

**EPSRC Centre for Doctoral Training
in the Advanced Characterisation of Materials**

**Project List and Outlines 2018/19**

1. **Mineralomics of the eye**

Defining pathological processes in age-related macular degeneration (AMD) is essential to limit the consequences of this major cause of legal blindness in the elderly. Clinical imaging methodologies, especially high-speed optical coherence tomography, are being used to define anatomical biomarkers that show increased risk of developing end stage AMD. Recently proposed risk biomarkers include the presence of calcified spherules in extracellular deposits like drusen and glistening nodules with hypo reflective interiors. This fourth biomarker is strongly associated with the advancement to geographic atrophy - the major form of end stage AMD. These structures have recently been identified by the supervisory team to be formed by apatite, an unexpected discovery that is being submitted to Nature Medicine. During this work, we learned that these kinds of studies require an interdisciplinary team with expertise in eye diseases (IL), high resolution analytical methods (SF) and soft tissue mineralization (SB). We discovered that there is varying hydroxyapatite crystallinity associated with all drusenoid structures in the human eyes. These suggest that there is complex, previously unrecognised chemistry taking place at cellular interfaces in the back of the eye. We proposed that understanding this calcium phosphate deposition is the key to slow the progression or in fact preventing the development of advanced AMD.

The major aim of the proposed PhD studentship will be to fully understand the chemistry, biochemistry and cell biology underpinning the mechanism leading to age related macular degeneration using high resolution molecular analysis techniques including SEM, TEM, FIB-SIMS, and ToF-SIMS to elucidate further the role of different mineral species in the development and progression to blindness in AMD.

1. **Optimising solar hydrogen production through studies of ultrafast dynamics**TiO2 remains the subject of intense research associated with its photocatalytic properties. Indeed, understanding how the TiO2/water system works at the level of individual atoms and molecules is one of the grand challenges of contemporary physical science. In this project we will focus on the dynamics, in particular that associated with plasmonic enhancement by gold nanoparticles. This will be studied in tandem with ultrafast interfacial energy-transfer processes associated with model photocatalysis and solar energy conversion involving TiO2. Although models to describe the associated phenomenon have been in place for many years, there have been no direct measurements of the electron state dynamics to test these ideas.
2. **Spin dependent transport in semiconductor nanostructures**The spin-orbit coupling in semiconductor nanostructures allows control of spins and spin dependent conduction in the absence of magnetic materials, such a phenomenon has many possible applications in spintronics and quantum computation. Although the effects are only observed at low temperatures the physical concepts which are acquired offer new perspectives for observing such phenomena at higher temperatures. In this project the objective is to combine the spin-orbit interaction with the lifting of spin degeneracy due to the electron interaction in narrow channels. We will establish a spin lattice by means of a nano-structural design of sequential pairs of patterned gates, which, when appropriately biased, allow control of spins. It is intended to establish pairs of electrons in which the spins are manipulated and then determine if the electrons are entangled so allowing a range of experiments with potential applications in quantum information processing. It is intended to introduce new findings in which the interaction between electrons can be manipulated between anti-ferromagnetic and ferromagnetic by control of separation during transport. The semiconductors utilised will be InSb, InGaAs and InAs quantum well heterostructures, patterned into nanostructures.
3. **Structural characterisation of neuropathological protein aggregates via fluorescence resonance energy transfer (FRET) and stimulated emission depletion (STED) spectroscopy**Protein misfolding and aggregation is one of the most important areas in current biomedical research. The failure of proteins to fold properly, or to remain folded, is a central feature of a number of increasingly widespread disorders (Parkinson’s and Alzheimer’s diseases to type II diabetes, and cystic fibrosis). One of the most common outcomes of protein misfolding is the formation of aggregates that result in the deposition of amyloid fibrils and plaques. By attaching fluorescent markers to individual proteins (ICL), e.g. -amyloid (Alzheimer’s) and -synuclein (Parkinson’s), we can follow structural changes and aggregation dynamics through steady state and time resolved fluorescence anisotropy (depolarization) measurements (UCL) and single molecule FRET (ICL). These measurements are sensitive to the close proximity and orientation of the fluorescent markers, allowing the structure of the aggregates to be characterised. We will also use two-photon excitation as a means of creating a higher degree of excited state order which is highly sensitive to molecular structure and FRET depolarization. This will be probed via new time-resolved STED spectroscopy techniques (UCL)
4. **3D Imaging of next generation quantum computers and integrated circuits**It is now possible to create atomically thin regions of dopant atoms in silicon patterned with lateral dimensions ranging from the atomic scale (angstroms) to micrometres. These structures are building blocks of quantum devices for physics research and they are likely also to serve as key components of devices for next-generation classical and quantum information processing. Recently our research group demonstrated the capability to image and electronically characterise three-dimensional phosphorus nanostructures using the emerging technique of scanning microwave microscopy (SMM). This project will involve developing the SMM technique, as well as scanning tunnelling spectroscopic techniques, to achieve high-resolution 3D imaging of buried nanostructures to a level where they will be useful for industrial applications.
5. **Nanomechanical characterisation of soft biomimetic materials**The project objective is to develop and utilise a suite of advanced analytical techniques, including optical tweezers and microfluidics, for characterising the (nano)mechanical properties of ‘soft’ biomimetic materials such as liposomes or biomembranes. The principal aims of this project are: to study the mechanical properties of biomimetic vesicles undergoing extreme deformations as a result of an applied external stress, e.g. optical, acoustic, or fluid shear forces; to study phase separation and rupture in artificial vesicles under external forcing; to use the result of the above studies to engineer membrane materials with properties optimised for applications including controlled drug release and microreactors.
6. **Probing the Importance of Nanostructure Design for Medical Imaging Agents using Precision Chemistry and Characterisation Techniques**Magnetic resonance imaging (MRI) is a powerful non-invasive imaging technique which becomes considerably more potent when contrast agents which enhance the relaxation of water protons are applied. Clinically approved contrast agents are usually based on paramagnetic gadolinium (Gd) but suffer from poor signal-to-noise, necessitating high dosages, with associated health concerns. Contrast agents based on nanomaterials have unparalleled capabilities to enhance this vital tool, with some already in clinical use. Silica nanoparticles with immobilised Gd chelates display significantly higher MRI contrast enhancement with much lower doses than traditional molecular agents. Recent work has discovered that the fine structure of the materials and the location of the contrast agent on their surfaces play a key role in MRI signal enhancement, however, this behaviour is poorly understood. This project aims to produce and characterise precision-engineered nanostructures which will provide important insights into the interaction of Gd chelates with nanosurfaces. Paramagnetic units will be immobilised on silica nanoparticles using carefully tailored chemical attachment techniques, which will control the flexibility and geometry of the paramagnet. Exploiting photoswitchable linkages, based on azobenzenes, surface proximity of the paramagnet will be controlled through light, allowing the impact of paramagnet flexibility, confinement and distance to the hydrated nanosurface to be characterised.
7. **Microdroplet-based nanoparticle characterisation**In the past 20 years, gold nanoparticles have emerged as a promising material platform for biochemical sensing, drug delivery, catalysis and optoelectronics.[1,2] Their surface properties govern key functional parameters such as solubility, molecular recognition or cell membrane interaction.[3,4] Yet, even today the characterisation of the nanoparticle ligand shell with nanometre resolution remains a challenge. The project will be centered around the study of gold nanoparticles with tunable size, shape and surface properties at liquid-liquid interfaces. A modular synthetic approach allows us to systematically tune structural properties and study effects on interfacial assembly and mechanically forced desorption. Further insights on crucial parameters of interfacial assembly and disassembly will lead to implementation projects, such as Pickering emulsions with stimuli-controlled uptake and release of active compounds, the alignment and deposition of supra-colloidal aggregates, and novel fabrication routes for nanoscopic devices. A comprehensive portfolio of material characterization techniques will enable the student to acquire a sound set of skills and get immersed in a very active and promising field of research
8. **Structural and compositional characterisation of resistive switching in silicon oxide (SiOx)**The proposed project builds on a recent highly successful preliminary collaboration between the UCL and ICL groups that has demonstrated the inhomogeneous structure of resistive switching SiOx and its evolution during electroforming and switching. Resistive switching in SiOx is an exciting new phenomenon with huge technological potential. Resistive switching devices are components whose electrical resistance can be varied by up to 106 by an applied field. They are promising candidates for next generation electronic memories, offering significant advantages over Flash memory: very high packing density; fast switching; low energy; 3D integration, and ease of processing. However, the mechanism of switching is poorly understood. Although it arises from the formation of conductive filaments within the oxide, the nature of the filaments is not known. To understand this requires a comprehensive structural and compositional study of switching oxides – ideally with in-situ measurements of changes during filament formation.
9. **Studying nanoparticle recognition of target analytes for improved biosensors in disease diagnostics and therapeutic drug monitoring**Nanoparticles provide a versatile toolbox for biosensing. A broad range of capping agents provides a multitude of recognition elements for target analytes as shown in Figure 1. Transduction and read-out may be pursued by colorimetric, fluorimetric, electric, electrochemical and other spectroscopic means. Meanwhile, a plethora of colloidal-based biosensing concepts exist but parasitic interaction with non-target species and quantitative sensing over a broad dynamic range remains a challenge. The project is based around the development of a reliable characterization platform geared towards the screening and validation of molecular receptors for target species in diagnostics and therapy. The group of Prof Stevens has developed numerous successful nanoparticle-based recognition pathways. Recent progress in the research groups of Dr Guldin now enables to routinely immobilise nanoparticles on the surface of a quartz crystal microbalance with dissipation monitoring (QCM-d). A modular two-step synthesis allows to decouple nanoparticle synthesis from surface functionalisation. The aim of this project is now to develop a characterization approach that provides straightforward and reliable feedback for effective receptor development.
10. **Nanoscale and GHz characterisation of novel superconducting spintronic interfaces**Although superconductivity has been known for more than 100 years since the Onnes's first discovery in mercury, it remains one of the most fascinating and in some cases mysterious phenomena in condensed matter physics. Undoubtedly, discovering a room temperature superconductor for example would have profound impact but the properties of such a material have yet to be established. Magnetism has a detrimental effect on the superconducting state, for ordinary superconductors. However, new class of high-Tc superconductivity was discovered in Fe-based materials around 15 years ago suggesting that more exotic forms of superconductivity may in fact rely on the proximity to a magnetic state. More recently spin-polarised supercurrents have been created by interfacing a superconductor with ferromagnetic layers which have spatially inhomogeneous spin states. These hybrid states offer great promise for a field known as superconducting spintronics, where the spin of an electron can be used to carry information, and the superconducting state means that devices will show zero or greatly reduced resistive losses. The forefront of current condensed matter physics is to use nanotechnology based sample engineering and state-of-the-art characterisation techniques to understand this exotic superconducting state at the nanoscale, for furthering our knowledge as well as developing new device concepts.
11. **Plasmonic Engineering of Photoelectrodes at Nanoscale for Entire UV-Visible-Near IR Light Harvesting**The current light harvesting by plasmonic materials has been limited by the narrowband enhancement using single type of plasmonic nanostructures, mainly in green region. The resonant photon wavelength of typical plasmonic metallic nanomaterials (Au, Ag, Cu, Al) ranges from ultraviolet to visible to near infrared. Therefore, in principle, it is possible to design a composite plasmonic/semiconductor system that can harvest photons over the entire solar spectrum. G- C3N4 has been recencently attracted emonours research attendtion due to its intrinsic advantages such as facile sunthesis, appealing electronic band struncture, high stability and earth abundant nature. The aim of this proposal is therefore to design a modular and scalable nano platform, for entire solar spectrum light harvesting, and for proof of concept in g- C3N4 based solar water splitting application.
12. **Quality and Toughness of Bone Interface Adjacent to Novel Bone Graft Materials**

Bone diseases are associated with increased fracture risk and are associated with a huge social and economic burden. For example, osteoporosis increases the risk of fragility fracture, and causes more than 8.9 million fractures annually worldwide. The total cost of treating osteoporosis is ~ $17 billion per year in the United States, which is projected to rise with an aging population. Fractures can have a significant impact on life and those which occur at the hip and spine result in disability, mortality and high healthcare costs. Current treatments for most bone diseases only focus on increasing strength by adding or preserving bone mineral density or bone density. Though these treatments improve the quantity of bone, they do not address changes in the quality of the tissue, i.e. bone’s composition, structure and organisation at the nanoscale that contribute to bone’s toughness independently of bone mineral density. Blunn has generated an inventory of bioactive BGS implanted into bone tissues, which are being evaluated for clinical trials. It is expected that specific implant chemistries/structures will be able to enhance bone quality and toughness, however, these metrics have not been characterised. This project will address this issue by correlating between high resolution electron microscopy and new nanomechanical testing methods developed at Imperial to characterise and measure bone’s quality and toughness at the nanoscale. These metrics will be vital for improved longevity of these biomaterials, for development of their use as new substitutes for osteoporotic tissues and future commercialisation.

1. **Characterisation of shape variant nanoparticles for sensing pathogens**Infectious diseases are tenacious and major public-health problem all over the world. This collaborative project aims to intergrate chemical synthesis, characterisation of nanomaterials and microfluidic device fabrication for plasmonic nanosensors for pathogens in infectious diseases or toxin in food. The morphology of nanomaterials will be characterised by TEM, HRTEM, the optical property will be determined using UV-Vis. The hydrodynamic size of NPs will be assessed by DLS. The crystallite size will be determined by XRD. The magnetic properties will be determined by SQUID. The size distrubtion of NPs will be chacterised by CPS.
2. **MR Fingerprinting Brain Tumours**Magnetic Resonance Fingerprinting (MRF) is a novel rapid imaging technique which aims to assess physical properties of different tissues using one short MRI sequence. Using innovative sequence development, MRF is able to extract quantitative magnetic relaxivity T1 and T2 values, as well as relative spin density and B0 inhomogeneity maps. It then exploits these characteristics to determine the unique signal evolutions that different tissue types will show. Much the same way as fingerprints can be used to determine the identity of a person, MRF requires the use of a dictionary to associate each of these unique signal evolutions with a specific tissue and has been applied in a pilot study on brain tumour patients with promising results. This PhD project will develop the physics for Magnetic Resonance Fingerprinting for the purpose of answering challenging clinical questions faced by Neuroradiologists, such as early determination of tumour transformation in patients with lower grade tumours and tumour response to treatment. The PhD student will investigate and optimise the physics of MRF and develop the dictionary to be used in brain tumours using machine learning. As MRF inherently measures a number of varying physical properties of the underlying tissue, it is hypothesized that it will provide additional information on the growth and development of brain tumours as compared to existing MR modalities.
3. **Light-matter-spin interaction in 2D materials**Atomically thin transition metal dichalcogenides (TMDCs), such as MoS2 and WSe2, exhibit direct-bandgap optical absorption that can be exploited for novel optoelectronics, ranging from flexible photovoltaic cells to harmonic generation and electro-optical modulation devices. These excellent optical properties in TMDCs are unique in a sense that other 2D materials, such as graphene, do not have a direct-bandgap in their electronic states. Research fields in TMDCs have been advancing rapidly, with a. main aim to use them a s a building block of optically active 2D heterostructures with tailored functionalities. A key challenge is to maximise light-matter-spin interactions within the materials, which are inherently weak due to their atomically thin nature. Light management around the 2D layers with the use of plasmonic nanostructures provides a compelling solution. Many of TMDCs have a strong spin-orbit coupling. Therefore, spin-dependence of optoelectronic responses in TMDs is expected. This area of research has not been extensively explored to date, yet having a potential to provide a future form of optoelectronic devices based on the spin degree of freedom. The main goal of this PhD project will be to fabricate novel 2D heterostructures and study their spintronics and optoelectronic properties. In particular we will aim to quantify key photovoltaic and plasmonic parameters in 2D materials and van der Waals heterostructures. This will broaden understanding of light-matter interactions in such systems. One of the main innovative aspects of the work is a study of optoelectronic properties under spin excitations (both GHz microwaves as well as dc magnetic fields).