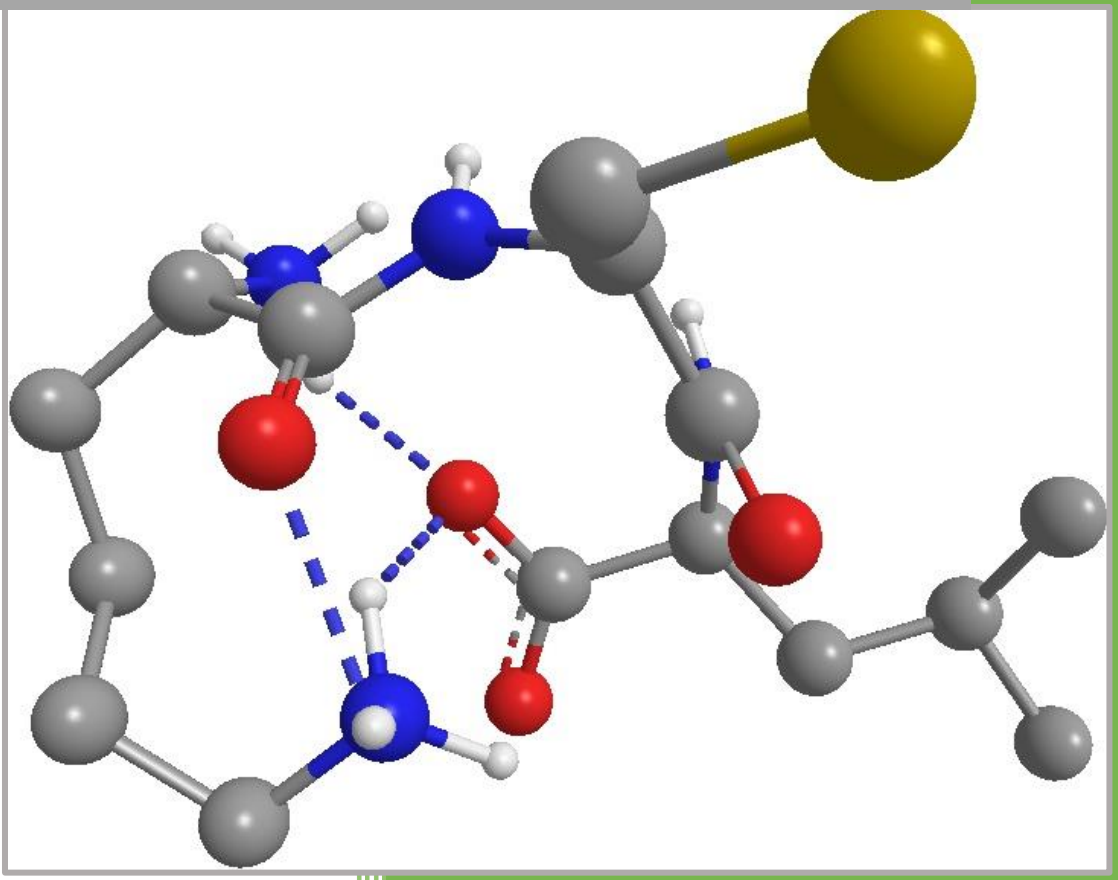
KING'S College LONDON

2021

Centre for Doctoral Training in Chemistry for a Healthy & Sustainable Society



Department of Chemistry

King's College London

Chemistry for a Healthy & Sustainable Society

We are delighted to announce the formation of the centre for doctoral training in Chemistry for a Healthy and Sustainable Society at King's College London. This ambitious programme beginning in 2021 will produce graduates who have expertise in Chemistry but whose experience transcends traditional boundaries and to become conversant in the languages of Biology and/or Physics. This is in line with the strengths of KCL Chemistry where we carry out state of the art research at the interfaces of chemistry and the life sciences and physical sciences. We believe that major global challenges such as **climate change**, **sustainable energy production**, **antimicrobial resistance** and **emerging pathogens** can only be solved by harnessing interdisciplinary research and state of the art techniques such as **synthetic biology, synthetic chemistry, single molecule techniques** and **molecular modelling**. This CDT aims to train outstanding chemists who are comfortable in multidisciplinary settings, can work in diverse teams to solve complex problems and will be agile enough to apply their knowledge to future scientific challenges.

To apply:

1. Read the projects detailed below. We recommend that you contact supervisors informally before you apply and have a first and second choice in mind. We will ask you to confirm your choice should you receive and offer.

2. Send your CV and a research statement as a single pdf to PGR-chemistry@kcl.ac.uk
   Your research statement must detail:
   a) Describe your previous research experience (final year projects, summer placements, year in industry etc).
   b) Why you want to do a PhD and why you chose this programme

3. Fill out an application on the Kings online application system here. **Please note that your references must be submitted within 7 days of the application deadline.**

The current application deadline can be found on FindaPhD.com

For information on eligibility and English language requirements see our website

The earliest start date for successful candidates will be Feb 2021

We look forward to welcoming you to King's Chemistry!

KCL Chemistry Department: Research Environment and Facilities

We are proud to have been ranked as the top Chemistry Department in London by the Guardian league table for the last two years and 13th in the Complete University Guide 2020.

King's College London has a unique multidisciplinary and collaborative environment. The growing Department of Chemistry at King's excels in interdisciplinary research where chemistry is a central science tying together physics and biology. The department is based in Britannia House, which was refurbished in 2018 with new labs and facilities for chemistry (including 400 MHz NMR, analytical and Prep HPLC, LCMS, LC-HRMS, GCMS, peptide synthesiser), biochemistry/microbiology and biophysics including an ongoing capital investment of £4 million. We have access to further excellent facilities in the Mass Spectrometry Centre (Franklin Wilkins Building, Denmark Hill), the Nikon Imaging Centre (Guys Campus) and our Cryo-EM facility. The KCL Centre for Biomolecular Spectroscopy covers high field NMR (including a 500 MHz Bruker instrument including a triple resonance ($^{1}H/^{13}C/^{15}N$) cryoprobe and 700 MHz Bruker instrument equipped with a quadruple resonance ($^{1}H/^{13}C/^{15}N/^{31}P$) cryoprobe), Biacore, ITC and native mass spectrometry. The NMR facility has recently been expanded to accommodate an 800 MHz instrument. KCL has fully equipped X-ray crystallisation services with extensive access to the Diamond synchrotron source via the block allocation system.

KCL Chemistry department is outward looking and has strong links to the Randall Division of Cell and Molecular Biophysics, Department of Imaging Chemistry, Physics and the Institute of Pharmaceutical Sciences within KCL and other London Chemistry Departments. King's excellence in Chemistry enhances its strength in Biomedical Sciences and we are members of King's Health Partnership and The Francis Crick Institute which can enable translation of scientific development toward clinical applications. We are members of other doctoral training centres (BBSRC LiDo and BiPAS). Equality is central to the ethos of KCL Chemistry, with a dynamic and fulfilling research culture for all, and an emphasis championing diversity and inclusion in science.

The Programme

The PhD programme is 4 years, including thesis writing. While the majority of your time on the programme will be spent carrying out state of the art research it is also important that you gain transferable skills, have the opportunity to fill gaps in your knowledge through taught modules and

have access to mentorship and feedback on your progress. To this end we have created a PhD doctoral training programme to complement and support this interdisciplinary research.

1. Transferable skills

While research in your chosen area will be your primary focus over the course of your 4 year PhD we believe that it is also important to develop transferable skills to both complement and enhance your research skills which will improve employability in your chosen industry. We require all students to take at least 10 days of transferable skills training each year.
KCL offers extensive PGR training courses from communicating your science to a lay audience, leadership skills, data management, presentation and writing skills.

Attendance of internal departmental seminars is mandatory. Additionally, all students are expected to attend external national and international conferences to present their work. Funds for travel are available.

2. Taught Modules to support your PhD research

All students can access of our taught modules in the Chemistry department and through our links with biochemistry, imaging and physics can also access modules in other departments which will complement their PhD studies and help to fill gaps in their knowledge.

Chemistry Frontiers, *Advanced Topics in Chemistry 1 & 2*, *Chemistry of Disease and Therapy* and *Catalysis*, *Protein Structure and Function* and *Advanced Biophysical Techniques* offer a range of topics that will help to support your research on the projects outlined below.
A full list of modules on our chemistry programme is available here.

3. Teaching and Outreach Opportunities

At KCL chemistry we are committed to delivering outstanding teaching to our undergraduates. We are lucky to have an engaged and diverse student body. Our department also has dedicated teaching staff who are engaged in education research and exemplify best practice. We offer all PhD students the opportunity to participate in teaching including lab demonstration and delivering small group teaching as well as supervision of undergraduates during their final projects. For all these teaching levels, training is provided as well as peer observation of teaching so you can improve your skills.

Beyond our internal teaching we have an active outreach programme, from staging public lectures to schools to bringing school groups to our labs and providing work experience opportunities for

students. There are opportunities for PhD students to be involved in these activities and with the widening participation unit at KCL.

4. Supervision and Mentoring

King's Chemistry is committed to ensuring all our PhD students receive excellent supervision and any additional support required during their studies. All projects have two supervisors and we anticipate that you will spend approximately equal time in both supervisors' labs. You will receive health and safety training from our excellent technical team and an induction course provided by the CDS as well as induction in Britannia House.

All PhD students will have a thesis committee which consists of both supervisors and a third academic staff member. The thesis committee and student meet within 3 months of the PhD starting and then between 9 and 12months. This second meeting involves a viva and allows the student to upgrade from MPhil to PhD. Meetings occur annually thereafter or as required. This process is intended to ensure students and supervisors understand their responsibilities and that students have ample opportunity for internal and external feedback and support. Additionally, the postgraduate tutor (Dr. Rivka Isaacson) meets all new PhD students and is available to offer support as needed and our excellent PGR administrator (Ruth Coughlin) is available for day to day administrative support. The departments seeks feedback and input from our post graduate community through our **PGR Student Staff Liaison Committee.**

Additionally, peer support is offered through ***PostDoc ChemComm*** our community of active PhD and Post doctoral researchers who have created an internal seminar series delivered by and for early career researchers. This includes research presentations by PGR and postdoctoral researchers as well as careers events.

Important contacts:

If you require support with the application process, please contact the Chemistry Postgraduate Administrator Ruth Coughlin PGR-chemistry@kcl.ac.uk

For informal enquires about the programme contact Dr. Sarah Barry sarah.barry@kcl.ac.uk

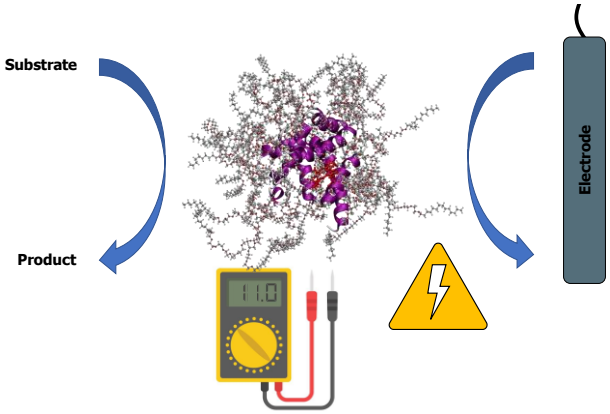
For informal enquiries about specific projects please contact academic supervisors directly. Contact details are included with project descriptions.

PhD Research Projects

Below is a list of the projects, followed by detailed descriptions, available to start in Feb 2021. The projects are all interdisciplinary and span techniques from organic synthesis to computational chemistry and take in themes from AMR to protein folding. Each project has a supervisory team of at least two chemistry academics. You can find more information on each research group on our website

Enhancing biocatalysis with electrons

Supervisory Team: Leigh Aldous, *Senior Lecturer in Chemistry*, Alex Brogan, *Lecturer in Chemistry* (with Ismael Díez-Pérez, *Reader in Physical Chemistry* as collaborator)
Email: leigh.aldous@kcl.ac.uk; alex.brogan@kcl.ac.uk



Enzymes are increasingly being used as biocatalysts for a number of industrial processes.[1] However, despite their great potential for biocatalysis, the current usage of enzymes in industry remains critically low. This low uptake is in part due to the reliance of many enzymes on prohibitively expensive cofactors such as NADPH, which is a significant hurdle for industry. This project seeks to explore the fundamental aspects of redox-active enzymes through a comprehensive study of enzyme structure, single molecule redox behaviour, the surrounding environment, and engineering of the electrode/protein interface for device application. Through rational design of the reaction media and chemical modification of enzymes, the project will investigate applications of redox enzymes in electron-fed biocatalytic processes and energy production (in bioelectrochemical cells).

The project will be centred around an exploration of the bioelectrochemistry, electron transfer, and associated biocatalysis by redox-active metalloproteins (such as heme containing cytochrome P450) and FAD-dependent-enzymes (such as glutathione reductase). The core purpose is to examine the possibility of replacing cofactors such as NADPH with a molecular mediator and an electrode to drive enzyme-catalysed processes with electrons alone, resulting in more green, sustainable, and controllable biocatalysis.[2] This will be benchmarked in aqueous media (known) [3] and the wider range of environments enabled by non-aqueous biofluids (unknown).

The **Aldous** group are experts in electrochemistry (including electroanalytical devices and energy harvesting) and the **Brogan** group are experts in stabilising enzymes in non-aqueous environments resulting in drastically enhanced activity (through chemical modification and biomaterial design).[4] The combined expertise here will allow for an in-depth study of the fundamental bioelectrochemistry of these enzymes in unique environments. The **Díez-Pérez** group are experts in biomolecular electronics [5] and will assist in detailed analysis of the bioelectrochemistry at electrode surfaces down to exquisite single protein level of detail.

The student will be trained in; the analysis of enzymes structure and stability (mainly using circular dichroism, FTIR spectroscopy, and UV/Vis spectroscopy), the fundamentals of dynamic electrochemistry and electron transfer, and the redox chemistry of enzymes in various environments using state-of-the-art electrochemical scanning tunnelling microscopy.

References: [1] B.B.Y Lau, T. Yeung, R.J. Patterson, L Aldous, *ACS Sustainable Chemistry & Engineering* 2015*,* **5***, 5320* [2] A. Aragonès, I. Díez-Pérez *et al. Nature* 2016, **531**, *88*. [3] T. Ha, M. B. Buckingham, L. Aldous, *manuscript in preparation.* [4] A. P. S. Brogan *et al*. *Nat. Chem.* 2018, **10**, *859* [5] M. P. Ruiz, I. Díez-Pérez, *et al. J. Am. Chem. Soc.* 2017, **139**, *43*, *15337*.

A biocatalytic approach to antibiotic derivatisation

Supervisory Team: Sarah Barry, *Senior Lecturer in Chemical Biology*,
Rivka Isaacson, *Reader in Chemical Biology*
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The rise of antibiotic resistance is an ongoing and slow burning global crisis. Diseases once thought irradicated, such as TB, are increasingly deadly due to the rise of multidrug resistant strains. This problem is exacerbated by the stagnation in antibiotic development.

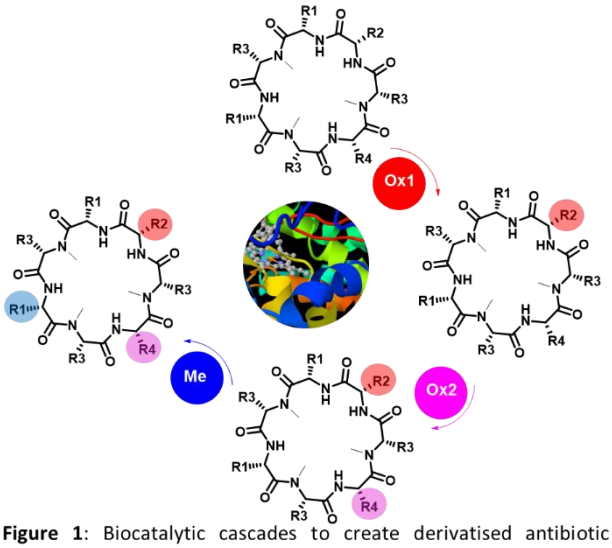

Figure 1: Biocatalytic cascades to create derivatised antibiotic peptides. Enzymes used will be biochemically and structurally characterised. The enzymes will be modified by mutagenesis and developed using directed evolution

Bacterial peptide antibiotics such as daptomycin and colistin are vital frontline drugs. However, derivatives are required to tackle resistance. These complex molecules are bacterial non-ribosomal peptides which are produced by fermentation. Generating derivatives of these complex natural products using traditional total synthesis is not economical. Engineering non-ribosomal multienzyme pathways to produce derivatives via synthetic biology also has many limitations [1, 2]. We aim to take a different approach to this problem by exploiting our knowledge of biosynthetic enzymology, we will develop chemoenzymatic routes to natural product peptide derivatives. Many biosynthetic enzymes have the ability to modify complex substrates with regio and stereoselectivity, frequently carrying out reactions that would be impossible using synthetic chemisty [3, 4]. The goal is to develop a chemoenzymatic route to natural product derivatives via biocatalytic cascades (Fig. 1).

The project will involve biochemical and structural characterisation of enzymes, as well as rational mutagenesis and directed evolution to produce modified enzymes. This exciting interdisciplinary project will produce new insight into antibiotic biosynthesis, inform synthetic biology approaches to antibiotic non-ribosomal peptide production and develop biocatalysts for peptide modification.

This project is highly interdisciplinary combining molecular microbiology, biochemistry, chemistry and structural biology [5].The project will suit someone with a degree in Chemistry or Biochemistry who is keen to expand their knowledge and skillset. They will spend equal time in the Barry and Isaacson groups and have the opportunity to present their results at national meetings and at an international conference.

References: [1] E. Winn *et al. Nat. Prod. Rep*. 2016, **33**, *317*. [2] C. B. Hubert *et al Biochem. Soc. Trans*. 2016, **44**, *738*. [3] E. Kim *et al. Nat. Chem. Biol.* 2015, **11**, *649*. [4] L. M. Alkhalaf *et al. J. Am. Chem. Soc.* 2019, **141**, *216*. [5] S. Martínez-Lumbreras *et al. Structure* 2018, **26**, *640.*

Single-molecule measurements for co-translational membrane protein folding

Supervisory Team: Paula Booth, *Professor of Chemistry*, Mark Wallace, *Professor of Chemistry*
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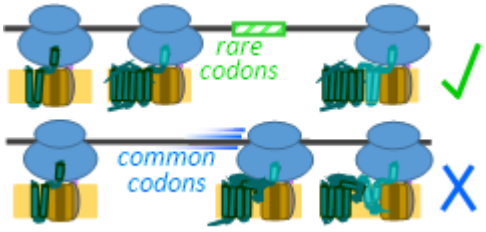
Self-assembly is an underpinning "Rule of Life". How biological systems assemble themselves efficiently to ensure normal, healthy function is however an enigma. The folding of newly synthesised proteins to their functional states epitomises natural self construction. The correct fold of a protein is vital for biological function and healthy cells. Knowledge of proper folding is also a pre-requisite to appreciate the implications of genetic errors and misfolding that can lead to disease.
This project will advance folding research – from conventional studies on full length, isolated proteins under artificial conditions, to the biosynthetic reality of co-translational folding. Furthermore, the project focusses on the important class of integral membrane proteins. These proteins underlie virtually all physiological processes and dominate drug targets.



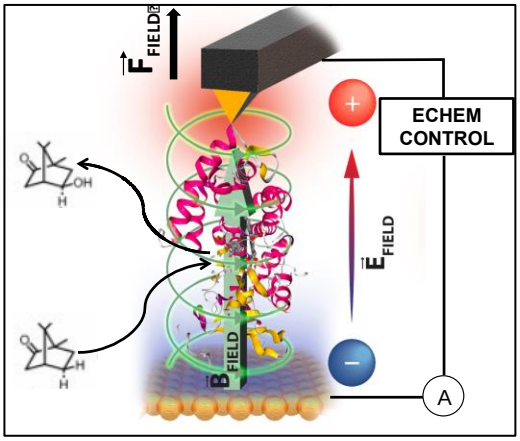
Nearly all helical membrane proteins insert into membranes and fold co-translationally, as the ribosome is translating mRNA. This project will develop new methods to probe a central premise of protein folding - that native structure is determined by primary amino acid sequence. This premise, however, may not be correct. Synonymous mutations are coming to light, where the amino sequence remains identical, but the codon sequence does not [1]. The degeneracy of the genetic code means that many amino acids are encoded by more than one codon, but these synonymous codons are not used equally. Rarely used codons slow translation, allowing more time for complex folding events. There is mounting evidence that this slower translation may be a key regulator of folding. Thus, although the primary amino acid sequence is the same, the codon sequence is different, and this could alter folding.
We will devise a method to measure translation rates of differing codon sequences for the same protein, directly in real time using a single molecule approach. Current approaches rely on the measurement of bulk systems and cannot differentiate effects of polyribosomes; in nature a single mRNA has several ribosomes bound at the same time, each at different stages of translation. Our simulations suggest that the presence of these extra upstream translating ribosomes can significantly affect the translation kinetics, which in turn affects measured folding rates.

A cell free (PURE) system will be used to synthesis and fold membrane proteins co-translationally in the presence of lipid membranes [2, 3]. Two single molecule approaches will be utilised to follow the growing polypeptide – single-molecule FRET (smFRET), and interferometric scattering microscopy (iSCAT) [4, 5]. Initial experiments will be performed using iSVSY, which can be used to measure single nano-scale objects without the need for fluorescent labels, including single proteins. smFRET will be monitored over time between donor and acceptor fluorophores attached to the nascent chain (via unnatural amino acids) and ribosome. The student will work in the labs of Booth and Wallace, which are very well set up for cell free co-translational folding work (using PURE, biophysical and biochemical methods) and single molecule spectroscopy (smFRET and iSCAT), respectively.

References: [1] J. L. Chaney and P. L. Clark, *Annu Rev Biophys*, 2015, **44**, *143*. [2] N. J. Harris, E. Reading, K. Ataka, L. Grzegorzewski, K. Charalambous, X. Liu, R. Schlesinger, J. Heberle and P. J. Booth, *Sci. Rep.*, 2017, **7**, *8021*. [3] N. J. Harris and P. J. Booth, *Trends Biochem Sci*, 2019, **44**, *729*. [4] H. L. E. Coker, M. R. Cheetham, D. R. Kattnig, Y. J. Wang, S. Garcia-Manyes and M. I. Wallace, Biophys J, 2019, **116**, *1085*. [5] P. M. Dijkman, O. K. Castell, A. D. Goddard, J. C. Munoz-Garcia, C. de Graaf, M. I. Wallace and A. Watts, *Nat. Commun*., 2018, **9**, *1710*.

Single-protein approaches to mechanoenzymology

Supervisory Team: Ismael Díez-Pérez, *Reader in Physical Chemistry*, Sarah Barry, *Senior Lecturer in Chemical Biology*
Email: ismael.diez_perez@kcl.ac.uk; sarah.barry@kcl.ac.uk;



Enzymatic catalysis is a prominent example of the rich, yet complex, dynamism inherent in any biomolecular process, and illustrative of how an atomic, but static, crystallographic picture of protein machinery is insufficient to provide a complete mechanistic description. Among the countless enzymes' families, **redox-active enzymes catalyse the most demanding reactions in biology with tremendous interest in bio-manufacturing** [1]. Today, most information on protein function comes from rational mutagenesis schemes based on crystal structure. While this *static picture* has been pivotal to identify key residues/chemical interactions in the enzyme active site that are directly involved in the catalytic process, studies have shown that even fully silencing such interactions still results in a 1000-fold catalytic activity versus same reaction in bulk [2]. This serves to illustrate the lack of understanding of the **physical forces that underpin enzymatic catalysis** [3] and give rise to enzymes' astonishing synthetic efficacy. This biological enigma has been long elusive due to the limited amount of experimental approaches able to directly address directional forces in an enzyme molecular machinery while monitoring its dynamic activity.

This project will focus on the cytochrome P450 family of redox enzymes. P450s enable most drug metabolism in cells and are of interest as biocatalysts due to their ability to activate inert C-H bonds and catalyse selective oxidation reactions *e.g.* hydroxylation [1]. P450s contain many flexible regions and undergo conformational change during catalysis. However, the effect of these changes on catalysis are poorly understood. To investigate, we will exploit cutting-edge biophysical approaches to trap individual enzymes in a nanoscale junction (see image) as a unique way to interrogate force stimuli (including mechanical forces) along crystallographic directions of the protein backbone. Precise electrical measurements of the single protein junctions [4] will allow detection of single enzyme turnover and generate insight into the relationship between protein dynamics/conformational change and catalytic function.

Such fascinating and strongly interdisciplinary proposal combining chemistry, molecular biology, enzymology and biophysics makes sense only when two supervisory teams covering the very different disciplines of the project join forces; the Díez-Pérez group is leader in the emerging field of BioMolecular Electronics and internationally recognized for its pioneering nanobiotech approach in single-protein electrical detection. The Barry group has extensive experience in discovery and characterisation of novel enzymes with emphasis in cytochrome P450s [5]. The student will have the opportunity to work in an emerging field with important applications to biotechnology.

References: [1] M. Girhard *et al*. in *Cytochrome P450* 451–520 (Springer International Publishing, 2015). [2] Carter, P. & Wells, J. *Nature* **332,** 564–568 (1988).[3] Arieh Warshel *et al. Chem. Rev.* **106,** 3210-3235 (2006).[4] M. P. Ruiz, Ismael Díez-Pérez, *et al. J. Am. Chem. Soc.* 2017, **139**, *43*, 15337-15346.[5] Alkhalaf, L. M et al *J. Am. Chem. Soc.* 2019, **141**, *216.*

Discovering chemical tools to target membranes

Supervisory Team: Ulrike Eggert, *Professor of Chemical Biology*, Martin Ulmschneider, *Reader in Computational Chemistry*
Email: ulrike.eggert@kcl.ac.uk; martin.ulmschneider@kcl.ac.uk

Lipids are critically important molecules underpinning a diverse range of essential biological functions. Together with proteins, they are major constituents of all cellular membranes. This means that lipids are involved in virtually every cellular and organismal process (e.g., viral infections, membrane and organelle biology, cell-cell interactions, tissue development and proper functioning of the immune system). Lipid dysfunction is associated with numerous diseases, including cardiovascular disease, cancer, diabetes, and many rare diseases.

Despite the huge importance of lipids, it is generally not well understood how lipids and proteins interact with each other within membranes. It has been challenging to study lipids because they cannot be imaged and manipulated as easily as proteins. We will address this issue by using a combination of experimental and computational tools that have been developed in the Ulmschneider and Eggert groups to design and characterise a new class of peptides that can distinguish between membranes of different lipid composition. Cells express many thousand distinct lipid species, leading to the hypothesis that one of the reasons for this diversity is that lipids and proteins interact specifically with each other, both directly and within larger groups called domains, and that these interactions determine membrane properties and function. The goal of this PhD project is to investigate this hypothesis using a highly interdisciplinary and innovative approach ranging from chemical biology, biophysics and computer modelling to cell biology.

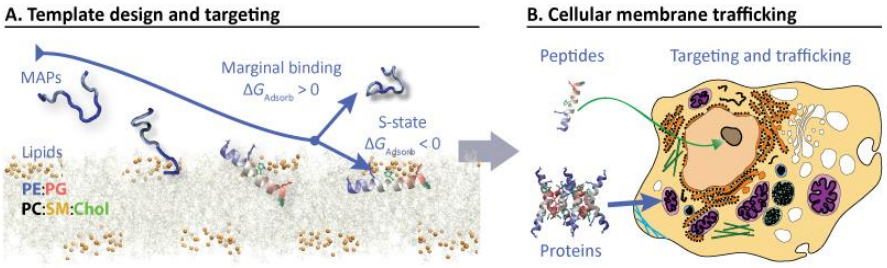


Figure 1. The project will employ simulation tools to investigate protein-lipid interactions and design novel lipid-targeting peptides (**A**), and experimental techniques to study membrane trafficking of designed peptides and cellular proteins (**B**).

In Year 1, you will identify lipid species that peptides bind to using lipidomic mass spectrometry, which is well established in the Eggert group. You will then use biophysical and biochemical studies to characterise these interactions. You will also be trained in molecular modelling and simulation-guided design of membrane-active peptides, a technique pioneered in the Ulmschneider group[1]. This will allow the generation of interaction models and membrane targeting peptides and proteins that will then be tested experimentally in future years.In Years 2 and 3, you will expand the analysis to proteins that are involved in membrane trafficking, an area of expertise in the Eggert lab. Membrane trafficking is important in the transmission of cargoes and signals within and between cells and is very suitable to this analysis because it involves vesicles and structures of different sizes, which are amenable to biophysical analysis of properties such as membrane curvature. In Year 4, you will finalise your experimental and computational work and will write your thesis.

You will be trained in a broad range of emerging techniques including computational modeling, biophysics, mass spectrometry microscopy and cell biology.

References [1] C. H. Chen *et al. J. Amer. Chem. Soc.* 2019, **141,** 12, *4839*. [2] J. G. Carlton. *Nat Rev Mol Cell Biol*. 2020, **21**, 3, *151*.[3] G. E. Atilla-Gokcumen et al. *Cell*. 2014, **156**, 3, *428*.

Co-chaperone/antioxidant interactions in cancer

Supervisory Team: Rivka Isaacson, *Reader in Chemical Biology,* Antoni Borysik*, Lecturer in Analytical Chemistry*
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Impaired protein quality control, in the crowded cellular environment, is associated with a wide range of diseases, including cancer. A greater understanding of the mechanisms by which co-chaperones, such as SGTA (Small, Glutamine-rich, Tetratricopeptide repeat protein Alpha), operate, may enable the development of innovative new strategies for targeting these pathologies. In prostate cancer cells, our collaborator has recently identified a novel interaction between SGTA and a complex which combats oxidative stress, is directly implicated in cancer and may serve to counteract otherwise lethal levels of reactive oxygen species.

A full understanding of SGTA has thus far remained elusive despite its importance for numerous cellular roles, many of which link with disease and, most pertinently now, for its interaction with a protein from SARS-CoV. We propose to structurally and functionally characterise the SGTA/antioxidant complex using an integrative structural approach. It is hoped that X-ray crystallography and/or cryo-electron microscopy (EM) can be used to produce atomic-resolution structures of the proteins bound together. Native mass-spectrometry (MS) and hydrogen-deuterium exchange (HDX) will provide information on the motions and oligomeric states of the complexes. Specifically, this project will exploit new online tools developed by the Borysik research group for high-resolution HDX-MS and HDX-guided protein modelling [2]. These methods permit HDX to be pinpointed to individual amino acids providing greater resolution for protein interaction sites and provide the facility to understand protein conformations directly from protein HDX-MS data. This studentship will be a great opportunity for the right candidate to apply these methods to a protein of high biological importance with a view to understanding the molecular basis of cancer. The insights gained from the structural experiments will shed light on the native function of the two proteins, whilst also informing on the likely effects of structural perturbations and how they tie into disease.

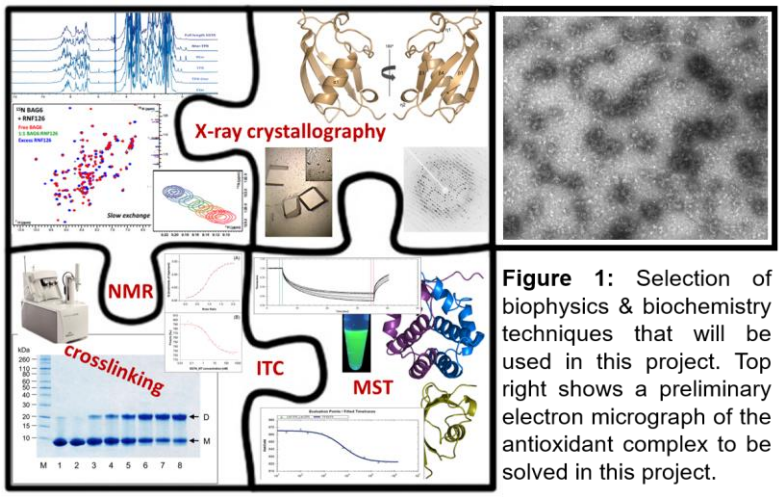


Figure 1: Selection of biophysics & biochemistry techniques that will be used in this project. Top right shows a preliminary electron micrograph of the antioxidant complex to be solved in this project.

This project is highly interdisciplinary and integrative (Figure 1) particularly exploiting the respective expertise of the two PIs in NMR and MS to achieve molecular level information about this complex and its role in cancer. The PhD student will drive the direction of the project in accordance with their interests and background with guidance from both supervisors. The student will attend group meetings as well as departmental/college seminars. They will have the opportunity to present their results at national meetings and at an international conference.

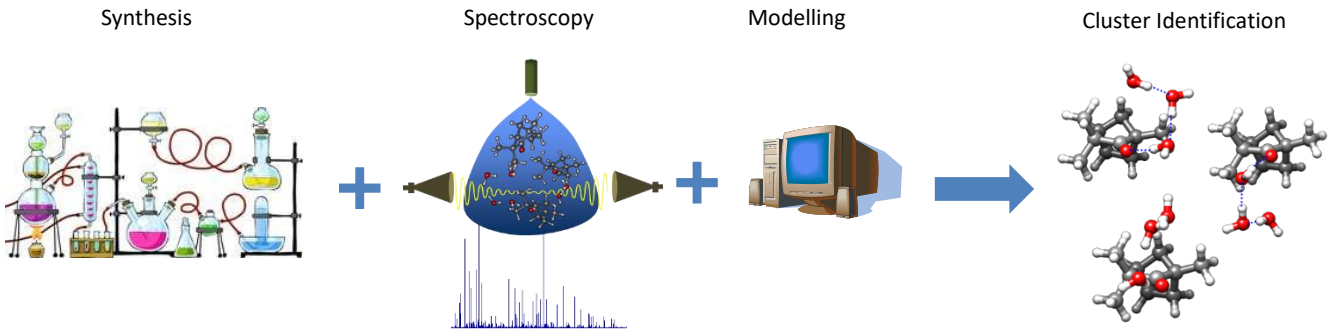
References: [1] S. Martínez-Lumbreras *et al. BMC Biol.* 2018, **16**, *76*. [2] A.J. Borysik Angew Chem Int Ed Engl. 2017, **32**, *9396*.

Understanding atmospheric nucleation of secondary organic aerosol: derivatives of monoterpenes and their clusters

Supervisory Team: Maria Eugenia Sanz, *Senior Lecturer in Physical Chemistry*, Andre Cobb, *Senior Lecturer in Organic Chemistry*
Email: maria.sanz@kcl.ac.uk; andre.cobb@kcl.ac.uk

One of the major challenges of our lifetime is climate change. Aerosols play a vital role in our climate by partially counteracting the warming caused by greenhouse gases. A main constituent of aerosol is secondary organic aerosol (SOA), formed from the reactions of organic matter in the atmosphere [1]. However, SOA is also one of the largest sources of uncertainty in climate modelling as its composition, formation and evolution are not well understood [2,3]. A critical process in the formation of SOA is atmospheric nucleation, which occurs when stable molecular clusters are formed spontaneously from gas phase molecules. However, knowledge on nucleation is limited, as information on the structures of the smallest molecular clusters that initiate the process is missing. Understanding the nature of critical clusters is the first step to reveal the formation mechanism of atmospheric particles and their composition. **The aim of this project is to determine the first aggregation stages of clusters of SOA precursors at the molecular level.**

Oxidised volatile organic compounds (VOCs) are the principal components of SOA. We will focus on oxidised monoterpenes that are identified to be precursors of SOA. We will synthesise these species and characterise their clusters with other atmospherically-relevant molecules using cutting-edge broadband rotational spectroscopy [4] in combination with high level molecular modelling. We will determine reaction pathways and the intermolecular forces driving aggregation.



References: [1] J. Zhu, J. E. Penner, G. Lin, C. Zhou, L. Xu and B. Zhuang, *Proc. Natl. Acad. Sci. U. S. A.*, 2017, **114**, *12685*. [2] M. Hallquist et al., *Atmos. Chem. Phys.*, 2009, **9**, *5155*. [3] H. Kroll and J. H. Seinfeld, *Atmos. Environ.*, 2008, **42**, I. [4] D. Loru et. al, *Phys. Chem. Chem. Phys.* 2019, **21**, *26111*.

The spark:
Electrochemical systems & the origin of life

Supervisory Team: Andrew Surman, *Lecturer in Chemical Biology*, Leigh Aldous, *Senior Lecturer in Chemistry*
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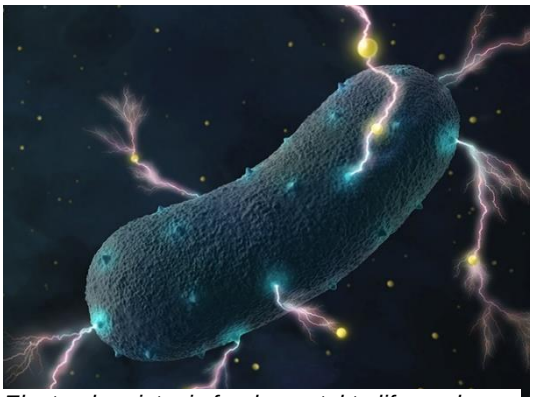
How life began – the transition from non-living chemicals to self-sustaining living systems – is one of science's Big Questions. It has been studied experimentally since the 1950s, when the field was kickstarted by Stanley Miller's 'spark discharge', modelling lightening on a primordial earth with high-energy sparks driving the formation of a 'primordial soup'. This experiment has been reproduced many times, and experimental study of the Origin of Life is currently undergoing a renaissance with the advent of Systems Chemistry.[1] However, compared to a 'spark', more subtle electrochemistry is rarely employed. This is despite the fundamental role of Electrochemistry in mediating control in biological systems.[2]



Electrochemistry is fundamental to life, and perhaps its Origin. (Amy Cao graphic, copyright UC Berkeley)

Systems Chemistry considers the emergence of more complex function from a set of molecules (living organisms being the ultimate demonstration). Therefore it considers not just the identities of the molecules composing a system, but what they DO when together (function). Electrochemistry is unique in providing access to both; for example, emerging function may be electrochemical, which electrical fields can manipulate/drive, and electrochemistry can analyse the systems (determine identities, and quantify them).

This PhD project will investigate new approaches to the electrochemical manipulation and analysis [3] of the kinds of very heterogeneous (or 'messy') [4] chemical systems considered models for conditions at Life's Origin. Whereas very high-energy sparks (*cf.* lightning) have driven previous studies, we will consider more moderate energy sources (*cf*. redox processes driven by geochemistry or bio-electricity). This project will explore their ability to maintain functional systems/supramolecular assemblies away from equilibrium (like living systems),[5] and the emergence of electrochemical function from the 'messy' chemistry thought to model the conditions leading to life's emergence ('primordial soup' models). Systems Chemistry's development depends on analytical developments, and we take the attitude that analytical and synthetic advances are naturally linked. Both the Surman (Supramolecular Chemistry, Complex Systems, Analytical Chemistry) and Aldous (Electrochemistry, Energy Systems, Electroanalysis) groups are interdisciplinary, dividing their time between making and measuring. This project will be no exception, involving synthesis (including electrosynthesis), lab-based analysis/testing, and data analysis. It would suit an independently-minded creative student, enthusiastic about working beyond narrow disciplinary boundaries. Experience of programming/scripting would all be valued (but not a requirement), as will a track-record of problem-solving, independence, and perseverance in any sphere.

References: [1] K. Ruiz Mirazo *et al. Chem. Rev.* 2012, **114**, *285*. [2] Levin, *et al*. *iScience*. 2019, **22**, *519*. [3] M. A. Buckingham et al. *Sustain. Energy Fuels* 2018, **2**, *2717*. [4] Surman *et al*. *Proc. Natl. Acad. Sci*. 2019, **116**, *5387*. [5] Rieß et al. *Chem* 2020, **6**, *552*.

Smart microcapsules through controlled macromolecular coating

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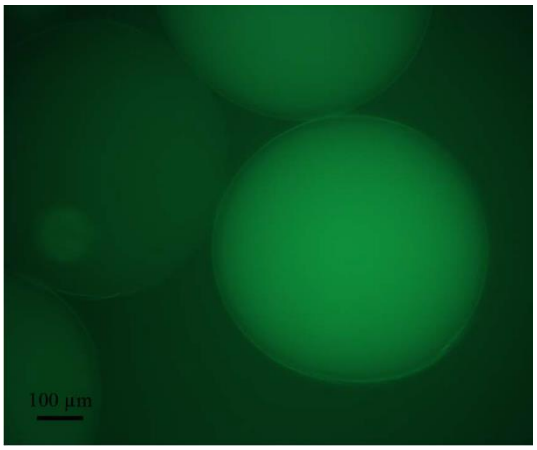
Microfluidic compartmentalisation technologies are increasingly used for high-throughput biomolecular analyses & screening.[1] Simple immiscible droplets dominate (e.g. water droplets in oil): tiny isolated 'test tubes' which can be made, manipulated, and observed in vast numbers (thousands to millions). As demand grows for advanced applications, the droplets' strength – being discrete compartments that do not break or mix – can become a weakness: it is difficult to add or remove compounds (for example, to feed growing cells). Alternative systems based on hydrogel "microcapsules ('beads' of jelly) dispersed in aqueous solvents suffer the opposite problem: limited control over movement between the aqueous solvents inside, and outside.



Polymer-coated hydrogel capsules can be engineered for selective permeability.

There have been early reports of gel microcapsules with selective permeability,[2] conferred by a polymer coating. These promise new opportunities, but selectivity in initial reports is limited (based on molecular size, over a very limited range). The limitations stem from only using a small range of commercially-available polymers to control selectivity.

This project will explore what selective permeabilities can be achieved when we move beyond the small range of commercially-available polymers. We will produce a variety of polymers [3] and assess their ability to assemble to coat gel capsules and the different selective permeabilities they confer, considering questions like: *How finely can we control in/out traffic? Can we model and predict selectivities for different polymers?[4] Can we control for properties other than size? Can that control be switched?* On achieving novel selectivities, we hope to collaborate with colleagues (in Tokyo and London; industry & academia) to consider whether this selectivity can be used to control cell culture conditions in droplets, or incorporated into artificial tissues.

This project is fundamentally interdisciplinary, requiring engagement with a range of areas. Both the Surman (*Supramolecular Chemistry, (Bio)Polymers, Analytical Chemistry*) and Ulmschneider (*Modelling, Microfluidics, Membranes, Peptides*) groups are extremely interdisciplinary. This project will be no exception, involving synthesis, self-assembly, microfluidic manipulations, data analysis, and modelling. It would suit an independently-minded creative student, enthusiastic about working beyond narrow disciplinary boundaries; ideally flexible to travel to collaborate. Experience of programming/scripting would all be valued (but not a requirement), as will a track-record of problem-solving, independence, and perseverance in any sphere.

References: [1] Mather *et al*. *Small* 2020, **16**, *1904321*. [2] Mao, *et al. Nature Materials* 2017, **16**, *236*. [3] Rodriguez et al *Nat. Comms.* 2015, **6**, *8385*. [4] Chen, *et al*. *Current Opinion in Structural Biology,* 2020, **61**, *160*.