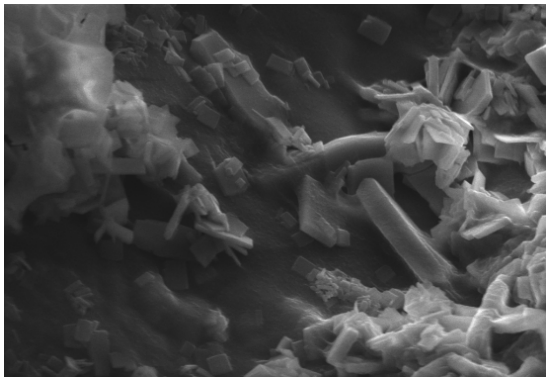
Biomedical Physics Honours Projects 2020

The projects below are indicative – you are welcome to negotiate research topics with potential supervisors.

Contents

Project title	Membrane Interaction of Small Molecules Capable of Improving Batten's Disease Cell Phenotypes
Name of supervisor(s)	Dr Charles Cranfield (UTS), Dr Alvaro Garcia (UTS), A/Prof Ron Clarke (USyd)
Email address	Evelyne.deplazes@uts.edu.au
Project description & aims (250 words max, summary written for prospective students)	Batten's disease is an inherited neurodegenerative disorder that is inevitably fatal. Onset typically occurs at the age of 5 – 10 years. Little is known about the causes of the disease and there are very few treatment options. Mutations in the protein CLN3 (also known as Battenin) cause the most common form of Batten's disease. Recently it was shown that the commonly used gap junction inhibitor *carbenoxolone* and other small molecules are able to improve phenotypes in CLN3 deficient mice. All of the molecules identified are steroid- or sterol-like molecules, which, due to their hydrophobic nature, would be expected to bind strongly to lipid membranes. The purpose of our project is to carry out an in-depth investigation on the effects of these molecules on a range of membrane properties. This will be achieved using a range of biophysical techniques that measure membrane property changes as a consequence of molecular membrane interactions. Discovering the mode of action of these molecules, would provide a rational basis for the design of improved treatments for CLN3 deficiency. The overall aim of our study is to uncover which property of biological membranes needs to be modified in order to observe a beneficial effect for sufferers of Batten's disease. This will provide essential knowledge for the future design of improved treatments.
Techniques the student would be working with	Our lab uses biophysics experiments such as quartz crystal microbalance (QCM) experiments, tethered bilayer lipid membranes as well as computational approaches, in particular molecular dynamics simulations using the UTS HPC cluster. The project and technique used can be matched to the student's background and interest. Full training is provided.
Infrastructure and support required for project execution	All equipment is available in the UTS Membrane Biophysics lab.

Project title	Microstructural Characterisation of Coral Skeletons
Name of supervisor(s)	Dr Annette Dowd, Dr Emma Camp and Prof Michael Cortie
Email address	Annette.Dowd@uts.edu.au
Project description & aims (250 words max, summary written for prospective students)	The impact of climate change on coral reef health is a subject of intense study however the focus has been on coral polyps (soft tissue). The hard coral skeleton, a biomineral known as aragonite, has been relatively neglected. There is preliminary evidence that the skeletal microstructure of a few coral species depends on environmental conditions although there is still little understanding of the underlying physical differences such as defects in the aragonite crystal structure. New characterisation techniques of coral variation will give marine biologists powerful tools for monitoring environmental impacts on coral reef growth. Moreover, variations in microstructure can have real implications for robustness of the coral reef. In this project the student will conduct a study the microstructure of the skeletal aragonite with several complementary spectroscopic and mapping techniques (see below). This will include studying recently acquired synchrotron data which showed anomalous low temperature behaviour of the biomineral. Specimens include several coral species collected from diverse environments by members of C3.  *Figure 1. SEM micrograph showing range of crystal morphologies in Seychelles coral biomineral skeleton by research student Anne Wright*
Techniques the student would be working with	X-ray diffraction (including synchrotron data), SEM-EDS, FTIR/Raman spectroscopy, biomineral specimen preparation
Infrastructure and support required for project execution	See techniques – all infrastructure is already available and in-place and specimen preparation techniques have been developed at UTS.

Project title	Molecular mechanisms of physical changes in the cell membrane
Name of supervisor(s)	Dr Annette Dowd
Email address	Annette.Dowd@uts.edu.au
Project description & aims (250 words max, summary written for prospective students)	The cell membrane is a self-assembled double layer structure of lipid molecules. From the physical point of view there are still unanswered questions about the different ways the lipid molecules are arranged within those layers and how the arrangement (packing) depends on the environmental conditions. We are developing a method to characterise lipid packing in bilayers using far-infrared (terahertz) spectroscopy. This frequency range allows us to simultaneously monitor signals from the different parts of the lipid molecules, the hydrogen bonding network, and the bound water molecules. Studies with this technique will contribute to our understanding of lipid bilayer stability and how it is affected by temperature, different ionic environments and membrane disrupting antimicrobial peptides.
Techniques the student would be working with	Far-IR spectroscopy (including synchrotron data), FTIR and Raman spectroscopy, biochemical specimen preparation.
Infrastructure and support required for project execution	See techniques – all infrastructure is already available and in-place and specimen preparation techniques have been developed.

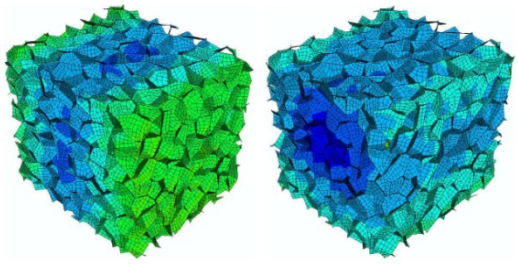
Project title	The interaction of a metamorphic protein with the cell membrane
Name of supervisor(s)	Dr Annette Dowd, A/Prof Stella Valenzuela
Email address	Annette.Dowd@uts.edu.au
Project description & aims (250 words max, summary written for prospective students)	Our traditional assumptions regarding the processes by which proteins insert into cell membranes are challenged by non-classical membrane proteins such as Chloride Intracellular Ion Channel CLIC1. It has the ability to spontaneously insert into the lipid membrane from a globular, soluble state but the precise mechanism remains a mystery. Knowledge about spontaneous membrane insertion will also have application in understanding some bacterial toxins which behave similarly. Cholesterol is known to dramatically influence the interaction of CLIC with the membrane, although its precise role is not known. Preliminary experiments suggest it forms a complex with CLIC before membrane insertion takes place. The aim of this project is to investigate any changes in the physical structure of CLIC when in its globular and cholesterol-complexed phases using small angle x-ray scattering (SAXS) data from ANSTO. These structures will be compared to structures determined with x-ray diffraction from protein crystals (solid phase) and FTIR of CLIC (solution phase). It may also be possible to use the SAXS-determined structure to analyse x-ray reflectometry measurements and establish any interaction of the CLIC with a lipid membrane.
Techniques the student would be working with	Far-IR spectroscopy (including synchrotron data), FTIR and Raman spectroscopy, small angle X-ray scattering (synchrotron data), data science, biochemical specimen preparation.
Infrastructure and support required for project execution	See techniques – all infrastructure is already available and in-place and specimen preparation techniques have been developed.

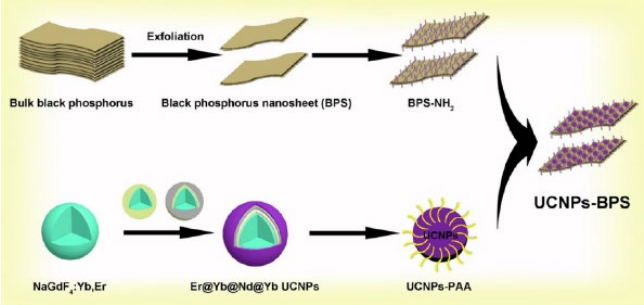
Project title	Conversion of marine structures (Nacre) to calcium phosphates for bone graft materials
Name of supervisor(s)	Dr Annette Dowd, Prof Besim Ben-Nissan, Ms Ipek Karacan
Email address	B.Ben-nissan@uts.edu.au
Project description & aims (250 words max, summary written for prospective students)	Marine shells are one group of biogenic materials composed of mostly calcium carbonate with excellent mechanical properties, essential for load bearing in orthopaedic applications. The conversion of seashells results in ceramic materials such as tri-calcium phosphates, hydroxyapatite and calcium phosphate ceramics, which are biomaterials for bone substitute and fillers. It has been shown that in the conversion of marine shells they retain their nano- and microstructures and can temporarily serve in a structural capacity for bone repair. The aim of this project is the production of hydroxyapatite from nacre (mother of pearl) and characterisation of the final products. The methods will involve hydrothermal conversion, XRD, SEM, FTIR, DTA/TGA and RAMAN. Powders and solid pieces will be converted and tested.
Techniques the student would be working with	XRD, SEM, Hydrothermal conversion, DTA/TGA, FTIR ,RAMAN and ICP.
Infrastructure and support required for project execution	All equipment available within the Faculty. Preliminary raw materials cost will be covered by Prof Ben-Nissan.

Project title	Characterising the cell membrane disrupting mechanism of the pH-sensitive peptide GALA using molecular dynamics simulations and biophysics experiments
Name of supervisor(s)	Dr Alvaro Garcia, Dr Evelyne Deplazes, Dr Charles Cranfield (School of Life Sciences)
Email address	Evelyne.deplazes@uts.edu.au
Project description & aims (250 words max, summary written for prospective students)	GALA is a peptide that was designed for the pH-sensitive disruption of membranes and is used for endosomal drug delivery. The peptide binds to cell membranes and once inserted, forms stable pores that allow the selective transport of ions across membranes. The peptide also shows antimicrobial properties. There are a number of open questions related to the mechanism of action of GALA. These include the role of lipid composition on the size and stability of the pore and how lipid composition affects the ability of GALA to disrupt cell membranes. Answering these questions is important for understanding the mechanism of GALA and for designing peptides that target specific membranes and/or used to deliver specific drug molecules and/or for the use of GALA as an antimicrobial agent. The overall aim of our study is to use MD simulations to understand how lipid composition affects the ability of GALA to form pores.
Techniques the student would be working with	Our lab uses both computational approaches, in particular molecular dynamics simulations using the UTS HPC cluster, as well as biophysics experiments such as quartz crystal microbalance (QCM) experiments, tethered bilayer lipid membranes. The project and technique used can be matched to the student's background and interest. Full training is provided
Infrastructure and support required for project execution	All equipment is available in the UTS Membrane Biophysics lab.

Project title	Characterising the cell membrane disrupting mechanism of the pH-sensitive peptide GALA using microfluidic devices.
Name of supervisor(s)	Dr Alvaro Garcia and Dr Evelyne Deplazes (UTS Biophysics lab), Dr Martin Stewart (School of Life Sciences)
Email address	Evelyne.deplazes@uts.edu.au
Project description & aims (250 words max, summary written for prospective students)	GALA is a peptide that was designed for the pH-sensitive disruption of membranes and is used for endosomal drug delivery. The peptide binds to cell membranes and once inserted, forms stable pores that allow the selective transport of ions across membranes. The peptide also shows antimicrobial properties. There are a number of open questions related to the mechanism of action of GALA. These include the role of lipid composition on the size and stability of the pore and whether lower concentrations of GALA could be used to deliver drugs or other agents into cells without causing cell death.
Techniques the student would be working with	Experiments with a microfluidics device will be used understand the interaction of GALA with living cells and their effect on the cell membranes. This can be combined with biophysics experiments such as quartz crystal microbalance (QCM) experiments, tethered bilayer lipid membranes in the UTS Membrane Biophysics lab. The project and technique used can be matched to the student's background and interest. Full training is provided.
Infrastructure and support required for project execution	All equipment is available in the UTS Membrane Biophysics lab and the School of Life Sciences.

Project title	3D cancer metastasis-on-chip model
Name of supervisor(s)	Dr Irina Kabakova, A/Prof Majid Warkiani, Dr Christine Poon
Email address	
Project description & aims (250 words max, summary written for prospective students)	Cancers are a leading cause of morbidity and mortality worldwide. The ability of cancer cells to metastasize, i.e. migrate and invade other tissues, greatly determines patient outcome. A key challenge in the development of anticancer therapies is that cells grown in 2D do not accurately represent their functions in 3D. Microfluidic cell culture aims to provide more biologically relevant preclinical models by capturing key physiologically-relevant parameters to better model tissues *in vitro*. This project will develop a simple 3D cancer metastasis model in a microfluidic chip device, where the rate of migration of cancer cells through the chip over time will be measured by a number of microscopic techniques. In particular, fluorescence microscopy will be applied to visualise cell migration and cell activity. In addition to that, label-free Brillouin microscopy will provide important information about cell stiffness in relation to metastasis, as well as other conventional biological imaging/assays. The effect of a drug on the metastatic ability of the cancer cells will also be measured for comparison. Overall, such a model will enable greater understanding of cancer metastasis pathways and development of more effective and targeted cancer therapies that disrupt the ability of cancer cells to spread.
Techniques the student would be working with	Cell culture, microfluidics, light microscopy, confocal fluorescent microscopy, confocal Brillouin imaging
Infrastructure and support required for project execution	PC1/2 Cell culture facility, Microfluidics laboratory, Brillouin Imaging laboratory (MAU), microscopy unit (CB04.level 7)

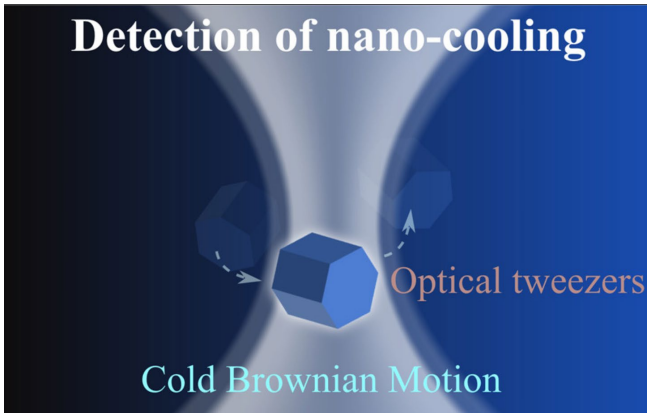
Project title	Light-sound interaction in soft porous materials
Name of supervisor(s)	Dr Irina Kabakova, Prof. Christopher Poulton
Email address	Irina.Kabakova@uts.edu.au, Christopher.Poulton@uts.edu.au
Project description & aims (250 words max, summary written for prospective students)	Biological materials, such as cells and tissues, are soft materials that consist of a solid porous network and liquid filling. The mechanical properties of these materials are linked to their function, and maintenance of appropriate elasticity levels is critical for their healthy life cycle. It has been recently shown that cells change stiffness with progression of several diseases (e.g. cancer, fibrosis etc.) Thus, it is important to understand the mechanisms that influence the cell and tissue's stiffness and be able to control it. In this project, numerical algorithms will be developed to assist with the understanding of mechanical and acoustic properties of soft porous materials. This will ultimately play a pivotal role in interpretation of experimental studies based on opto-acoustic interactions in biological materials such as those using Brillouin microscopy and spectroscopy.  (a) Uniaxial tension (b) Shear This project is suitable for someone with an ability to solve problems using theoretical and computation approaches. Some experience in programming (MATLAB preferred, but other programming languages such as python and C++ are also appropriate). Knowledge of the finite element software package COMSOL is a bonus but is not required.
Techniques the student would be working with	Finite-element modelling (MATLAB, COMSOL), development of analytical models based on energy bounds approach
Infrastructure and support required for project execution	A COMSOL multi-user license is available for student and supervisors within full duration of the project.

Project title	Synthesis and biomedical applications of hybridized black phosphorus – upconversion nanoparticles
Name of supervisor(s)	A. Prof. Charlene Lobo, Dr. Helen Xu
Email address	Charlene.lobo@uts.edu.au
Project description & aims (250 words max, summary written for prospective students)	Emerging two-dimensional (2D) materials such as hexagonal boron nitride (h-BN) and 2D black phosphorus (BP) have unique combinations of properties, including direct, tunable bandgaps (in the ultraviolet and infrared respectively) and biocompatability. Prior studies have demonstrated that unprotected BP nanoparticles undergo degradation in air and in aqueous buffer solutions, resulting in the formation of nontoxic phosphates and phosphonates[1-2]. This project will develop methods of fabricating and functionalizing stable BP nanoparticles for use as biomedical sensing probes and therapeutic agents. Nanoparticle synthesis will be conducted using conventional wet chemistry methods, and the synthesized nanoparticles will then be appropriately functionalized to yield well-dispersed nanoparticles in aqueous media. BP nanoparticles will then be hybridized with upconversion nanoparticles (UCNPs) to yield biocompatible imaging and contrast agents (see figure and references below).  References 1. Lee, H. U.; Park, S. Y.; Lee, S. C.; Choi, S.; Seo, S.; Kim, H.; Won, J.; Choi, K.; Kang, K. S.; Park, H. G.; Kim, H. S.; An, H. R.; Jeong, K. H.; Lee, Y. C.; Lee, J., Black Phosphorus (BP) Nanodots for Potential Biomedical Applications. *Small* **2016,** *12* (2), 214-219. 2. Shao, J. D.; Xie, H. H.; Huang, H.; Li, Z. B.; Sun, Z. B.; Xu, Y. H.; Xiao, Q. L.; Yu, X. F.; Zhao, Y. T.; Zhang, H.; Wang, H. Y.; Chu, P. K., Biodegradable black phosphorus-based nanospheres for in vivo photothermal cancer therapy. *Nat. Commun.* **2016,** *7*, 13.
Techniques the student would be working with	Chemical and photochemical synthesis, confocal and UV-visible spectroscopy, mass spectrometry, electron microscopy, thermogravimetric analysis, among other techniques.
Infrastructure and support required for project execution	All research facilities are available in the School of Mathematical and Physical Sciences and the Institute for Biomedical Materials and Devices, UTS.

Project title	Combined super resolution microscopy and optical trapping for non-adherent cell imaging
Name of supervisor(s)	David McGloin, Fan Wang
Email address	david.mcgloin@uts.edu.au; fan.wang@uts.edu.au
Project description & aims (250 words max, summary written for prospective students)	Super resolution microscopy is a technique in which images can be produced that break the normal resolution of an optical imaging system, which is typically half the wavelength of the light used. It has significant application in biological imaging systems, and the general techniques won a Nobel Prize in 2014. In this project you will develop and build a super resolution microscope based on the idea of *structured illumination microscopy* (SIM). In this technique multiple images of a sample illuminated with an optical pattern are combined to extract extra information from the image than would be possible with a single image. The patterned light can be produced in a number of ways, and you will explore the use of *spatial light modulators* (SLMs)for this purpose – these devices are able to shape a simple laser spot into a complex pattern, and to do this in real time, allowing the necessary images to be built up to form the final high-resolution pattern. At the same time, you will explore how such a system can be combined with a technique called *holographic optical tweezers* which use lasers to trap and hold (and rotate) microscopic objects to allow non-adherent cells to be trapped and rotated to allow 3D super resolved images of cells to be built up. The project will involve the development and building of the microscope and tweezers, along with developing software for controlling the instruments and analysing data.
Techniques the student would be working with	• Optical design and engineering • Microscopy • Labview/Matlab/Python • Algorithm development and implementation • Image Analysis • Use of lasers • Beam shaping • Cell handling
Infrastructure and support required for project execution	The project will be based in the photonics laboratories at Tech Lab, and will make use of existing infrastructure: lasers, spatial light modulators, microscopes etc.

Project title	Holographic microscopy for bioaerosol analysis
Name of supervisor(s)	David McGloin, Fan Wang
Email address	david.mcgloin@uts.edu.au; fan.wang@uts.edu.au
Project description & aims (250 words max, summary written for prospective students)	Holographic microscopy enables the 3-dimensional tracking of fast moving particles without the need for any scanning parts or labelling of the particles under study. It is well suited for the analysis of particles such as aerosols or dynamic biological organisms. It works by examining how light that scatters from the particle of interest interferes with light that is unscattered. By recording the interference patterns and then applying an algorithm that links the recorded pattern to the expected pattern the position of a particle can be inferred. In this project you will develop a simple holographic microscope suitable for analysing aerosol production from a medical nebulizer as part of a wider project on exploring the interaction of aerosols with optical and electric fields, and as a measure as to how simple lung-on-a-chip devices might be analysed in real time. The project will involve the building of the microscope and the development of the software to analyse the particle behaviour. There may be scope to examine simple machine learning algorithms to analyse the image data as well. The project will initially focus on imaging solid particles in fluid before moving to more challenging samples, such as airborne droplets with an end goal of looking at many thousands of particles in a nebulizer stream. There is also an opportunity to examine applications in the analysis of bioaerosols such as pollen, for environmental monitoring applications.
Techniques the student would be working with	• Optical Design and Engineering • Use of lasers • Microscopy • Nebulizers • Modelling using inverse algorithms • Optical scattering • Labview/matlab/Python • Data Analysis • Instrument control
Infrastructure and support required for project execution	The project will be based in the photonics laboratories at Tech Lab, and will make use of existing infrastructure: lasers, optical components etc

Project title	Computational Modelling for the solution of Inverse Problems occurring in Biomedical Imaging
Name of supervisor(s)	Ananda Sanagavarapu
Email address	Ananda.Sanagavarapu@uts.edu.au
Project description & aims (250 words max, summary written for prospective students)	The aim of the project is to solve inverse problems that occur in biomedical imaging using computational Modelling.
Techniques the student would be working with	Computational techniques, Numerical Modelling and MATLAB
Infrastructure and support required for project execution	MATLAB

Project title	Bio-refrigeration: nanoscale laser cooling in physiological environments
Name of supervisor(s)	Dr. Fan Wang
Email address	fan.wang@uts.edu.au
Project description & aims (250 words max, summary written for prospective students)	Laser refrigeration, also called laser cooling, is a technique to reduce the temperature of an object by applying laser beams. Laser refrigeration of nanoparticles requires optical tweezers to confine particle movement, maximise the energy transfer rate and measure the local temperature at the nanoscale from the cold Brownian motion of particles. Lanthanide-doped fluoride nanoparticles have been found to have a high potential for nanoscale laser refrigeration. However, due to their small size and low refractive index, these nanoparticles have extremely small polarisability compared with other optical tweezering probes. This poses a challenge in detecting 3D Brownian motion. As a result, it has not been demonstrated that Ln-NPs smaller than 300 nm can act as a cooling probe. Whether a small Ln-NP and its surrounding medium can be cooled through existing mechanisms is still unknown. The project aims to overcome the problems of motion detection and force generation in nanoscale optical tweezers, leading the way to the discovery of nanoscale laser cooling in a physiological environment. This nanoscale cooling shows great potential as a unique tool to enable the investigation of many fundamental questions in biophysics, such as how metabolism regulates cellular proliferation and how integrin coordinates with endogenous force. The student is supposed to use both cold Brownian motion and emission spectrum of the optical trapped particle to detect its temperature during laser cooling. 
Techniques the student would be working with	Optical engineering, LabVIEW programming, Machine learning programming
Infrastructure and support required for project execution	Optical tweezers system in biophotonics lab at level 5, building 7