Discovery through Innovation
Manchester Institute of Biotechnology
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MANCHESTER INSTITUTE OF BIOTECHNOLOGY
Driving discovery through innovation

The Manchester Institute of Biotechnology (MIB) is one of the leading biotechnology research institutes in the world. Focusing on advanced quantitative approaches to specific biotechnology challenges at the interface, the MIB enjoys a unique pluralistic and open research culture that is realised through a coherent and integrated research concept and the establishment of a unique multi- and inter-disciplinary community of researchers committed to working across discipline boundaries.

The MIB is based at the John Garside Building and houses over 500 research staff and students from 52 research groups from across The University of Manchester from the Faculties of Engineering and Physical Sciences, Life Sciences, and Medical and Human Sciences. With a strong emphasis on translational research, knowledge transfer and discovery through innovation, our philosophy has placed us in a strong position to address a series of Grand Challenges and showcasing a selected portfolio of projects that illustrate the diversity, quality and dynamism of our research teams. Our reputation as an international leader in the biotechnology field is evidenced with over 1400 publications, since 2009, in major journals and the impact of the Institute’s research is evident from a sustained commitment to the successful translation of basic science into commercial success.

Harnessing the synergy of interdisciplinarity
Focusing on specific challenges in biotechnology the co-localisation of researchers from distinct disciplines generates interdisciplinary teams with unique capabilities.

Design promotes interaction
Reflecting the needs of interdisciplinary science, the MIB features open-plan, multifunctional laboratories and extensive specialist research facilities.

Discovery through innovation
Delivering internationally recognised programmes across all disciplines, with a strong emphasis on translational research, knowledge transfer and discovery through innovation.

Innovation in action
Advancing economic and societal development through knowledge generation and transfer. Enabling companies of all sizes to benefit from our research technology and expertise. Exploiting commercially significant innovation through licensing and the creation of spin-out companies.

Nigel Scrutton
Director

Fig. 1.0
Discovery through Innovation Pipeline

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The Manchester Institute of Biotechnology is committed to the pursuit of research excellence, education, knowledge transfer and discovery through innovation whereby a coherent and integrated interdisciplinary research community work towards developing new biotechnologies that will find applications in areas such as human health, the economy, food security, industrial transformations and the environment.
The University of Manchester

Our goal, outlined in the Manchester 2020 strategic plan, is to establish the University as a major centre for interdisciplinary research.

The large scale and quality of our activity at Manchester sets us apart. We are able to combine disciplines and capabilities to meet both the challenges of leading-edge research and the external demands of society, business and other stakeholders.

The University of Manchester is one of the world’s leading centres for biomedical and biotechnology research that sits at the forefront of new discoveries in science and engineering. Research is at the heart of the University and the sheer scale, diversity and quality of our research activity is unrivalled in the UK. We have a distinguished history in research, innovation and enterprise stretching back over 180 years with many of the major advances of the twentieth century having been discovered at the University.

Our institutes carry responsibility for several of the University’s key research priorities, working in areas where we have achieved or aspire to world-leading status. The Manchester Institute of Biotechnology was the first university-based, purpose-built interdisciplinary research institute of its kind in the UK. Through the establishment of multi-skilled interdisciplinary teams applying pioneering approaches to major global challenges in biotechnology it has evolved into one of the leading biotechnology research institutes in the world.

We are committed to enhancing the lives of all people, through knowledge transfer and education and this commitment is firmly embedded in the global challenges that constitute the unique research vision of the MIB whose role is integral to the advancement of the research mission of the University.

Professor Luke Georgiou
Vice President for Research

Expanding cross campus collaboration

We continue to develop collaborations across the University campus with current research grant funding aligned with 83 research groups from all four Faculties. Recent funding successes and applications endorse a closer alliance with other University of Manchester Institutes: Photon Science Institute, Manchester Institute of Innovation Research, and the Institute for Science, Ethics and Innovation. The development of our synthetic biology (Sybs) activity has developed closer alliances with members of the Faculty of Humanities and broader, more comprehensive, links with the Faculty of Engineering and Physical Sciences and with the Faculty of Life Sciences. Our interactions with the Faculty of Medicine and Human Sciences have developed significantly through the appointment of Professor Clare Mills, but also in the metabolomics area through Professor Roy Goodacre and in spectroscopy through Professor Peter Gardiner. Our system/modeling/text mining activities continue to assemble cross-faculty teams of researchers to deliver innovative research at the forefront of medical biotechnology.

Cross-disciplinary feasibility

There are numerous areas of research within the biological and biomedical field that require the ability to quantitatively analyse single cells and large cell populations. For example, metabolomic studies have the potential to yield understanding of complex disease processes, drug toxicity and cellular function whilst the development of innovative tools for accurate measurement of transcripts and proteins necessitates novel sample handling, analyte amplification and use of miniaturisation and microfluidics to assist with high throughput measurements to achieve sensitive detection.

In a programme funded by the EPSRC the MIB engaged in a suite of short-term speculative activities to consolidate the cross-disciplinary culture within the Institute. In one project, Professor Peter Gardiner in collaboration with Professor Mark Dunne (PhLS) differentiated four separate cell lines in pancreatic stem cells using FTIR cell population imaging technologies.

Following on from earlier work led by Professor John Vickeriwan which utilised imaging Mass Spectrometry for 2D and 3D cellular characterisation in an Alzheimer’s study, Professor Roy Goodacre and Professor Nick Lockyer will join a collaborative team of researchers from PhLS led by Professor Alan Dickinson that will seek to describe and understand the heterogeneity of stem cell populations at the molecular level. A stem cell model has been selected that has major promise in drug discovery research. To date, the key limitation to the exploitation of stem cells has been their scarcity. Furthermore, even when it is possible to source stem cells, there is still the formidable task of purification and sorting of the usable cells from cells that have differentiated into unusable types. Presently, stem cells are labelled with markers and then sorted one-by-one using very expensive instruments. Despite the very high speed of modern cell sorters the relatively small numbers obtained and the addition of labelling reagents mean that these methods are not suitable for widespread application of stem cell therapy. Stem cells have yet to find global application, because of their rarity. This project proposes to change the current stem cell sorting methods from low throughput one-by-one techniques to very high throughput alternatives that will be capable of sorting millions of cells simultaneously.

The key to this will be the design of a series of filters that behave as smart sieves. The stem cells will be poured through new filters that will recognize the cells by their shape, size, flexibility and their chemical signature, without the addition of any extra reagents. A set of filters will be assembled; one on top of the other, to allow rapid screening of a mixture that contains both the valuable and unwanted stem cells, alongside less useful cells. This research programme will focus on the design of these filter stages, and use cutting edge science and technology to generate a completely new approach to stem cell purification. Specialist techniques such as microfluidics, nanotechnology, rapid microstructure prototyping will be combined with the latest ideas in cell biochemistry and cell bio-recognition to fulfil the primary objective of making it easier, cheaper and faster to harvest useful stem cells. The benefit to society will be huge, making the possibility of stem cell therapy a reality for everyone.

This is an EPSRC funded project involving partners from across the University: Professor Nick Goddard in collaboration with Professors Cathy Merry (Materials), Cay Kythe (PhLS), Tony Day (PhLS), Chris Ward (Dentistry) from The University of Manchester and Professors Steve Eichhorn from the University of Exeter and Peter Fielden from Lancaster University.

Stem cell fractionation using interactions with artificial matrices

There has been a recent explosion in interest in and potential applications of stem cells. Their potential for therapeutic medical applications is particularly exciting, with the real prospect of growing replacement tissue and bone to overcome a wide variety of disease conditions. Stem cells also have an important role in diagnostics, and have already shown promise in drug discovery research. To date, the key limitation to the exploitation of stem cells has been their scarcity. Furthermore, even when it is possible to source stem cells, there is still the formidable task of purification and sorting of the usable cells from cells that have differentiated into unusable types. Presently, stem cells are labelled with markers and then sorted one-by-one using very expensive instruments. Despite the very high speed of modern cell sorters the relatively small numbers obtained and the addition of labelling reagents mean that these methods are not suitable for widespread application of stem cell therapy. Stem cells have yet to find global application, because of their rarity. This project proposes to change the current stem cell sorting methods from low throughput one-by-one techniques to very high throughput alternatives that will be capable of sorting millions of cells simultaneously. The key to this will be the design of a series of filters that behave as smart sieves. The stem cells will be poured through new filters that will recognize the cells by their shape, size, flexibility and their chemical signature, without the addition of any extra reagents. A set of filters will be assembled; one on top of the other, to allow rapid screening of a mixture that contains both the valuable and unwanted stem cells, alongside less useful cells. This research programme will focus on the design of these filter stages, and use cutting edge science and technology to generate a completely new approach to stem cell purification. Specialist techniques such as microfluidics, nanotechnology, rapid microstructure prototyping will be combined with the latest ideas in cell biochemistry and cell bio-recognition to fulfil the primary objective of making it easier, cheaper and faster to harvest useful stem cells. The benefit to society will be huge, making the possibility of stem cell therapy a reality for everyone.

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Beyond The University of Manchester we have a strong portfolio of national and international collaborations and networks with academics and industry. The diversity and quality of our research programmes is reflected in publications in major journals, with over 500 publications with over 280 research institutes from over 65 countries. The impact of the Institute's research is evident from a sustained commitment to the successful translation of fundamental science into commercial success.

Our EU portfolio continues to grow, with current live awards in the region of £14 million, through collaborative research programmes and major EU training networks.

A number of EU and RCUK funded projects are tackling some of the key barriers to chemical manufacture in the 21st century. CHEM21 (Chemical manufacturing methods for the 21st century pharmaceutical industries) is a public-private partnership (PPP) that was launched at the end of 2012, led by Professor Nicholas Turner and was launched at the end of 2012, led by Professor Nicholas Turner and Professor Paul Popelier who is developing innovative QSRR models and expert systems for predicting toxicity of ionic liquids in the provision of safe green solvents for the future. The Manchester Centre for Integrative Systems Biology (MCISB) is involved in SYNPOL (Biopolymers from syngas fermentation) working alongside 13 partners across Europe. This project aims to develop a platform integrating biopolymer production through modern processing technologies, with bacterial fermentation of SYNGAS, and the pyrolysis of high complex bio waste enabling the treatment and recycling of complex biological and chemical wastes and raw materials in a single integrated process.

In contrast, the National Centre for Text Mining joins OSSMETER (Automated measurement and analysis of open source software) working with 8 partners on platform development that will support decision makers in the process of discovering, comparing, assessing and monitoring the health, quality, impact and activity of open-source software. The Linked2Safety project (Advancing clinical practice and data security in clinical research) brings together 11 partners to develop a secure framework to facilitate the efficient and homogenised access to shared distributed Electronic Health Records (EHRs) which would impact enormously across the healthcare sector. The diversity of our research in the biomedical and healthcare arena received an EU funding boost with GlycoBioM (Tools for the detection of novel glyco-biomarkers) bringing together Europe’s leading scientists to study glycosylation. Hailing from Croatia (Genos), Denmark (UCPH), Germany (UKE and Galab), Ireland (NIBRT) and the UK (UNIMAN), the team is identifying new biomarkers and tools for detection and diagnostic screening which could be used to develop personalised treatment for cancer and related diseases.

SYBIL (Systems biology for the functional validation of genetic determinants of skeletal diseases) will see Professor Roy Goodacre and a consortium of world-class scientists, systems biologists, disease modellers, information technologists and industrialists validate the genetic determinants of common and rare skeletal diseases to gain a mechanistic understanding of disease processes and age-related changes.

In March 2013, the world’s biggest ever study of allergies was officially launched at the MIB led and coordinated by Professor Clare Mims funded by the European Commission under the 7th Framework Programme, iFAAM (Integrated Approaches to Food Allergy and Allergy Risk Management), will develop evidence-based approaches and tools for the management of allergens in food. The Manchester team will work with 38 partners including, industrial stakeholders (represented by Unilever and Eurofins), patient groups representing people at risk of severe allergic reactions from Germany, UK and Ireland and a risk manager and assessor group including the UK Food Standards Agency. The project will work with the clinical community, working in collaboration with the European Academy of Allergy and Clinical Immunology.

Further details of our live portfolio can be found in the ensuing research pages.
International collaborations

Building links with China
Professors Eriko Takano and Nigel Scrutton have recently secured funding through a Synthetic Biology China Partnering Award, co-funded by the BBSRC, the Chinese Academy of Sciences (CAS) and the EPSRC to partner and develop long term fruitful relationships with Chinese scientists.
We have strong links with the National University of Defence Technology in China and currently host a number of their visiting scientists and PhD students.
In addition we have hosted events with two Chinese Universities (Hebei University of Science & Technology and Jilin University) to encourage scientific and teaching exchanges and collaborations. We continue to welcome a high proportion of overseas students and postdoctoral fellows to the Institute.

Brazil beginnings
In November 2012, academics representing the nine schools that comprise the Faculty of Engineering and Physical Sciences visited the top universities in Brazil to explore research synergies. MIB’s Dr Chris Blanford and Dr Neil Dixon, two members of the delegation, hosted a reciprocal visit in March 2013 to establish collaborations based on mutual strengths in industrial biotechnology and bioenergy. This has led to several joint funding applications and paper submissions.

MIB researcher secures National Institute of Health grant
Dr Alexander P Golovanov from The University of Manchester has established a new and exciting collaboration with one of the world’s leading virology groups, led by Professor Rozanne Sandri-Goldin at the University of California-Irvine to jointly study the molecular mechanisms behind the critical protein interactions which lead to the herpes virus hijacking the cell.

Herpes simplex virus 1 (HSV-1) causes a wide range of diseases, from recurrent painful skin lesions to more serious conditions such as encephalitis.

Recently, studies here in Manchester led by Professor Ruth Itzhaki suggested that HSV-1 can be a risk factor in Alzheimer’s disease, and that antiviral drugs might be effective at slowing down its progression. Unfortunately, no effective antiviral treatment is currently available, which suppresses viral replication efficiently. Finding a ‘weak spot’ in the HSV, which can be targeted by the therapies of the future, would therefore make a significant breakthrough.

During the infection, HSV expresses and uses a key multifunctional protein called ICP27, which among other regulatory functions, helps the virus to hijack the cellular machinery which normally exports the cellular mRNA from the nucleus to cytoplasm. Instead this machinery is used to export viral mRNA. Earlier NMR studies performed in the MIB (Tunnicliffe et al, PLoS Pathog, 2011, 7(1), e1001244) established the first atomic-resolution structure of the complex between viral ICP27 and cellular mRNA factor.

This five-year project funded by the National Institute of Health (NIH) will look into further details of how the assembly of multicomponent complexes between viral and cellular proteins is organised and regulated, ultimately promoting viral replication. The identification of critical binding interfaces in these complexes may help to design new drugs, which will interfere with this complex assembly and HSV replication.

This collaborative project consists of two complementary parts: virology and in vivo studies will be conducted in the University of California Irvine, in Sandri-Goldin’s group, while high-resolution structural studies, mainly using NMR spectroscopy, will be conducted here in the MIB in Dr Golovanov’s group. What we learn about ICP27 mechanism of action may be helpful in developing drugs targeted at other herpes viruses such as KSHV which causes cancer in these viruses also encode ICP27 homologues.
New discoveries in biotechnology are applied to medical processes that can find applications in such areas as pharmacogenomics and drug production. The development of modern medicines requires an understanding of molecules and networks at the molecular and systems levels which involves imaging and spatial mapping of cell responses in health and disease and in response to drug challenges. Our research ranges from structural and dynamic modelling of potential drug targets and their interactions including establishment of early phase drug discovery pipelines through the challenges of systems mapping of the “virtual human.”

Degenerative disease researchers make breakthrough in bid to find treatment for Parkinson’s and Huntington’s

A significant breakthrough has been made by scientists at the MIB towards developing an effective treatment for neurodegenerative diseases such as Huntington’s, Alzheimer’s and Parkinson’s. The work, published in the journal Nature, was led by Nigel Scrutton, Professor of Molecular Enzymology, and details how an enzyme in the brain interacts with an exciting drug-like lead compound for Huntington’s disease to inhibit its activity, demonstrating that it can be developed as an effective treatment for neurodegenerative diseases.

Working with colleagues at the University of Leicester and the University of Lisbon in Portugal, researchers identified the molecular structure of the enzyme lysine-specific monomethyltransferase (KMO), which is found in the human brain. It took five years for the team to establish the crystal structure of KMO – the first time it has ever been done. The scientists then studied how the compound UPF 648 binds incredibly tightly to the enzyme to act as an inhibitor. Previous studies with animal models of neurodegenerative disease have showed that switching off the enzyme activity through drug binding should be effective in the treatment of brain disorders. Professor Nigel Scrutton said: “UPF 648 works very well as an inhibitor of enzyme activity. However, in its current form it does not pass into the brain from the blood. The search is on for related compounds that can both inhibit the enzyme and pass into the brain. Our research detailing the molecular structure of the enzyme now enables a search for new KMO inhibitors that are able to cross the blood-brain barrier. This provides real hope for developing drug therapies to target neurodegenerative diseases such as Huntington’s, Alzheimer’s and Parkinson’s disease.”

Dr Flaviano Gergi, the team’s neurogeneticist from the University of Lisbon, said: “This is a big move forward for the development of new KMO inhibiting drugs. It is hoped that such compounds may ultimately be tested in clinical trials and prove beneficial for patients.”

Professor Sarah Tabrizi is the head of the Huntington’s disease research team at University College London’s Institute for Neurology. Commenting on the research she said: “Unlocking the crystal structure of KMO is a real boost to our efforts to find treatments for this devastating disease. It provides a solid basis for the optimisation of inhibitor drugs like UPF 648 that are being developed by the global Huntington’s disease research community. KMO is one of our top drug targets, and the crystal structure is a significant step along our roadmap to clinical trials of KMO inhibitors in patients.”

New drug treatments for Alzheimer’s – adopting a drug repositioning strategy

Current drugs for Alzheimer’s can only delay symptoms for about six months, so new effective drugs are desperately needed. Several thousand chemical libraries exist, and each contains thousands of compounds with the potential to have desirable side effects, though they were designed to treat other conditions. Old drugs that are effective in cellular models for Alzheimer’s disease can be rapidly progressed to clinical trials in humans, since many of the essential steps in drug development, such as toxicity testing in animals and people, have already been done.

A few hundred drugs have been tested so far in cells and a promising hit called A.77636 has been found which was first discovered in the 1980s as a possible treatment for Parkinson’s disease and cocaine addiction, by Abbott Laboratories, but not tested for Alzheimer’s. Abbott’s laboratories showed that A.77636 can enter monkey brains when taken orally, a crucial requirement for an Alzheimer’s drug. A new company, Pharmaceutics, founded by Professor Andrew Doig and Dr Farid Khan launched in 2012 will take A.77636 forward and test thousands of other known drugs. Hits found in cell culture will be examined to find out how they work and then tested in mouse models of Alzheimer’s and, if successful, ultimately in human volunteers with Alzheimer’s.

Bacteria to shed light on new drug targets for inherited cancers BRCA1 and BRCA2

Scientists at the MIB and the Cancer Research UK Manchester Institute have succeeded in purifying a protein found in bacteria that could reveal new drug targets for inherited breast and ovarian cancers as well as other cancers linked to DNA repair faults. The team are the first to decipher the structure of a protein called PARG, which plays an important role in DNA repair and acts in the same pathway as PARP.

PARG removes these chemical tags after the DNA damage has been repaired. So the researchers believe that, similar to PARP inhibitors, drugs designed to block the action of PARG could be effective in treating cancer.

Lead author Dr Ivan Ahel, based at the Cancer Research UK Manchester Institute said: “For decades scientists have wanted to find out the structure of PARG, but its large size makes it very hard to produce in the lab. By studying a smaller version of PARG found in bacteria, we’ve been able to create a 3D map that researchers can use to understand more about how PARG works. The next step will be to investigate whether drugs that block its activity might be an effective way of treating cancers driven by faults in DNA repair genes.”

“Obtaining the crystal structure of PARG is a first and key step to guide and illuminate future drug-design efforts aimed at treating certain cancers. Knowing what this enzyme looks like, and having a good idea of how it operates, makes designing such drugs less of a shot in the dark.”

David Leys
Professor of Structural Biology

Handling of protein crystals for x-ray crystallography

A cartoon representation of Saccharomyces cerevisiae lysine-specific monomethyltransferase (KMO). Inhibition of KMO, an enzyme in the eukaryotic tryptophan catabolic pathway, leads to amelioration of Huntington’s-disease-relevant phenotypes. The figure shows a flavin adenine dinucleotide (FAD) highlighted in red (stick representation) with the cocrystallised inhibitor UPF-648 depicted as purple spheres.

GlycoBioM bringing us one step closer to understanding cancer

A cure for cancer has become the Holy Grail for many medical researchers but studying the changes that occur in cells and cell structure may bring us one step closer to understanding this elusive and complex disease. Keeping up with the cell changes associated with cancer is no easy task. A key cancer-related cell process known as glycosylation could advance our understanding significantly, leading to better diagnosis and smarter drugs since all cell surfaces, and more than half of the proteins in our bodies, are linked to sugar chains.

GlycoBioM (Tools for the detection of novel glyco-biomarkers) is a FP7 funded project which brings together Europe’s leading scientists to study glycosylation of biomolecules in cells, a process seen in many cancers. The team, led by Professor Sabine Flitsch, is identifying new biomarkers and tools for detection and diagnostic screening that could be used to develop personalised treatment for cancer and related diseases.

In cancer cells, recognition between cells is disturbed, leading to invasive growth and dissemination of tumour cells. This phenomenon is reflected in the glycosylation of the cell coat, which is of particular interest to researchers.

“Recombinant glycan receptors are used to identify tumour associated carbohydrates in the glycosyl coat of tumour cells. The recombinant receptors are used in different ways, such as for identifying tumour associated carbohydrates to carcinoma cells in tissue sections, and recognizing sub-populations of leukaemia cells. The GlycoBioM team is also using the receptors to identify soluble glyco-biomarkers in tumour patients’ blood samples.”

Professor Christoph Wagener
University Medical Center Hamburg-Eppendorf (UKE), Germany
In parallel, project members from The University of Manchester, in collaboration with The University of Liverpool, have been working on an analytical tool to capture and characterise glycan binding proteins which could eventually be used to pinpoint sugar biomarkers in diseases such as cancer. This project has also progressed our understanding of diabetes, in particular the discovery of a novel glycan biomarker related to the disease, and the team expects to develop a system that will enable patients to check for maturity-onset diabetes of the young (MODY), a form of diabetes that is caused by mutations in a number of different genes.

The GlycoBiom project is truly a European success story, with partners from opposite ends of Europe all contributing to ground-breaking results. When the Croatian team found that certain glycans can predict the speed at which colon cancer will progress (which could lead to tailored therapy – or ‘smart drug’ – for individual patients), the Danish team took up the baton, developing a new glyco profiling method to reduce false-positive cancer diagnoses. This is expected to help women in ovarian cancer. Apart from having developed a new blood test for ovarian cancer, the team has made commendable progress in unravelling the complexities of breast cancer and hopes that these results lead to better stratification of patients regarding the choice of the most appropriate therapy. This project also featured in the Royal Society Summer Exhibition – see Science and Society section.

Characterization of a superior biocatalyst for pravastatin production

Andrew Munro, Professor of Molecular Enzymology and Research Associate Dr Kirsty McIntyre, together with industrial partner DSM, have used directed evolution and structural biology in order to redesign an enzyme catalytically (a cytochrome P450) to exploit the technology for the manufacture of pravastatin. Initially an engineered biocatalyst (monoamine oxidase), which has been optimised by successive rounds of directed evolution, is used to convert a cheap chemical into the active material to be used in the drug Telaprevir™, which combines biocatalysis with multi-component chemistry.

A fragment-based screening approach to rationalizing M. tuberculosis P450 molecular selectivity

Expanding their work on cytochrome P450 enzymes Professor Andrew Munro and David Leys together with Dr Kirsty McIntyre and Dr Alistair Revell from the School of Mechanical, Aerospace and Civil Engineering (SMAC) at the University of Manchester, in collaboration with Professor Romano Ortu and Dr Alfaisal Rehman from the Free University of Amsterdam, has devised an efficient screening strategy for selectivity against tuberculosis (Mtb) P450 molecular selectivity.

The glycome of breast cancer and it is hoped that these results lead to better stratification of patients resulting in more accurate diagnoses for these diseases.

Orthogonal profiling reveals heterogeneous cancer cell populations

Another major challenge in treating various chronic diseases is to move away from broad-spectrum therapies (such as monoclonal antibodies) require frequent and high dosages of an active ingredient protein in a small volume of liquid (e.g. >10mg/ml) for subcutaneous (SC) injections using a prefilled syringe or auto-injection device. There is a need for underpinning research to support industrial development of novel protein therapeutics for more convenient delivery of products by subcutaneous injection. This is an increasing priority for biopharmaceutical companies enabling patients to administer medicines at home, rather than having to visit hospital for lengthy infusions. The challenge for bioprocessing research is to dissolve the dose of protein required in a small volume to enable self-injection. This challenging project will be led by Dr Xue-Feng Yuan, Reader in Biochemical Physics in collaboration with MB colleagues Dr Robin Curtis and Dr Alexander Gribanov from the School of Mechanical, Aerospace and Civil Engineering (SMAC).

In parallel, project members from The University of Manchester, in collaboration with DSM, experts in industrial researchers at DSM, experts in microbial fermentation and screening techniques, together with the Munro group, experts in enzymology and protein crystallography, led P450 catalysis to perform the desired reaction with much greater stereoselectivity than other chemical-enzyme-based approaches. This new biotechnologically advanced method forms the basis of a patented process for efficient production of the blockbuster drug pravastatin.

Hepatitis C is a major global health problem that currently affects approximately 200 million people worldwide. Many of the infected people live in countries where access to modern expensive treatments is a major issue. Recently a new class of drugs has been developed that are highly effective in tackling the infection and in the majority of patients result in complete removal of the virus from the bloodstream. Telaprevir™, which was launched in 2011 by Vertex, is currently the leading medicine in this area although in order to make it widely available at an affordable cost it is necessary to develop inexpensive manufacturing routes to the molecule. Professor Nicholas Turner, in collaboration with Professor Romano Ortu and Dr Alistair Revell from the Free University of Amsterdam, has devised an efficient screening strategy for selectivity against tuberculosis (Mtb) P450 molecular selectivity.

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World’s biggest ever study of food allergy gets underway

Up to 20 million European citizens suffer from food allergy, a disease that can be conquered, if critical steps are taken. However, management of both food allergy by patients and health practitioners, and allergies, by industry, is thwarted by lack of evidence to either prevent food allergy developing or protect adequately those who are already allergic. European Commission-sponsored research, known as the Integrated Approaches to Food Allergen and Allergy Risk Management (iFAAM), will set the stage for facilitating such steps to be taken. This research will produce evidence-based approaches and tools for the management of allergens in food and integrate knowledge derived from their application and new knowledge from intervention studies into food allergy management plans and dietary advice. The resulting holistic strategies will reduce the burden of food allergies in Europe and beyond, whilst enabling the European food industry to compete in the global market place.

The Manchester team will work with 38 partners including, industrial stakeholders (represented by Unilever and Eurofins), patient groups representing people at risk of severe allergic reactions from Germany, UK and Ireland and a risk manager and assessor group including the UK Food Standards Agency. The project will work closely with the clinical community, working in collaboration with the European Academy of Allergy and Clinical Immunology.

This study involves 38 partners and is headed by MB’s Clare Mills, Professor of Allergology, from the Allergy and Respiratory Centre of The University of Manchester’s Institute of Inflammation and Repair. Based in the Manchester Institute of Biotechnology, Professor Mills said: “This is a massive research project that will have far reaching consequences for consumers and food producers. The evidence base and tools that result from this will support more transparent precautionary “may contain” labelling of allergens in foods which will make life easier for allergy sufferers as they try to avoid problem foods.”

Dr Bert Popping, Eurofins Scientific Director, said: “Eurofins is excited to be part of this European Commission project. We are looking forward to sharing our newly-developed multiple allergen detection method and making a meaningful contribution to this crucial initiative.”

This research study featured in the BBC series “Trust Me I’m A Doctor” presented by Dr Michael Mosley. This £9 million project builds on an earlier €4.3 million research study EuroPrevail also headed by Professor Mills which involved 62 partners from 17 countries.

Professor Mills was recently elected to the International Academy of Food Science and Technology, a distinguished group of outstanding scientists representing the international community of food science and technology. The induction ceremony for new Fellows took place at the IUFoST* World Congress of Food Science and Technology held in Foz do Iguaçu, Brazil.

*Mentioned with kind permission of Food Science and Technology

Developing a technological platform for the design of novel biomaterials

In a project that will contribute significantly to the field of healthcare technologies as well as biomaterials and tissue engineering research Dr Alberto Saiani, Reader in Molecular Materials, has received an EPSRC Research Fellowship to develop a technological platform for the design of novel biomaterials that can be used across a number of applications. The use of non-covalent self-assembly to construct materials has become a prominent strategy in materials science offering practical routes for the construction of increasingly functional materials for a variety of applications ranging from electronic to biotechnology. A variety of molecular building blocks can be used for this purpose such as de-novo designed peptides. With a library of 20 natural amino acids available it often the ability to play with the intrinsic properties of the peptide such as structure, hydrophilicity, charge and functionality allowing the design of materials with a wide range of properties.

The main challenge facing scientists in this field is being able to rationally design these peptides to gain control over the physical properties of the resulting self-assembled materials. This requires not only an in depth knowledge of the self-assembling processes at all length scales, but also a detailed understanding of the specific requirements of each application targeted. For example, injectable materials need to be developed for cell delivery while for drug delivery oral cavity sprayable systems could be required. For cell culture and tissue engineering the issue of adaptability of material properties is even more critical as depending on cell type, origin and intended behaviour, cells have very different requirements in terms of the environment, (i.e. material properties and functionality) in which they are placed. Finally, one other key element is the cost of these materials. When used as structural materials, as in hydrogels, the quantity of peptide required is significant.

Dr Saiani is currently developing this technological platform by furthering our understanding of the self-assembly process of these short peptides and designing novel responsive and increasingly functional materials for a new field of applications.

Through engagement with academic and industrial end-users throughout the development process the team will ensure that the materials designed will be relevant whilst exploring new potential fields of application.

MIMIT celebrates 4 years

MIMIT (Manchester: Integrating Medicine and Innovative Technology) has celebrated its four year anniversary during which time it has developed 27 projects, requiring £1 million initial investment (project and infrastructure), based on 116 unmet clinical needs. To date projects have leveraged £3 million, 3 clinical research fellowships, numerous publications and patents. One of the first developments reached the market place mid-2013 and resulted in 1 licence agreement with a SME, £5 million VC funding and 1% estimated net returns of £250m per annum. Royalty returns will be shared between the NHS, academia and inventors. Two other project have leveraged £2 million VC and £1 million Pharma investment between them and 9 projects have received UMP Proof of Principal investment to get them ‘Investor ready’.

One of the early projects supported by MIMIT Phagenesis won Bionow Healthcare Project of the year 2012. Congratulations also went to Curtis Dobson, MIMIT Site Manager for the award of Biomedical Project of the Year 2012 to Microsensor, a novel infection sensing technology.
INDUSTRIAL BIOTECHNOLOGY

Industrial Biotechnology (IB) is a set of cross-disciplinary technologies that use biological resources, such as algae, plants, marine organisms, fungi and micro-organisms, for the production and processing of chemicals, energy and materials. A multidisciplinary approach is essential to transform the traditional chemical and chemical-related sector to a more sustainable and competitive one which draws on disciplines such as organic and synthetic chemistry, biochemistry, molecular biology, enzyme kinetics, genomics, proteomics, bio-informatics and bioprocessing.

With major recent grant awards in Industrial Biotechnology and strategic participation in national and international forums over the past year, the widely recognised expertise in IB@MIB has seen major research programmes initiated.

Rapid evolution of enzymes and synthetic micro-organisms for the development of industrial biocatalysts

In collaboration with GlaxoSmithKline, one of the world's largest pharmaceutical companies, this project seeks to develop an accelerated laboratory evolution platform for the rapid optimisation of biocatalysts for industrial applications in a matter of weeks rather than the months it currently takes, resulting in a much greener approach to the production of a wide variety of products.

This EM project is funded under the BBiRC iLoCa initiative in partnership with GSK.

Developing next generation biocatalysts

BIONEXGEN, led by Professor Nicholas Turner, will develop the next generation of biocatalysts to be used for eco-efficient manufacturing processes in the chemical industry. It will also develop and integrate, with chemical steps, the biotechnological manufacturing routes for the synthesis of fine and specialty chemicals especially amine oxo-acids and renewable polymer intermediates which are better in terms of eco-efficiency, economic potential, complexity and for specificity of the synthetic pathways than those currently employed. The consortium consists of 17 institutions from university research groups, small and medium sized companies, to BASF, the world's leading chemical company.

The consortium have identified the key technology fields of amine synthesis, polymers from renewable resources, glycoscience and wider oxidase application as four key areas where the next generation of biocatalysts that will lead to improvements in both economic and environmental performance of the chemical manufacturing industries. This programme, funded under the EU 7th Framework Programme, will enable industry to use renewable resources with reduced greenhouse gas production as compared to their fossil counterparts and deliver biotechnological routes with reduced energy consumption and less toxic wastes compared to conventional chemical processes. Routes to specialised, high-value chemicals (e.g. chiral chemical compounds) normally require long chemical synthetic routes involving complex reaction steps with toxic side products and waste streams. This project will allow these methods to be replaced by clean biocatalysis routes. To broaden the range of fine and specialty chemicals and intermediates produced by biotechnological routes, research will address 1. the design and optimisation of enzymes to be used in synthetic chemistry; 2. the selection/development of modified microorganisms which are resistant to heat, pressure or low pH when used in the production of chemical entities and allow 3. the integration of biotechnological steps into conventional chemical processes.

Biocatalytic tools for industry

Professor Nicholas Turner will also lead BIOX (Developing a validated technology platform for the application of oxygen dependent enzymes in synthesis and transformation of alcohols), a collaborative FP7 project involving 11 partners from leading European companies and universities to develop new, eco-safer, and safer manufacturing processes for the chemical industry and end-users. This programme will develop the tools for the implementation of bio-oxidation to synthesise and oxidise alcohols for applications in flavourings and fragrances, and fine chemicals. The aerobic biocatalytic oxidation reaction currently has the potential for the biggest impact on the future uptake of industrial biotechnology (IB) in Europe. Bionexgen have the potential to overcome the hazardous nature and high environmental impacts of current chemical oxidation processes. Biocatalysis for oxidative chemical manufacture processes can deliver a major advantage to the European chemical-using industries and the environment, and it is expected that this new technology platform will allow the rapid development of bio-oxidations as a routine technology for the IB industry and support the European knowledge based biotechnology. The four-year, £7.4 million project will be promoted by a dynamic public engagement and dissemination programme within the scientific community and the wider public, especially schoolchildren, to create extra value for the European Union.

Directed evolution of enantiocomplementary malonate decarboxylases

This project is led by Professor Jason Micklefield, in collaboration with Professors David Lyes and Nicholas Turner, and is funded by BBiRC and BASF through the Industry Partnership Award (IPA) Scheme. The MB team used structure-guided directed evolution to create new malonate decarboxylase enzymes that can produce a wide range of carboxylic acids, which are particularly common intermediates in the manufacture of pharmaceuticals, agrochemicals and other valuable products. The new decarboxylase enzymes are also attractive because the substrates can be generated from malonic acid, a natural precursor derived from renewable sources (fermentation). The availability of chiral carboxylic acids, which are single enantiomers (one of two possible stereoisomers that are non-superimposable mirror images) is of critical importance, particularly for pharmaceutical production.

Industrial chemicals of the monoterpoid class realised through synthetic biology and pathway engineering

In partnership with GSK, Professors Nigel Scrutton, John Gardiner, David Lyes and Pedro Mendes have engineered bacterial strains to produce flavours and fragrances that belong to the monoterpoid family of compounds using synthetic biology and enzyme engineering approaches.
Bio- or ‘natural’ routes to the synthesis of these compounds significantly enhance their market value and this research will transform the industrial production of medicines. By providing ‘natural’ routes to these compounds, avoiding problems associated with classical chemical synthesis, bio-routes will reduce the environmental impact associated with classical synthesis and release industry from the constraints of limited availability from natural resources. This project is funded by the EPSRC as part of the Industrial Partnership Award (IPA) Scheme.

Pharmaceuticals and universities working together on multi million pound project

Europe’s largest public-private partnership (PPP) dedicated to the development of manufacturing sustainable pharmaceuticals was launched at the end of 2012 and is led by Professor Nicholas Turner and the pharmaceutical company GlaxoSmithKline. The introduction of biotechnology to the manufacturing processes for medicines will limit the drain on the world’s resources and have a lasting benefit on the environment.

CHEM21 brings together six pharmaceutical companies, 13 Universities and four small to medium enterprises from across Europe in a £21.2 million project with the aim of developing sustainable biological and chemical alternatives to finite materials, such as precious metals, which are currently used as catalysts in the manufacture of medicines. CHEM21 will run initially for four years with funding from the Innovative Medicines Initiative. The project will establish a European research hub to act as a source of up-to-date information on green chemistry. It will also develop training packages to ensure that the principles of sustainable manufacturing are embedded in the education of future scientists.

“The networks will drive new ideas to harness the potential of biological resources for producing and processing materials, biopharmaceuticals, chemicals and energy. Each has a particular focus, such as unlocking the potential of food waste and by-products to produce chemicals and biomaterials; unlocking the industrial biotechnology potential of microalgae, producing high value chemicals from plastic; and making use of plant cell walls (lignocellulosic biomass) to produce chemicals and biofuels.”
Dr John Baldeoni GlaxoSmithKline.

IBCarb - Glycoscience tools for biotechnology and bioenergy

Professor Sabine Flitsch, University of Manchester and Professor Rob Field, John Innes Centre

Carbohydrates constitute the largest source of biomass on Earth and their exploitation for novel applications in biorenewables, energy, food and health will be critical in moving away from dependence on hydrocarbons to develop sustainable biotechnologies and reduce GHG emissions, ensuring both energy and food security. Glycoscience is a broad term used for all research and technology involving carbohydrates, ranging from cell biology, human nutrition and medicine to carbohydrate-based materials and the conversion of carbohydrates to energy.

The analysis, synthesis and biosynthesis of carbohydrates and their modification to industrial products are, therefore, central challenges in both industrial biotechnology and bioenergy. The last twenty years have seen a number of fundamental changes in the glycosciences generating a technology push with respect to carbohydrate synthesis and modification, enzymology and glycemic analysis. At the same time, there is a technology pull – great demand and opportunities in diverse areas such as biopharmaceuticals (8 out of 10 top selling drugs worldwide are glycoproteins), foods (prebiotics designed for the human gut microbes), antimicrobials (targeting cell surface recognition and biosynthesis), materials (from bioresorbable polysaccharides) or energy (digesting the indigestible). IBCarb is an interdisciplinary network that will allow for exploitation of opportunities presented by glycoscience.

Network in biocatalyst discovery, development and scale-Up

Professor Nicholas Turner, University of Manchester and Professor John Ward (University College London)

This network aims to develop new tools to accelerate biocatalyst research, discovery and development. The network will provide the framework and coordination to allow research groups from industry and academia to easily access and develop a truly broad range of biocatalyst panels and technologies for screening whilst providing a pipeline through to scale-up, manufacture and commercial use of novel enzymes.

Industry-academia networks in industrial biotechnology and bioenergy

The Biotechnology and Biological Sciences Research Council (BBSRC) announced in December 2012 an investment of £18 million in 13 unique collaborative ‘Networks in Industrial Biotechnology and Bioenergy’ (BBSRC NIBB) to boost interaction between the academic research base and industry, promoting the translation of research into benefits for the UK. The University of Manchester secured four networks, three of which will be led from MIB. These national networks pool skills from academia and business to develop research projects with the potential to overcome major challenges in the industrial biotechnology and bioenergy arena whilst allowing new members to come on board with skills that can benefit the group.

Natural Products Discovery and Bioengineering Network (NPRONET)

Professor Jason Micklemfield, University of Manchester and Professor Barrie Wilkinson, John Innes Centre

Building on the UK’s established world-leading expertise in natural product chemistry, biosynthesis and microbiology Professor Jason Micklemfield and Professor Barrie Wilkinson will lead this network, devising methods to activate the expression of biosynthetic gene clusters to discover novel natural products. Natural products are small molecules produced predominantly by microorganisms and plants that have inspired the development of many blockbuster drugs including anticancer and immunosuppressive agents including most of the antibiotics in clinical use today. Natural products are also used in agriculture as herbicides, pesticides and fungicides to increase crop yields. In addition, bioengineering methods and synthetic biology tools will be developed to enable rapid structural diversification and optimisation of the most promising natural product molecules for therapeutic, agrochemical and other applications.

“The networks bring together a number of internationally competitive, cross-disciplinary communities capable of undertaking innovative research that will attract further investment from the UK and abroad. They provide a new opportunity for the research community to make significant contributions to the UK’s biocatalysis, drug transformational bioscience into industrial processes and products; creating wealth and jobs; and delivering environmental benefits, such as CO2 reduction.”
Dr Celia Caulcott
BBSRC Executive Director, Innovation and Skills

Working closely with industry to advance the field of chemical biology

Funded by EPSRC, BBSRC and MRC and with commitments from its 10 industrial partners, the Manchester Chemical Biology Network brought together more than 50 research groups from a range of disciplines across The University of Manchester to share expertise with industrial partners, including companies such as AstraZeneca, GSK and Pfizer.

This collaboration between research groups provides a more effective platform to tackle the major challenges associated with the discovery of new drugs and other products of importance to human health and wellbeing, using expertise ranging from synthetic chemistry through to cell biology.

“Improving the sustainability of our drug manufacturing processes through collaborations such as CHEM21 will not only reduce our industry’s carbon footprint, but will provide savings that can be reinvested in the development of new medicines, increase access to medicines through cost reduction and drive innovations that will simplify and transform our manufacturing paradigm.”
Dr John Baldeoni GlaxoSmithKline.
Our contribution to the energy agenda focuses in particular on the biological aspects of energy including fuel cells, solar energy and 2nd/3rd/4th generation biofuels. Research into alternative biofuels includes utilising biomass from both agricultural and marine sources to the development of novel biofuel pathways. Fill your car with petrol or diesel today, and the fuel you buy will likely contain a small (5%) proportion of biofuel. Could we use more and limit our reliance on fossil fuels? Almost certainly yes but current biofuels are not fully compatible with modern, mass-market internal combustion engines. The cost of modifying vehicles and fuel supply infrastructure to run on blends containing 20% or more bioethanol or biodiesel is the major limiting factor. The grand challenge is to produce a biofuel with the same chemical structure as conventional diesel fuel in commercial volumes. Biofuels with these characteristics are being termed ‘drop-in’.

Bacteria making “oil”
Solutions that seek to reduce our dependency on fossil oil are being tackled by Professors David Leys, Andrew Munro and Nigel Scrutton who are working on a BBRC Industry Partnership Award with Shell combining state-of-the-art genomics and laboratory evolution techniques with synthetic biology to make organisms produce “oil”, bypassing the need to drastically adapt oil-dependent processes. The team will focus, in particular, on production of linear alpha-olefins, a high value, and industrially crucial intermediate class of hydrocarbons that are key chemical intermediates in a variety of applications. At present, no “green” alpha-olefin production process is available, a situation which this project seeks to change.

Aquatic photobiology – exploring the potential
Biological fuel production is already a commercial reality with biology expected to contribute further towards fuel-production in both intermediate and future energy systems, particularly with the advancement in technologies that enhance economic sustainability.

During the next two decades the chemical industry will undergo a major transformation. As both oil and natural gas begin to run out, there will be a growing need to switch from oil based starting materials to those derived from biomass. Biotechnology-based processes will need to be developed to efficiently convert inexpensive raw materials to high value products such as pharmaceutical drugs, cosmetics and fuels. Underpinning this research is the transfer of technology into the marketplace. The University of Manchester has a range of world-class activities supporting the need for solutions that can play their part in meeting the global energy challenge.

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Aquatic photobiology – cultures of photosynthesizing cyanobacteria which are the hosts for alkane production
Photosynthetic organisms are able to utilize water, CO2 and sunlight to directly synthesise fuel or chemical precursors - all in one-engineerable package capable of both self-amplification and internal self-repair. Terrestrial-grown plants however display poor overall solar energy conversion efficiency. An alternative to land-based biomass are aquatic photobiological organisms, eukaryotic algae or cyanobacteria. These organisms display simple nutritional requirements and are in some cases even cable of nitrogen fixation. The cultivation of eukaryotic algae or cyanobacteria can be carried out on land that is not suitable for agriculture in constructed enclosed systems that do not utilize soil. By choosing aquatic instead of terrestrial systems for harnessing sunlight it should be possible to minimize the potential conflict between food-producing agriculture and photobiological fuel production. Aquatic photobiological organisms are also capable of potentially greater solar energy conversion efficiency compared to terrestrial plants. This EU FP7 collaborative project involves four Universities from across Europe and the US, together with Chemtex Italia and Photon Systems Instruments with the aim of developing photobiologically active algae that catalyse direct conversion of solar energy and carbon dioxide to engine-ready fuels.

SYNPOL – Biopolymers from syngas fermentation (SYNPOL) SYNPOL is an EU FP7 KBBE collaborative project (Knowledge-Based Bio Economy – Noodles) involving 14 European partners from academia and industry. The basic idea of the SYNPOL project is the establishment of an integrated processing technology for the efficient synthesis of cost-effective commercial new biopolymers using the products derived from fermentation of SYNGAS: generated from very complex feedstocks. This revolutionary project will see the establishment of a platform which integrates fermentation of modern processing technologies, with bacterial fermentation of syngas, and the physiology of highly complex biowaste as a microbial commercial grade, agricultural enzymatic feedstocks for the development of advanced biopolymers. The SYNPOL project is focused on the development of innovative photobiological, downstream and synthetic technologies to produce a wide range of new biopolymers, based on a number of novel and mutually synergistic production methods, and including an assessment on the environmental benefits and drawbacks related to the concept. The knowledge generated through this innovative biotechnology approach will not only benefit the environmental management of terrestrial wastes, but also reduce the harmful environmental impact of petrochemical plants.

In its first phase funded through the Biotechnology and Renewable Energy Centre for Integrated Systems Biology (BRC), prepared a catalogue toolbox from computational analytics through experimental approaches to data handling and organisation. The results of this early research can be found as a set of tools and resources and in the most recent issue of Methods in Enzymology devoted to Systems Biology by the MCBIE.

The MCBIE continues to be involved in two EUREKA TechnoRegions projects supported in the ELITE programme giving rise to a range of international collaborations and various recognition (eg as a best practice case by the EUREKA Executive Office).

IONTOX Safe green solvents for the future
In silico predictive chemometric models for selected toxicity endpoints of ionic liquids

Ionic liquids (ILs) are a modern addition to the world of chemical compounds, deployed in areas ranging from electrosynthesis, over organic synthesis, to cleaning, extraction and separation technology. Their unique negligible vapor pressure, non-flammability, enhanced thermal stability and outstanding solvation potential make them green solvents but their toxicity needs to be understood and controlled. Reliable toxicity prediction can only be achieved through computational means. Quantitative structure-property relationships, known as QSAR, solve the problem created by stringent environmental regulations and costly and time consuming experimental determination.

This EU International Incoming Fellowship will see Professor Paul Popelier develop ecotoxicological models for ILs in silico, obeying OECD principles, based on available toxicity data against various endpoints.
Considering the ever-growing interest in ILs, truly predictive QSAR models will be highly advantageous in designing the desired ILs. This project combines complementary expertise in physicochemical parameters rooted in quantum chemistry and rigorous chemometrics. Professor Popelier aims to establish collaboration with experimental toxicologists at The University of Manchester for experimental validation of the developed models delivering innovative QSAR models and expert systems for predicting toxicity of ILs, ready for European regulatory purposes.

**Enzymes for energy conversion**

Fuel cells are electrochemical devices that directly convert chemical energy into electrical energy. These function like a battery but have the reactants like hydrogen and oxygen fed from outside the cell. These devices frequently rely on expensive platinum-group metals to speed up the energy conversion process. Some metal-containing enzymes such as hydrogenases and multicopper oxidases carry out the same functions as efficiently as the precious metal catalysts and use small amounts of abundant elements such as iron, nickel, and copper.

Dr. Christopher Blanford’s recent EPSRC fellowship work focused on exploiting multicopper oxidases to create miniature components for portable fuel cells that could be used to power consumer devices like mobile phones. Two of the key challenges to adapting biological catalysts to replace inorganic ones are immobilising the enzymes to have the most efficient possible transport of reactants, products and electrons, and maximising the longevity of these immobilised enzymes.

Dr. Blanford and his group have discovered numerous biomimetic surface modifications, essentially using the enzyme’s natural partners to orient the macromolecules for efficient electron transport while preserving their activity for months. As part of the group’s research into rational electrode surface modification, they discovered a unique copper configuration that could be adapted to produce more efficient fuel-cell enzymes in common expression systems like E. coli.

The group also use an electrochemical quartz crystal microbalance (EQCM) to test how real-world usage conditions affect the longevity of fuel cell electrodes. While the enzymes remain viable for days when a constant output is required, rapidly varying the electric current extracted from the electrodes could diminish their lifetime to minutes. The group found that these destructive effects can be mitigated by limiting the electrode’s output potential.
In the wake of the human genome project, microbiology is currently undergoing a major transition: we are now capable of obtaining a comprehensive molecular view of the entire cellular circuitry of our microbes of interest, followed by an equally comprehensive re-engineering of their cellular functions, called Synthetic Biology. Synthetic Biology aims at the rational design of biological systems and living organisms using engineering principles, to achieve new useful functions in a modular, reliable and predictable way. It has the potential to drive a new industrial revolution in biotechnology, with applications in many sectors, including healthcare, sustainable energy, green chemistry, pharmaceuticals, novel materials and bioremediation. It requires cutting-edge research at the interface of biology, engineering, chemistry and computing science. The Manchester Institute of Biotechnology has assembled one of the strongest interdisciplinary teams with world-class expertise in all these areas in a single state-of-the-art facility.

SynBio®MIB - Synthetic Biology advancing synthetic biotechnology

Through active collaborations with a large variety of industry partners the Centre for Synthetic Biology of Sustainable Chemicals and Natural Products (SYNBIOSCHEM) at the MIB is harnessing the power of synthetic biology to propel chemicals/natural products production towards ‘green’ and more sustainable manufacturing processes, and boost UK research capacity by stimulating innovation with industry and other key stakeholders in the chemicals/natural products sector.

Major EU funded projects in synthetic biology include BIONEXGEN, BIONTENEN and BIOBOX, focused on developing the next generation of biocatalysts for industrial chemical processes.

Strategic links in this field have been developed with a number of SMEs as well as large global companies through regular Industry Days hosted at the MIB bringing together academia and industry in focused groups to explore future perspectives in synthetic biology. In addition we have links with international Centres of Excellence including the Austrian Centre for Industrial Biotechnology (ACIB), CSIRO biofuel cluster in Australia, SynBio in the US (multi-university SynBio Centre), Beijing Genomics Institute and the Chinese Academy of Sciences as well as several SynBio centres across Europe.

Emerging societal, ethical, and regulatory challenges associated with this rapidly advancing new technology are addressed in close interaction with social scientists and economists across The University of Manchester.

MIB-based synthetic biology researchers


Associated researchers

Andrew Balmer, School of Sociology Sarah Chan, Faculty of Life Sciences Philip Shapiro, MIB

We actively link across campus with network partners as part of a wider synthetic biology strategy.

Industry stakeholders-partners

We have an established track record of leadership in industry and stakeholder collaborations in the chemicals/natural products sectors including:

ACIB, AtoZenza, BASF, Bayer, Bruker, CatSci, Charmwood Consulting, Codexis, Dr Reddy’s, Evolva Biotech, GlaxoSmithKline, Janssen, Orion, Lonza, Merck, Pfizer, Novo, Synthace, Syngenta, Shell, Syngenta, Unilever and more.

EU science and training programmes in synbio

We enjoy ‘hub status’ for major EU science and training programmes in this sector, including the Innovative Medicines Initiative award CHEM 21 (ICSM), EU training networks (MAGIC, PARITY) and EU FP7 consortia awards (DIRECTFUEL, BIONEXGEN, AMBIOCAS, BIONTENEN, SUPRABIO).

Networks

BBBRC Natural Products Discovery and Bioengineering Network (PRONET) led by Jason Micklefield (MIB, UoM) and Barrie Wilkinson (John Innes Centre)

Technology Platforms

TP1 Rapid identification of components and accelerated directed evolution for SynBio

TP2 Bioengineering technologies and chassis design

TP3 Metabolomics, analytical science and metabolic engineering platforms

TP4 Computational systems biology, bioinformatics and genomics

Computational and systems modelling of prototypical pathways in engineered chassis; pathway/biocatalyst control (e.g. orthogonal regulatory circuits, riboswitches); chassis engineering (e.g. yeast, bacteria) for robust and high yield industrial producers; informatics and genomics/metagenomics to facilitate building block discovery; enzyme engineering and evolution to generate new biocatalytic technologies; robotics for accelerated host optimization and refactoring; metabolomics/analytical science supporting chassis optimization and intermediates/product analysis; pathway refactoring/assembly comprising assembly of building blocks and pathways and regulatory components.

These technology platforms are integrated through iterative (n) cycles of (circuit design—computational modelling—experiment—data analysis—modelling—redo) (n). These cycles will be implemented at different levels, within individual platforms as well as between platforms, to establish a semi-automated and integrated pipeline for the discovery and re-engineering of biocatalysts building blocks and engineered pathways.
Exploiting natural product assembly line genomics and synthetic biology for discovery and optimisation of novel agrochemicals

Harnessing world leading expertise in natural product synthesis, this project brings together Professor John McFadden, Professor of Chemical Biology (Wits), together with Professors Gisela Schwartz (Marie Curie), Peter Leadlay (Cambridge) and Russell Cox (Bristol) to develop a platform technology that can exploit the potential of microbes for the production of useful compounds for use in agriculture and medicine.

Many microorganisms produce beneficial compounds, including antibiotics and fungicides. Synthetic biology can be used to engineer a fungus with most microbes having the capacity to produce many more compounds than are actually observed. If their full potential can be activated then it could provide new compounds for the testing of medicines and agricultural chemicals.

This grant funds an ambitious programme to rapidly sequence the genomes of 40 microorganisms with the known ability to produce potential compounds that benefit agriculture. The team will work with partners in the international agrochemical company Syngenta to develop these as new herbicides, insecticides and fungicides, while partners at the biotechnology company Biotica will focus on compounds with use in human medicine.

This £3M project is funded under the BBRC/Sci4U initiative in partnership with Syngenta and Biotica.

**Development and application of next generation synthetic biology tools**

Dr Dixon seeks to develop novel protein production and metabolic engineering tools, and demonstrate the applications of these novel synthetic biology tools in the context of the bioprocessing industry. Although biopharmaceuticals offer many health benefits along with substantial commercial opportunities, their production remains a significant technical challenge. Dr Dixon will develop and demonstrate four important features of a novel gene co-expression technology, to allow modular protein products to be produced more effectively, along with the potential to provide a simpler and more efficient manufacturing process.

Additionally, these co-expression technologies will be used to optimise a number of multifactor co-expression challenges, helping to guide metabolic engineering efforts leading to improved bioprocessing efficiencies, with the potential to reduce both drug development times and manufacturing costs.

Dr Dixon has also been awarded a Technology Science Board (TSB) feasibility grant entitled ‘Rapid Engineering of Cellular Factories’ working alongside collaborators from UCL and Synact to advance the industrial application of synthetic biology. This is a collaborative R&D project, with the goal of demonstrating the rapid creation of bacterial cellular factories, for fine chemical production that is both economically and environmentally sustainable, based on industrial biotechnology, and advanced synthetic biology and bioprocesses.

**Engineered compartments for monoterpenoid production using synthetic biology**

TERPENOSOME is led by Professor Enrico Takano, and together with Professor Nigel Scrutton and partners across Europe, it will use synthetic biology to engineer novel organisms for the overproduction of monoterpenoids in microbial hosts. The project aims to generate a portfolio of generic methods for the compartmentalization of biosynthetic pathways for bioactive molecules, improve the biosynthetic enzyme systems for more efficient bioprocessing and overproduce industrially relevant terpenoids, for commercialization by one of the partners.

The generic compartmentalisation methodology will be exploited by industrial partner, Life Technologies, in synthetic biology projects on a wide range of biotechnologically relevant high-value compounds. The second industry partner, ACS International, will exploit the improved production strains for the widely used precursor material limonene, as well as the two high-value compounds that are the major target molecules of TERPENOSOME.

**Delivering next generation antibiotics**

One of the major challenges in healthcare is the provision of new antimicrobial agents that can combat antibiotic-resistant pathogens (superbugs), which are widely recognised as a major global threat. New antibiotics are urgently needed to combat the emerging critical problem of bacterial resistance. The European Centre for Disease Prevention and Control has estimated that antimicrobial resistance costs the EU about 1.5 billion euros in healthcare each year. The UK government has made clear actions into fighting antimicrobial resistance with a 5 year Antimicrobial Resistance Strategy Report published in September 2013.

Despite this, the majority of antimicrobial agents used today belong to old classes of antibiotics discovered before 1970. In partnership with GSK, Professors Jason McFadden, David Leys and Enrico Takano will investigate the biosynthesis and bioengineering of lipoygycoprotein antibiotics of the ramoplanin and enduracidin family. The lipoyglycopes are highly potent antibiotics which have considerable clinical potential, with ramoplanin having entered phase III clinical trials. The team will develop alternative biosynthetic engineering approaches to enable the rapid structural diversification of this class of antibiotics, providing access to large numbers of lipoyglycopeptide variants with potentially improved antimicrobial activities, for subsequent development with industrial partners.

The new biosynthetic insights will be used to guide the development of bioengineering strategies aimed at altering the glycosylation, halogenation and lipoylation patterns, as well as the amino acid sequence of the lipoyglycopes. The bioengineering methodologies developed here will be used to engineer a wide range of derivatives for other promising classes of antibiotics as well as other natural product variants for alternative therapeutic and agrochemical applications.

In a complementary project, funded by the TSB, Professor Enrico Takano aims to use synthetic biology as a key technology to discover and develop new antibiotics overcoming common problems associated with antibiotic discovery from natural sources, such as poor understanding of the antibiotic producer, poor growth characteristics, reproducibility, poor yield and lengthy delays to market. Demunis Ltd, an SME with expertise in natural product discovery, has identified a promising broad-spectrum antibiotic but it is produced in low quantity. In collaboration with Croda, a large chemicals company with established routes to market, the team will fully unlock the potential of this promising broad-spectrum antibiotic using synthetic biology approaches.

Bioinformatics and biosynthetic gene cluster refactoring will be used for optimum expression and for introducing additional diversity of the chemical structure. The optimized biosynthetic machinery will then be introduced into Demunis’ optimised production host for maximum yield required for commercialization. In addition, the methods established in this work will be utilised for the activation of novel silent gene clusters identified from the genome-sequence of the broad-spectrum antibiotic producer and the products identified and characterised for potential industrial applications.

**China Partnering Award**

Professors Enrico Takano and Nigel Scrutton have secured funding through a Synthetic Biology China Partnering Award, co-funded by the Biotechnology and Biological Research Council (BBSRC), the Chinese Academy of Sciences (CAS) and the Engineering and Physical Sciences Research Council (EPSRC) to partner and develop long term fruitful relationships with Chinese scientists. The funding is provided for up to four years and it is anticipated that the partnerships will lead to new joint grant applications and high impact research.

Professors Enrico Takano and Nigel Scrutton will collaborate with Professor Lien Zhang at the Chinese Academy of Sciences Institute of Microbiology to establish cooperative research on the use of synthetic biology approaches for production of high-value fine chemicals.

**STREPSYNTH: Rewiring the Streptomyces cell factory for cost-effective production of biomolecules**

Professor Roy Goodacre is bringing his expertise to bear on STREPSYNTH, an EU FP7 funded project involving 15 partners and led by the UK’s largest biotechnology company Biotica. STREPSYNTH aims to establish a Streptomyces-based industrial production platform (SNP) for high value added biomolecules.

Streptomyces lividans was chosen as a bacterial host cell because it has already shown itself to be highly efficient in antimalarial production of a number of heterologous molecules that vary chemically, has a robust tradition of industrial fermentation and is fully accessible to genetic intervention. In setting up SNP the consortium chose two classes of biomolecules with obvious immediate industrial value and application: heterologous proteins (industrial enzymes, biomaterials, diagnostically and small molecules (antipartheptide and anti-inflammatory) for use in the production of industrial enzymes and antibiotics.

It is envisioned that SNP is a modular platform that can be reprogrammed for diverse future applications. Professor Goodacre is very excited to be involved in this novel synthetic biology programme. His role is to develop a metabolomics and fluxomics toolbox which aims to establish standard experimental procedures for robust and reproducible fluxomics in Streptomyces lividans TCH4.

**“Synthetic biology is an exciting new field with enormous potential to bring benefits to people around the world in all sorts of ways, for example producing better antibiotics or manufacturing low carbon fuels. Co-funded initiatives such as this scheme will see British and Chinese scientists learning from each other’s expertise and benefiting from the globalisation of excellent science.”**

Professor Douglas Kell, Chief Executive of BBSRC

**“We at CAS attach great importance to international collaboration. The idea of this programme is to put the best minds together. Together our scientists and those from the UK can advance this field more efficiently. In the progress of our cooperation, I hope they will further strengthen their linkages and collaboration, and tackle bigger challenges for the needs of mankind.”**

Cao Jinghua,
Deputy Director-General of Bureau of International Cooperation of CAS

**“EPSRC is pleased to be part of this joint international call which demonstrates the wide scope for synthetic biology to create impact in many academic fields. It has the potential to create new solutions to address pressing global challenges, such as the need for new fuels, better waste management and new medicines.”**

Professor David DeLey, Chief Executive of EPSRC
MIB iGEM team take Best Undergraduate Human Practices Award at the World Championships Jamboree

For the first time in history an undergraduate team from The University of Manchester competed in the International Genetically Engineered Machine competition (iGEM), the world’s premiere iGEM Synthetic Biology competition. Student teams are given a kit of biological parts at the beginning of the summer from the Registry of Standard Biological Parts. The teams use these parts together with new parts of their own design to build biological systems and operate them in living cells.

Along with 60 other teams from across Europe the Manchester iGEM team presented their project at the regional iGEM Jamboree held in Lyon on 11 – 13 October 2013 gaining gold medal status and Best Undergraduate Human Practices Award which they went on to win at the World Championship Jamboree in Boston.

“We are very proud of what the team has achieved – the Manchester iGEM team is the only first-time undergraduate team to win the award without the benefit of building on the experience of earlier teams from the same university. This makes their achievement all the more amazing. The team includes first year to last year students working very closely together”

Professor Eriko Takano
Team Leader iGEM

Manchester Centre for Integrative Systems Biology (MCISB)

The Manchester Centre for Integrative Systems Biology (MCISB) at The University of Manchester was founded in 2006 having been awarded £6.4M by the BBSRC of Manchester was founded in 2006 and received the first full endowment from the Wellcome Trust. It is a Centre of Excellence for Systems Biology, funded by the UK’s Biotechnology and Biological Sciences Research Council (BBSRC) and the Engineering and Physical Sciences Research Council (EPSRC) as part of the UK systems biology programme.

The centre is led by Professor Pedro Mendes and brings together approximately 75 scientists from a range of disciplines from within The University of Manchester and further afield. They are working on the development of new methods for the quantitative study of biological systems, the production of tools for their analysis, and the application of these tools towards comprehensively addressing biological problems of major societal relevance.

Interest (ChEBI)

Chemical Entities of Biological Interest (ChEBI) acts as a resource for small molecules that act on and within these biological structures. In the service of its application to facilitate whole-systems research into biology enabling the integration of metabolomics and systems biology.

COPASI (Complex PATHway Simulator)

Bioinformatics research is becoming increasingly dependent on construction and simulation of computational models as the technical aspects of modelling and simulation are often overwhelming to a large number of biomedical researchers. COPASI provides the appropriate numerical algorithms shielded by a user interface to assist the researcher in conducting the required simulations. This project aims to extend the capabilities of COPASI by adding the means to simulate
models with explicit time delay, providing
a mechanism for easy calculation of summaries
of entire simulations and groups of
simulations and incorporating a new feature
that will allow researchers, for the first time,
to be able to navigate the entire history of
a model, such that the reasons for changes
that took place are formally identified, as
even as decisions on the model structure.
The project will also improve and extend
the software's interoperability and standards
compliance to allow bioscience researchers
to freely exchange data and models.

COPASI (Complex Pathway Simulator)
is based on the GEPASI simulation software
(General Pathway Simulator) that was
developed in the early 1990s by Professor Pedro Mendes. It is the result of an
international collaboration between The
University of Manchester (UK), the University of Heidelberg (Germany), and the Virginia
Bioinformatics Institute (USA). The initial
development of COPASI was funded by
the Virginia Bioinformatics Institute, the
Klaus Tschira Foundation, the BBSRC and
EP SRC. Professor Pedro Mendes has received
additional follow on funding from the BBSRC
to maintain and develop this important
resource.

Study maps human metabolism
in health and disease

Scientists from the MIB working with
researchers from Cambridge, Edinburgh,
Berlin, Nijmegen and San Diego among
others have produced an instruction manual
for the human genome that provides
a framework to better understand the
relationship between an individual's
genetic make-up and their lifestyle. The team have
mapped 65 different human cell types and half
of the 2,600 enzymes that are known
drug targets in order to produce the network
model, providing the most comprehensive
model yet to explain why individuals react
differently to environmental factors such
as diet or medication. Pedro Mendes,
Professor of Computational Systems Biology commented:

"This research is the second, important
stage of our understanding of the human
genome. If the sequencing of the human
genome provided us with a list of the
biological parts then our study explains
how these parts operate within different
individuals. It provides a network mapping
to all the molecular transactions that
define what goes on with these so-called
metabolites in human biochemistry. The
results provide a framework that will
lead to a better understanding of how an
individual's lifestyle, such as diet, or a
particular drug they may require is likely
to affect them according to their specific
genetic characteristics. The model takes us
an important step closer to what is termed
'personalised medicine', where treatments
are tailored according to the patient's genetic
information."

Douglas Kell, Professor of Bioanalytical
Science at the MIB said: "To understand
the behaviour of a system one must have
a model of it. By converting our biological
knowledge into a mathematical model,
this work provides a freely accessible
tool that will offer an in-depth understanding
of human metabolism and its key role
in many major human diseases. It offers
the most complete model of the human
metabolic network available to date to
help analyse and test predictions about the
physiological and biochemical properties
of human cells. Pharmaceutical drugs get
into cells by 'hitchhiking' on the transporter
proteins that normally serve to move small
molecules around. An area of particular
interest is thus the incorporation into our
metabolic network map of knowledge of
pharmaceutical drug transport."

Dr Nicolas Le Novère, from the Babraham
Institute in Cambridge (UK), said:

"This is a model that links the smallest
molecular scale to the full cellular level. It
contains more than 8,000 molecular species
and 7,000 chemical reactions – no single
researcher could have built this alone. Having
large collaborations like these, using open
standards and data-sharing resources, is
crucial for systems biology."

SYBIL provides insight into skeletal diseases

SYBIL (Systems biology for the functional
validation of genetic determinants of skeletal
diseases) is a large scale collaborative project
that brings together a complementary group
of world-class scientists, disease modelers,
information technologists and industrialists.
The overall concept of this project is to
functionally validate genetic determinants of
common and rare skeletal diseases to
gain a mechanistic understanding of disease
processes and age-related changes, and
to deliver new and validated therapeutic
targets.

Rare skeletal diseases (RSDs) are an extremely
diverse and complex group of diseases that primarily
affect the development skeleton. There are more than 450 unique and well-
characterised phenotypes that range in
severity from relatively mild to severe and
lethal forms. Although individually rare, as a
group of related orphan diseases, RSDs have
an overall prevalence of at least 1 per 4,000
children, which extrapolates to a minimum of
225,000 people in the 27 member states and
candidate countries of the EU.

Dr Jean-Marc Schwartz will lead one of the
work packages and, alongside Professor
Roy Goodacre, provide the core qualitative
systems biology analyses for the consortium.
Roy has over 18 years experience in mass
spectrometry (MS), advanced data analysis
applied to spectroscopic, mass spectrometric
and metabolomic data and over 11 years in
vibrational spectroscopy. He has published
over 180 peer-reviewed papers and has
col-edited books on metabolic profiling
and systems biology. He is the Editor-in-chief
of the journal Metabolomics and on the
editorial board of the Journal of Analytical
and Applied Physics. Finally, he is a founding
director of the Metabolomics Society and
director of the Metabolic Profiling Forum.

Perfecting drug combinations
to combat severe diseases and conditions

A multidisciplinary team of researchers, led
by Professor Douglas Kell, have found a
way of identifying ideal drug combinations
from billions of others which would prevent
inflammation from occurring. The findings,
published in Nature Chemical Biology,
could be the first step in the development of new
drug combinations to combat severe diseases and conditions.

Most non-infectious disease, such as cancer,
stroke and Alzheimer’s are worsened by
inflammation, which is the body’s natural
defence mechanism. Inflammation has evolved
to help fight infection but can also be very
damaging in long term disease, prolonging suffering and ultimately risking
premature death. After a stroke, the body
reacts to the injury as if it were an infection,
causing further damage. By blocking the
inflammation, the chances of survival or
higher quality of life following a stroke are
thus greatly enhanced. This can be achieved
by quickly and effectively identifying
combinations of drugs which can be used
together.

Existing ‘clot-busting’ stroke drugs are only
effective if administered within three hours
after the stroke – often very difficult to
achieve as people are often unaware they
are having a stroke – and even then do not
completely solve the problem, often leaving
sufferers with serious disabilities.

However, using ideal drug combinations
the researchers suggest they can block
inflammation and therefore greatly reduce
the damage caused by non-communicable
diseases such as stroke. Although the
researchers have initially concentrated
on stroke, they believe the process can
be applied to all drugs and for a huge
variety of diseases. The team developed
an evolutionary computer program which
rapidly sifted through nine billion different
combinations of potential drugs.

Sorting and testing 50 drug combinations
at a time using robotics in the laboratory,
the scientists were able to find effective
combinations and then refine them as
many times as necessary to find ideal
combinations. Ultimately, they hope this will
lead to the development of tailored therapies
for treating inflammation.

Another advantage of choosing ideal drug
combinations is that it allows patients to
take smaller doses, which reduces potential
toxicity concerns.

Erythrocyte and fibrin imaging for
disease diagnosis

In a separate study, Professor Douglas Kell has
demonstrated that ungalvanized iron is responsible for
a large number of degenerative and inflammatory
diseases. In collaboration with Prof Resia Pretorius
(University of Pretoria, South Africa), he has now
demonstrated that this model is highly aberrant
morphologies of fibroin - the protein responsible
for blood clotting - and or red blood cells. Work
is in progress to use these kinds of measurements
for the rapid, cheap, and minimally invasive
diagnosis of the severity of such diseases and the
effectiveness of their treatment.
PathText: reconstructing pathways with evidence from text

To understand complex biological systems in detail we need to incorporate knowledge scattered over millions of scientific publications. Using conventional means, Pathway model reconstruction and maintenance is a manual and expensive curation process due to new discoveries. However, PathText links pathway models with textual evidence by combining and ranking relevant information from the literature using text mining methods.

PathText integrates and ranks the evidence from text using a number of text mining tools and services including the identification of reactions, genes, proteins and metabolites in their semantic context, from text automatically. NaCTeM’s interoperable text mining infrastructure links the text analysis components and text mining workflows with an annotation environment to further support curators in their task.

PathText currently links CellDesigner with NaCTeM’s text mining services FACTA+(mining direct and indirect associations between concepts and bioprocesses), KLEIDO (advanced semantic faceted search based on bio-entities) and MEDE (semantic search based on bio-ontologies). Novel methods such as automatic event and biological process recognition from texts have facilitated this task.

This project was led by Professor Sophia Ananiadou in collaboration with Professor Jun’ichi Tsujii, Professor Douglas Kell, and Professor Hironori Kito (Systems Biology Institute, Japan). It was funded by BBSRC. Event extraction in collaboration with AmaZenica.

http://www.nactem.ac.uk/pathtext/
http://www.nactem.ac.uk/facta/

NaCTeM receives three first place rankings at Biocreative IV

NaCTeM’s text mining tools were recently ranked highest in three separate tasks to develop software that can identify important information in chemical text. In particular, NaCTeM was ranked first out of 12 groups in the recognition of chemicals, and the recognition of genes, and first out of 23 teams in a task involving the recognition of chemical names.

BioCreative IV is the latest in a series of text mining challenges in which teams from both academia and industry apply their technology to extract a range of types of information from text.

The National Centre for Text Mining (NaCTeM) provides text mining systems and infrastructure at large scale

NaCTeM has developed text mining tools, resources and services to support the automatic extraction of information and knowledge from the growing amount of literature in an efficient, manageable and comprehensive manner at large scale. Applications areas include: drug discovery, chemistry, systems biology, clinical trials, public health, medical historical archives, newswire analysis, pathway reconstruction and advanced search systems. NaCTeM, led by Professor Sophia Ananiadou and Dr John McNaught, is a fully sustainable text mining centre. It has been funded by BSC, BBSRC, MRC, AHRC, Wellcome Trust, NH and industrial partners.

Text mining software facilitates the discovery, extraction and structuring of relevant knowledge from unstructured text. The output of text mining systems can enrich documents with semantic information, which can in turn be used to develop search systems that allow users to locate information of interest more quickly and efficiently than is possible using traditional search methods.

Europe PubMed Central

Europe PMC forms a European version of the PubMed Central repository, in collaboration with the National Institutes of Health (NIH) in the United States. NaCTeM collaborates with the European Bioinformatics Institute (EBI), MIMAR and the British Library. NaCTeM’s contribution to this major project is the provision of advanced semantic search over full papers, involving massive analysis at the level of individual facts (some 83M sentences have been analysed so far for our EvidenceFinder application).

The objectives are to deliver content from annotated documents, such as concepts, e.g. anatomical entities, genes, chemical compounds, links to databases, and relations amongst concepts, through a sophisticated search facility. EvidenceFinder presents the user with a list of questions relating to his query, where these questions are derived from the abovementioned analysis and indexed facts, thus are known to have answers. For example, given the query “5.2-”, EvidenceFinder will present questions such as “What inhibits 5.2 receptor?”, “What binds to 5.2 receptor?”, etc., for the user to click on. This allows information to be located that might otherwise be missed, and to quickly establish which articles do and do not contain information being sought. EUPMC funded led by Wellcome Trust.

Evidence-based public health

Evidence-based public health (EBPH) reviews play a central role in public health policy, practice and guidance. Their development currently involves first searching, then screening and synthesizing evidence from the vast amount of literature. Unlike systematic reviews, EBPH reviews require dynamic and multidimensional views of relevant information from the literature, without relying on a priori research questions.

As a result, EBPH reviewing is a time consuming and resource intensive process that can take more than a year to complete. Since crucial information can be difficult to locate, and indeed understand given the complex nature of EBPH problems, the multiple causes and interrelations between interventions, diseases, populations and outcomes can remain hidden.

EvidenceFinder, an MRC funded project between Manchester (Ananiadou, McNaught), NICE and the University of Liverpool will address these limitations by exploring new research methods, which combine text mining and machine learning to produce novel search while screening tools for public health reviews. Text mining methods will discover automatically new knowledge from unstructured data and machine learning will support the prioritisation and ranking of the extracted information into meaningful topics. The combination of text mining and machine learning methods will reduce the burden of producing public health reviews which will be completed more quickly, thus meeting policy and practice timescales and increasing their cost efficiency. They also allow more timely and reliable reviews, thus improving decision making across the health sector.

Interoperability, text mining processing, and annotation are supported by Argo, a Web application for analysing (primarily annotating) textual data. The workbench supports the combination of elementary text-processing components developed by the centre to form comprehensive processing workflows. It provides functionality to manually intervene in the otherwise automatic process of annotation by correcting or creating new annotations, and facilitates user collaboration by providing sharing capabilities for user-owned resources.

The workbench builds upon a previous, standalone application (U-Compare) that currently hosts over 100 text-processing components. Argo benefits users such as text analysts by providing an integrated environment for the development of processing workflows; annotators/curators by providing manual annotation functionalities supported by automatic pre-processing and post-processing; and developers by providing a workbench for testing and evaluating their automatic text analytics.

These platforms have been funded by the EC in the framework of META-LE and by the BBSRC.

http://argo.nactem.ac.uk
http://nactem.ac.uk/ucompare/

Open Source Software receives funding boost

This EU FP7 funded project will see NaCTeM working with 8 partners across Europe on OSSMETER which aims to extend the field of automated analysis and measurement of Open Source Software, and develop a platform that will support decision makers in the process of discovering, comparing, assessing and monitoring the health, quality, impact and activity of open-source software. To achieve this, OSSMETER will compute trustworthy quality indicators by performing advanced analysis and integration of information from diverse sources including the project metadata, source code repositories, communication channels and bug tracking systems of Open Source.

Supporting evidence-based public health interventions using text mining

Funded by the Medical Research Council (MRC) this project will address current limitations in Evidence-based public health (EBPH) interventions by exploring new research methods which combine text mining and machine learning to produce novel “search while screening” tools for public health. This is a collaborative project with NICE and the University of Liverpool.

Mining the history of medicine

Funded by the Arts and Humanities Research Council (AHRC) this cross-disciplinary collaboration between the National Centre for Text Mining (NaCTeM) and the Centre for the History of Science, Technology and Medicine (CHSTM) at the University of Manchester, seeks to demonstrate the potential of text mining in medical history. Initially an asset will be created out of two very large, long-running digital sources, the British Medical Journal (BMJ) (1840 - present) and the London-area Medical Officer of Health (MOH) reports (1848-1972), by applying text mining methods to these data with semantic annotations. The project plans to extend its impact to the following sectors: public health, public policy, publishing, media and libraries, with a view to ensuring sustainability and wider uptake of methods and technologies.
Tackling early cognitive decline – a text mining perspective

Critically only 50% of people with dementia ever receive a diagnosis that could lead to them receiving medical care and support. Professor John Keane is collaborating with Professor Alastair Burns and Dr Hiroa Leki from FMHS as part of a joint programme, with Lancaster University and King’s College, London to look at novel ways in which data and text-mining techniques, combined with adaptive user interfaces, may enable sufferers’ new opportunities for self-referral.

Supported by the EPSRC, the project is entitled SAMS: Software Architecture for Mental Health Self-Management.

By exploiting novel data and text mining techniques, combined with adaptive user interfaces, SAMS will validate thresholds by non-intrusively examining changes in people in established cognitive dysfunction and mild Alzheimer’s disease and begin to explore the potential for technology-enhanced detection of early cognitive dysfunction. Patterns of computer use and content analysis of e-mails, such as forgetting topics, expressions of concern, emotion, etc., will be analysed and coupled to feedback mechanisms to enhance users’ cognitive self-awareness, enabling them to self-refer themselves for expert medical advice.

This project is supported by the EPSRC, Dementias Neurodegen Network (DeNDRoN), The Alzheimer’s Society, Microsoft Research, the University of British Columbia and Johns Hopkins University School of Medicine.

Linked2Safety: advancing clinical practice and data security in clinical research

Electronic Health Records (EHRs) contain an increasing wealth of medical information. They have the potential to support clinical and medical research, improve health policies, ensure and empower patients’ safety and improve the overall quality of healthcare. The Linked2Safety project is funded through the EU 7th Framework Programme and involves ten partners from eight EU countries including MB researchers, Professor John Keane and Dr Goran Nenadic, together with colleagues from the School of Computer Science.

The project aims to advance clinical practice and accelerate medical research by providing healthcare professionals, pharmaceutical companies and patients with a secure framework facilitating the efficient and homogenised access to shared distributed Electronic Health Records (EHRs). Linked2Safety facilitates the use of EHRs in clinical research to support early detection of potential patient safety issues based on the genetic data analysis and the extraction of the bio-markers associated with an identified type of an adverse event. It also aims to support sound decision making and effective organization and execution of clinical trials.

The underlying architecture will be based on a common shared semantic infrastructure including linked data, ontologies, common medical vocabularies and state-of-the-art clinical data analytics techniques.

Mass Spectrometry@MIB

Gas-phase ion chemistry research provides an enhanced understanding of the analytical techniques that underpin proteomics, metabolomics and the investigation of other molecules of biological significance. New developments in quantitative mass spectrometry provide much needed information for modelling of biological networks, while techniques are being developed for the analysis and quantification of a variety of post-translational modifications.

In September 2013 we were delighted to welcome Professor Perdita Barran to the MIB as Chair of Mass Spectrometry and Director of the Michael Barber Centre for Collaborative Mass Spectrometry. The Barran group have developed and maintained many successful collaborations within academia and industry in developing and applying gas phase methods to problems of biological and medical relevance. Through the adoption of solvent free methodologies they are able to provide an understanding of structure function relationships of proteins and peptides at the molecular level and have developed IM-MS (ion mobility-MS) instrumentation, in collaboration with Walter, to investigate changes in protein conformation to understand biological systems using MS-based techniques which have widespread application. The Barran group is currently developing two new ion mobility instruments, one to provide higher resolution cross section measurements and one to also allow for photo-interaction.

An extremely successful area of multidisciplinary investigation is the structure activity relationship of a group of anti microbial peptides known as β-defensins, where Barran led a platform grant (EPSRC) funded team comprising 7 academic groups. Research in this area continues to be fruitful, and has recently been extended to examine other chemokines in collaboration with Professor Brian Vollman (Wisconsin, USA) and chemokine GAG interactions with Professor Rob Woods (Georgia USA). Barran is currently collaborating with Professor Cal MchPhee and Dr Tilo Kunath (Edinburgh) and Professor David Albro (Lancaster) to look at pre-fibrillar amyloid aggregates of neurodegenerative proteins.
Professor Perdita Barran joins MIB

Perdita graduated from The University of Manchester with a degree in Chemistry with Industrial Experience in 1994. She went on to obtain a PhD in Chemical Physics in 1998 from Sussex University under the supervision of Professors Tony Stace and Sir Harry Kroto. Following postdoctoral appointments in the UK and USA she was awarded an ERC Advanced Research Fellowship to study “The Structure and Energetics of Peptides and Small Proteins” which she took up at the University of Edinburgh where she helped to establish a Centre of Proteomics (SHARCAMS).

Since 2009 she has published 38 papers with five currently in review. She has a total publication list of 70 peer reviewed papers (over 900 citations, in Factor 23). This impressive output spans work on the fundamentals of Ion Mobility Mass Spectrometry, including instrument development all the way to application to biomedical problems. Barran has communicated 2 book Chapters, and an entry for the European Encyclopaedia of Biophysics (2012). Perdita was awarded The Dicky Memorial Prize for Innovation in Separation Science in 2005, and the Joseph Black award from the Royal Society of Chemistry 2009 for her significant developments in the fields of mass spectrometry and separation science, especially ion mobility techniques. Recently she was appointed as an Editor of the International Journal of Mass Spectrometry.

Adopting a combined experimental-computational approach

Many advances in biology, medicine, chemistry and materials science of the last few decades owes much to the structural information that has been obtained for proteins and nucleic acids by X-ray crystallography and NMR spectroscopy, and which has revolutionised our view of how life works. Unfortunately, these techniques are far too difficult to apply to the main class of biomolecules - carbohydrates. Despite carbohydrates constituting over half of the biomass of our planet and performing an almost limitless number of roles in living systems, we don’t really understand how they work in the same way that we do for proteins and DNA. The lack of definitive data means there is still considerable debate as to how we even define structure in carbohydrate polymers. In order to best capitalise on the immense potential of carbohydrates in both science and industry we have to understand in more detail the molecular principles that govern their assembly, organisation and interactions with other molecules which requires alternative approaches to studying carbohydrate structure.

Paul Popelier, Professor of Chemical Theory and Computation has joined forces with Dr Ewan Blanch, Reader in Biophysics and a Raman spectroscopist on an EPSRC funded project to develop a combined computer modelling and spectroscopic lab-based approach to characterising the structures of carbohydrates, from simple sugars to full carbohydrate polymers known to be involved in regulating biological functions generating a uniquely incisive new tool for glycobiology. The team will be combining high level quantum chemistry calculations, molecular dynamics simulations and highly detailed Raman spectra to develop and validate novel computer modelling tools that will provide new insights into many other areas of research, such as protein-ligand interactions and DNA-drug molecule binding.

Although the resulting development of new computational tools will be focused on the structures and behaviour of carbohydrates, the end product will also be widely applicable to all other biomolecules, particularly proteins and nucleic acids.

Forensics and archaeology

ZoMS - short for ZooArcheology by Mass Spectrometry - is a pioneering new technique called “collagen fingerprinting” which uses the persistence and slow evolution of collagen as a molecular barcode to read the identity of bones. The method, developed by Dr Mike Buckley during his PhD, uses a well-established approach, peptide mass fingerprinting, allied to high throughput Time of Flight Mass Spectrometry. Bones are identified by differences in the mass of the peptides which arise as a result of sequence differences between species.

Palaeobiology and vertebrate evolution

Recently, Dr Mike Buckley was approached by Dr Natalia Rybczynski, a vertebrate palaeontologist with the Canadian Museum of Nature to identify bone fragments dating from three- and a-half million years ago. By extracting minute amounts of collagen, the dominant protein found in bone, from the fossils and using chemical markers for the peptides that make up the collagen, a collagen profile for the fossil bones was developed. Dr Buckley then compared the profile to 37 modern mammal species, as well as that of a fossil camel found in the Yukon. The collagen information, combined with the anatomical data, demonstrated that the bone fragments belonged to a giant camel as the bone is roughly 30% larger than the same bone in a living camel species.

Discovery of detailed genotype of a historic strain of M. tuberculosis

The study of ancient DNA enables the prevalence of diseases in past populations to be determined by analysis of skeletons for the presence of pathogen DNA. In a recent study of Mycobacterium tuberculosis (MTB) published in PNAS, Terry Brown, Professor of Biomedolecular Archaeology, together with researchers from York and Durham, have obtained the detailed genotype of a historic strain of M. tuberculosis from a female adolescent buried sometime between 1840 and 1911 in a crypt in Leeds, England through the use of pioneering new methods based on next generation sequencing.

M. tuberculosis is the second deadliest infectious agent worldwide, yet little is known about the bacterium’s historic genetic variations and how such historic strains have evolved over time. The genotyping of historic strains of M. tuberculosis could enable comparisons between strains from different geographic locations and time periods, and may yield clues about the pathogen’s evolutionary history. The group are particularly interested in linking strain variations to changes in TB virulence during the medieval period, when Britain became increasingly urbanised. They are also comparing strain data for TB in Europe with similar results from the Americas, the latter helping us to understand why many native Americans died of TB after first contact with Europeans even though strains of TB had been endemic in the New World for many years prior to contact. The Brown group have worked on several diseases, including malaria and syphilis, and most recently on tuberculosis and leprosy.

Secondary Ion Mass Spectrometry (SIMS)

SIMS is developed and used for the analysis and imaging of chemical and biological systems, including advanced materials, single cells and biological tissue. The aim is to relate novel insights into the chemical and spatial organisation and function of these systems at the molecular level. Nick Lockyer and Professor John Vickerman are developing applications of SIMS in areas involving the characterisation and classification of cells and tissue at the molecular level. They are also working closely with industry to develop new instrumentation and analytical protocols to advance SIMS applications in biosciences.

The High Arctic camel on Ellesmere Island during the Pliocene warm period, about three-and-a-half million years ago. The camels lived in a boreal-type forest. The habitat includes larch trees and the depiction is based on records of plant fossils found at nearby fossil deposits.

CREDIT: Dr. Julius T. Csotonyi, scientific illustrator (csotonyi.com)
“This project will provide a new dimension to our understanding of early European agriculture and also inform work on the impact that future environmental change could have on the sustainability of modern cereal cultivation.”

Ramsay spectroscopy and cells: lighting up sub-cellular research

Raman spectroscopy is a physical-chemical method based on the interaction of light with matter. In Raman scattering a molecular vibration yields light of a different wavelength. This enables a very powerful and non-invasive analysis of the chemical and structural information of a sample; indeed one can use this to measure protein structure and posttranslational modifications. Moreover, it is highly sensitive and when coupled with atomic force microscopy (AFM) it has exquisite spatial resolution (<20 nm). In the MIB we are developing Raman to analyze cells and their components and this has recently been facilitated via three new approaches: (i) optical trapping of eukaryotic cells using Raman tweezers; (ii) coupling in situ cell growth facilities within the instrument so that drugs and metabolites can be mapped within cells; (iii) the very recent acquisition of an AFM-Raman system which shall be developed for tip enhanced Raman spectroscopy (TERS) imaging, following on from our pioneering work in bacterial surface enhanced Raman scattering (SERS).

Fingerprinting food

MB researchers using MALD-TOF-MS and chemometric approaches have found new applications as a fast and accurate viable bacterial detection and quantification method for routine use in the milk and meat industry. Major food adulteration and contamination events seem to occur with some regularity, such as the widely publicised adulteration of milk products with melamine and the recent microbial contamination of vegetables across Europe for example; and more recently the horsemeat scandal, which has rocked consumer confidence in the food supply chain. With globalisation and rapid distribution systems, these can have international impacts with far-reaching and sometimes lethal consequences. These events, though potentially global in the modern era, are in fact far from contemporary, and deliberate adulteration of food products is probably as old as the food processing and production systems themselves. Professor Roy Goodman’s critical review “Fingerprinting food: current technologies for the detection of food adulteration and contamination” features on the inside cover of the September 2012 edition of Chem Soc Rev. This review first introduces some background into these practices, both historically and contemporary, before introducing a range of the technologies currently available for the detection of food adulteration and contamination. These methods include the vibrational spectroscopies: near-infrared, mid-infrared, Raman; NMR spectroscopy, as well as a range of mass spectrometry (MS) techniques, amongst others. This subject area is particularly relevant at this time, as it not only concerns the continuous engagement with food adulterers, but also more recent issues such as food security, bioterrorism and climate change. It is hoped that this introductory overview acts as a springboard for researchers in science, technology, engineering, and industry, in this era of systems-level thinking and interdisciplinary approaches to new and contemporary problems.

Ribs from the female adolescent skeleton 4006 from St. George’s Crypt, Leeds. Bone formation possibly indicative of pulmonary TB is visible on the surface of the ribs within the area indicated by the boxes.
Manchester Centre for Biophysics and Catalysis (MCBC)

MCBC is a state-of-the-art cross-disciplinary platform technology centre integrating biophysical, structural, and computational methods to address contemporary problems in catalysis and the dynamical properties of biological macromolecules. The MB has recently emerged as a world-leader in integrated biophysics and catalysis, with capabilities spanning all aspects of biological structure determination, magnetic resonance spectroscopies, time resolved and single molecule spectroscopy and biological chemical computation. By going beyond simple structure determination of biological molecules MCBC is driving the new ‘dynamics determines function’ paradigm through temporal analysis of dynamic transitions relevant to biological function and catalysis from the femtosecond to second timescale.

MCBC is home to a number of platform technologies in the biophysical and catalysis areas. At Manchester we emphasize the integration of these technologies to address major biological challenges at the molecular level. This molecular insight is crucial in developing larger scale understanding of biology at the systems level. We also place emphasis on developing new technologies and the translation of molecular-based research. MCBC develops programmes with external partners in most areas of research expertise and works with a number of industrial partners ranging from SMEs to large pharmaceutical companies (ie. Shell, AstraZeneca, DSM, Tgk) on a range of projects. MCBC also works with instrument developers to generate next generation biophysical instruments, for example specialised applications in laser-induced red spectroscopy, high pressure NMR spectroscopy and high pressure optical spectroscopy. State-of-the-art facilities in the MB include: unattended facilities, bioengineering and evolution, chemical biology and synthesis, computation and theory, electron microscopy, electron paramagnetic resonance, laser facilities, microfabrication and nanotechnology, nuclear magnetic resonance, single molecule approaches, structural biology, time resolved spectroscopy and x-ray crystallography facilities.

Robots are already part of the pharma industry’s development process, but could they ever take over completely? Ross King, Professor of Machine Intelligence, and his colleagues have spent a decade developing Robot Scientists – machines designed to automate the discovery of scientific knowledge.

The King group built two Robot Scientists. “Adam” was designed to understand how the components of cells work together (functional genomics) and is the first machine to have discovered some novel scientific knowledge. New Robot Scientist “Eve” is designed to automate drug screening and design. Eve has been applied to the discovery of leads for neglected tropical diseases such as malaria, African sleeping sickness, Chagas disease etc.

“...the motivation for our work is partly philosophic and there is a strong view that holds that we do not fully understand a phenomenon unless we can replicate it. “What I cannot create, I do not understand” [Richard Feynman from The Universe in a Nutshell]. Automating science is an excellent test bed for AI as it involves formal reasoning with interaction with the real-world. However the most important motivation is that we wish to make scientific research cheaper and more cost-effective”.

Ross King
Professor of Machine Intelligence

The MIB pursues and is engaged in challenging research projects that enable us to make significant advances in science to benefit industry and society. Through innovative research, we can help you advance your business, solve technical problems, improve your processes, develop new products and build the technical capabilities of your staff. We understand the importance of adapting the approach to meet the needs of the project.

There are a number of ways for commercial businesses to benefit from the academic expertise fostered in the MIB. We run a successful programme of networking events with industrial partners and other stakeholders that focus on developing practical strategies to create short-term, mid-term and long-term relationships for mutual benefit. Our partnerships range from collaborative research programmes to joint studentships and instrumentation-technologies development across the chemical, biotechnology and biopharmaceutical sectors.

Collaborations
We actively engage with a wide range of companies from large pharmaceutical to smaller SMEs. Existing partnerships include companies from the Chemical, Biotechnology and Biopharmaceutical sectors as outlined in our research portfolio including Bruker, BASF, GSK, Novartis, Shell, Siemens, Solvay, Syngenta and Unilever.

We offer an unrivalled environment that presents opportunities for placements in industry across a variety of research disciplines. Our portfolio of industrially sponsored postgraduate studentships includes Bruker Ltd, Lonza, Unilever, AstraZeneca, Tgk, Christtech, Shell and GlassSmithKline.

We also host European biotechnology training networks in Industrial Biotechnology including P4fifty and BIOTRAINS, for the support for the chemical manufacturing industries and MAGIC (MAGnetic Innovation in Catalysis).

Benefits of collaborative research with MIB include:
• the cost effective trialling and testing of products, drugs and compounds using University facilities and expertise
• the development of close long-term relationships with academic staff to build a relevant and comprehensive portfolio of research and expertise needed to meet your company’s specific needs.
• the transfer of innovative techniques and practices from the laboratory to the manufacturing process
• the direct licensing of innovative technologies and processes
• the accessing of government and European Union funds for academic research that would be out of reach for purely commercial projects

INNOVATION IN ACTION
**Technology Transfer**

The University of Manchester Intellectual Property Limited (UMIP) assists in the commercialisation of any innovative technologies and processes that may be derived from collaborative research. UMIP has over a 20 year history of Intellectual Property (IP) commercialisation and works closely with MIB to ensure that any IP is fully developed to maximise technology transfer.

In the FY2012-13 the MIB has secured over 31 invention disclosures which represents a 48% increase from the previous year and filed 1 priority patent and 2 new licences.

**Spin-out companies**

**CAK**, known as Conformetrix, founded by Dr Andrew Almond, is focused on the optimisation of drug discovery and design using NMR-based technology to accurately solve bioactive three-dimensional molecular structures. Conformetrix Ltd and AstraZeneca signed a research collaboration agreement under which Conformetrix’s proprietary NMR-based technology will be applied across AstraZeneca’s pre-clinical therapeutic pipeline to enhance lead discovery and hit identification.

**Pharmakure**, founded by Professor Andrew Doig and Dr Farid Khan, launched in 2012 to explore new Alzheimer treatments through the screening of existing drugs. Pharmakure is a new drug discovery company focused on Alzheimer’s disease through the discovery of new uses for old drugs, offering great promise for delivering new therapeutic options to patient care.

**PeptiGelDesign** was founded in 2013 by Drs Aline Miller and Alberto Saiani. A new drug discovery company focused on exploring new Alzheimer treatments through the screening of existing drugs.

**Biotechnology YES 2012 - MIB team triumphs in National competition to be the biotechnology stars of the future**

Members of Jason Micklafford’s research group secured a place in the final of a national competition to find the entrepreneurial biocatalysts of the future. Matthew Styles, Anna-Winona Struck, Sarah Shepherd, Brian Law and James Leigh formed team Enzomax and beat off stiff competition from 377 competitors across 82 teams in five regional workshops held in October and November in the Biotechnology Young Entrepreneurs Scheme (Biotechnology YES) 2012 competition. The team flew the flag for Manchester in December at the UK finals held in London. Although the team did not scoop the top prize, which went to Calvitium Solutions, they were the category for “Best consideration of IP strategy” sponsored by Potter Clarkson.

Enzomax have a proprietary platform technology, known as Enzomax SHIELD™, which they use to deliver cost-effective solutions for maximising the performance of enzymes in industrial biotechnology.

**PepitoPeptiDesign** was founded in 2013 by Drs Aline Miller and Alberto Saiani. A new drug discovery company focused on exploring new Alzheimer treatments through the screening of existing drugs.
Research Institutes

The University has established a number of prestigious interdisciplinary Research Institutes in addition to existing specialist research centres and groups. Research institutes incorporate the acknowledged research strengths across the University into core research priorities. Researchers in the MIB have strong links with the following institutes:

Phantom Science Institute
www.manchester.ac.uk/pci

Institute for Science Ethics and Innovation
www.isi.manchester.ac.uk

Cancer Research UK Manchester Institute
www.cruk.manchester.ac.uk

Research Facilities

We have an impressive range of specialist research facilities in the MIB which are maintained by dedicated experimental officers offering flexible and tailored use of our facilities, ranging from walk-in service to formal collaborations. Services and equipment are available to University, academic and external users from academia and industry.

Protein Science – an integrated approach

The Protein Science Facility at the MIB provides a comprehensive set of facilities for the high level expression and purification of recombinant proteins.

Biophysics

Enquiries: Dr Deryn Hayes
deryn.hayes@manchester.ac.uk
Tel: +44(0)161 306 5159

The Biophysics Facility is one of the largest, academic ‘Kinetics and Spectroscopy’ facilities for bio-science research in the world and consists of over £1.5 million of state-of-the-art instrumentation. We offer cutting-edge biophysical equipment, which can be used to study many different chemical and biological processes over a range of timescales and temperatures. The facility is actively involved in a wide range of research topics and has contributed to a number of publications in a broad range of high impact journals.

The facility has developed the use of advanced spectroscopic tools to study catalysis, binding and structural dynamics of biological macromolecules, including advanced fluorescence techniques; Circular Dichroism (CD) spectroscopy; electrochemical approaches to probe redox properties of biological molecules using potentiometry apparatus; Fourier Transform Infrared (FTIR) spectroscopy; isothermal titration calorimetry (ITC) and surface plasmon resonance (SPR).

Complementary spectroscopic techniques are available in MIB in EPR spectroscopy (Steve Rigby) and Raman spectroscopy (Elwin Blanch/PhD Goodacre/Peter Gardiner). In addition to the above we offer a number of kinetic instruments to study biological and chemical reactions on the fs – sec timescale.

Manchester Protein Expression Facility

Enquiries: Dr Eddie McKenzie
edward.a.mckenzie@manchester.ac.uk
Tel: +44 (0)161 306 4170

The facility provides a comprehensive resource for the high level expression and scale-up production of recombinant proteins. Currently we offer a choice of four expression systems: bacteria, pichia, insect and mammalian cells. Depending on particular needs we are able to provide either small scale production facilities for biochemical analysis and antibody production or larger scale production for structural studies. Equipment includes:

• ATP/press Protein Purification systems;
• Biomek iP4 liquid handling robot;
• Syngene Chromatoimage imaging system and a 10 litre wavebag (GE Healthcare) for insect cell scale up.

The facility collaborates extensively across departments in the University that includes:

• Michael Smith building, AV HI, Stopford Building, St Mary’s Hospital, Patterson Institute and MIB.

External collaborators have been growing over the last two years now and some examples are: Sheffield University, Abcam, Syngenta, Takara & Heptares.

The protein expression team have recently been named on two successful grants (£210,000 EuReromics Eu FP7 Collaborative project & £157,000 from Kidney Research UK) with Professor Paul Brenchley at St Mary’s Hospital to study the role of the protein PLA2R in the disease membranous nephropathy.

Manchester Protein Structure Facility

Enquiries: Dr Colin Levy
colin.levy@manchester.ac.uk
Tel: +44(0)161 306 5185

X-ray crystallography utilises X-ray diffraction by single protein crystals to elucidate three dimensional structures at atomic resolution. The technique plays a pivotal role in understanding how individual amino acids interact with small molecule ligands and cofactors.

The facility provides a complete service pipeline, taking you from purified protein to crystal structure. Meeting the often rate limiting challenge of crystallization are two complimentary high throughput routine dispensing robots (Mosquito & Phoenix) allowing rapid screening and optimisation.

The facility also houses two rotating anode X-ray generators and associated data collection equipment. These in-house facilities are further supplemented with regular synchrotron access.

Nuclear Magnetic Resonance (NMR)

Enquiries: Dr Matthew Cripps
matthew.cripps@manchester.ac.uk
Tel: +44 (0)161 306 4229

Nuclear Magnetic Resonance (NMR) spectroscopy is one of the principal techniques used to obtain physical, chemical, electronic and structural information about molecules. It is a powerful technique that can provide atomic resolution information on the topology, dynamics and three-dimensional structure of molecules in solution and the solid state. The breadth and quality of information attainable from NMR measurements makes it unique among spectroscopic tools.

In March 2012 the MIB took delivery of a new 800 MHz Bruker NMR spectrometer, along with upgrades to existing 600 and 500 MHz spectrometers. These new additions to our facility will open up a substantial number of new research programmes focusing on the structures and dynamics of complex macromolecular systems.

We have close links with Bruker who have contributed four 4-year fully funded industrial PhD studentships.

MIB has both state-of-the-art very high field and more economical lower field instruments.

Computational Chemistry

Enquiries: Linus Johannisson
linus.johannisson@manchester.ac.uk
Tel: +44 (0)161 306 4559

Simulating protein function and dynamics using computational methodologies including protein dynamics & conformational change (MD simulations); free energy calculations (umbrella sampling, metadynamics); ligand binding ( Docking, metadynamics) and catalytic mechanisms (QM & QM/MM calculations).

Mass Spectrometry

Enquiries: Dr Raynald Spiess
raynald.spiess@manchester.ac.uk
Tel: +44 (0)161 306 5157

Gas-phase ion chemistry research provides an enhanced understanding of the analytical techniques that underpin proteomics, metabolomics and the investigation of other molecules of biological significance. New developments in quantitative mass spectrometry provide much needed information for modelling of biological networks, while techniques are being developed to aid in the analysis and quantification of a variety of post-translational modifications.

Additional capabilities include:

• Mass Spectrometry (including Secondary Ion Mass Spectrometry (SIMS) and Fourier Transform Ion Cyclotron Resonance (FTICR), Electron Paramagnetic Resonance (EPR), Infrared and Raman Spectroscopy, Fluorescence Spectroscopy (including anisotropy decay).

Secondary Ion Mass Spectrometry (SIMS)

Enquiries: Dr Nick Lockyer
nick.lockyer@manchester.ac.uk
Tel: +44 (0)161 306 4479

SIMS is developed and used for the analysis and imaging of chemical and biological systems, including advanced materials, single cells and biological tissue. The aims involve novel insights into the chemical and spatial organisation and function of these systems at the molecular level.

Nick Lockyer and John Vickerman are developing applications of SIMS in areas involving the characterisation and classification of cells and tissue at the molecular level. They are also working closely with industry to develop new instrumentation and analytical protocols to advance SIMS applications in biosciences.

Bioimaging Facility

Olympus BX51 upright fluorescence snapshot microscope for routine fixed specimen imaging and specialised microscopes including multimode-picoscope atomic force microscopy (AFM); IPX: cellimaging AFM; TAM: Toluidine Blue Imaging for scanning fluorescence and subcellularised gels and an Olympus BX51 upright fluorescence snapshot microscope with colour and monochrome cameras.

In addition a large selection of confocal and specialist microscopes are available in the Michael Smith Building Biomaging Facility.

Bionanotechnology and Imaging

Enquiries: Dr Steven Mardan
steven.mardan@manchester.ac.uk
Tel: +44 (0)161 306 5186

This facility includes instrumentation for the imaging, manipulation or measurement of single biomolecules or single molecule biochemical reactions. Recent AFM projects include imaging of graphene on silicon oxide in air, fixed xenopus embryos in PBS, protein fibrils, mcsin, gold nanoparticles, etched troughs and pits in silicon, and to end protein stretching and a selection of cell and surface indentation experiments on the IPX:cellimaging AFM.

The facility offers a range of microscopes for routine fixed specimen imaging and specialised microscopes including multimode-picoscope atomic force microscopy (AFM); IPX: cellimaging AFM; TAM: Toluidine Blue Imaging for scanning fluorescence and subcellularised gels and an Olympus BX51 upright fluorescence snapshot microscope with colour and monochrome cameras.

In addition a large selection of confocal and specialist microscopes are available in the Michael Smith Building Biomaging Facility.

Mass Spec@Manchester

Mass spectrometric research has a long and rich history at The University of Manchester. In this network we attempt to bring together the experience and expertise of these researchers under one umbrella.

Bioimaging Facility
**POSTGRADUATE AND TRAINING**

The MIB offers a unique environment to carry out multidisciplinary research with open-plan laboratory and write-up areas designed to promote open communication between researchers from diverse and hybrid scientific backgrounds. Home to over 250 PhD students and 80 MSc students we endow our interdisciplinary investigators with the key skills to enable them to work successfully across the disciplinary interfaces at the forefront of biotechnology.

In addition to the traditional UK doctoral training programmes we host a number of EU training networks (P4FIFTY, Biocatalysts and MAGIC). Students join a vibrant and dynamic international community of researchers and students from across the EU and around the world including China, Egypt, Saudia Arabia, India, Pakistan, UAE, Mexico, Chile and Thailand amongst others.

We offer an unrivalled environment that presents opportunities for placements in industry across a variety of research disciplines. The MIB team has successfully developed new methods for catalysis have a key role and they are necessary for screening libraries generated either from sampling the biosphere or from divergent generation methods. The technique suitable for HTS must be rapid and cost effective and reflecting the desired functions.

In the search for new enzymes and biocatalysts, high-throughput screening methods for catalysis have a key role and they are necessary for screening libraries generated either from sampling the biosphere or from divergent generation methods. The technique suitable for HTS must be rapid and cost effective and reflecting the desired functions. The MIB team has successfully developed new fluorescence based HTS methods for several biocatalytic reactions. This HTS method will be used to screen bacterial, plant, fungal (and their mutants) P450 libraries for hydroxylation activity against a set of standard compounds which have to give specific reaction with human P450s. Another aspect of MIB efforts will be to develop P450s active in both conventional and alternative solvents (such as fluorinated solvents) providing engineering solutions for large scale application to be investigated.

The mechanistic importance of coupled motions and quantum chemical effects. In turn these novel methods will transform current experimental capabilities and will be applied to a range of important biological catalysts to probe the mechanistic importance of coupled motions and quantum chemical effects. In turn these novel methods will transform current experimental capabilities and will be applied to a range of important biological catalysts to probe the mechanistic importance of coupled motions and quantum chemical effects.

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**MAGIC** brings Marie Curie success to Manchester

The concept of team-based activity is well founded across research groups in MIB-PSI and will enrich the training experience bringing multiple skills embedded in these teams to MAGIC programmes. These novel methods will transform current experimental capabilities and will be applied to a range of important biological catalysts to probe the mechanistic importance of coupled motions and quantum physics-chemical effects. Innovative physical sciences magnetic resonance techniques (NMR and EPR) will be developed and implemented in a life sciences context to contrast studies of enzyme mechanisms and catalysis, and ultimately rational design.

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**“Our aim is to train the future generation of leading investigators of biological catalysis/ enzymes with a view to developing new enabling technologies that can advance physical understanding of catalysis and mechanism. Collaborative research projects will explore the mechanistic detail of enzyme systems by adopting innovative, versatile and unique experimental techniques to probe the contributions of motions across multiple spatial and temporal timescales and quantum chemical effects.”**

Professor Nigel Scrutton

Director

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**“The MIB has a reputation for pushing the boundaries in technology development and innovation. I was delighted to join the MIB as it promotes interdisciplinary, challenge oriented science that is supported by an outstanding structural biology infrastructure.”**

Claudio Santos

Ph.D Biochemistry, 2nd Year Bruker Studentship

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**“The MIB is an exhilarating environment in which to carry out research, I enjoy associating with peers from around the world, and the up-to-date facilities mean the research undertaken here is of the highest quality. I also believe that the integration of different experimental approaches provides a key advantage over other competing groups and institutions.”**

Alex Geddes

Ph.D Biochemistry, 2nd Year Bruker Studentship
BIOTRAINS – leading the green chemical training push

The ‘European biotechnology training network for the support of the chemical manufacturing industries’ (BIOTRAINS) programme brings together microbiologists, enzymologists, chemists, engineers and process development experts involved in the training of the next generation of scientists who will develop green manufacturing methods for the chemical industry. Led by Professor Nicholas Turner, Director of the Centre of Excellence for Biocatalysis, Biotransformations and Biocatalytic Manufacture (CoEBio3: www.coebio3.org), this four-year project involves eleven partners from academia and industry who will recruit and train research fellows and another six industrial partners who are offering placement training that is expected to make a major contribution to efforts to replace traditional chemical manufacturing – reliant on highly toxic chemicals and solvents – with so-called ‘white biotechnology’. The term covers the manufacturing of chemicals, alternative energy and biomaterials and has the potential to enable economies to become less dependent on fossil fuels by employing the power of natural biocatalysts and modern manufacturing techniques to deliver safer and less-environmentally damaging industrial methods. It is a term used mainly in Europe for the application of nature’s catalysts, such as enzymes and cells, in biotechnology for industrial purposes. The use of the word ‘white’ distinguishes it from other biotechnologies such as ‘red’ (medicinal) and ‘green’ (plant) biotechnology.

SCIENCE AND SOCIETY
Informing... consulting... collaborating

We work closely with the University Public Engagement team, Manchester Museum and the Museum of Science and Industry (MOSI) to deliver events and activities including the Manchester Science Festival and National Science and Engineering week.

We continue to host students as part of the Nuffield Bursary Placement Scheme enabling students to work alongside professional scientists, technologists, engineers and mathematicians. In particular the scheme encourages from schools in difficult social circumstances, and students who do not have a family background of higher education or STEM professions.

On Friday 9 November 2013 the MIB opened its doors to 200 A-A/S students from 12 schools/colleges from across the North of England providing them with a unique opportunity to visit a world class interdisciplinary research institute. Students witnessed and participated in a number of activities throughout the day including interactive research stands followed by guided tours of the research laboratories with an opportunity to talk with researchers about their work. MIB postdocs and research students developed a number of laboratory demonstrations that covered topics as diverse as NMR, protein expression and robotics. A variety of interactive stands showcased the rich array of MIB research from the developing enabling technologies (including micro fluidics, nanotechnology and spectrometry/spectroscopy), protein science and genomics through to systems and computational biology.


Tour demonstrations included: Protein Structure | Mass spectrometry | NMR | Protein Expression | Robotics | Enzyme reactions.

"... a distinctive feature of the University is its commitment to a social responsibility agenda. This ethos is embedded in our outreach activity at the MIB and we are committed to engaging with our wider community with the aim of increasing awareness, interest, and understanding of science and hopefully inspiring the next generation of scientific leaders."

Dr Rosalind Le Feuvre
MIB’s Research and Planning Manager
The stand demonstrated how the study of carbohydrates such as sucrose, starch, pectin and alginate can help improve many aspects of our lives from producing renewable energy and materials to generating new medicines. How cell sugars interact with foreign molecules have applications in a variety of areas, including improving human fertilisation therapies, developing anti-flu medicines and diagnostic tools, and creating new anti-cancer treatments. Identifying the difference in glycoalyx between cells can help scientists distinguish between pandemic, seasonal and bird flu and develop the correct therapies for flu outbreaks. As the glycoalyx also differs between individuals, it provides a method for producing advanced diagnostic tools for personalised medicines. One of the main exhibition activities was focused on cell surface sugars and visitors were encouraged to build a cell surface sugar and explore its interaction with cell invaders both on a cell surface and also a gold glycan array. This activity was very popular and designed to highlight and directly promote the GlycoBioM work. As part of the exhibition the team also commissioned a three minute animation which provided an introduction and overview of the whole area of carbohydrate science. This video has since had over 700 views. They were also successful in the Royal Society Games Jam competition with their game, ‘Cell Invaders’, which was voted the best game at the exhibition and won £2,000 worth of development and is now available to download on PC and iPad.

“it was very exciting to be selected to exhibit at the Royal Society and we very much enjoyed interacting with the students. Our exhibit demonstrated how the study of these sugars can help improve many aspects of our lives from producing renewable energy and materials to generating new medicines. Understanding the glycoalyx and its interaction with other molecules will provide a wide range of opportunities for the development of new foods, medicines and healthcare treatments”

Sabine Flitsch
Professor of Chemical Biology

Faculty of Life Sciences

ALKON, Andrew - 3D-structure and function of biologically important oligosaccharides and polysaccharides.
BELLA, Jordi - extracellular matrix proteins: structure, design possibilities and biomaterial applications.
BLANCH, Ewan - biophysical single molecule analysis using Raman spectroscopy.
BREITLING, Rainer - metabolomic systems biology and postgenomic data analysis.
BROWN, Terry - biomolecular and structural biology using DNA to study the past.
BUCKLEY, Mike - determination of species-specific biomarkers in bone for studying vertebrate palaeobiodiversity.
DIXON, Neil - function of biologically important oligosaccharides and polysaccharides.
DOIG, Andrew - protein structure, bioinformatics, amyloidosis.
GOLOVANOV, Alexander - biology: structure, mechanism and engineering of new properties.
HAY, Sam - quantum and theoretical biophysics.
HAYES, Finbarr - molecular engineering of a DNA trafficking nanomachine.
LEY, David - structural biology to look at new metabolic pathway novel enzymes systems; structural insights guide rational engineering/synthetic biology applications.
LU, Hui - redox regulation and biogenesis of mitochondrial proteins.
MUNRO, Andrew - structure and enzymology of biotechnologically and biomedically relevant redox enzymes.
PRINCE, Steve - structural biophysics of membrane-proteins and protein-protein interactions.
RIGBY, Stephen - biological electron paramagnetic resonance (EPR) spectroscopy and related techniques.
SCRUTTON, Nigel - enzyme biophysics, structure and mechanism, enzyme engineering, enzyme biocatalysis, biofuels.
TAKANO, Eriko - synthetic biology of bioactive molecules/antibiotics.
WARWICKER, Jim - models for structural cell biology.

Faculty of Medical and Human Sciences

BAYAT, Ardeshir - wound healing, tissue repair & regeneration, biological engineering.
MILLS, Clare - why are some proteins allergens and not others; what makes certain types of foods or pollens more allergenic; why do only some people become allergic?

Institute of Population Health

DAY, Philip - single cell analyses within heterogeneous populations of cancer cells.
Faculty of Engineering and Physical Sciences

School of Chemical Engineering and Analytical Science

CURTIS, Robin - weak protein-protein interactions, protein aggregation, bioprocessing, biomolecular thermodynamics.

De VISser, Sam - computational studies of enzyme mechanism and function.

GARDNER, Peter - vibrational spectroscopy of bio and biomedical systems.

GODDARD, Nick - microfluidics; sensors (electrochemical/optical); high throughput platforms; microexposures (electrokinetics); multiphase microfluidics; micro- and nano-fabrication.

MILLER, Alina - application of physical principles to mimic, manipulate and improve biomolecular self-assembly to create materials for regenerative medicine.

SUTcliffe, Mike - computational enzymology & protein modelling.

WESTERHoff, Hans - integrative systems biology.

YUAN, Xue-Feng - rheology of complex fluid/soft matter such as biofluids and biomaterials in living system: quantitative rheological and structural characterization under physiological conditions, integrated multiple scale modelling.

School of Chemistry

BARRAn, Perdita - mass spectrometry, instrument development and RMMS fundamentals.

FLITSCH, Sabine - glycosciences and biocatalysis.

GARDNER, John - carbohydrate chemistry/chemical biology, biocatalysis, dendrimer synthesis and heteroacryc biocorganic chemistry.

GOODACre, Roy - integrative omic analyses and vibrational spectroscopy for understanding biological systems.

HENCHMAN, Richard - biomolecular structure and dynamics.

KEANE, John - development of clinical decision support systems (DSS) and analytics of multi-modal (structured, semi-structured, unstructured, image) data for bio-health applications.

KELL, Douglas - development and application of novel analytical methods at the interface between postgenomic biological systems, quantitative bi analytical science and machine learning, with a special emphasis on evolutionary computing and systems biology.

LOCKyer, Nick - imaging Mass Spectrometry (SIMS), instrument development.

MICKLEFIELD, Jason - chemical biology and synthetic biology.

POPELler, Paul - predictive modelling of structure and dynamics from first principles; drug design; chemical insight from modern wave functions.

TURNer, Nicholas - discovery and directed evolution of tailored biocatalysts: applications in industrial biotechnology including fine chemicals, pharmaceuticals and biofuels.

WEBB, Simon - supramolecular chemistry, biomimetics, understanding biomembrane behaviour, biosensor design.

WONG, Lu-Shin - combining chemical biology and nanotechnology applications in the life sciences: Biocorporation and surface behaviour towards nanoscale protein arrays.

School of Computer Science

ANANIADOU, Sophia - biomedical text mining, information extraction, terminology management, semantic interoperability of resources.

KING, Ross - interface between computer science and biology/chemistry.

MCAUGHT, John - text mining.

MENDES, Pedro - computational systems biology.

NENADIc, Goran - text mining and automatic knowledge structuring (ontologies, concept maps) in life sciences and health-care.

School of Materials

BLAnFORD, Chris - sensitive measurements of protein-surface interactions in electrocatalyst enzymes.

SAIANI, Alberto - understanding the chemical architecture - thermodynamics - structure - physical property correlations in complex polymeric systems.

School of Mechanical, Aeronautical and Civil Engineering

BArTOLO, Paulo - biomaterials and mechanical design of scaffolds for tissue engineering.

School of Biomedical Sciences

MIB Fellowship Opportunities

The MIB actively promotes new career track research fellowships at the interface between engineering, the physical sciences and bioscience. Applications are encouraged from proactive individuals keen to participate in interdisciplinary research and interact in key societal and strategic research areas of interest to the MIB. For further information on our fellowship scheme visit our web pages at www.mib.ac.uk.

Our research facilities are outstanding offering a unique infra-structure, research environment and culture, all specifically designed to remove the barriers between disciplines and to promote innovative science.

We offer an attractive fellowship extension scheme for fellows bringing in 4-5 years of external funding (regardless of the source of the fellowship, BBSRC/EPSRC etc), whereby we will top up fellowships by 1 or 2 years additional support. We are confident in the quality of the fellows we wish to recruit and recognise the importance of stability at this career stage to enable our fellows to reach their full potential. Additional start up monies may also be available depending on the nature and level of the externally funded research fellowship. These fellowships are seen as early stage entry into independent academic careers at Manchester. Throughout the 6-year period you will benefit from close manager and mentor support from senior colleagues in the MIB. You will become a member of one of the University Faculties – Human and Medical Sciences (HMS), Life Sciences (LS) or Engineering and Physical Sciences (EPS).
Douglas Kell was awarded a CBE for services to science and research in the Queen’s New Year Honours 2014. He has been a pioneer in many areas of computational biology and experimental metabolomics, including the use of evolutionary, closed-loop methods for optimisation. He also contributed to the discovery of the first bacterial cytokine, currently on trial as part of a vaccine against tuberculosis.

Douglas studied at Oxford University focusing on the development and exploitation of novel methods for the study of (mainly microbial) bioreactivities. He was awarded a Personal Chair at the University College of Wales (now Aberystwyth University) in 1992 and from 1998-2002 was Director of Research at the Institute of Biological Sciences. He co-founded Aiber Instruments, that received the Queen’s Award for Export Achievement in 1998.

In 2002 he accepted an RSE/ESRC-funded Chair in Bioanalytical Sciences at UMIST. From 2005-2008 he was Director of the Manchester Centre for Integrative Systems Biology at The University of Manchester. From 2008 until 2013 he was Chief Executive of the Biotechnology and Biological Sciences Research Council (BBSRC).

He has a Doctor of Science Honoris Causa from Cranfield University (2011), and is a fellow of the Learned Society of Wales (2012), of the American Association for the Advancement of Science (2012), and of Aberystwyth University (2013). He has published over 400 scientific papers with 18,000 citations in WoK (H-index 72). In Google Scholar H=83 and citations >26,000.

Douglas Kell is Professor Douglas Kell CBE MSc DPhil FSB FLSW FAAAS Chair in Bioanalytical Science. He is a fellow of the Learned Society of Wales (2012), of the American Association for the Advancement of Science (2012), and of Aberystwyth University (2013). He has published over 400 scientific papers with 18,000 citations in WoK (H-index 72). In Google Scholar H=83 and citations >26,000.

### Selection of Publications

  - doi: 10.1038/nature12039

- **Bredt J, Bʌy AK, Lypkiń B, Kell DB. Prestosia E. High fertiliy limits have major effects on the morphology of epithyothes in Alzheimer’s disease. Front Aging Neurosci. 2013 5:86.**
  - doi: 10.3389/fnagi.2013.00088

  - doi: 10.1039/c3cc48065j

  - doi: 10.1038/ncomms14188

  - doi: 10.1038/nchem.1817

  - doi: 10.1073/pnas.1209444109

  - doi: 10.1021/ac303265q

  - doi: 10.1038/ncomms1889

  - doi: 10.1038/ncomms1889

  - doi: 10.1038/embor.2012.116

  - doi: 10.1039/c2cs35573b

  - doi: 10.1021/ja4051235

  - doi: 10.1021/ja4051235

  - doi: 10.1039/c3nr06181a

  - doi: 10.1039/c3nr06181a

  - doi: 10.1016/j.tibtech.2013.05.004

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**Douglas Bártolo joins the MIB**

Professor Paulo Bártolo BEng, MSc, PhD Chair in Advanced Manufacturing

Paulo Bártolo joins the MIB in Spring 2014 from Polytechnic Institute of Leiria, Portugal. Paulo holds a PhD degree in Polymer Physics from the University of Reading (UK) and a Master of Science and Licenciatura in Mechanical Engineering, both from the Technical University of Lisbon (Portugal). His research interests focus on biomaterial manufacturing and computer-aided design of scaffolds for tissue engineering. He developed different bottom-up and top-down approaches for bone, cartilage and skin applications. The design of smart and functionally graded scaffolds to promote tissue interfaces is also an important topic of his research. He investigated the relationship between the material processing and the mechanical, biological and degradation characteristics of scaffolds, as well the fabrication of scaffolds with controlled oscillotropy. Different materials (PCL, PLA, PCL/PLA, PCL/HA, PCL/TPC, PC/Phospholipids, PC/bioglass, Alginate, Dextran) and cell lines (fibroblasts, keratinocytes, osteoblasts, chondrocytes and hMSCs) were used in their research works.

Paulo Bártolo is author and co-author of more than 400 publications in journal papers, book chapters and conference proceeding papers. He also edited 13 books and holds 10 Portuguese Patents. His research work has been published in high impact factor journals like Progress in Polymer Science, Nanomedicine, Acta Biomaterialia, Biofabrication Journal, Carbohydrate Polymers. He is also Editor-in-Chief of Virtual in Physical Prototyping Journal published by Taylor&Francis, and member of the Editorial Board of several Journals like the Biofabrication Journal, the Rapid Prototyping Journal, the International Journal of Precision Engineering and Manufacturing, the Journal of Biomaterials and Tissue Engineering, the IBRM Tissue Engineering and the International Journal on Mechatronics and Manufacturing Systems.


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