The University of Nottingham
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For further information, please contact:
**Research, Enterprise and Graduate Services (REGS)**
e: **regs@nottingham.ac.uk**
t: **+44 (0)115 74 84 555**


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# The University of Nottingham

## Industrial Biotechnology Capability Statement

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# Foreword

Industrial Biotechnology (IB) will underpin the future of a successful sustainable global society and will contribute substantially to the Bioeconomy.

The University of Nottingham is already contributing to advances in IB and has a global reputation for high quality research in the many academic disciplines which cut across IB.

It is now looking to integrate and expand its considerable activities in IB-related research, identify complementarity between academic groups and, importantly, to understand what those companies which draw on IB need and want for their growth and sustainability.

This Industrial Biotechnology Capability Statement seeks to draw together the many and various strands of research expertise across the University's campuses to showcase what is available and highlight to companies the many opportunities for mutually beneficial research and development collaboration.

As the Vice-Chancellor's advisor on IB, I am committed to Nottingham's quest to be a beacon for Industrial Biotechnology research in the UK. This Capability Statement is an excellent step towards that goal.

I trust that you will find the following pages useful and use them to guide you to appropriate expertise within the University that will be of benefit to you and your company.

**Professor Ian Shott** CBE FREng
Managing Partner Shott Trinova LLP

# Contents





# What is Industrial Biotechnology?

Over the past three decades, modern biotechnology has been most associated with the medical and pharmaceutical sectors. However, the Human Genome Project (HGP) heralded a technological revolution in synthetic and computational biology which has created transformational opportunities in providing cost effective and more sustainable processes. Today, many products are manufactured from fossil fuels using energy intensive petrochemical technology. In the age of the genome, casting off the shroud of the previous age, many products will stem from cell factories underpinned by Industrial Biotechnology.

Industrial Biotechnology is the application of knowledge gained from synthetic, molecular and computational biology; enabling the adaptation and modification of natural organisms, bioprocesses, bioproducts and biosystems to produce goods and services. Industrial Biotechnology may be harnessed to:

- **create new products**
- **modify and develop new industrial processes for chemical feedstocks, platform chemicals, fuels, speciality products, materials and active ingredients**
- **make the process manufacturing industry more competitive**
- **reduce the environmental impact of manufacturing towards more sustainable processes**

The potential for a vibrant bio-economy is substantial, as successful implementations of Industrial Biotechnology now span the globe. Examples abound in pharmaceuticals, chemicals, plastics, textiles, leather and hazardous waste management; providing productivity gains, more efficient processes and faster access to larger consumer markets.

# How to use this document

**This Industrial Biotechnology Capability Statement draws together all of the research activities conducted at The University of Nottingham that are either central to Industrial Biotechnology (IB) or that add value to core IB activities.**

The Capability Statement is a living document which aims to be a one-stop shop for all things IB-related at Nottingham. It is a ready reference guide, primarily aimed at companies seeking IB expertise, but also for academics to identify new collaborative partners who can add value to their research. Whilst IB approaches can offer effective solutions to many industrial problems, there are a number of common needs and challenges facing industries that utilise IB. A brief summary of these is given on page 9.

Research at Nottingham in the area of IB covers a very diverse range of disciplines but is focused around five Capability themes depicted in the colour-coded flow diagram on page 10 and 11. These themes cover core production processes from feedstock to end product as well as associated enabling technologies including economic, social and environmental aspects.

For ease of reference, the IB themes and associated capabilities in this brochure have been grouped to fall into the five colour-coded Capability themes laid out on pages 12 to 15. Further details of each individual Capability, together with key contacts, can be found by either clicking on the hyperlinked-titles, or by scrolling to titles of interest in the A-Z list of capabilities on pages 16 to 53. The colour bar associated with each capability identifies to which of the five themes the Capability is relevant.

Details of relevant training and business opportunities at The University of Nottingham can be found on pages 54 to 59.

General contact details can be found at the end of the document.





# Current Industrial Biotechnology needs and challenges

**1) Feedstock:**

- (a) Selection and characterisation of feedstocks, optimisation of composition and replacement with renewables.
- (b) Utilisation of waste feedstocks.
- (c) Utilisation and deconvolution of complex mixtures.
- (d) Carbon-efficient utilisation of feedstocks such as C1 gases, glycerol and C5/C6 sugars.

**2) Improved process efficiency in terms of economics, energy and environmental impact:**

- (a) Robust, process compatible biocatalysts.
- (b) Process integration and intensification, including catalytic cascades and in-situ purification.
- (c) Improved enzymes and pathways for enhanced efficiency, broad substrate and functionality range and stereoselectivity.
- (d) Improved product export from whole cell biocatalysts.
- (e) Relieve yield restrictions due to product toxicity.
- (f) Continuous biomanufacturing.
- (g) Improved process design with fewer stages, reduced purification demand and alternate processing routes.
- (h) Increased process intensity with shorter cycle times to improve process velocity and reduce working capital needs.
- (i) Modelling and engineering of complex reaction systems and downstream processing, especially when using highly complex mixtures of reagents and co-products.

**3) Waste reduction and reutilisation:**

- (a) Waste reduction and reuse through feedstock or process improvement, product recovery and re-use of materials.
- (b) Data management on where waste and by-products are created, how they can be collected as a consistent supply of feedstock from waste.
- (c) Waste valorisation of high value products localised to avoid transport costs and systems to justify investment in low-profit margin products.

**4) Innovative manufacturing and product development:**

- (a) Product and market development for 'circular' products such as novel, bio-based intermediates and innovative materials.
- (b) Application of synthetic biology approaches through the development of new platform tools, chassis discovery and optimisation including: bio-parts and standardisation, gene construct assembly automation and enzyme discovery.
- (c) The creation of new products, or modification to the standards of current products, to meet changing regulatory requirements in particular in respect of recycled content.

**5) Socioeconomic and environmental considerations:**

- (a) Developing robust life cycle analysis methodologies.
- (b) Techno-economic analysis and life-cycle analysis.
- (c) Public engagement.
- (d) Assessing public acceptance of novel processes and products.
- (e) Applying responsible innovation.
- (f) Minimising adverse impacts on the environment through, for example, reductions in greenhouse gas emissions and reduced carbon footprints.

# Capability theme areas

## Enabling technologies

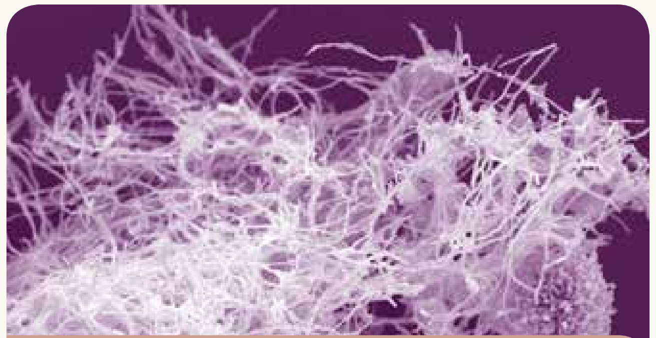
**Analytical capabilities**
- Transcriptomics
- Proteomics
- Metabolomics

**Synthetic biology tools**
- Metabolic engineering
- Enzyme engineering
- Epigenetics

**Systems biology – In silico capabilities**
- Bioinformatics
- Big data management
- Metabolic pathway design

### Feedstock

- C1 gases
- Lignocellulosic biomass
- Glycerol
- Municipal solid waste
- C5 and C6 sugars
- Wastewater



### Processing

- Physio-chemical
- Downstream processing
- Enzyme catalysis
- In situ product recovery
- Metabolic engineering
- Bioprocess design
- Engineered microrganisms
- Waste water treatment
- Bioreactor technology
- Waste minimization

### Products and co-products

- Biofuels
- Nutraceuticals
- Bulk industrial chemicals
- Medical applications
- High value added chemicals
- Pharmaceutical compounds
- Agricultural products

## Economic, social and environmental

- Business and entrepreneurial
- Life cycle analysis
- Techno-economic evaluation
- Resource management
- The circular economy
- Responsible research and innovation

# Themes and associated capabilities

## Enabling technologies

### Analytical capabilities

- Biophysics and NMR structural biology to study biomolecular interactions
- Biopolymer stability against processing
- Geophysical techniques for subsurface characterisation
- Mass spectrometry to study biomolecular interactions
- Nutritional diagnosis and metabolite analysis
- Surface and nanoscale imaging of biomaterials
- X-ray computed tomography: non-destructive microstructural characterisation of biomaterials

### In Silico capabilities

- Advanced bioinformatics analysis
- Big data in computational modelling for protein engineering
- Computational chemistry in biology
- Computational approaches in synthetic and systems biology
- Differential equation modelling in dynamic systems
- Mathematical modelling of bioreactors
- Mathematical modelling of multi-scale complex systems
- Mechanistic mathematical modelling
- Modelling of human decision making
- Molecular modelling of biomolecules

### Tools for synthetic biology

- Advanced bioinformatics analysis
- Allergenicity and functional *in vivo* produced biotinylated recombinant proteins
- Cellular redox and electrical communication
- Chemical biology and epigenetics
- Computational approaches in synthetic and systems biology
- Controlling cellular processes with smart novel electrochemical nano-systems
- Functional annotation of bacterial coding sequences
- Gene delivery methods and recombineering
- Genome manipulations in prokaryotic and eukaryotic organisms
- Molecular mechanisms: bacterial DNA replication, host-pathogen interactions, modulation of bacterial virulence, bacterial biofilms and antimicrobial resistance
- Novel peptide ligand discovery
- Post transcriptional RNA modifications
- Reporter systems for bacterial translation and protein secretion
- Synthetic biology and metabolic engineering of bacteria
- Synthetic biology: genome editing and generating novel CRISPR tools
- Transitory modulation of gene expression for clinical and biotechnological uses





## Feedstock

- Bacterial metabolism: fermentation of C1 gases
- Exploitation of lignocellulosic feedstocks for the production of transportation biofuels
- Modulation of plant cell walls for improved raw material quality
- Synthetic biology and metabolic engineering of bacteria
- Valorisation of food waste streams
- Wastewater treatment

## Processing

### Physio-chemical

- Catalytic methods to synthesise chemical building blocks
- Chemical reaction mechanisms and molecular interaction for biological processes
- Microwave pre-treatment to produce sugar derivatives and bio-based chemicals
- Sustainable chemistry using ionic liquids

### Enzyme catalysis

- Artificial enzymes
- Big data in computational modelling for protein engineering
- Biocatalytic chemical production from renewable feedstocks
- Biophysics and NMR structural biology to study biomolecular interactions
- Developing biocatalysts for applications in the chemical industry
- Development of enzymes and other proteins as biologics biopharmaceutics
- Modular polyketide synthases
- Molecular modelling of biomolecules
- Protein evolution and chemical modification
- Protein structure determination and engineering
- Wastewater treatment

### Improving microorganisms

- Fungal biotechnology
- Synthetic biology and metabolic engineering of bacteria

### Metabolic engineering

- Bacterial metabolism: fermentation of C1 gases
- Biocatalytic chemical production from renewable feedstocks
- Synthetic biology and metabolic engineering of bacteria

## Products and co-products

### Agricultural products and applications

- Chemical reaction mechanisms and molecular interaction for biological processes
- Dairy cow health and production
- Development of veterinary vaccines and diagnostic assays
- Geophysical techniques for subsurface characterisation
- In-field molecular diagnostics and UV-mediated control of plant diseases
- Modulation of plant cell walls for improved raw material quality
- Novel food structures as delivery vehicles
- Nutritional diagnosis and metabolite analysis
- Optimising welfare and performance in ruminant agriculture
- Rational vaccine design through pathogen interactions
- Secondary plant products for industrial and medical use
- Use of yeast to produce value added products
- For applications related to food and drink, download a copy of the **Food and Drink Capability Statement.**

### Biofuels

- Bacterial metabolism: fermentation of C1 gases
- Exploitation of lignocellulosic feedstocks for the production of transportation biofuels
- Fungal biotechnology
- Sustainable chemistry using ionic liquids
- Synthetic biology and metabolic engineering of bacteria

### Bulk industrial chemicals

- Bacterial metabolism: fermentation of C1 gases
- Biocatalytic chemical production from renewable feedstocks
- Synthetic biology and metabolic engineering of bacteria

### Medical and pharmaceutical applications

- Allergenicity and functional *in vivo* produced biotinylated recombinant proteins
- Artificial cells for drug delivery
- Artificial enzymes
- Biomaterials development to influence mammalian cell behaviour
- Biosynthesis of novel anticancer compounds in plants
- Development of enzymes and other proteins as biologics biopharmaceutics
- Engineering mammalian cells: screening for immunologic active protein and lipid compounds
- Fungal biotechnology
- Mathematical modelling of bioreactors
- Mathematical modelling of multi-scale complex systems
- Modelling of human decision making
- Molecular mechanisms: bacterial DNA replication, host-pathogen interactions, modulation of bacterial virulence, bacterial biofilms and antimicrobial resistance
- Next generation biomaterials discovery
- Novel peptide ligand discovery
- Post transcriptional RNA modifications
- Regenerative medicine bioproducts
- Scaffolds and synthetic methodology for small molecule drug discovery
- Secondary plant products for industrial/medical use
- Signalling and communication in prokaryotes
- Synthesis of polymers for biomedical applications
- Synthetic biology: genome editing and generating novel CRISPR tools

### Others

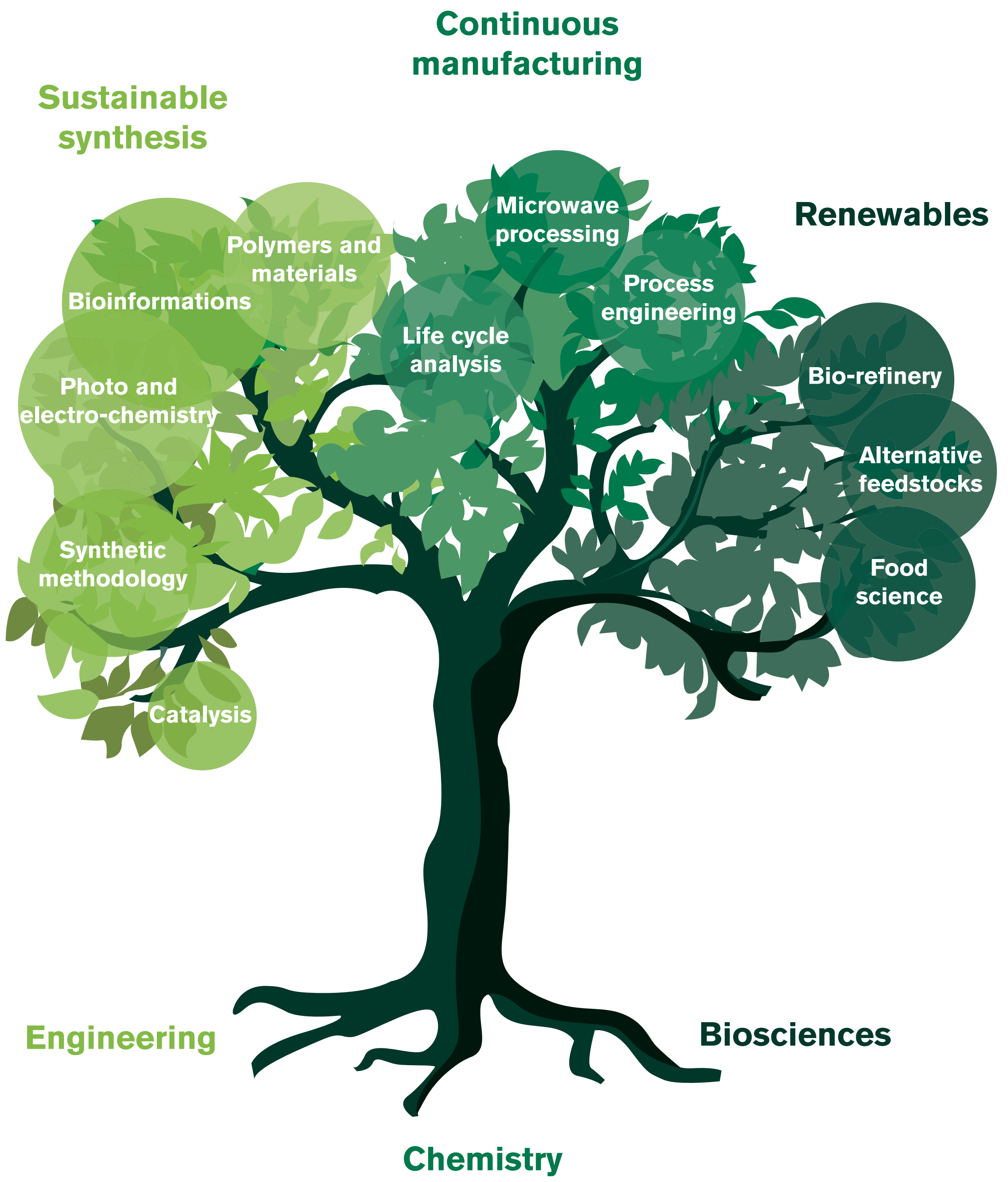
- Applications of functionalised spider silk
- Wastewater treatment





## Economic, social and environmental aspects

- Assessment of conservation value of constructed reedbeds
- Clinical guidelines for animal owners and veterinary professionals
- Entrepreneurial development and commercialisation
- Framework of Innovative Uncertainties
- Integrating Responsible Research and Innovation (RRI)
- Life cycle assessment and techno economic modelling
- The bioeconomy: social and ethical dimensions
- The circular economy
- Wastewater treatment



# A-Z list of capabilities

## Advanced bioinformatics analysis

**Key contact:** Richard Emes

The development of cost effective high throughput DNA sequencing has revolutionised biomedical research with increased emphasis on stratified or precision medicine. Our team at the Advanced Data Analysis Centre (ADAC) has experience in the identification and functional prioritisation of genomic variants related to human and animal health, including the development of methods and software for bespoke analysis.

To fully understand a biological system requires effective integration of high throughput data from different systems, such as genomic, proteomic and transcriptomics. Whilst these individual methods are becoming commonplace, the integration of them is still a specialist endeavour. At ADAC, we have demonstrable experience of undertaking these studies and a recognised infrastructure to ensure the effective delivery of large-scale studies.

Auto sampling for HPLC analysis

## Allergenicity and functional *in vivo* produced biotinylated recombinant proteins

**Key contacts:** Marcos Alcocer

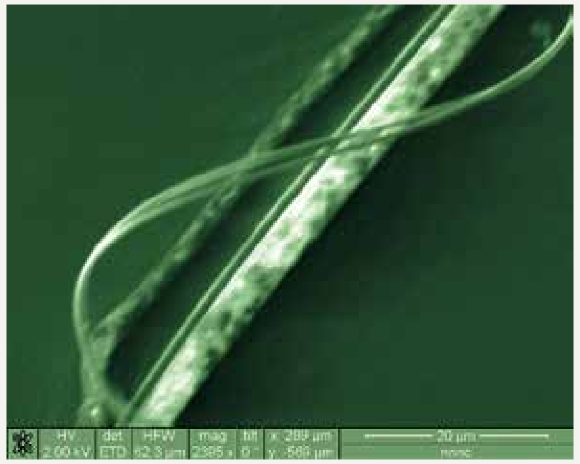
Our research interests fall into two main areas:

- **Food allergy:** where we are trying to understand why common food proteins are recognised by the immune system as 'foreign' while other proteins with similar structures are tolerated. Using purified proteins and lipids as a model system we investigate how these ingredients interact with particular cells of the immune system and the signals generated from the interaction. We are learning how the ingredients are taken up and processed, which genes are upregulated and which cytokines are produced.
- **Protein expression and folding:** we have developed effective strategies for the production of properly folded, *in vivo* biotinylated recombinant proteins (for example antibodies and allergens) in a yeast (*Pichia pastoris*) system. Our controlled single-point biotinylations allow the production of functional multimeric proteins which we use in the production of major allergenic probes for diagnostic systems and for the development of new nanoparticle and phage display tools, completely bypassing the animal immunisation stage.

This work is generating essential information for diagnostics and prediction of allergenicity of novel proteins – a major industrial bottleneck for the registration of new products.







## Applications of functionalised spider silk

**Key contact:** Sara Goodacre and Neil Thomas

Our interests lie in the studies of spider silk at the molecular level, with our research group currently working on projects to characterise the likely mechanisms through which diversification of the spider silk gene family has occurred through natural evolution. We are exploring the characteristics of the natural diversity of silk proteins, which remain as yet largely poorly described. In parallel we are working collaboratively with organic chemists to synthesise synthetic silk proteins with novel industrial applications based upon newly described silk motifs.

## Artificial cells for drug delivery

**Key contact:** Cameron Alexander

Our research examines the synthesis of container materials and synthetic chassis formats which can encapsulate drugs, proteins, genes and existing biological cells. These containers are built from synthetic polymers, and can be engineered to respond to changes in pH, temperature, redox status and light. The main applications for these materials are in sensing and in controlled release. Current projects are evaluating materials for drug, gene and cell delivery in the medical sector. The same materials can be employed for encapsulating enzymes for biotransformations, bacteria and yeast for fermentations, and gene circuitry for fine chemicals and biomaterials production. The advantages of synthetic polymers for these applications over existing materials lie in the ability to make the containers and chassis responsive or under control of external operator controlled stimuli.

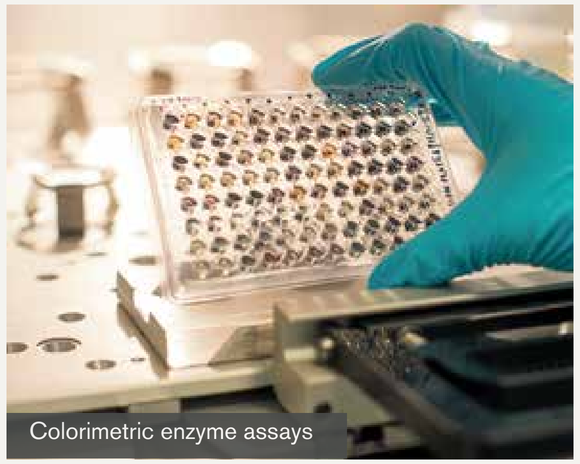
## Artificial enzymes

**Key contact:** Anca Pordea

We design and engineer enzymes for applications in chemicals synthesis:

- Design of enzymes for non-natural chemical transformations. The main focus is the incorporation of metal-based chemical catalysts into proteins, to create hybrid catalysts. This combines the non-natural activity of the metal with the ability of the protein to bind and activate hydrophobic substrates. In addition, the protein can act as a shield against deactivation of metal catalysts in aqueous environments.
- Cascades of chemical catalysts with enzymatic or whole-cell catalysts.

The methods we use are bioconjugation of small molecules to proteins, synthesis and catalytic applications of ligands and metal complexes compatible with proteins.



Colorimetric enzyme assays

## Assessment of conservation value of constructed reedbeds

**Key contact:** Tom Reader

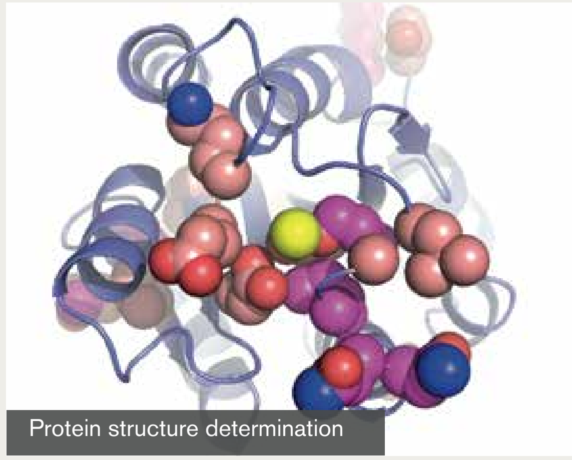
Constructed reedbeds are artificial wetlands, planted with common reed (*Phragmites australis*), which are used to treat waste water from domestic, agricultural and industrial sources. We work with reedbed designers and end-users to evaluate the conservation impact of these 'green' waste-water solutions, with the aim of assessing their value, and providing advice about site design and management.

## Bacterial metabolism: fermentation of C1 gases

**Key contact:** Nigel Minton, Klaus Winzer and Alex Conradie

As microbiologists with a longstanding interest in bacterial physiology and metabolism we are trying to genetically modify bacteria to produce fuels and chemical commodities from waste gases. Our main research areas include:

- bacterial metabolism – the fermentation of C1 gases and carbohydrates
- metabolic engineering and synthetic biology
- bacterial cell to cell communication
- interactions between bacteria, nano-machines and materials


Protein structure determination

## Big data in computational modelling for protein engineering

**Key contacts:** Jon Garibaldi

Our current research into predictive computational modelling for protein engineering incorporates computationally demanding simulations and the creation and analysis of large amounts of simulation data. Quick and efficient data analysis methods need to be incorporated into such projects in order to retrieve meaningful information for the next steps in rational enzyme design.

## Biocatalytic chemical production from renewable feedstocks

**Key contact:** Gill Stephens, Alex Conradie and Anca Pordea

Our research focuses on biocatalytic methods to produce chemicals, primarily from renewable feedstocks. Our applications-focused projects include metabolic engineering to produce bulk chemicals and monomers from renewable feedstock, and enzymatic depolymerisation of lignin. As a group we also work on process and method development for biocatalysis. Our areas of competence include:

- design of metabolic routes to produce bulk chemicals
- identification of enzymes to form non-natural chemical products
- overcoming product inhibition in microbial processes
- integrating microbial fermentations with chemical catalysis
- discovery of cell and enzyme friendly ionic liquids for use in biocatalytic processes
- improved delivery of water-insoluble substrates and polymers using ionic liquids
- biphasic ionic liquid/water systems for product recovery
- toxicity evaluation for substrates and products in bioprocesses
- anaerobic biotransformations

Our research is supported by both public-funding and company sponsorship.



Industrial Biotechnology Capability Statement

Fermentation of lignocellulosic sugars for bioethanol


NMR facilities





## Biomaterials development to influence mammalian cell behaviour

**Key contacts:** **Felicity Rose, Kevin Shakesheff, Lee Buttery, James Dixon, Jing Yang and Lisa White**

Collectively we have extensive expertise in scaffold design, fabrication and analysis. We work with both natural and synthetic polymers to produce an array of scaffolds and microparticles with controlled size, shape, controlled release profiles and structure. We lead the UK Research Councils UK Regenerative Medicine Platform – a cellular hub which leads the UK research effort in producing materials for regenerative medicine applications for a range of tissue types.

In addition to scaffold fabrication we are experts in mammalian cell biology, including stem cells, and their interactions with biomaterials, not only for regenerative medicine but for the production of *in vitro* models.

Our technologies include 3D bio-printing with a particular interest in liver, peptide delivery to cells to express proteins important in the regenerative process, electrospinning to form scaffolds that mimic the extracellular matrix, and in the use of optical tweezers to manipulate the arrangement of cells to form controlled cell niches.

## Biophysics and NMR structural biology to study biomolecular interactions

**Key contact:** **Mark Searle**

We use biophysics and NMR structural biology to research studies on protein engineering and design, biomolecular interactions in cell signalling, DNA replication, autophagy, the immune response, and nucleic acid structures and interactions. High-field NMR provides insights into molecular structure and dynamics at high resolution. Complementary techniques such as Crystallography, Isothermal Titration Calorimetry (ITC), Circular Dichroism (CD) and molecular simulations are used in parallel to solution NMR studies in collaborative projects with colleagues in a range of disciplines.

## Biopolymer stability against processing

**Key contacts:** **Steve Harding and Gary Adams**

Our team at the National Centre Macromolecular Hydrodynamics has world-leading expertise on the characterisation of molecular integrity (molecular weight and conformation), interactions and stability of macromolecules in the environment where most occur naturally. We address problems in food such as:

- polysaccharide barriers against gluten intolerance
- biopharma: antibody stability and controlling aggregation in high viscosity solutions
- ability to characterise stability and reliability of glycovaccines to FDA criteria, against for example, meningitis and in bio-archaeology, such as biopolymer consolidants

Our main technique is analytical ultracentrifugation – the Food and Drug Administration 'gold standard' technique. We have four various specifications: reinforced by static or dynamic light scattering methods, Size Exclusion Chromatography, and high precision viscometry, densimetry and spectroscopy – including Fourier transform infrared spectroscopy.

Our research is reinforced by the MSc in Applied Biomolecular Technology (founded in 1997) with its Industrial Placement, MSc in Applied Biopharmaceutical Biotechnology and Entrepreneurship – with the School of Business Studies, and the MRes in Industrial Physical Biochemistry. Our team has provided scientific expertise for GSK vaccines in patent cases with a 100% success rate and also to the government think-tank for diabetes.

## Biosynthesis of novel anticancer compounds in plants

**Key contacts:** Rupert Fray, Chris Hayes and Graham Seymour

Since its isolation from the pacific yew (*Taxus brevifolia*), and subsequent FDA approval in 1992, taxol and its close derivatives continue to be used as frontline drugs for the treatment of cancer. Tomato fruit contain very high levels of a key precursor compound that can be converted to high value taxanes. Our research uses a transgenic plant approach coupled with subsequent in vitro modification as a vehicle for generation of novel taxanes using synthetic biology approaches.

## Catalytic methods to synthesise chemical building blocks

**Key contact:** Hon Lam, Simon Woodward and Liam Ball

We are working on the development of new catalytic methods to synthesise chemical building blocks more efficiently. Areas of interest include:

- new methods for the functionalisation of C-H bonds to give shorter synthetic routes to compounds
- enantioselective catalysis to prepare chiral compounds in enantiomercially enriched form
- searching for new reactions using first-row transition metal catalysts to increase the sustainability of chemical processes

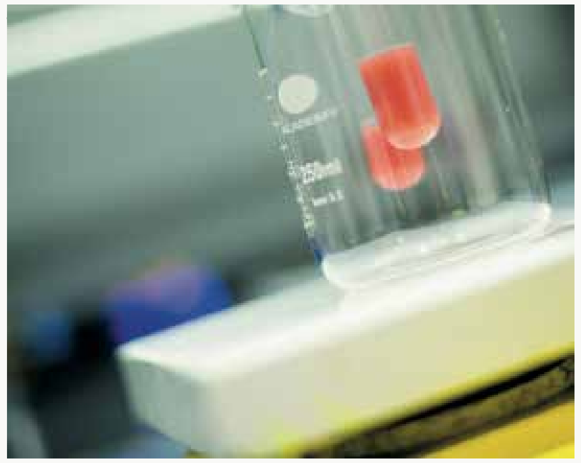
Our research addresses industrial biotechnology needs through downstream conversion of enzymatically produced chemicals into more complex, value-added products. We can provide chemical expertise to guide the development of new enzymatic routes to important chemicals, such as chiral and enantiomerically enriched chemicals.

Our research lends itself well to other disciplines: we design and synthesise small molecules which are required for the development of biological applications, and we can provide chemical expertise to help develop manufacturing routes to target molecules.

## Cellular redox and electrical communication

**Key contacts:** Frankie Rawson and Cameron Alexander

Our group investigates new ways of molecular engineering conducting surfaces, which have the capability of electrically ‘wiring’ biological cells. This then facilitates electrical communication between the conducting surface and cells. The applications of our research are broad and include the development of new biosensor diagnostics, through to use within bioenergy generation via the production of cellular fuel cells and development of new bioelectronic based medicine. Additionally, we aim to utilise cell electrical communication systems to drive chemical reactions, thereby forming immune stimulating bioactive polymers which have the potential to find applications as a therapeutic.



## Chemical biology and epigenetics

**Key contact:** Christoph Loenarz

As a research group we focus on pushing the frontiers in epigenetics research by investigating connections between post-translational modifications, such as histone lysine methylation and metabolic pathways of pathophysiological relevance. We are extending our knowledge of their oxygen-dependent mechanism that enables modulation of protein synthesis accuracy and antibiotic resistance. We employ techniques encompassing organic synthesis and chemical biology approaches such as proteomics, intact protein mass spectrometry, enzymology and reporter assays, as well as cellular studies using yeast genetics and human cell culture.





NMR machine

## Chemical reaction mechanisms and molecular interaction for biological processes

**Key contact:** Anna Croft

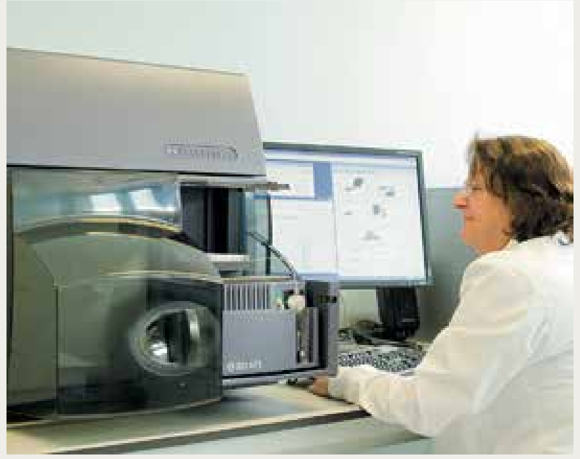
Our work focuses on understanding free-radical enzyme reactions for biocatalytic cascades and as bio-inspired catalysts; the use of ionic liquids to direct reaction outcomes and aid in the extraction and production of chemicals and materials; development of biological antioxidant chemistry in the context of functional foods; the utilisation of analytical methodologies such as NMR, Mass spectrometry, high-throughput spectroscopy and computational modelling to optimise and redesign bio- and chemo-processes; and work with biopolymers and biomolecules that includes natural antioxidants, amino acids, peptides, proteins (including both enzymes and structural proteins such as keratin and silk), lignin and lipids.

## Clinical guidelines for animal owners and veterinary professionals

**Key contacts:** John Burford, Sarah Freeman, Gary England, Rachel Dean, Marnie Brennan and Adelle Bowden

Clinical guidelines are designed to recommend care based on the best available evidence and reduce inappropriate variation in practice. They are well established in human healthcare situations such as the process of triage, whereby treatment priority is quickly assessed on primary presentation often in conjunction with ‘red flag’ protocols. These are aimed at the early identification of symptoms which are associated with particular pathologies requiring rapid diagnosis and treatment.

The use of clinical guidelines is poorly established in veterinary practice and there is little evidence on how this information should be disseminated into both the lay horse owning community and to veterinary professionals. Our team is working both on developing guidelines for diseases of equids with high mortality and morbidity – and therefore the greatest impact on equine welfare, and also to investigate how this knowledge should be delivered. Currently our particular focus has been on equine colic where reducing the time taken to diagnose critical conditions can make the difference between life and death, and the amount of pain and suffering a horse undergoes.



## Computational approaches in synthetic and systems biology

**Key contact:** Jamie Twycross

We use computational modelling, data analytics and machine learning to address a wide range of problems in synthetic and systems biology, and have a strong track record of successful interdisciplinary collaborations with researchers from a wide range of disciplines. We have applied computational approaches to investigate various prokaryotic and eukaryotic organisms including bacteria, archaea, plants and humans.

We have expertise in modelling cellular systems at a variety of scales, from modelling of regulatory, signalling and metabolic networks, to multi-scale spatial models of cellular populations, and expertise in developing and applying machine learning and bioinformatics approaches for optimisation and data analytics.

We currently have a number of computational biologists co-located in the Nottingham Synthetic Biology Research Centre (SBRC) who are investigating the construction of genome scale models, metabolic pathway discovery, RNA device design, and chassis optimisation.

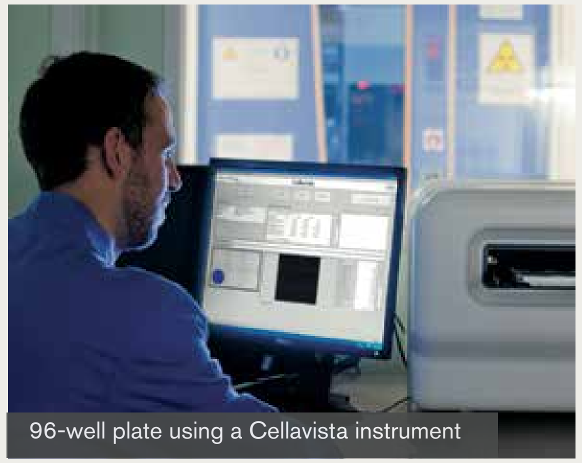
## Computational chemistry in biology

**Key contact:** Jonathan Hirst

Fuelled by the dramatic progress in computer hardware development and the deluge of biological data emerging from genome sequencing, the application of computational chemistry to challenging problems in biology is now one of the most vibrant fields in computational biology.

Much of our research centres on understanding how proteins fold into their preferred biologically active shapes. This protein folding problem has been called 'the second half of the genetic code' and, if solved, would revolutionise molecular biology and medicine by permitting real exploitation of genome sequence data.

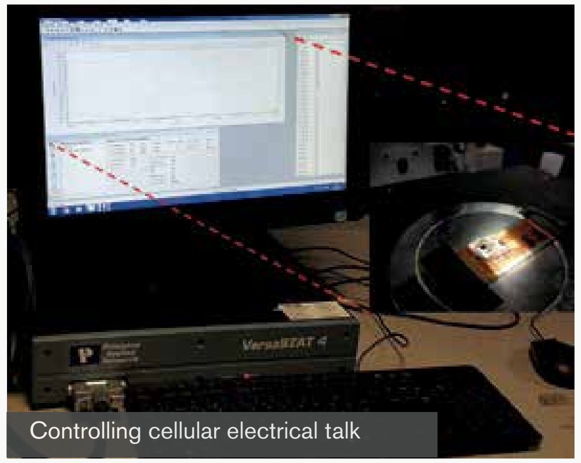
Outside of this, our research spans from the quantum chemistry of small molecules and the spectroscopic properties of proteins to the application of state-of-the-art statistical and computer science methodology, through to drug design and bioinformatics. We are now interested in developing novel computational tools to guide the optimisation of protein function; an area of significant academic and industrial interest ranging from fundamental biological questions through to areas like drug discovery, synthetic biology and industrial biotechnology to develop improved or novel biochemical activity.



96-well plate using a Cellavista instrument



Industrial Biotechnology Capability Statement



Controlling cellular electrical talk

## Controlling cellular processes with smart novel electrochemical nano-systems

**Key contact:** Frankie Rawson

Our interests centre on the development of a smart novel electrochemical nano-system for studying and controlling cellular processes on a molecular scale. This involves fundamental studies of charge transfer from prokaryotic and eukaryotic cells in addition to breakthrough methodologies of surfaces functionalisation and control on the nano-scale.

Our research spans multiple disciplines and has the scope to lead to the generation of new technology and biological routes to harness a sustainable electricity source, through to bioelectrochemical and cellular electrochemical controlled development and production of therapeutics, electroceutics and diagnostics.

Our research adds value to the understanding of electrochemical processes that underpin cell signalling and microbial fuel cell development as well as the molecular tailoring of surfaces for functional properties such as that required in energy production.

## Dairy cow health and production

**Key contacts:** Martin Green, Jon Huxley and Phil Garnsworthy

At the Centre for Innovation Excellence in Livestock, part of the national Agri-tech Centres of Innovation in Agriculture, we are currently focusing research on the following three key areas:

### Optimising health and wellbeing

Conducted in a flexible housing facility, research on interactions between the cow and her environment is used to identify optimal methods to keep and manage dairy cows and to further enhance their health and wellbeing. Research expertise includes endemic disease (mastitis, lameness and infectious disease), reproductive biology, epidemiology and computational biology, genetics, bioinformatics, microbiology and immunology.

### Nutrition

In response to industry demands for large trials, our research is carried out within a new, state-of-the-art Nutritional Research Unit. Up to 100 high yielding milk cows can be individually fed with continuous recording of feed intake, milk yield, live weight, activity, and rumination linked to detailed measurements of cow metabolism and physiology.  Research expertise and themes include feed efficiency, metabolic physiology, nutrient utilisation, digestion and impact on the cow, the environmental impact of feedstuffs (such as nitrogen and methane emissions), interactions between nutrition, fertility and health, rumen function and the rumen microbiome.

### Antimicrobial resistance

An integrated category 2 laboratory facility with milking equipment has been created to further develop research into host pathogen interactions, vaccinology, and mitigation of antimicrobial resistance.

Dairy cow health and production

## Developing biocatalysts for applications in the chemical industry

**Key contacts:** **Elaine O'Reilly, Francesca Paradisi, Neil Thomas, Pete Licence, Anna Croft, Steve Howdle, Thorsten Allers, Martyn Poliakoff, Gill Stephens, Alex Conradie and Anca Pordea**

Our research in the School of Chemistry focuses on developing robust enzymes and optimised biocatalytic industrial processes. A range of projects are undertaken including:

- applications of alcohol dehydrogenases, transaminases and glycosyl hydrolases from a variety of extremophilic organisms in the synthesis of intermediates for the pharmaceutical, cosmetic and food industries (Paradisi)
- biocatalysis allows us to reevaluate synthetic strategies and enables disconnections that are not possible using traditional chemical synthesis or catalysis. We focus on the development of new synthetic routes to high-value chiral molecules by employing key enzymatic steps (O'Reilly)
- development and application of robust biocatalysts, including transaminases, aldolases and oxidases using directed evolution or rational design (O'Reilly)
- immobilisation of biocatalysts on solid supports for flow chemistry (Paradisi)
- developing catalytic systems involving immobilised enzymes, crosslinked enzyme crystals and aggregates (CLECs, CLEAs) and hydrophobically ion-paired enzymes in these solvents in order to maximise yield and enzyme stability, and to simplify product work-up (Thomas)
- development of non-conventional expression systems for industrially relevant enzymes (Paradisi)
- use of non-aqueous solvents for enzyme catalysed reactions including ionic liquids In order to maximise the yields of certain reactions. It is necessary to use enzymes in non-aqueous solvents either because the substrates are poorly soluble or unstable in aqueous solution or in the case of hydrolytic enzymes, if these are being used in amide, ester or glycoside bond formation. Alternative solvents include organic solvents, ionic liquids, fluorous solvents, supercritical fluids and multiphase systems (Thomas, Licence, Howdle, Croft, Poliakoff)
- the enzymatic synthesis of polymers has also been demonstrated (Howdle)
- use of enzymes from the halophilic archaeon *Haloferax volcanii*, which are optimised to function in the presence of molar salt concentrations. *Haloferax* enzymes are also able catalyse reactions in the presence of organic solvents and are therefore compatible with chemical reactions where the substrates or products are insoluble in water. This opens up a wealth of novel industrial and biomedical applications (Allers)
- produce new materials from renewable feedstocks by using biocatalysis to synthesise building blocks/monomers (Howdle)

We also have experience of combining enzymes with inorganic or organometallic catalysts in order to conduct multistep reactions including dynamic kinetic resolutions.


Colorimetric analysis of enzyme reactions

## Development of enzymes and other proteins as biologics biopharmaceutics

**Key contact:** **Neil Thomas**

Our research interests include:

- the development of enzymes and other proteins as biologics or biopharmaceutics
- the design, synthesis and evaluation of enzyme inhibitors as temporal modulators of metabolic pathways
- the use of enzymes in non-aqueous solvents for synthesis of high value chemicals
- the development of new enzyme activity assays based on fluorescence, MRI and luminescence

Our work has the potential to add expertise to other research areas including availability of molecular probes (such as Fluorescence and MRI), controlled release antibiotics and anti-cancer drugs. Furthermore, our research would add value to work on bespoke enzyme inhibitors, novel protein scaffolds such as protein nanoparticles and spider silk fibres, un-natural amino acid mutagenesis and mechanistic enzymology.









## Development of veterinary vaccines and diagnostic assays

**Key contact:** Janet Daly

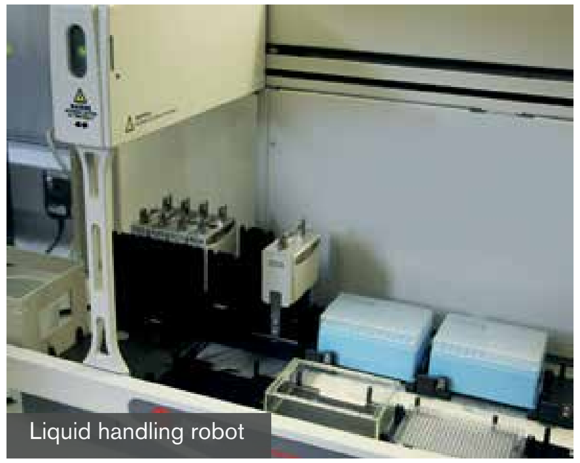
We have a broad range of expertise in the development and testing of veterinary vaccines and diagnostic assays for companion and livestock animals. Our work is largely funded through government agencies in partnership with sponsoring SMEs. Our work on animal infection and immunity encompasses research on bacteria, parasites, phage and viruses. Our experts act as consultants to veterinary pharmaceutical companies and other industry bodies, such as levy boards, on various infectious diseases.

## Differential equation modelling and dynamical systems

**Key contacts:** John King, Etienne Farcot, Markus Owen and Jonathan Wattis

We, along with the Centre for Mathematical Medicine and Biology (CMMB), specialise in developing mathematical methods to provide insights into biological and biomedical phenomena. We aim to promote the application of mathematical modelling to medicine and the biomedical sciences, and to stimulate multi-disciplinary research within the University and beyond.

- Mathematical methods including dynamical systems and differential equation modelling allow to gain quantitative insights into biological systems even when the experimental knowledge is otherwise only sufficient to provide an overall qualitative understanding.
- The Centre for Mathematical Medicine and Biology (CMMB), based within the School of Mathematical Sciences, is one of the largest of its kind in the UK. It comprises members of The University of Nottingham with a wide range of mathematical specialities and a long experience of applying mathematics to biological and biomedical sciences.



Liquid handling robot

## Engineering mammalian cells: screening for immunologic active protein and lipid compounds

**Key contacts:** Marcos Alcocer, Ashfaq Ghumra, Maria Neophytou, Franco Falcone and Lucy Fairclough

What makes a protein an allergen is not well defined. Recently, activation of the innate immune system has been demonstrated to be a critical step in the initiation of immune responses to allergenic proteins. Accumulated evidences suggest that factors other than the protein composition might be important for the response. Complex lipids in particular from a variety of sources can act as ligands for cells of the human immune system (via CD1) and activate potent drivers (NKT cells) of allergic sensitisation.

We have an established track record of working with industry. For example, in partnership with a large multinational company we are humanising stable mouse NKT cell lines and producing fluorescent cell reporter systems. By using modern gene editing tools, a pool of receptors from primary donor cells and robotic handling stations we are establishing a screening assay able to select commercially interesting materials with a reduced risk of immunomodulation. These cells, and other engineered basophil systems previously developed, are part of our ongoing efforts to define an allergen and produce *in vitro* systems for their assessment.

Biotechnology YES Final 2015

## Entrepreneurial development and commercialisation

**Key contacts:** Simon Mosey and Hannah Noke

The Haydn Green Institute manages the Biotechnology YES competition that has developed the entrepreneurial skills of over 5,000 early career researchers. The team has also worked with biotech and bioenergy entrepreneurs and large corporations globally to help manage the adoption of radical new technologies to address industrial and societal challenges.

## Exploitation of lignocellulosic feedstocks for the production of transportation biofuels

**Key contact:** Greg Tucker

The exploitation of lignocellulosic feedstocks for the production of biofuels such as ethanol and butanol requires reduction in the inherent recalcitrance of the feedstock to enzymatic degradation and the availability of microorganisms with higher tolerances to the inhibitors generated by the process. Additionally, the process requires a large amount of water. We are investigating these barriers to commercialisation.

Our research includes a study of the use of selective breeding to enhance the digestibility of wheat straw along with the production of yeast strains with higher tolerances to inhibitors such as acetic acid.

We are also testing the replacement of fresh with sea water in the process and new strains of marine yeast have been identified that may facilitate this approach. Furthermore, we are investigating a range of potential feedstocks including wheat and rice straw, and municipal solid waste.

## Framework of Innovative Uncertainties

**Key contacts:** Stelvia Matos and Jeremy Hall

Our team at the International Centre for Corporate Social Responsibility has developed the Technological Commercial Organisational and Societal (TCOS) Framework of Innovative Uncertainties – an analytical tool to identify respective key issues at early phases of a technology's development to improve commercialisation and avoid potential controversies that can hamper success.

In addition to technological challenges, the causes of innovative uncertainties include lack of knowledge regarding commercial applications and user needs, whether organisations possess the competencies, intellectual property protection and complementary assets that will allow them to appropriate the benefits of their invention, and whether they have an adequate understanding of the social perception of the technology, sustainability aspects and unintended impacts that it may have on stakeholders.

We have applied the TCOS framework in a number of industries including agriculture biotechnology (transgenics), forestry (biomass based resins and carbon fibre) and food (vanillin flavouring). The framework helps identify hurdles that prevent innovations from making the leap from lab to living room, and how corresponding levers can be exploited for more efficient technology translation and diffusion. In particular, we found that eco-value propositions – technologies that can address health, safety and environmental impacts – are likely to be a key drive but are often overlooked.


Exploiting agricultural wastes for biofuel



Industrial Biotechnology Capability Statement

Petri dish growing *Aspergillus Fumigatus.* ©iStock Linde1



## Functional annotation of bacterial coding sequences

**Key contact:** James Leigh

Within the School of Veterinary Medicine and Science our team is researching genome sequence data, which is now readily available and can be produced in a rapid, cost effective manner for numerous applications. Accurate annotation of such data and, more precisely, annotation in relation to the function of interest is more difficult. We have developed a molecular biology work-flow and bioinformatic pipeline that enables detection of those genes that play a functional role in selectable biological processes such as growth, survival and colonisation.

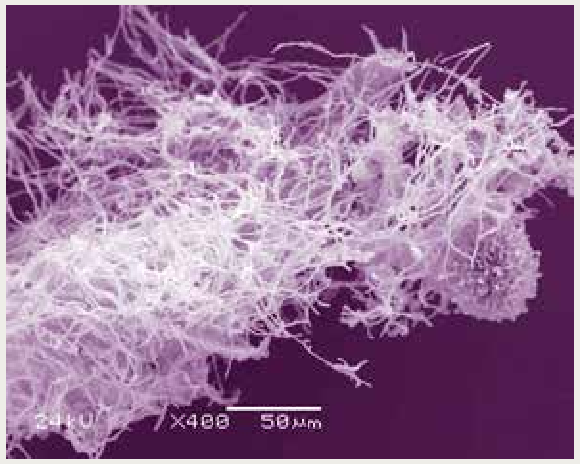
The original application of this technology was the investigation of disease pathogenesis by streptococci. We have shown that it is now possible to employ a similar process following the same principles for any bacteriumin which insertional or transposon mutagenesis is known to work.

Essentially, the genomic sequences flanking the point of insertion from a population of mutated bacteria are generated using next generation sequencing of an enriched target and the resulting sequences are mapped back to the genome of interest in a quantitative manner. Detection of those sequences that are not mutated or carry fewer mutations following the desired selection permits alignment of specific sequences and genes to specific phenotypic traits. Appropriate selection of the phenotype under investigation enables rapid detection of new targets for the future development of prophylactic and/or therapeutic agents for disease control.

## Fungal biotechnology

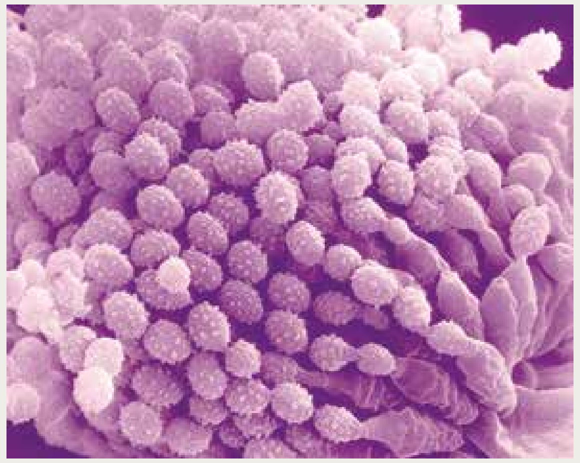
**Key contacts:** Simon Avery, Matthias Brock, Paul Dyer and David Archer

Filamentous fungi and yeasts are of considerable importance within the biotechnology, food and pharmaceutical sectors. Some have beneficial properties, but some have detrimental properties, being responsible for animal and plant diseases and spoilage and decay. Our group has expertise in fungal (yeast and filamentous fungi) biology and the tools required for genome manipulation (recombinant DNA and sexuality). We use fungi as models of disease. Our work encompasses fungal primary and secondary metabolites, with applications in synthetic chemistry, biofuels, foods and beverages, medicine, and opportunities for pathway manipulation by synthetic biology. By way of examples, we develop novel antifungal treatments for combatting fungal infections of crops and humans including *in vivo* imaging for investigating therapy efficacy in murine models.




We provide specific expertise in:

- protein secretion
- regulation of gene expression
- fungal enzymes for biofuels, and anti-fungals used in food
- development of novel combination-antifungals and mode of action discovery
- analysis of stress responses and phenotypic heterogeneity
- strain improvement by sexual selection and genetic manipulation for improved fungal drug or food production
- genome analysis
- purification and characterisation of fungal natural products
- regulation of secondary metabolism
- heterologous expression systems
- *in vivo* imaging of fungal infections




DNA quantification

## Gene delivery methods and recombineering

**Key contact:** Ronald Chalmers

Our primary interests are in tool and method development in DNA recombination and genomics. This research includes gene delivery methods and recombineering in higher eukaryotic organisms. We are also interested in understanding the roles that transcriptional networks and epigenetics play in phenotypic development.

## Genome manipulations in prokaryotic and eukaryotic organisms

**Key contact:** William Brown

We have developed a set of unidirectional serine recombinases that can be used for sophisticated genome manipulations in a wide variety of organisms, both prokaryotic and eukaryotic. These include the construction of transgenic segments several hundred kilobase pairs in length, deletions and translocations. We are using these reagents to investigate centromere assembly in the fission yeast *Schizosaccharomyces pombe.*

## Geophysical techniques for subsurface characterisation

**Key contact:** Li Bai

Soil, plant, and groundwater resources are important for biotechnology and the bioeconomy. In collaboration with the British Geological Survey, we work on geophysical imaging techniques such as Electrical Resistivity Tomography (ERT) for characterising the shallow subsurface, the uppermost part of the Earth's crust, which is of primary importance for agriculture. The geophysical techniques help us understand fluid (groundwater, contamination and nutrient) flow in the subsurface, soil-water-plant interactions, and geothermal energy exploration.


In-field molecular diagnosis

## In-field molecular diagnosis and UV-mediated control of plant disease

**Key contact:** Matthew Dickinson

Our molecular diagnostics work has involved the development and validation of Loop-mediated isothermal amplification (LAMP) assays, for rapid detection of plant pathogens (viral, bacterial and fungal) in non-lab based settings. This has involved development of robust field-based DNA extraction techniques that can be combined with real-time LAMP assays using minimal equipment, and the capacity for integrating these methods into remote-sensing. For example, combining the assays with real-time spore trapping for monitoring air-borne inoculum of pathogens is now being investigated. With industrial partners we have developed the use of UV-C and UV-B based commercial equipment for control of plant diseases, primarily in horticultural crops. The UV-C based technology aims to treat plants in glasshouses with pulses of UV-C to induce systemic resistance mechanisms within the plants to help them fend off diseases, whilst the UV-B based equipment is aimed at post-harvest treatment in storage facilities to remove ethylene from the storage areas and potentially reduce the damage caused by post-harvest rots of fresh produce.





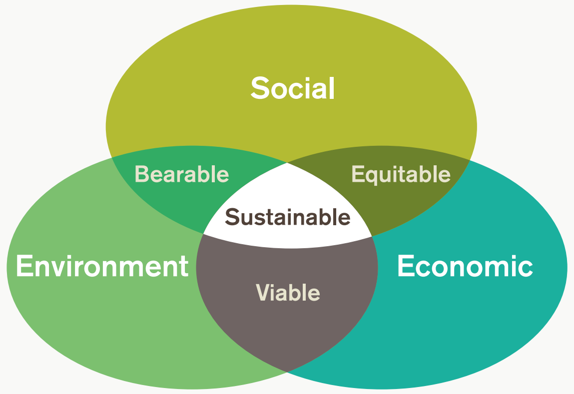
## Integrating Responsible Research and Innovation (RRI)

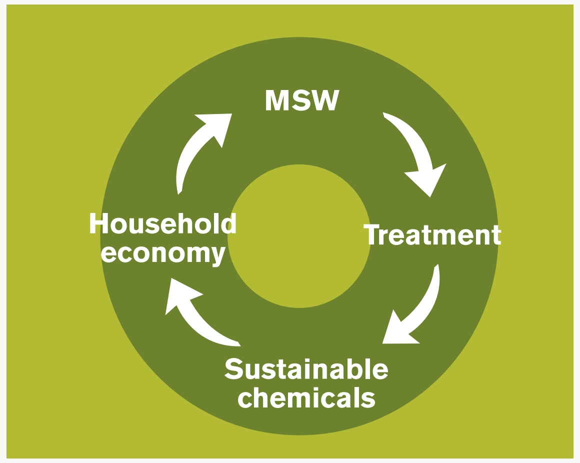
**Key contacts:** Brigitte Nerlich, Carmen McLeod, Sujatha Raman and Alison Mohr

A number of recent initiatives attempt to bring about significant shifts in the institutional relationships between research funders, researchers and the public. These include the 2010 Concordat for Engaging the Public with Research, the work of EPSRC on responsible innovation, and the emergence of RRI as a policy framework for Horizon 2020 in the European Commission. Central to these initiatives are moves to better articulate the social responsibilities of different parties involved in promoting innovation.

As part of our programme of research we are developing specifications to clarify what RRI means and what it requires from research management, funders, universities and industry as well as researchers. We are also investigating ways in which the public can contribute to or benefit from responsible innovation, and developing training materials to enable a bottom up engagement of researchers with this new policy landscape. In recently completed work funded by the BBSRC we have applied concepts of RRI to clarify options for responsible innovation in biofuels, biorefining and the bioeconomy.

RRI is a key aspect of Synthetic Biology, both in the initial UK 'Roadmap' and in the UK Government's strategic plan published in 2016. At the Synthetic Biology Research Centre (SBRC), we are committed to implementing RRI within our research programme. The RRI strand of our research programme engages both with scientists and members of the public and also critically studies how RRI works in theory and practice.




## Life cycle assessment and techno-economic modelling

**Key contact:** Jon McKechnie

We focus our research lens on life cycle assessment (LCA) and the techno-economic modelling of bioenergy and biorenewable chemical production and use. This includes assessing environmental benefits of industrial biotechnology processes and products, the identification of hot-spots to help prioritise ongoing research, and determining compliance with relevant regulations such as biofuel GHG emissions reduction requirements.

Our research helps to bridge lab-scale research and development with potential impacts at future commercial-scale deployment. By simulating full-scale production we are able to better understand feedstock supply requirement and potential environmental impacts, production process impacts, potential markets for end products and benefits from displacing current products.

This approach can identify processes and inputs of concern in order to help prioritise ongoing research and the optimisation of processes to balance financial and environmental objectives. Assessment methods developed in undertaking this research will contribute to streamlining LCA and other whole system assessment tools. Standardised assessment methods will make it easier to communicate results to key stakeholders, including industry and policymakers as well as the general public. This will also help inform ongoing policy development that regulates and incentivises biorenewable fuels and chemicals production.


Spectrophotometry

## Mass spectrometry to study biomolecular interactions

**Key contacts:** David Barrett and Neil Oldham

Our research focuses on using MS-based methods to monitor and understand cellular metabolism. This includes work on quantitative bioanalysis, metabolic profiling, metabolomics, biomarker discovery, and surface and imaging mass spectrometry using some of the most advanced systems available.

Of particular interest is the study of non-covalent protein-ligand and protein-protein interactions by electrospray-mass spectrometry, ion mobility spectrometry, and chemical footprinting.

## Mathematical modelling of bioreactors

**Key contacts:** Paul Matthews and Richard Graham

Tissue engineering is an important and expanding research field with an aim to grow human tissue, seeded from a patient's own cells, in a bioreactor to form a structure that can then be returned to the patient's body. We have worked on the mathematical and computational modelling of the growth process within the bioreactor, which involves complex interactions between the cells, the nutrient and the fluid used to supply the nutrient. Our research centres on the design of the scaffold structure, the cell seeding structure and the flow regime in order to create an environment for efficient, even and effective cell growth.

## Mathematical modelling of multi-scale complex systems

**Key contacts:** Cornelia de Moor, Andy Salter, Ian MacDonald, John King, Tim Parr, John Brameld, Ian Dryden, Rachel Gomes, Jamie Twycross and Etienne Farcot

Formulation and analysis of mathematical models of complex systems in a number of different areas:

- Regulatory networks, metabolism, mRNA production and degradation, and drug side-effects e.g. insulin sensitivity. Of particular interest are problems involving nonlinear kinetics or regulation, such as may occur in systems with catalytic or inhibitory feedback mechanisms. This has applications in complex chemical systems, biological networks such as the metabolism of carbohydrates and fats in the body, or other gene-protein regulatory networks.
- Aggregation or coagulation-fragmentation problems, in which there is a size distribution which evolves over time, for example in cluster formation, or polymers, where lengths may change.
- Crossing scales from subcellular gene to metabolic and signalling networks, and macroscale process modelling.


Modelling root growth and development

## Mechanistic mathematical modelling

**Key contact:** John King

Our research interests include mathematical modelling, systems and synthetic biology, and industrial mathematics. Our work has the potential to aid mathematical modelling across scales from subcellular dene to metabolic and signalling networks, and macroscale process modelling.





## Microwave pre-treatment to produce sugar derivatives and bio-based chemicals

**Key contacts:** Eleanor Binner, John Robinson, Ed Lester and Sam Kingman

Pre-treatment of biomass can be achieved in a number of ways using microwave heating in a controlled and selective manner. Aqueous phases can be harnessed to extract valuable chemicals from the plant matrix with reduced treatment times and energy use, without the use of toxic solvents and under milder processing conditions. Controlled biomass transformation can also be carried out, converting cellulose into Levoglucosan or other platform chemicals at lower temperatures than conventional thermal processes. The barriers to the development of these processes stem from a lack of understanding of the fundamental mechanisms by which microwaves enhance extraction and transformation processes. Our group has developed an established track record for industrial scale-up of microwave heating processes, and our industrial partners have benefitted from reduced energy requirements, simplified process flowsheets, lower capital costs and increased feedstock flexibility when microwave heating is used.

Our research focuses on understanding how biomass interacts with microwaves, with the aim of developing microwave heating systems to enable the use of sustainable and non-conventional feedstocks for biotechnological processing.

## Modelling of human decision making

**Key contact:** Jon Garibaldi

Our research interests centre on the modelling of human decision making, primarily in the context of medical applications. Work so far has concentrated on utilising fuzzy logic to model the imprecision and uncertainty inherent in medical knowledge representation and decision making but can also have application in industrial biotechnology.

This approach has been applied in areas such as classification of breast cancer, identification of Alzheimer's disease, and the assessment of immediate neonatal outcome. Of particular interest to us is the transfer of medical intelligent systems into clinical use, which has led to the study of methods of evaluating intelligent systems and mechanisms for their implementation. Our work spans to generic machine learning, such as clustering, classification and optimisation, particularly when applied to the optimisation of decision making models, and in the study of adaptive and time-varying behaviour.

## Modular polyketide synthases

**Key contact:** Neil Oldham

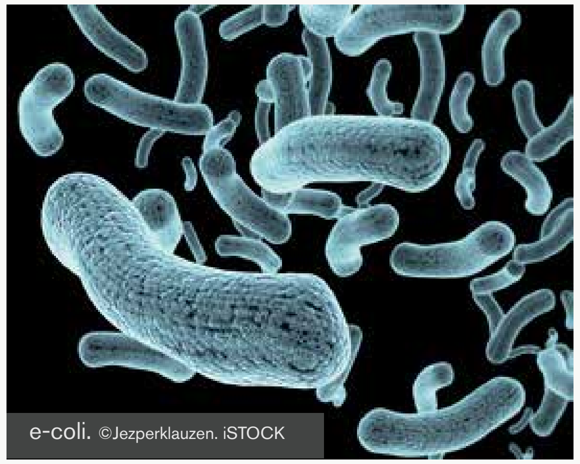
We produce novel recombinantly expressed catalytic domains from polyketide synthases, which carry a range of enzymatic activities, including C-C bond forming reactions such as Claisen condensation, ketoreduction, dehydration and enoylreduction.


Micrograph of tomato cells ©WAVEMOVIES ISTOCK

## Modulation of plant cell walls for improved raw material quality

**Key contacts:** Graham Seymour, Rupert Fray and Tim Foster

Building on decades of expertise in plant genetics and gene manipulations we use RNAi and CRISPR technology as tools to modulate cell wall remodelling enzymes in plants. For example, in tomato, altered cell wall activity can dramatically affect the structure and functional properties of pectins for use in processed food products. A major target for application is improved raw material quality for tomato puree and paste.


e-coli. ©Jezperklauzen. iSTOCK

## Molecular mechanisms: bacterial DNA replication, host-pathogen interactions, modulation of bacterial virulence, bacterial biofilms and antimicrobial resistance

**Key contact:** Panos Soultanas

Our expertise is in the area of mechanistic biochemistry, in particular:

- bacterial DNA replication and priming
- DNA repair and site-specific recombination

Our work has diversified into research into antimicrobials, host-pathogen interactions and the effects of human cytokines on bacterial virulence as well as the development of anti-biofilm agents.

## Molecular modelling of biomolecules

**Key contacts:** Jonathan Hirst, Elena Besley, Charlie Laughton, Anna Croft and Christof Jaeger

A number of groups perform research in this area:

- Within the Computational and Theoretical Chemistry Group a broad range of computational techniques is used to study systems ranging in size from a few atoms through to nanoscale materials and devices to biologically relevant species such as enzymes and proteins. This requires the use of an extensive pallet of techniques from state-of-the-art quantum mechanical electronic structure methods to large scale molecular modelling and statistical approaches. Our group is actively involved in finding new and innovative approaches to make methods appropriate to problems on different scales work effectively together to deliver new insight into chemical and biological systems (Hirst, Besley, Laughton, Croft).
- Computational approaches for predictive *in silico* protein design and engineering, with the goal to develop enzymes with novel catalytic features for their use in industrial biotechnological applications. One area of particular interest is the study of radical enzymes. Processes using radical enzymes offer opportunities to combine sustainable chemistry approaches with the high potential of free radicals – chemical intermediates that are difficult to control in industrial processes, but which nature has been able to harness to produce valuable materials such as antibiotics, anticancer and antiviral drugs. Our research addresses the need for new enzymes to expand the biocatalytic toolbox for the synthesis of chemicals, and includes the combining and developing of efficient workflows and strategies based on a wide range of computational chemistry methods that are transferable over a range of projects in the form of predictive modelling. This leads us to a deeper understanding of the underlying molecular biology and chemistry, and opens the gateway to rational enzyme design. From different simulation approaches we gain insights into the dynamic behaviour of enzymes, catalysis, aggregation behaviours and other features, all of which feed into a deeper understanding of the systems necessary to improve their properties for biotechnological applications (Jaeger).

## Next generation biomaterials discovery

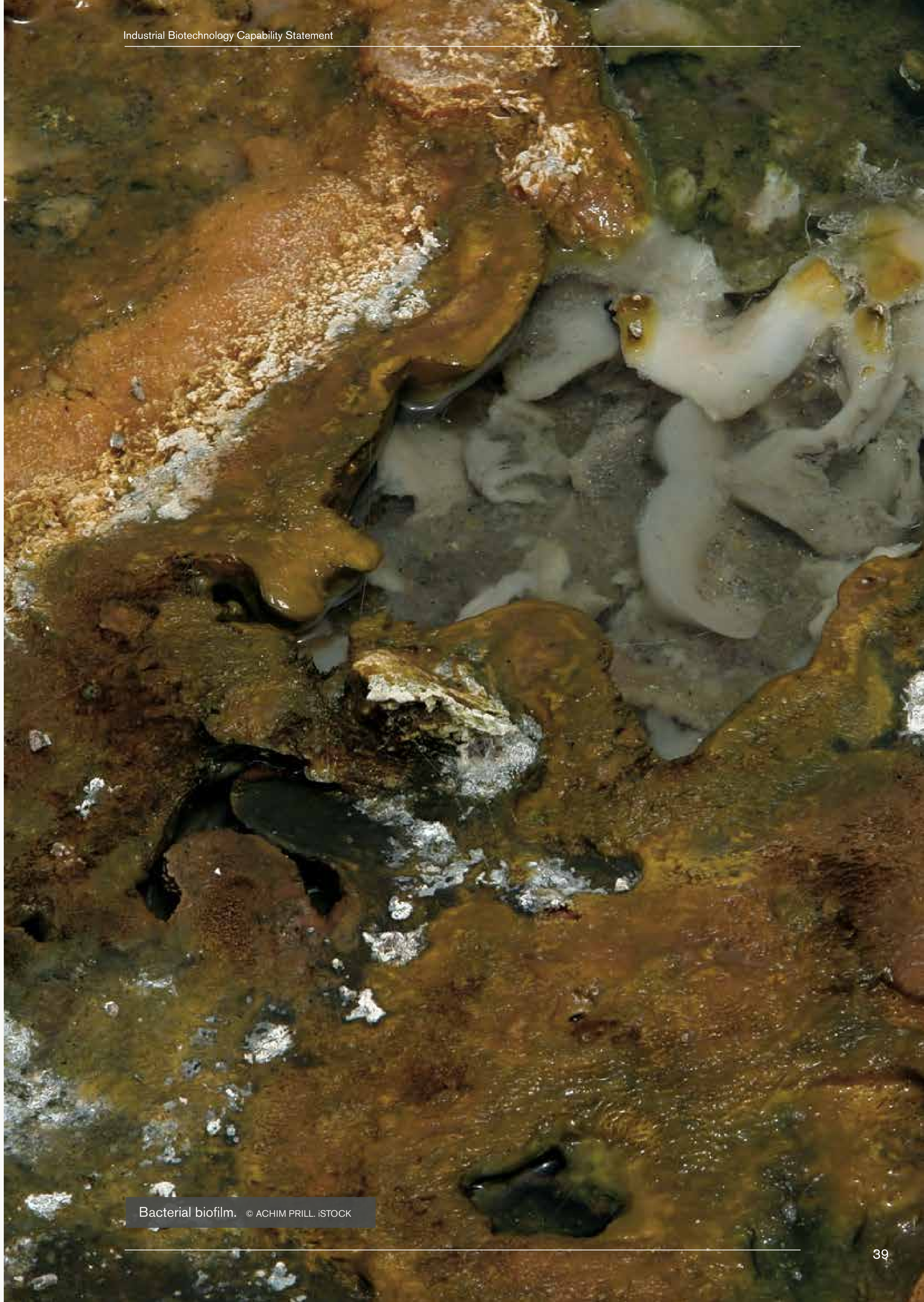
**Key contacts:** Morgan Alexander and Elizabeth Hudson

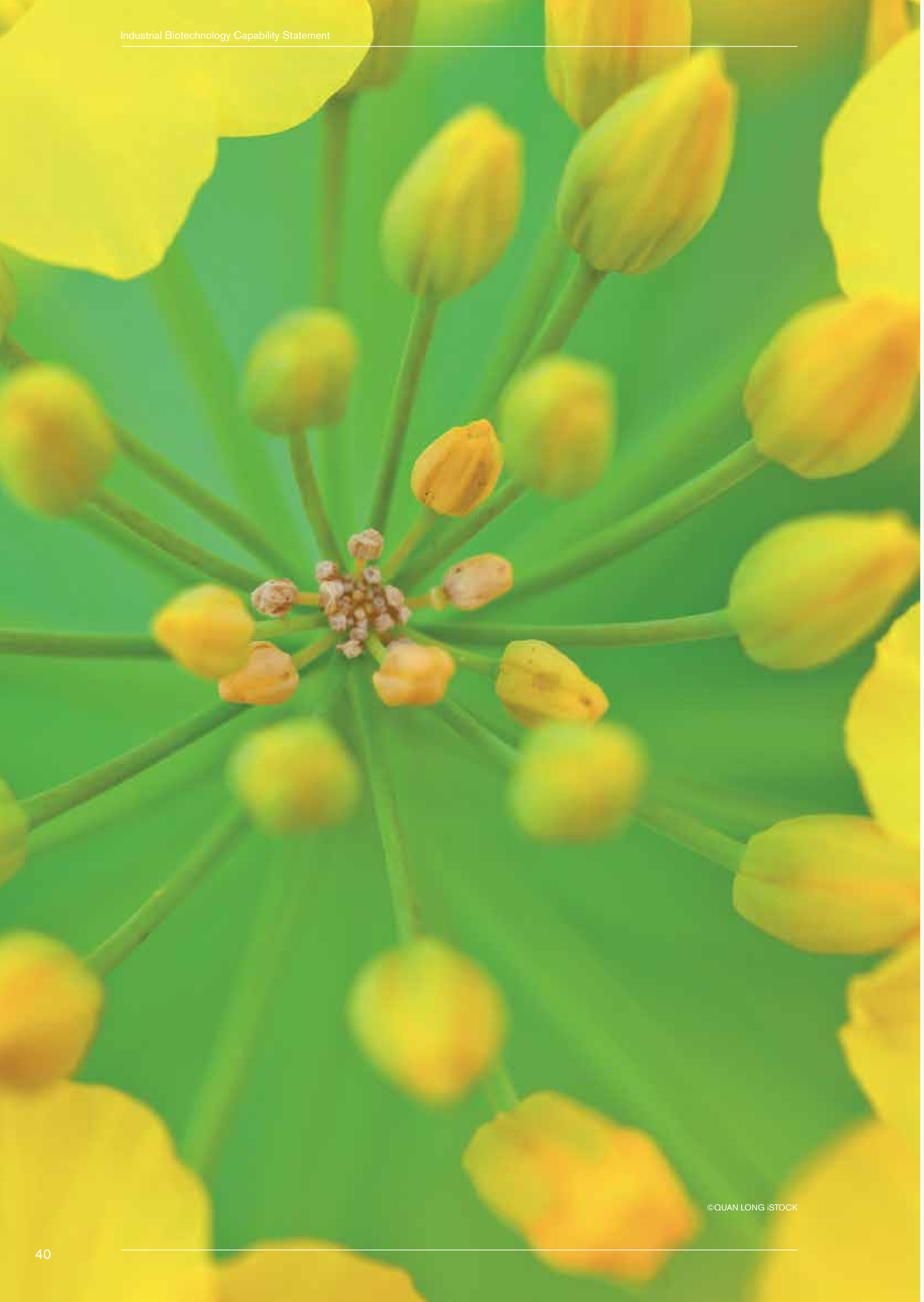
Advanced biomaterials are an essential part of meeting future challenges facing our society, such as antimicrobial resistance. Companies who have unmet materials needs benefit from the capability of our Laboratory in Biophysics and Surface Analysis (LBSA).

Our multi-disciplinary team of experts across the University are collaborating with leading international groups. This work can benefit a wide range of sectors from new advanced materials (including regenerative medicine), the pharmaceutical industry, medical devices, high value manufacturing, and industrial biotechnology and materials. For example we have discovered polymeric materials which control the attachment of microbes. This research aims to realise the vision of materials discovery in 3D, allowing the development of bespoke materials identified for specific applications.






Bacterial biofilm. © ACHIM PRILL. iSTOCK



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## Novel food structures as delivery vehicles

**Key contact:** David Gray

Our group's research interests include novel, bio-innovative approaches of incorporating lipids into the diet to improve health and to reduce impacts on the environment. Other interests include:

- lipid: extraction, analysis, and the study of phytonutrient (vitamins A and E) availability
- biological material: oilseeds, green leaf material, chloroplasts, and microalgae
- intracellular organelles: oil bodies, oleosomes, lipid droplets, chloroplasts, natural emulsions, and milk fat globules
- digestion: oils and fats, lipids, functional food ingredients
- sustainability: novel processing of oilseeds, recovering value from green plant waste material

Our research has the potential to add value to industry through the physical processing of biomass (including waste) to recover organelles with functional properties as food and feed ingredients.

## Novel peptide ligand discovery

**Key contacts:** Kevin Gough and Ingrid Dreveny

We have developed advanced methodology by exploiting the vast diversity of phage display peptide libraries, which contain tens of millions of distinct peptides and coupling it with the screening power of next generation sequencing technologies. This combined methodology allows the screening of tens of thousands of binding events in parallel and facilitates the efficient identification of peptides that bind to immune reagents produced upon infection or disease and peptides against target proteins. Applications include:

- mapping interaction sites on proteins that have important biological roles, such as those implicated in pathologies such as cancer. The aims of this are to discover both the binding sites on the protein and also their binding partners; both approaches have the potential to inform the discovery of synthetic peptide mimetic drug-like molecules
- identifying panels of infection and disease-specific synthetic peptides that mimic immunogens and can be used for the design of novel diagnostics and vaccines

Veterinary facilities at Sutton Bonington

## Nutritional diagnosis and metabolite analysis

**Key contact:** Nigel Kendall

At the NUVetNA laboratory we offer nutritional diagnostic services specialising in mineral and trace element monitoring. We are also able to measure a variety of metabolites and markers.

We have routine blood, liver and urine services where our clients are predominantly veterinarians but also nutritional companies and farmers. We also perform custom diagnoses to meet research and commercial requirements.

We routinely utilise colorimetric clinical chemical capabilities, Inductively Coupled Plasma mineral analysis and ELISAs for immunoassays.

## Optimising welfare and performance in ruminant agriculture

**Key contacts:** Martin Green, Jon Huxley, Chris Hudson and Jasmeet Kaler

In the Dairy Herd Health Group and Sheep Flock Health Group within the School of Veterinary Medicine and Science we aim to improve the understanding of factors affecting health, welfare and efficiency of farming systems, with a view to facilitate the sustainable intensification of the industry to meet growing demands from limited resources.

We have extensive experience of using advanced statistical and computational techniques to derive maximum value from data recorded in the ruminant agriculture sector as well as extensive capability in data engineering and agri-informatics; unlocking potential from routinely recorded farm data.

Our other interests include evaluating novel methods of animal-level data collection using biosensing. Cutting edge analytical techniques are applied to the data to ensure that results are robust but intuitive to interpret.

We have an outstanding track record in deriving impact from our research, with an extensive network of contacts both amongst the livestock veterinary community and within the wider agricultural industry. Established routes to impact have included the development and roll-out of a national control scheme for a major endemic disease of dairy cows (the DMCP, associated with an estimated benefit to the UK industry of £5 – 10 million pa) and development of sophisticated decision support tools.


Welfare of dairy cattle


Tomato plant research

## Post transcriptional RNA modifications

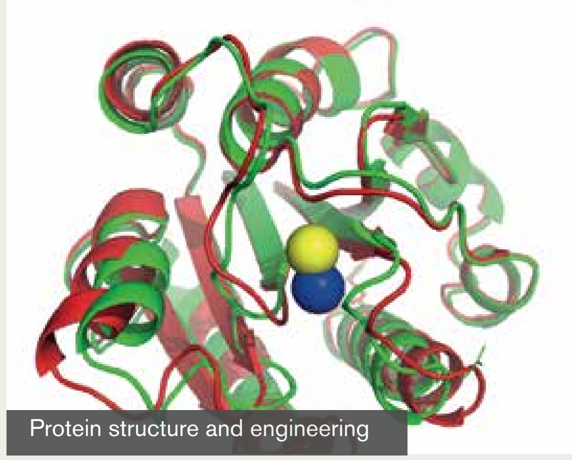
**Key contact:** Rupert Fray

Our research has three interlinked themes:

- Re-engineering carotenoid producing plant and bacterial systems (Tomato and Pantoea ) as platforms for the production of high levels of paclitaxel precursors. We use the Tomato system for taxadiene synthesis and accumulation which facilitates a simple purification pathway. This naturally synthesized taxadiene is used by our organic chemistry colleagues for *in vitro* semi-synthesis approaches for production of various taxane analogues that may have applications such as novel anti-cancer therapeutics.
- Exploring and manipulating RNA modifications for the post transcriptional regulation of gene networks and improved transgene expression. We have developed monoclonal antibodies for recognition of modified nucleotides, which have been licensed to two companies and which form the basis of a commercial analytical test kit.
- The introduction into plants of bacterial pathways to bypass photorespiration and improve photosynthetic efficiency. We have strong collaborative links with academic colleagues in China whio are transforming our systems into target plants and conducting controlled field trials.




Robotic milking system



Protein structure and engineering

## Protein evolution and chemical modification

**Key contact:** Neil Thomas

We modify proteins to add additional functionality (imaging agents, drug molecules, stabilizers, immobilisation tags and catalytic activity) using chemical methods, enzymatic methods (such as biotinylation) or site-directed mutagenesis with either natural or un-natural amino acids. These approaches have been shown to increase the thermal stability of enzymes involved in biocatalysis and allow proteins such as antibodies to deliver and release cytotoxic drug molecules selectively at tumour tissues, or to be used to image tumour tissues *in vivo*.

Modifications include:

- pegylation that enable proteins to evade the immune system and proteolytic breakdown *in vivo* to improve their pharmacokinetics
- the incorporation of un-natural amino acids that allow the attachment of a wide variety of ligands to the protein of interest using ‘click’ chemistry
- biotinylation of proteins that allows them to be immobilised using a streptavidin/avidin column

These modifications can be carried out along with protein evolution to impart new catalytic activity or increased stability.

## Protein structure determination and engineering

**Key contact:** Ingrid Dreveny

Our research focuses on the determination of protein structures in the presence and absence of binding partners using X-ray crystallography. Knowledge of a protein’s three-dimensional structure and structure-based protein engineering provide unique opportunities for both academic and industrial applications. Some of the potential benefits and applications include:

- optimisation of an enzyme’s substrate specificity
- enhancement of a protein’s stability or solubility
- insights into a protein’s function that may lead to new applications
- structure based drug design

Sheep welfare

## Rational vaccine design through pathogen interactions

**Key contacts:** Sabine Tötemeyer, Tracey Coffey, Peers Davies, Richard Emes and Jasmeet Kaler

We are developing complex cell and organ culture models to study host pathogen interactions in a representative system while reducing the use of animals in research.  In parallel, we investigate pathogenic bacterial populations of animal welfare concern, develop typing systems and use high throughput sequencing technologies to identify vaccine targets.

We are applying our models and are working towards vaccine targets to multi-bacterial infections such as Foot-rot, which remains of great welfare and economic concern for sheep farmers and veterinarians worldwide as current vaccines are short-lived and poorly effective.





## Regenerative medicine bioproducts

**Key contact:** Virginie Sottile

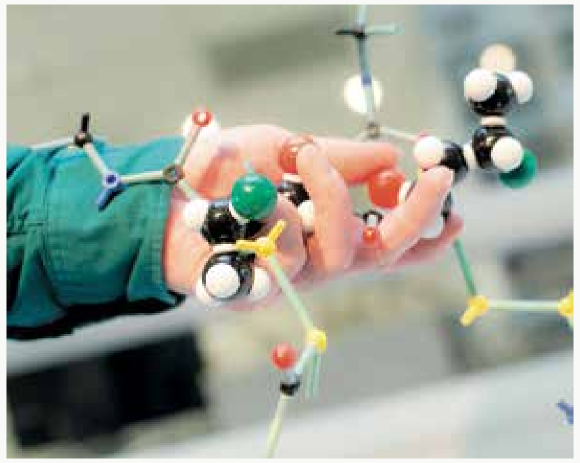
Our group studies the development of regenerative medicine bioproducts, which requires the manufacture of stem cells and derived tissue equivalents in a controlled and optimised biotechnological environment. We have a particular interest in developing non-invasive, live-cell monitoring analytical indicators and technologies in order to enable the in-line control of therapeutically relevant cell products in a manufacturing context.

## Reporter systems for bacterial translation and protein secretion

**Key contact:** Phil Hill

We develop reporter systems to measure bacterial transcription, translation, protein secretion and surface anchoring of bacterial proteins. We recently developed a high throughput screen for inhibitors of bacterial sortase, a potential anti-infective target. Furthermore, we have developed methods based on covalent attachment of ligands to bacterial surfaces to construct artificial bacterial consortia for modification of substrate flow between strains with different catalytic activities.

We use our applied molecular microbiology knowledge to advance industrially-relevant science. For example we are modifying carotenoid-producing bacterial chassis to accumulate high levels of paclitaxel intermediates as substrates for in *vitro* modification to produce novel bioactives and pharmaceuticals.



## Scaffolds and synthetic methodology for small molecule drug discovery

**Key contacts:** Chris Moody, Simon Woodward, Chris Hayes, Hon Lam, David Amabilino, Rob Stockman, John Moses, James Dowden, Ross Denton, Liam Ball, Martyn Poliakoff, Mike Stocks, Peter Fischer and Barry Kellam

We have an extensive track record of developing novel synthetic methodologies that enable chemical processes to operate with greater chemical stereo-specificity, reduced use of toxic solvents, fewer stages, less purification demands, lower temperature and pressure, and lower environmental impact. Our research in this area has been applied to:

- new scaffolds for drug discovery
- novel catalysts for chemical processes
- new functional materials synthesis
- the development of green technologies such as super critical fluids and photochemistry as an alternative to existing industrial processes
- automated process optimisation

The outputs of our research have clear industrial applications. For example we recently described the use of a photochemistry approach to a key intermediate in the synthesis of the anti-malarial drug Artemisinin.

Tomato tagging to assess development





## Secondary plant products for industrial and medical use

**Key contact:** Graham Seymour

Our research focuses largely on the tomato; a crop which, in its fresh and processed states, is worth $55 billion annually. We have three main areas of interest:

- Secondary metabolites from tomato; the identification and isolation of compounds with health benefits.
- Using tomato fruits as factories for the synthesis of novel compounds, such as taxanes.
- CRISPR DNA editing: we have knockout lines for all the major cell wall remodelling genes in ripening tomato and for the first time we have been able to modulate fruit softening. Our insights into remodeling cell walls will have a massive impact on tomato processing quality through increased paste viscosity creating a more natural product, obviating the need for modified starch in processed products.

## Signalling and communication in prokaryotes

**Key contact:** Steve Diggle

Our research interests focus upon the evolution of signalling and communication, cooperation and conflict in microbial populations, and the implications for the evolution of virulence and antibiotic resistance during infection. Our main emphasis is on chronic infections such as those found in non-healing wounds and the cystic fibrosis lung. We are exploring the development of compounds which disrupt biofilm formation. If we can prevent bacteria from attaching to surfaces and forming biofilms, this could have great relevance and be of direct value to a number of industrial processes.

With increasing concerns over antibiotic resistance, we are looking back in time to learn from the past. We develop recipes in the laboratory based on ancient medieval recipes for the treatment of infectious disease which are translated from ancient texts, and test them against antibiotic resistant bacteria such as *Pseudomonas aeruginosa* and *Staphylococcus aureus*.

We have recently developed a recipe using instructions from the 10th century text Bald's Leechbook that has significant anti-Staphylococcal activity.

Nanotechnology facilities

## Surface and nanoscale imaging of biomaterials

**Key contacts:** Andrei Khlobystov, Chris Parmenter and Karen Alvey

Nanoscale and Microscale Research Centre (NMRC) is a new cross-discipline centre housing over 20 major pieces of instrumentation for nanoscale research, including 12 electron microscopes, an advanced surface characterisation suite and nanofabrication facilities. We have developed unique protocols (FIBSEM) suitable for the extraction of small regions of sample, particularly biomaterials, at cryogenic temperatures using a cooled micromanipulator enabling label free imaging of biological materials. This significantly improves the analysis and interpretation of biological, medical, pharmaceutical, food and other organic samples in their native, unaltered form.

The NMRC has considerable experience in the investigation and characterisation of biological materials at the micro and nano scale. This has included a breadth of work including: assessing the position of nanoparticles within cells and tissue, characterising drug delivery systems (including emulsion, liposomes, conjugated nanoparticles etc.), and imaging *in situ* hydration-dehydration of hydrogels.

## Sustainable chemistry using ionic liquids

**Key contacts:** Pete Licence and Jairton Dupont

Our research team in the GSK Carbon Neutral Laboratories for Sustainable Chemistry (CNL) is using ionic liquids for a range of applications to improve the environmental impact of chemical manufacture and processing, including:

- using ionic liquids for biomass pre-treatment and processing prior to biofuel synthesis
- developing novel catalysts for industrial processes
- capturing carbon dioxide and transforming it using ionic liquids

Pete Licence is also the chemistry lead for the EPSRC and BBSRC Multidisciplinary Research Centre on Synthetic Biology making petrochemical feedstocks from C1 off gases.

## Synthesis of polymers for biomedical applications

**Key contact:** Cameron Alexander

Our research interests include making synthetic containers to encapsulate functional biological molecules and machinery, incorporation of cell-signalling or cell-signal interference components, and encapsulants for biological cells and cell communities. Our approaches have applications in drug delivery, industrial processing and in the control of bacterial populations for example in health-care settings.

## Synthetic biology and metabolic engineering of bacteria

**Key contact:** Nigel Minton

Our main research interest is, through Synthetic Biology approaches, the metabolic engineering of microbial chassis to produce chemicals and fuels from sustainable feedstocks, either C1 waste gases (CO, $CO_2$, $CH_4$) or lignocellulose-derived C5/C6 sugars and glycerol. Principle chassis are:

- anaerobic acetogens *Clostridium autoethanogenum;* and *Acetobacterium woodii*
- saccharolytic clostridia; thermophilic *Geobacillus thermoglucosidasius*
- aerobic methylotroph, *Methylococcus capsulatus*
- chemolithoautotroph, *Cupriavidus necator*

We have developed a number of patented ‘tools’ to facilitate metabolic engineering in our chassis and we are establishing Nottingham for the UK as the leading European centre exploiting Gas Fermenting microbes. We build on the firm base of our research council funded Synthetic Biology Research Centre and research council funded Network in Industrial Biotechnology (NIBB): C1net which brings together those academics and industries globally with commercial interests in exploiting C1 gases.

Our research team, numbering over 100 people, includes metabolic engineers, molecular biologists, synthetic biologists, fermentation experts, *in silico* genome and pathway modellers as well as process engineers.

Our work provides the basis for the sustainable manufacture of materials using a disruptive technology based on cheap abundant feedstocks that directly reduce GHG emissions.



Industrial Biotechnology Capability Statement

## Synthetic biology: genome editing and generating novel CRISPR tools

**Key contact:** Ed Bolt

Our research into genome editing widely utilises the CRISPR-Cas tools by adapting the enzyme Cas9, plus its guide RNA, to alter DNA sequences in cells and *in vitro*. Cas9-based editing allows cutting of DNA but relies on a natural process called Homologous Recombination (HR) to complete the editing via 'paste' mechanisms. HR is complex, mutagenic and to some extent unpredictable, negatively influencing control and efficiency that can be exerted over Cas9 genome editing reactions. We are beginning to develop new CRISPR-Cas enzyme hybrids that contain both cut and paste activities, thereby potentially removing the need for HR. This aims to generate novel enzymes for genome editing independently of HR and its associated complexity, such as:

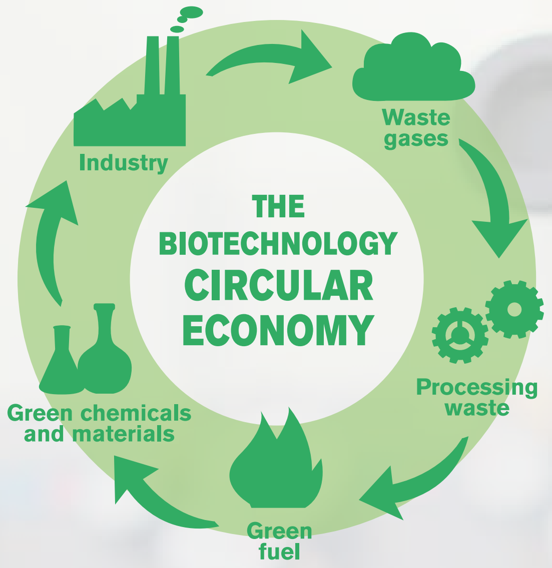
- protein-nucleic acid interactions in CRISPR-Cas and homologous recombination
- analysis and manipulation of CRISPR-Cas genome editing enzymes (for example Cas1-2, Cas9, Cpf1, Cas3)
- antibiotic resistance that targets essential protein-DNA interactions through genome-wide screens for novel anti-bacterial agents

## The Bioeconomy: social and ethical dimensions

**Key contacts:** Pru Hobson-West and Kate Millar

The Centre for Applied Bioethics has a national and international reputation for research related to the social and ethics issues related to science, technology and the bioeconomy. Our research interests include the following themes:

- how we sustainably feed a growing population
- how we meet increasing energy needs
- how we reduce reliance on scarce natural resources
- how to increase the health of our population across the life-course




## The circular economy

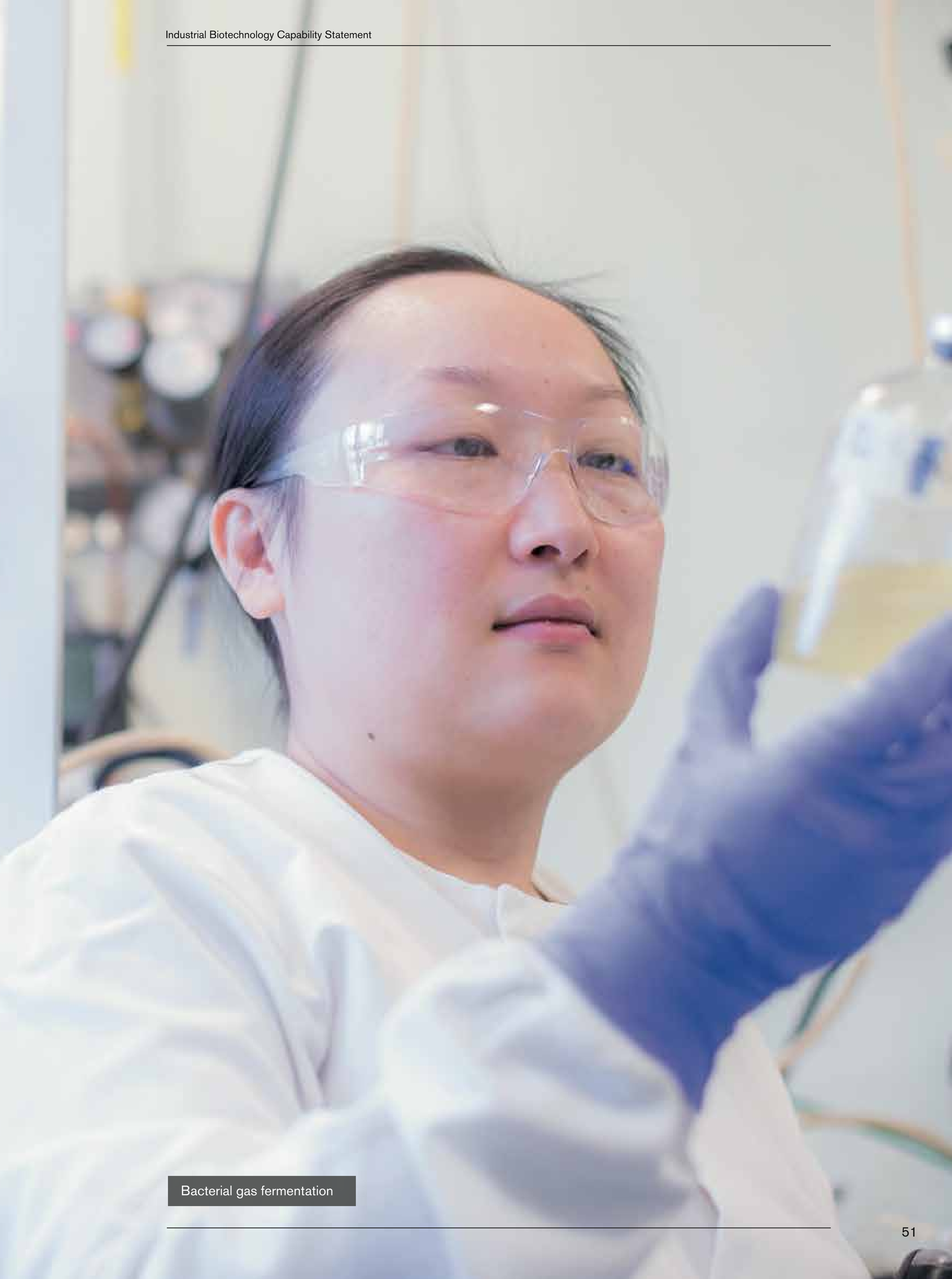
**Key contact:** Richard Smith

A transition towards a circular economy in which waste streams increasingly become resources provides a focus to challenge the environmental and sustainable performance of waste management technologies. Working with industry and regulators, specific research areas include:

- application of risk assessment principles
- optimisation of waste treatment processes
- waste characterisation
- fate and transport of contaminants
- industrial symbiosis for example wastes as fuels
- materials recovery and utilisation of byproducts for example utilisation of $CO_2$ from anaerobic digestion for food and beverage grade manufacturing
- emissions control and mitigation
- sustainability metrics







Bacterial gas fermentation

Sterile cabinet and stem cell robot

## Transitory modulation of gene expression for clinical and biotechnological use

**Key contact:** Victoria James

The development of CRISPR technologies to delete and modify genes in somatic cells has rapidly advanced the biotechnology industry and is successfully transitioning to clinical use. The disadvantage of this type of technology is its irreversibility, which limits its clinical use in diseases where permanent modification of non-diseased tissue would be detrimental and in situations where biological adaption to these permanent modifications commonly occurs.

To advance this area of biotechnology we are developing a system that allows for transient modification of gene expression at the gene (DNA) level, thus alleviating the issues associated with irreversibility.

Non-coding RNAs are naturally occurring molecules in the cells of most species. The role of non-coding RNAs is to transiently regulate gene expression via the recruitment of specific protein machinery. We have very recent evidence that supports non-coding RNA mediated pathways in the silencing and activation of genes. Leveraging these non-coding RNA dependent pathways is likely to allow the development of a system that allows not only the transient silencing of genes (equivalent to the effect of CRISPR) but also the activation of genes. This latter function would greatly benefit future clinical applications of the technology but also significantly enhance the biotechnology industry that supports research and development.

## Use of yeast to produce value added products

**Key contact:** Simon Avery

Our research  is concerned with applications based on fungal phenotypic traits. We have three main areas of interest:

- Exploring cell individuality: the population heterogeneity of phenotypes (such as stress resistance) between genetically-uniform cells. This work is of relevance to the performance of cell populations in biotechnology, food spoilage and pathogenesis.
- Mode of action: the mechanistic basis for the actions of drugs and environmental toxicants (such as metals) on cells.
- Food security and pathogen control: the development of novel antifungal combinations to inhibit undesirable fungi.

We are working with the agri-chem and biocide industries to develop novel fungicide combination treatments, and we are working with companies concerned with food-preservative resistance due to fungal population heterogeneity.

## Valorisation of food waste streams

**Key contacts:** Greg Tucker, Roger Ibbett, Tim Foster, David Gray and Ian Fisk

Our research centres on the characterisation of food waste streams to identify potential value added end use products. This may be in terms of nutrient recycling, food structuring capability or the extraction and purification of individual compounds such as bioactives or functional polymers. Examples include:

- structuring agents such as polysaccharides, antimicrobials and flavouring compounds
- developing processing technologies for the communition of food waste streams and for functional end uses such as structuring agents, purees or as a source of bioenergy
- developing methodologies for the extraction and purification of value added products
- assessing the commercial opportunities afforded by the resultant processes and products

These approaches can be applied to a number of food streams, such as low grade fruit and vegetables, processing bi-products such as fruit peel or residuals such as distillers spent grain. Exploitation of these bi-products or waste streams can add value to the overall process and also reduce costs associated with potential landfill disposal.






## Wastewater treatment

**Key contact:** Rachel Gomes

We are focusing on the utilisation of microorganisms and enzymes for the processing of materials and chemicals within the wastewater treatment or manufacturing environments.

Our research interests cover:

- biobased treatment technologies to remove pollutants from wastewater matrices and water reuse
- bioanalytical techniques enabling process design evaluation and efficiency
- emerging pollutants (for example pharmaceuticals and antimicrobial resistance) in dairy farming; understanding real world interactions and the role of enzymes in waste treatment and reuse
- analytics and predictive modelling to evaluate the influence of complex process environments on biocatalyst activity

Of particular interest is the use of bio-sourced feedstocks or catalysts. These increase system complexity because of the the inherent variability exhibited by biological materials. We are working to ensure that developing and evaluating sustainable processes to produce wastewater fit for reuse and the manufacture of chemicals to the desired specification understand and account for this complexity.

## X-ray computed tomography: non-destructive microstructural characterisation of biomaterials

**Key contacts:** Craig Sturrock and Sacha Mooney

We use x-ray computed tomography (CT) to characterise biomaterials. X-ray CT scanners allow characterisation and measurement of the interior structure of a material in 3D non-destructively. X-rays are used to create a series of cross-section images through the sample allowing constituent materials to be measured. Routine measurement include defect detection, void or bubble structure of materials (pore, volume, surface area, void ratio, size distribution), wall thickness, fibre orientation, and actual and nominal comparison to CAD data. A key benefit of our technique is that no or very little sample preparation is required facilitating rapid investigations at high spatial resolutions in their natural state. Data created are highly suited for integration in mathematical modelling applications.

At our facility, we have three high-performance scanners that offer the flexibility to investigate a wide range of materials and sample sizes. Some examples include electronic components, geological samples, soils, food products, carbon fibre, bone, and plant leaves.

X-ray computed tomography

Industrial Biotechnology Capability Statement

# Training and business interaction

# Doctoral Training Programmes

Doctoral Training at The University of Nottingham

### BBSRC Doctoral Training Partnership (DTP)

Here at The University of Nottingham we have a leading BBSRC funded £12.5 million doctoral training centre, within which a key area of interest is research into Biotechnology, Biofuels and Bioeconomy. At the centre we offer an innovative integrated four-year doctoral programme that provides our PhD students with world-class training in Biotechnology and Biological Sciences.

Our DTP programme students gain laboratory experience in varied environments, often crossing discipline boundaries, and focus on research projects from three key research themes:

- Agriculture and Food Security
- Industrial Biotechnology and Bioenergy
- Molecules, Cells and Organisms

A number of our schools are involved in the delivery of our DTP programme, including:

- Biosciences
- Chemistry
- Engineering
- Life Sciences
- Mathematical Sciences
- Medicine
- Pharmacy
- Psychology
- Veterinary Medicine and Science

### Research Training

Our DTP delivers a wide range of skills development to prepare students for a successful research career, and generates a community for the exchange of ideas and experiences across student cohorts.

In addition to their research project, all students enlist on a common programme of training for the first six months of PhD study, split equally into high-level modular training and laboratory rotations. All DTP students participate in a programme of researcher development based on the Researcher Development Framework (RDF and takes part in a three month Professional Internship Placement (PIP) designed to be outside of their core research area to broaden their horizons, experience and employability.
**For further information please contact:**
bbdtp@nottingham.ac.uk



Industrial Biotechnology Capability Statement

### Professional Internship for PhD Students (PIP)

The PIP is a three month placement not directly related to the student's research programme. It offers DTP students experience in one of a number of career sectors such as teaching, policy-making, media and industry.

Businesses are able to take doctoral students on a placement to assist in looking at strategic projects or technical challenges that may benefit from an external viewpoint.
**For further information please contact:**
bbdtp@nottingham.ac.uk

To hear students talking about how their time in industry has influenced their future career plans visit **http://bit.ly/2a3Gyl5**, and for blogs about our student placements visit www.ncub.co.uk/blog/food-econ-placements and www.ifst.org/work-experience-blogs

### EPSRC Centre for Doctoral Training in Sustainable Chemistry

We have been awarded £5.3 million to establish the EPSRC Centre for Doctoral Training in Sustainable Chemistry. The centre is being developed in collaboration with Industry and as a partnership of several disciplines including chemistry, engineering, biosciences and business. The Centre aims to train students in the development of sustainable processes and compounds for the chemistry-using industries. The defining principle that has driven the co-creation of the CDT training programme is a shared vision and commitment to foster a new generation of champions for sustainable chemistry – these individuals will be equipped with the skills and experience to lead chemistry-using industries towards a more sustainable future.

EPSRC CDT in Sustainable Chemistry research falls under these three broad research themes:

- Renewables (bio-refinery, alternative feedstocks and food science)
- Sustainable Synthesis (polymers and materials, biotransformation, photo-and-electro-chemistry, synthetic methodology)
- Continuous Manufacturing (life cycle analysis, microwave processing, process engineering)

We welcome applications from science graduates and professionals with chemistry, engineering or bioscience backgrounds, who are interested in learning more about sustainability in the terms of chemistry and chemical-based supply chains. The programme is designed to provide students with the technical and theoretical competences to equip them for a leading career in the chemical sciences or chemical user community.
**For further information please contact:**
**Perislava Williams**
perislava.williams@nottingham.ac.uk

### SynBio Doctoral Training Programme

The Synthetic Biology Research Centre has an associated doctoral training programme in Synthetic Biology which interacts with our BBSRC DTP scheme and the EPSRC CDT in Sustainable Chemistry to not only develop scientists but provide them with a broad understanding of industrial biotechnology. The programme funds 25, four-year PhD studentships recruiting on average six students per annual cohort with intakes from 2014 to 2017. Projects are cross-disciplinary by design, include an industry placement option and explore synthetic biology approaches in fields ranging from microbial metabolic engineering to Techno-economic analysis.
**For further information please contact:**
**Dr Klaus Winzer**
klaus.winzer@nottingham.ac.uk

### Mathematics for a Sustainable Society (MASS)

MASS is an interdisciplinary doctoral training centre established to tackle the ongoing global problems of food shortages, water scarcity and insufficient clean energy. It brings together mathematicians with researchers from across the University developing improved crops, bioenergy sources and biological methods to clean contaminated water; renewable energy sources, storage and distribution. Mathematics plays a crucial role in helping to understand resource use by quantifying and predicting the effects of alternative approaches through predictive modelling, statistical analysis and uncertainty quantification.

The programme funds 15 fully-funded four-year PhD scholarships over three intakes. The first cohort of students started in September 2015.
**For further information please contact:**
**Professor Marcus Owen**
marcus.owen@nottingham.ac.uk

# Placements and Knowledge Exchange

Knowledge Transfer Partnerships

### Undergraduate and MSc placements

**Key contact: Rob Howarth**

Placement students are available to help businesses with a range of projects such as research, testing, planning and analysis. Students can partner with businesses on collaborative projects, using their expertise and knowledge to provide high quality work.

Placements and projects can vary from short term projects (two to three months) to longer placements (12 months) and are usually between the student's second and third year of study.

### Knowledge Transfer Partnerships (KTP)

**Key contact: Paul Yeomans**

KTP is a leading programme that aims to assist businesses in maintaining a competitive edge, increasing productivity and creating a more strategic innovation through greater use of shared knowledge, technology and skills that reside within the UK knowledge base. Our KTP scheme has being running for almost 40 years and its longevity is due to the unprecedented level of success for all involved.

A KTP involves an alliance between three partners:

- The business partner
- Knowledge base partner
- One or more associates – (recent graduate)

The University provides access to cutting edge research and development which can facilitate and utilise specialist skills of a recently qualified associate who can embed their expertise in your business.

The Associate will work on a project integral to your needs, working to enhance the long-term capability of the business, while being jointly supervised by your company and a senior academic.

"The University has worked with over 60 businesses to develop new products and business improvements. The KTP scheme is a great way for companies to work with universities to deliver bottom line benefits."
Dan King, Head of Knowledge Transfer, Business Engagement and Innovation Services.





# Innovation support for business

The University of Nottingham provides a wide variety of services to help make your business grow and become more profitable. The University has built a strong reputation for the quality and impact of its collaborative work, with a range of services that include research and development, offering new technology for licensing and other forms of commercialisation, providing consultancy expertise to solve business issues, and delivering training to meet staff development needs.

Support for business and industry at the University of Nottingham is organised through our Research, Enterprise and Graduate Services (REGS) department. The department provides a range of services for both major corporate businesses and the SME business sector, with support and advice services delivered through a number of dedicated teams:

**Corporate Partnerships Team** – develops and manages long-term strategic relationships with key corporate businesses in order to enhance the relevance and impact of the University's research and training activities, derive increased industrial income and further the University's external reputation.

**Ingenuity** – a support programme for small and medium-sized enterprises – the Ingenuity programme's main aim is to transfer knowledge and expertise from the University into the local and regional SMEs sector, thereby helping them innovate and grow by providing access to funding, graduate placements and Knowledge Transfer Partnerships (KTPs). Ingenuity provides SMEs with opportunities to attend events and workshops delivered by experts on business and innovation as well as being part of a business directory of over 1000 other businesses. It also works with and supports many SMEs from outside the East Midlands in both the UK and overseas thereby providing significant networking and supply chain brokerage opportunities.

**Intellectual Property Commercialisation** – The University of Nottingham takes a pragmatic and realistic approach to management of intellectual property, working with industrial collaborators and prospective licensees to develop IP for mutual benefit. We support the commercialisation of technologies which have been developed through research by licensing to third parties, utilising joint ventures to develop technology further and through investing in spin-out companies which frequently retain close links to the university. With our strong links to industry and investors, the University's IP Commercialisation Office provides valuable market knowledge and experience to guide translation of research outputs into marketable products and processes.

**Asia Business Centre** – helps businesses establish links with the University's international campuses helping them to exploit opportunities available in the rapidly expanding markets of South East Asia. By working with the Asia Business Centre, businesses can access our world leading research and development, our renowned training and education programmes and our state-of-the-art facilities. We have also championed unique and flexible skills development programmes and qualifications to meet the needs of employers globally. With campuses in China and Malaysia, Nottingham continues to enhance its growing international reputation.

**If you would like to know more about how to engage with the University, please contact:**

**Rob Howarth**
**Senior Executive Corporate Partnerships**
Industrial Biotechnology Sector
Phone: 0115 74 84 356
Email: regs@nottingham.ac.uk