Supervisor: Prof Adrian Liston (al989@cam.ac.uk)

Website: https://www.liston.babraham.ac.uk/

Department / UPI: Babraham Institute

Research area:

The brain is a site of relative immune privilege, long considered isolated from the peripheral immune system. We recently identified a population of resident T cells in the healthy mouse and human brain, important for the maturation of microglia (Pasciuto et al, Cell 2020). By analysing the kinetics of migration between the blood and brain, we found that the key bottleneck controlling the number of anti-inflammatory regulatory T cells in the brain was the high rate of cell death the cells exhibit when housed within the brain. Through developing a unique tool, with potential therapeutic application, we were able to deliver a biologic directly to the brain and enhance the size of the regulatory T cell population (Yshii et al, Nature Immunology). The approach protects mice from brain damage following traumatic brain injury, stroke and multiple sclerosis. In this project we wish to explore the immunological processes that drive damage during neuroinflammation, and to harness immune-modulating biologics to prevent damage to the brain.

BBSRC DTP secondary strategic theme: Biosciences for an integrated understanding of health

Supervisor: Prof Florian Hollfelder (fh111@cam.ac.uk)

Website: https://hollfelder.bioc.cam.ac.uk/

Department / UPI: Biochemistry

Research area:

Nature has evolved the most amazing functional biomolecules that operate in complex networks. We want to know how they work, individually and collectively. We use extreme miniaturisation of experiments (into picoliter droplets made in microfluidic devices) to answer fundamental questions. Using an eclectic mix of techniques we extend the mechanistic lessons learned to potential applications in biotechnology, synthetic chemistry and medicine. Specifically we address these areas:

(1) Protein Engineering. Enzymes are the all-purpose catalysts that make the Chemistry of Life run smoothly and efficiently, under the mildest, 'greenest' conditions – and protein binders are involved in governing many biological processes. Directed evolution allows us to explore 'protein fitness landscapes' and UHT analysis in droplets enables us to go faster than any other analytical system. By combining this functional readout with next generation sequences we create 'maps' that direct evolution efforts better.

[see Nat Commun. 2022, doi: 10.1038/s41467-022-28396-4; ACS Cent Sci. 2022, doi: 10.1021/acscentsci.2c00576; Trends Biochem Sci, 2022, doi:10.1016/j.tibs.2021.11.001; Nat Commun., 2020, doi:10.1038/s41467-020-19687-9; Nat. Commun., 2020, DOI:10.1038/s41467-020-17061-3; Proc Natl Acad Sci U S A. 2018; doi: 10.1073/pnas.1607817115]

(2) Protein discovery. We use UHT in droplets to screen metagenomic libraries for useful catalysts, at rates > 10e6 per day. This functional metagenomics approach reveals completely novel enzymes that cannot be predicted by sequence homology and provides insight into new

mechanisms as well as useful ne catalysts, e.g. for plastic degradation, fince chemical synthesis, degradation of biomass to generate biofuels etc.

[see Nat Chem Biol 2022, DOI: 10.1038/s41589-022-01071-x, Microbiome, 2020. 10.1186/s40168-020-00911-z; Nat. Commun., 2015,. doi: 10.1038/ncomms10008]

(3) Single cell transcriptomics. We have developed a droplet-based total RNA single cell sequencing method 'Vasa-Seq' that allows a uniquely comprehensive analysis of transcriptional programmes in developmental biology, e.g. in stem cell biology (especially pluripotency across species), the development of embryos, development of organoids etc. We also design 3D environments in droplets, that provide a matrix for cell development more akin to their natural environment, which helps us to create better conditions for growth, maintenance of pluripotency and development (and analyse these states by Vasa-Seq).

[see Nature Biotechnology, 2022, DOI: 10.1038/s41587-022-01361-8; Nature, 2022, doi:10.1038/s41586-022-05246-3; Nat Cell Biol. 2022 doi: 10.1038/s41556-022-00984-y; Nature. 2022, doi: 10.1038/s41586-022-04953-1]

BBSRC DTP secondary strategic theme: Biosciences for renewable resources and clean growth

Supervisor: Dr Lorenzo Di Michele (ld389@cam.ac.uk)

Website: https://www.dimichelelab.org/

Department / UPI: Chemical Engineering and Biotechnology

Research area:

Our group works at the interface between nucleic acid (NA) nanotechnology and (bottom-up) synthetic biology. We use NAs to create nanodevices and materials that mimic and enhance biological systems. By combining our nanodevices with other materials (e.g. lipid membranes, polymers) and functional elements (enzymes, nanoparticles), we aspire to build "synthetic cells" (SynCells) that replicate behaviours typically observed in cells, including motility, communication, homeostasis, biosynthesis, tissue/biofilm formation, growth and division. SynCells promise to underpin Transformative Technologies in healthcare (drug delivery, biosensing, cell therapies), biosynthesis (materials, pharmaceuticals) and environmental remediation (pollutant sequestration and degradation), while opening exciting routes to Understand the Rules of Life through a "learning-by-building" approach.

BBSRC DTP secondary strategic theme: Understanding the rules of life

Supervisor: Prof Roisin Owens (rmo37@cam.ac.uk)

Website: https://www.ceb.cam.ac.uk/research/groups/best

Department / UPI: Chemical Engineering and Biotechnology

Research area:

3D in vitro models of the gut-brain-microbiome axis with integrated electronic monitoring

BBSRC DTP secondary strategic theme: Biosciences for an integrated understanding of health

Supervisor: Prof Steven Lee (sl591@cam.ac.uk)

Website: https://www.ch.cam.ac.uk/person/sl591

Department / UPI: Chemistry

Research area:

Advanced microscopy, super-resolution imaging. T cell immunology

BBSRC DTP secondary strategic theme: Understanding the rules of life

Supervisor: Dr Pietro Sormanni (ps589@cam.ac.uk)

Website: https://www.ch.cam.ac.uk/person/ps589

Department / UPI: Chemistry

Research area:

Antibodies play key roles in biomedical and biotechnological research, as well as in the diagnosis and treatment of many diseases, including cancer and neurodegeneration. By using a multidisciplinary approach that encompasses computational method development and in vitro experiments, we work to develop and establish novel technologies of antibody design at a computer. These advances are making it possible to complement well-established laboratory-based methods of antibody discovery and optimisation with fast computational approaches, and to offer time- and cost-effective novel alternatives. We carry out both fundamental research projects to develop novel technologies of antibody design, and translational research projects to obtain novel antibodies for specific needs, including for diagnostic or therapeutic applications.

BBSRC DTP secondary strategic theme: Biosciences for an integrated understanding of health

Supervisor: Prof Ozgur Akan (oba21@cam.ac.uk)

Website: http://ioe.eng.cam.ac.uk

Department / UPI: Engineering

Research area:

Biological Communications, Molecular Communications, Communication Networks inside Human Body, Neural Communications, Fundamentals of Olfactory Communications, Internet of Bio-Nano Things

BBSRC DTP secondary strategic theme: Understanding the rules of life

Supervisor: Dr Gemma Bale (gmb49@cam.ac.uk)

Website: http://www.eng.cam.ac.uk/profiles/gmb49

Department / UPI: Engineering

Research area:

The Neuro Optics Lab is a new, multidisciplinary research group that operates jointly between the Departments of Physics and Engineering at the University of Cambridge. Led by Dr Gemma Bale, we develop and validate new optical methods to monitor brain function and metabolism non-invasively. The lab currently focusses on near infrared spectroscopy (NIRS)-based methods to perform in-vivo monitoring of metabolic markers such as haemoglobin oxygenation, mitochondrial function and blood flow. We are interested in pioneering tools and techniques to monitor relevant physiology for both basic science and medical applications. Our work is highly translational and we work closely with clinical partners in Addenbrooke's Hospital to deliver technologies that progress medical therapeutics.

BBSRC DTP secondary strategic theme: Biosciences for an integrated understanding of health

Supervisor: Dr Andre Cabrera Serrenho (ag806@cam.ac.uk)

Website: http://www.eng.cam.ac.uk/profiles/ag806

Department / UPI: Engineering

Research area:

Projects will be offered on climate change mitigation interventions. These projects will include the identification of feasible opportunities to deliver our future needs for transport, buildings, materials, and food without emissions within the next few decades. This involves developing modelling approaches to understand the way we use energy and materials to satisfy a variety of human needs, and the identification and exploration of the most meaningful interventions to accelerate change across various sectors.

BBSRC DTP secondary strategic theme: Bioscience for sustainable agriculture and food

Supervisor: Dr Yan Yan Shery Huang (yysh2@cam.ac.uk)

Website: https://biointerface.eng.cam.ac.uk/

Department / UPI: Engineering

Research area:

Synthetic and bionic circuits for organ-on-a-chip and environments.

BBSRC DTP secondary strategic theme: Transformative technologies

Supervisor: Prof George Malliaras (gm603@cam.ac.uk)

Website: http://www.eng.cam.ac.uk/profiles/gm603

Department / UPI: Engineering

Research area:

One of the most important scientific and technological frontiers of our time is the interfacing of electronics with the human brain. This endeavour promises to help understand how the brain works and deliver new tools for diagnosis and treatment of pathologies including epilepsy and Parkinson's disease. Current solutions, however, are limited by the materials that are brought in contact with the tissue and transduce signals across the biotic/abiotic interface. Recent advances in electronics have made available materials with a unique combination of attractive properties, including mechanical flexibility, mixed ionic/electronic conduction, enhanced biocompatibility, and capability for drug delivery. A range of projects will be made available in the Bioelectronics Laboratory (https://bioelectronics.eng.cam.ac.uk/), where the PhD candidate will leverage advances in electronics to develop new tools to interface with the brain.

Supervisor: Dr Sebastian Pattinson (swp29@cam.ac.uk)

Website: https://www.sebastianpattinson.com/

Department / UPI: Engineering

Research area:

Enabling 3D printers to learn how to bioprint better.

BBSRC DTP secondary strategic theme: Understanding the rules of life

Supervisor: Prof Florin Udrea (fu10000@cam.ac.uk)

Website: http://www.eng.cam.ac.uk/profiles/fu10000

Department / UPI: Engineering

Research area:

The power devices field has seen tremendous changes in the last decade. The traditional power MOSFET has been largely replaced by a new class of power devices based on the Silicon Sueprjunction concept, while the Insulated Gate Bipolar Transistors (IGBTs) are now fabricated on 12 inch wafers and have access to the latest thin wafer/trench/fine dimension technologies. However most of the innovation and flavor in the field comes from the emergence of Wide Band Gap semiconductors – and in particular the Gallium Nitride and Silicon Carbide. Extensive research is also carried out in single crystal Diamond and Gallium Oxide materials. The market of power devices has reached ~$M40 with exponential growth in wide bandgap materials reaching CAGRs in excess of 30% in the next 3-5 years.

The PhD project will deal with new designs and architectures of power semiconductor devices using SiC or GaN technologies

Supervisor: Prof Ji Zhou (ji.zhou@niab.com)

Website: https://www.niab.com/about/people/professor-ji-zhou

Department / UPI: NIAB

Research area:

Ji leads NIAB's Data Sciences department, which focuses on developing multi-scale indoor and in-field plant and crop phenotyping, ranging from cellular to population level. We use satellite, Agri-Drones (field level), LiDAR (field and plot level), low-cost remote sensing (plant level), Videometer (seed and tissue levels) and Opera HCS system (high-throughput cellular phenotyping) to conduct plant and crop phenotyping, based on which beyond state-of-the-art AI algorithms and automated trait analysis solutions are developed to assess genetic gain, trait stability, yield/quality prediction, early disease detection, and genotyping- to-phenotyping linkage for agricultural and horticultural crops such as wheat, rice, Brassica and orchard fruits (e.g. apple).

Some recent impactful work from Ji's lab includes high-throughput 3D crop mapping and NUE varieties screening using LiDAR (CropQuant-3D, Plant Phys., 2021), low-cost distributed phenotyping platforms (CropQuant UKIPO, GB1709756.9; and CropSight, GigaScience, 2019), large-scale aerial phenotyping to enable crop genetic mapping and marketable yield prediction (AirMeasurer, New Phyt. 2022; and AirSurf, Hort. Research, 2019), automated seed science research platform (SeedGerm, New Phyt. 2020), and cellular trait analysis (PDQuant, Plant Cell, 2013; StomataMeasurer, Traffic, 2018). Also, he is an associate editor for the Crop Journal, Plant Phenomics, and Horticulture Research.

BBSRC DTP secondary strategic theme: Bioscience for sustainable agriculture and food

Supervisor: Prof Mark Howarth (mh2186@cam.ac.uk)

Website: https://www.phar.cam.ac.uk/research/Howarth

Department / UPI: Pharmacology

Research area:

Inspired by extraordinary molecular features from the natural world, we engineer and evolve proteins for fundamental analysis and biotech application.

• The gut is highly effective at degrading proteins, preventing the use of antibodies for targeting in the GI tract. We established a new antibody mimetic with exceptional protease resilience. We are developing this targeting platform towards applications in pathogen and microbiome modulation, for human and veterinary application.

• Our Plug-and-Protect platform facilitates the rapid assembly of vaccines to induce strong antibody responses. Through building mosaic vaccines, we can induce neutralizing responses across a family of bat and human viruses. One project is to tailor antigens and protein nanoparticles, to harness better immune signalling and maximize protection for rapidly evolving One Health threats.

• The lab's SpyTag/SpyCatcher technology for covalent ligation is being widely applied for basic research and biotechnology. A new project uses SpyTag to enhance how antibodies can be combined to allow combinatorial control of cell behaviour.

BBSRC DTP secondary strategic theme: Biosciences for an integrated understanding of health

Supervisor: Dr Ioanna Mela (im337@cam.ac.uk)

Website: https://www.ioannamela.com/

Department / UPI: Pharmacology

Research area:

Antibiotic resistance is an emerging health issue, with major socio-economic implications. We are combining biological with engineering principles, to develop tools that will help control this crisis. Our research focuses on the design and synthesis of DNA nanostructures that can specifically sense, attach to, and destroy bacterial targets. We are interested in how multivalent, targeted delivery can potentiate the action of existing and new antimicrobials and on the discovery of new ways with which to attach DNA nanostructures to bacteria. We are working on aptamer selection with which we can bind and block outer membrane bacterial proteins, so that we can refine the targeting aspect of our work.

To achieve these goals we use a variety of classic molecular biology and biochemistry approaches, together with high-speed atomic force microscopy, correlative atomic force microscopy with fluorescence microscopy, and super-resolution microscopy.

Our work is strengthened and complemented through several collaborations within and outside the University.

BBSRC DTP secondary strategic theme: Understanding the rules of life

Supervisor: Dr Leila Muresan (lam94@cam.ac.uk)

Website: https://www.pdn.cam.ac.uk/staff/muresan

Department / UPI: Physiology, Development and Neuroscience

Research area:

Quantification and extraction of information from fluorescence microscopy images is paramount to the understanding of imaged biological processes. My research focuses on developing approaches adapted to cutting-edge microscopy techniques including single molecule localisation microscopy, lightsheet imaging, two-photon microscopy, single shot 3D (lightfield) microscopy.

More specifically, we focus on the following issues:

• Image reconstruction and enhancement, that allow better downstream processing and analysis such as rapid multi-view image reconstruction (fusion) and restauration based on spatially variant deblurring adapted to the specific light sheet image formation model.

• Segmentation, detection and characterisation of objects of interest in microscopy images based on state-of-the art approaches in data science, such as deep learning based methods.

• Analysis of dynamical processes at various scales, from single molecule tracking to 3D flows.

BBSRC DTP secondary strategic theme: Understanding the rules of life

Supervisor: Prof Ben Lehner (lehner.ben@gmail.com)

Website: https://www.sanger.ac.uk/programme/human-genetics/

Department / UPI: Sanger Institute

Research area:

Understanding, predicting and engineering biology and genetics using massively parallel mutagenesis and machine learning

After 70 years of molecular biology, we remain strikingly limited in our ability to predict how biological systems respond to even simple perturbations such as point mutations and we struggle to engineer them to have desired properties. As a consequence, the vast majority of the millions of genetic variants in our genomes are 'variants of uncertain significance'. That the fundamental 'encoding' problems of molecular biology remain unresolved after decades of research suggests that a new approach is required. We believe that practical solutions to these problems will come from combining large-scale data generation – primarily massively parallel perturbation experiments using DNA synthesis, selection and sequencing – with modelling and machine learning. Towards this goal we are developing and applying methods to quantify in parallel the properties of hundreds of thousands of protein and RNA variants. Applied at scale, these approaches allow us to generate reference atlases of mutational effects for clinical genetics and, more fundamentally, datasets of sufficient size and diversity to tackle the foundational problems of molecular biology using modelling and machine learning. Current projects in the lab are focussed on understanding, predicting and engineering from sequence protein and RNA stabilities, affinities, specificities, allostery, expression and dynamics i.e., the sequence-to-activity relationships that underlie essentially all of biology.

BBSRC DTP secondary strategic theme: Understanding the rules of life