence Lee
Victor Chang Cardiac Research Institute
Email: l.lee@victorchang.edu.au
Tel: +612 9295 8644
Research area: Synthetic biology

Professor Richard Lock
Children's Cancer Institute Australia for Medical Research
Email: richard.lock@unsw.edu.au
Tel: +612 9382 1846.
Research area: Molecular mechanisms of drug resistance; new therapeutic approaches in childhood acute leukaemia

Dr Karen Mackenzie
Children's Cancer Institute Australia for Medical Research
Email: k.mackenzie@unsw.edu.au
Tel: +612 9382 1829
Research area: The regulation of telomere length in haematopoietic cells

Dr Anne Mai-Prochnow
CSIRO North Ryde
Email: anne.mai-prochnow@csiro.au
Tel: +612 9490 8451
Research area: Interactions of gas plasma with bacterial biofilms; intersection of microbiology, chemistry and physics; biofilms; microbial inactivation, protein identification, plasma nanoscience, food science.

Dr Greg Neely
Garvan Institute of Medical Research
Email: g.neely@garvan.org.au
Tel: +612 9295 8455
Research area: Novel disease genes affecting the nervous and cardiovascular systems

Professor Bill Rawlinson AM
Virology Division, Dept. of Microbiology, SEALS Prince of Wales Hospital
Email: w.rawlinson@unsw.edu.au
Tel: +612 9382 9113
Research area: Molecular biology of viruses, particularly congenital cytomegalovirus, clinical virology, enteroviruses and diabetes, and respiratory viruses

Dr Catherine Suter
Victor Chang Cardiac Research Institute
Email: c.suter@victorchang.edu.au
Tel: +612 9295 8720
Research Area: epigenetic variation and epigenetic inheritance in mammals
Frequently Asked Questions

1. **Can I start Honours in semester 2?**
   Yes, the School of BABS offers a mid-year intake as well as a semester 1 intake.

2. **What is included in the overall WAM and stage 3 Science WAM?**
   Every course completed in stages 1 to 3 is included in the overall WAM. This includes general education courses. Stage 3 Science WAM includes level 3 courses run by the Faculty of Science (level 3 courses with the prefix: AVIA, BIOS, BEES, CLIM, GEOS, IEST, MSCI, ENVS, BABS, BIOC, BIOT, MICR, CHEM, COMP, FOOD, MATS, MATH, ANAT, NEUR, PATH, PHAR, PHSL, PSYC, PHYS, VISN, SCIF).

3. **I only have one more course left to complete for my program. Can I start Honours and complete my last course at the same time?**
   No. Students must successfully complete all requirements from stages 1 to 3 of their degree before commencing Honours.

4. **I have one more course to complete for my program but I will be completing this in the summer session before Honours commences in Semester 1. Am I still allowed to apply for a Semester 1 start?**
   Yes. Your Honours application will be assessed as normal (see Honours application process timeline on p.53). If your application is successful, you will be given a conditional offer based on you passing your remaining summer session course.

5. **I have met with a potential supervisor and they have agreed to supervise me. Does this mean I am guaranteed acceptance into Honours?**
   No. Potential supervisors may express their interest in supervising you for Honours and you may include them in your Project Preference List, however only the School can formally accept students into Honours and allocate students to supervisors.

6. **Why is there a limit on the number of external supervisors we can nominate in our project reference list?**
   There are two reasons for this limit. (1) to ensure that a sufficient number of students undertake their Honours project within BABS; and (2) to ensure students have the best possible chance to be allocated a supervisor/project (external supervisors are restricted to only 1 student per intake making placements very competitive).

7. **Can I request an external supervisor not on the external supervisor list?**
   No. Students may only nominate approved BABS external supervisors. If you include any external supervisors on your preference list that are not approved, they will be ignored.
BABS Honours Application Form – 2015 Entry


<table>
<thead>
<tr>
<th>Closing Date – Applications close at 4pm on:</th>
<th>Semester Start</th>
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<tbody>
<tr>
<td>Semester 1 2015: Monday 3 November 2014</td>
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<td>Semester 2 2015: Friday 1 June 2015</td>
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Personal Details

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<th>Surname:</th>
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<th>UNSW Student ID (if applicable)</th>
<th>Current UNSW Program (if applicable)</th>
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Address:

**Phone contact (business hours):**

**Email address (external students only)*

*Existing UNSW students will be contacted via their UNSW student email address

**Honours Project Preferences** (Rank 5 projects/supervisors in order of preference).

<table>
<thead>
<tr>
<th>No.</th>
<th>Project Title</th>
<th>Project Supervisor</th>
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NB: At least 3 nominated projects must be with supervisors based within the School.

Ensure you attach:

1. Current curriculum vitae
2. Complete transcript of your grades
3. Brief list of research interests

Return this form and accompanying documentation to:

BSB Student Office
Room G27, Ground Floor, Biological Sciences Building
UNSW Australia, Kensington NSW 2052
Email: BABStudent@unsw.edu.au

NB: if you are not currently enrolled at UNSW, you also need to apply for admission to UNSW. Admission guidelines can be found at: [http://www.unsw.edu.au/future-students-domestic-undergraduate/your-application/how-apply](http://www.unsw.edu.au/future-students-domestic-undergraduate/your-application/how-apply)

**NB: MPhil (BABS) candidates must apply online at:** [UNSW Apply Online website](http://www.unsw.edu.au/apply)