

MSc Projects - chosen in 2014-2016

Biomaterials and Tissue engineering

Protein-templated nanoparticles for targeted delivery

Delivery of metal and metal oxide nanoparticles directly to specific biological targets enables both imaging and therapy of diseases such as cancers. To target specific cell types and tumours, nanoparticles need to be chemically bound to selected protein or peptide molecules requiring complex multi-step chemistry that can limit applicability. An alternative approach is to use protein molecules directly as nucleation sites for nanoparticle growth, i.e. to grow particles directly within the protein molecules of interest. The project will investigate the potential of this approach for generating disease-targeting nanoparticles.

Nanoparticles for Cancer Treatment

Small bioactive glass particles can be taken up by cells without them changing cell behaviour. The aim of this project is to develop particles that will be taken up by cancer cells and when they are inside the cancer cells release ions that will kill the tumour cells. The project will be lab based and involve particle synthesis and testing, including imaging and degradation studies.

Antibacterial titanium implants

As resistance to antibiotics increases, alternatives for fighting/ preventing infection are needed. Silver ions are known to kill bacteria. Titanium alloy implants are the most common medical devices in orthopaedics and dentistry. Smith and Nephew, a multinational medical device company, have developed a process for introducing silver into the surface of their implants. They do not yet know in what form the silver is incorporated, its 3-D distribution and depth, or what variables affect silver ion release.

Project Aims:

To investigate process (manufacturing) variables on the nanoporosity of the surface and incorporation of silver and its release into simulated body fluids. The project will be in close collaboration with Smith and Nephew. It will involve doing the surface treatment of titanium implants provided by the company and characterising the product.

Hybrid scaffolds for cartilage tissue engineering

Tissue engineering combines biology and materials engineering principles to regenerate damaged tissue to its original function. Temporary templates (scaffolds) must be developed to guide tissue repair with different mechanical properties depending on the application. For cartilage regeneration, the scaffolds must have mechanical properties mimicking cartilage. Composites are required, but conventional composites will not work. This project will involve the development of new hybrids (nanocomposites) and the tailoring of their properties to match cartilage. The project will be lab based and involve materials chemistry, processing and then characterisation by imaging, degradation studies and mechanical testing. Successful scaffolds will be tested in cell culture.

Extracellular induction of hematopoietic maintenance genes by human mesenchymal stem cells

Human mesenchymal stem cells (hMSCs) are an invaluable part of the hematopoietic stem cell (HSC) niche in bone marrow. However, the extracellular cues that stimulate expression of HSC maintenance genes in hMSCs remain unexplored. In this project, we are taking a modular, bottom-up approach to identify outside-in signals for inducing up-regulated or de novo expression of HSC maintenance genes in order to construct an in vitro recapitulation of the complex bone marrow microenvironment.

Graphene oxide polymer particles for therapy

Graphene oxide has many interesting properties. This project will focus on the photothermal property of graphene oxide that can be used to kill bacteria and cancer cells. Specifically graphene oxide $\frac{1}{2}$ polymer based nanoparticles will be investigated. Polymers will be used in order to stabilise graphene oxide in water and facilitate the attachment of further functional groups. This study will involve both the fabrication and characterisation of polymers and the graphene oxide-polymer particles.

Biomechanics and Mechanobiology

Device for measuring femoral movement at the knee

How the knee moves during normal activities is difficult to quantify accurately. This is mostly due to significant relative movement between the skin surfaces and the underlying skeletal structures. In this project a prototype method for allowing the tracking of the femur at the knee will be re-engineered to better quantify femoral movement. This is a highly relevant clinical project that will result in a device to be used in an orthopaedic outpatient clinic.

Various projects involving fluid mechanics in the eye

The eye is an exquisite organ that is filled with two main fluids: vitreous humour and aqueous humour. Many processes that are vital for maintaining the health and function of the organ are dependent on the mechanics underlying them. It is possible for this project to be chosen by more than one student, as there are several subprojects available, each involves different skills. Subprojects include:

- a. Modelling flow in the tear ducts of the eye*
- b. The tear film of the eye*
- c. Modelling of the motion of vitreous humour within the eye*
- d. Investigation of the artiflex lens device in the eye*
- e. Improved treatment for retinal detachment - scleral buckle*

Functional Electrical Stimulation to lower joint contact forces

Functional electrical stimulation (FES) allows muscle contractions to be driven by an external stimulus. This has the prospect of changing how people move and load their bones and joints so that the effects of joint disease and pain are reduced. In this project FES will be used to reduce loading on the knee joint. This work will be in collaboration with researchers in the group who are using FES and musculoskeletal modelling for other pathologies of the knee.

Composite surrogate material for lung tissue

The lung is a very complex mechanical system. Lung like many soft tissues in the body has a very complex mechanical behaviour when subject to various loading conditions. Most soft biological tissues also exhibit significant strain rate sensitivity. This project aims to develop and test a surrogate soft solid composite material to match the bulk visco-elastic/plastic properties of lung tissue.

The project will involve determining initial estimates of lung properties under compression and shear. This data will then be compared to a surrogate material such as gelatine. This gel will then be modified using filler material to create pores and inclusions. Micromechanical approaches will be exploited to design this composite to match the rate sensitive behaviour of lung tissue.

Mechanical behaviour of human trabecular bone during across strain rates measured with multi-scale imaging techniques combined with mechanical testing

Strain rates applied to body tissues can vary enormously, from that seen during normal walking, estimated as in the range of 0.002 s^{-1} , rising to 0.05 s^{-1} during downhill running. Higher rates will be seen during sport or recreational activities, rising even higher in the instance of traumatic injury. The strain rates experienced during blast can be orders of magnitude higher, with an associated increase in the damage sustained. It has been shown previously increase in stiffness and reduced toughness in bone tissue during high strain-rate loading cannot be explained by macro level mechanical tests alone, but must involve changes in the bone lamellar and osteon and fibrillar level. The precise mechanisms for this behaviour have not been shown in previous studies. Therefore the aim of this study is to investigate mechanical behaviour of trabecular bone during cross strain rates using multi scale imaging techniques such as high speed videography, synchrotron X-ray diffraction and confocal microscopy and linked those mechanical properties to macroscopic bones fractures seen in blast injuries. Student will carry out tensile and compression mechanical testing on human trabecular bone specimens using a custom made mechanical testing machine at Imperial College London and UK synchrotron X-ray facility at Diamond Light Source Ltd. Oxfordshire.

Medical Physics and Imaging

Single ultrasonic element with dual non-invasive therapy and monitoring capabilities

Advances in focused ultrasound technologies have led to the development of a wide range of noninvasive therapeutic techniques. In these methods, ultrasound is generated from a curved transducer, which propagates through several layers of tissue and converges to a small focal volume deep in the body. The localised ultrasound can heat, push, expand, and contract the tissue leading to a wide range of bioeffects including heating of tumours to destroy cancer, opening of brain capillaries to enhance drug uptake, pore formation in cell membranes to enhance cell transfection, and clot

dissolution to treat blocked arteries. Yet the same noninvasive feature, which makes this technology clinically attractive, makes controlling of thermal and mechanical forces deep in the body difficult. Previous studies including the supervisor's previous work have developed methods to listen to the acoustic emissions generated from the diverse range of ultrasonic phenomena in order to predict therapeutic outcomes. Yet the ultrasound excitation elements and detection elements are typically distinct from each other, forcing the placement of the elements at separate locations. This arrangement reduces achievable excitation volumes and detection resolutions while increasing the cost of the ultrasonic system. The aims of this project is to (1) understand how ultrasound can be generated and captured from the same transducer, (2) design the appropriate transducer and filters to extract received emissions, and (3) create a single ultrasonic element transducer capable of both therapy and monitoring of ultrasonic applications.

Numerical simulations and experimental investigations of microbubble doppler effects in long-pulse ultrasound therapy

Focused ultrasound in conjunction with pre-formed systemically administered microbubbles have emerged as a non-invasive and targeted therapeutic system with potential use in the treatment of various pathologies. Bioeffects induced by the interaction of ultrasound and microbubbles are mostly dictated by the microbubble dynamics within the vasculature. Whereas a large body of work has focused on imaging applications, there remains poor understanding of these dynamics in the therapeutic regime.

The aim of this project is to successfully model the microbubble cloud movement within a vascular network under long-pulse therapeutic ultrasound exposure and understand the correlated acoustic emissions. The student will develop numerical models of the ultrasound-microbubble-surrounding medium interactions, i.e. primary radiation forces, secondary radiation forces, drag forces etc. Many-body simulations (MBS) applied in other areas of Physics (based on methods such as the particle mesh or the PM-Tree) will be implemented here to approach the complex problem of the microbubble cloud mechanics during long-pulse therapeutic sonication. Theoretical results will be compared with optical and acoustic experimental data acquired by the student, with focus on the detected Doppler shifts in the acoustic emissions of the translating microbubbles.

The successful applicant will join the Noninvasive Surgery and Biopsy laboratory and will have the opportunity to work in a vibrant and multidisciplinary environment, in collaboration with experts in Engineering, Physics, Computer Science and Biology. The project can be extended according to the interests of the student.

Real-time monitoring of ultrasound therapy

Focused ultrasound and circulating microbubbles have been successfully tested in vivo in diverse therapeutic applications such as targeted drug delivery, capillary-opening techniques, sonoporation etc. The success and the safety of an ultrasound-based, microbubble-seeded therapy largely depend on the spatiotemporal distribution of the acoustic cavitation activity within the focal volume, where the therapeutic effect occurs. Thus, a reliable method of spatiotemporally resolving the microbubble acoustic activity is needed.

An emerging approach for the real-time monitoring of cavitation activity is the Passive Acoustic Mapping (PAM) method. Briefly, in PAM acoustic signals are captured using a multi-element linear array and then post-processed in order to localise the emitting sources. Whereas the resolution of the technique in the lateral dimension is satisfactory, interference patterns arising in the reconstruction process result in poor axial resolution. Furthermore the technique is so far restricted in 2-D maps, thus rendering the localisation of acoustic sources beyond the elevational focus impossible.

The aim of this project is to develop algorithms in order to enhance the performance of the PAM technique, especially regarding the amelioration of its axial resolution. Briefly, we will apply the available beam-forming approaches in our system (starting from the Robust Capon Beamforming algorithm) and investigate ways to optimise the acoustic map reconstruction process. Furthermore, the idea of acquiring 3D passive acoustic maps will be explored, by using our automated 3D positioning system. The student will conduct in vitro phantom experiments in order to test the performance of the algorithm and, if applicable, will be given the opportunity to analyse in vivo data. The project can be extended according to the interests of the student.

Device for temporary loop ileostomy

Temporary loop ileostomy is carried out in order to protect a distal bowel anastomosis (bowel join) is carried out in order to protect a distal bowel anastomosis (bowel join). Following the bowel surgery the ileostomy protects the bowel during healing. Once the bowel has healed the ileostomy is reversed but this requires a further operation.

The project is to design a fluid switch that be used to divert the colon contents to the ileostome, and then be reversed without a further operation. The device will be a plastic part, perhaps with remote

operation.

Interventional MRI positioning using an IR sensor

This work will help develop a clinical tool and protocol to support imaging during interventional work at St Marys Hospital. An optical/IR sensor array will be used to track a positioning device and navigate through a series of images in 3D. This will include some programming and possibly building a wireless transmitter. This project would be most suited for someone with a strong interest in electronics and some experience in programming in MatLab.

Phase Encoded Artefact Suppression

Phase-Encoded Artifact Suppression (PEAS)

A student is required to assist in development of a novel pulse sequence for reduced-artefact imaging of metal implants.

This sequence will use a phase-encoded-only acquisition for 3D imaging, which is traditionally a method too slow to be put to clinical use. The student will conduct research to find a suitable method of undersampling (compressed sensing) and implement this into the PEAS pulse sequence on a Siemens MRI system, and also handle the corresponding offline reconstruction algorithm. A good working knowledge of MATLAB software and interest in image-processing would be desirable for this project.

Neurotechnology

Cyathlon: Development of Powered Arm Prosthetic

A project to develop a powered arm prosthetic to take part in the Cyathlon. Details of the Cyathlon can be found at: <http://www.cyathlon.ethz.ch/en/>

Three-dimensional mapping of the dopamine pathway to the prefrontal cortex

Working memory (WM) allows us to temporarily store task-relevant information, such as performing mental arithmetic or remembering a phone number. A central locus of working memory processing is the prefrontal cortex (PFC), where some neurons display sustained elevations in firing during WM tasks. Interestingly, when a WM task is unsuccessful, these sustained firing rates are not present, indicating a link between this neural activity and success or failure of the WM task.

One reason why we might fail at a working memory task is the presence of a distractor, which interrupts the neural activity in the PFC and destroys the WM representation. Our ability to resist these distractors seems to crucially rely on dopamine (DA) levels in the PFC, as people with imbalances in DA (such as schizophrenic or ADHD patients) have profound deficits in WM performance.

PFC DA originates from DA neurons in the midbrain, the axons of which traverse many millimeters to reach their destination. However how and where exactly DA has its effect in PFC is unknown. We are now able to selectively label the DA pathway projecting to PFC, enabling a thorough characterization of this innervation.

This project would involve using novel whole-brain imaging techniques to map the pathway of DA neurons to the PFC in 3D, and analyzing density distribution of DA axons within different PFC areas and different cortical layers. Therefore this project would be ideally suited to a person with interests in large-scale neural anatomy and good knowledge of image processing techniques.

Online optogenetic manipulation of neural populations in vivo

Neural spike trains in primary cortical areas can reliably encode many features of sensorimotor activity. Our understanding of this code is far from complete, but there is ample evidence that stimulus features are encoded through alterations in neural firing rate (a rate code). However, individual neurons typically only respond to a small subset of stimulus space: for example, individual neurons in the auditory cortex only fire spikes in response to relatively narrow bands of sound frequency. As such, accurate representations of the sensory world typically require the concerted activity of large numbers of neurons (a population code).

Novel recording technologies now allow experimenters to record from many different cortical sites simultaneously and to control neural activity with light (via optogenetic probes such as channelrhodopsin). In our lab, we use silicon microelectrodes with up to 64-closely spaced electrode recording sites. These electrodes allow the spiking activity of up to 100 neurons to be recorded simultaneously. However, extracting the responses of each individual cell from these recordings requires complex processing which requires time (usually several hours), so neural responses must be determined offline. Therefore, because we know little about the individual tuning of cells during the recording, only low-resolution receptive field mapping is possible.

The aim of this project is to develop an algorithm in Matlab and/or LabView to perform online conversion of light evoked neural spike trains. This information will be used to calibrate the laser power

to optimally stimulate distinct populations of neurons.

This project requires the manipulation of large data sets, and ideally the implementation of a flexible user-friendly interface, therefore excellent coding skills are a must. Data and guidance will be provided by a postdoc in the lab and there will be an opportunity to observe and assist in the collection of electrophysiological recordings.

Automated home-cage behavioural testing in rodents

To understand the function of the brain it is necessary to understand the language of the brain, the neural code, and the thoughts and actions it's function leads to. This requires two approaches: measurement of the neural code (often in animals) and measurement of the behaviour it relies on (often in humans). The accuracy of these data relies on two assumptions: the first is neurons in animals must do the same things as neurons in humans and the second is that this underlies the same behaviour in animals as it does in humans. Recently there has been a greater drive to collect neural data in awake-behaving animals allowing neural data to be compared directly with behaviour of the same subject it was collected from.

Unfortunately training animals to complete the same simple tasks as a person is often not possible. In essence humans are smarter than animals. This means that training animals on psychophysical tasks can often take months using up much of the neuroscientists time. In addition even after months of training the animal might turn out to be poor at the task. The reason this takes so much time is that animals are only trained during brief periods of the day where the experimenter transports the animal to a test area and the supervises learning (or lack thereof). This process is fraught with problems, for example transporting and handling the animals often scares the animal, the animal is then expected to learn in a brief time window and the whole time the researcher must be present. One way this could all be avoided is by using an automated behavioural setup located inside the animal's home cage. This way the animal would not need to be moved or handled by the experimenter, the animal could initialise at any time of the day and as often as it likes and (best of all) the experimenter would not need to supervise learning. This would allow large quantities of animals to be trained with the minimum of effort.

This project would be to design and build a simple operant behavioural rig to test auditory discrimination of mice in their home cages. This project suits a person with a hands-on approach but with some knowledge of basic coding e.g. in Matlab.

Computational modelling of the peripheral nervous system

Bioelectronic medicine, in which devices connected to groups of individual nerve fibres are used to control the patterns of electrical signals to restore health to organs and biological functions, has been suggested to have the potential to make major advances in the treatment of conditions resistant to drugs, including diabetes, obesity, hypertension and pulmonary diseases (Famm et al, Nature 496:159-61, 2013). The development of bioelectronic medicines, however, is contingent upon the existence of suitable technology for monitoring and perturbing activity in peripheral nerve fibres; in particular, being able to "read out" and interpret signals carried by a peripheral nerve fibre is an essential milestone.

In this project, we will develop a detailed computational model of the electrical activity of peripheral nerves, including in particular the vagus nerve. This model should take into account the presence of multiple fibres with differing properties (fibre diameter, myelinated versus unmyelinated, etc) and produce as an output the type of signals produced by nerve cuff electrodes. We will make use of NEURON compartmental modelling software, wrapping it in Python in a similar way to the analogous LFPy. The project will suit a student with a strong computational and programming background, and preferably experience with Python.

Decoding algorithms for interfacing with the peripheral nervous system

Bioelectronic medicine, in which devices connected to groups of individual nerve fibres are used to control the patterns of electrical signals to restore health to organs and biological functions, has been suggested to have the potential to make major advances in the treatment of conditions resistant to drugs, including diabetes, obesity, hypertension and pulmonary diseases (Famm et al, Nature 496:159-61, 2013). The development of bioelectronic medicines, however, is contingent upon the existence of suitable technology for monitoring and perturbing activity in peripheral nerve fibres; in particular, being able to "read out" and interpret signals carried by a peripheral nerve fibre is an essential milestone. In this project, we will develop decoding algorithms capable of reading out both continuous physiological signals, and discrete "events", from peripheral nervous system (PNS) electrical signals. These algorithms will be applied to a variety of datasets collected by members of a research network in Bioelectronic Medicines.

The project would suit a student with a strong background in signal processing machine learning, information theory or similar areas, and experience with programming in MATLAB.