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# Editorial

*Foreword by Professor Mike Hoare*

Welcome to this first edition of *BioProcessing Matters*.

UCL and the Advanced Centre for Biochemical Engineering have always driven research excellence and this newsletter provides a snapshot of some of the bioprocess leadership activities currently being undertaken with our industrial partners.



This particular edition focuses on current research from our Innovative Manufacturing Research Centre (IMRC), Bioconversion-Chemistry-Engineering Interface (BiCE) and Regenerative Medicine (ReMeBio) programmes, such as our DTI-funded project with Plasticell and the National Institute for Biological Standards to develop robotics for the automation of stem cell research. Additionally, we are delighted to announce that our MBI® Training Programme is going from strength to strength with the development of a new Design of Experiments for Bioprocess Optimisation module and the launch of four e-learning modules.

Whatever your interests, we hope that this newsletter gives you a real insight into how the Centre is leading the way in turning the UK into a bioprocess design workshop for the world.

If you would like to find out more about any of the stories, follow the web links at the end of each article or contact us by email using the addresses provided.

A handwritten signature in black ink that reads "Mike".

*Mike is Professor of Biochemical Engineering, Head of the Department of Biochemical Engineering and Director of The Advanced Centre for Biochemical Engineering. He is a Fellow of the Royal Academy of Engineering and of the Institution of Chemical Engineers.*



## Department news

**Dr Farlan Veraitch** joined the Department in July 2006 as a Lecturer. Farlan studied for his MEng in Chemical with Biochemical Engineering here at UCL and then obtained his PhD in Genetic Optimisation of Mammalian Cell Bioprocesses from Birmingham University. His research interests include automation of stem cell isolation, expansion and differentiation; downstream processing of differentiated stem cells; dynamic control of the physiological environment during expansion and directed stem cell differentiation; mechanically induced signalling pathways and their impact on stem cell phenotype; nutritional requirements of stem cells and their derivatives and the development of scalable biphasic co-culture systems. He has a central role in the delivery of both the Mammalian Cell Processes and Stem Cell & Regenerative Medicine Bioprocessing MBI modules. Please feel free to contact him on 0207 679 2648 or email him at [f.veraitch@ucl.ac.uk](mailto:f.veraitch@ucl.ac.uk).

**Dr Karen Smith** joined the Department in October 2006 as the Director of Bioprocess Leadership. She comes from the University of Cambridge where she was the Business Director of the Computational Biology Institute and the Acting Head of the Partnership Group (Corporate Liaison Office). Karen has worked for many years with the pharmaceutical and biotechnology industries as a senior consultant with Ernst & Young and IMS Health Global Consultancy. Karen's role involves responsibility for enhancing bioprocess leadership activities across the department and expanding sponsor relationships through vehicles such as MBI<sup>®</sup>, ReMeBio, BiCE and the IMRC. She has two Masters degrees and a PhD in Neuroscience from Emmanuel College, Cambridge, and has published numerous scientific papers and thought leadership articles. Please feel free to contact her on 0207 679 4411 or email her at [karen.smith@ucl.ac.uk](mailto:karen.smith@ucl.ac.uk).

**Dr Nicolas Szita** joined the Department in February 2007 as a Senior Lecturer. Nicolas has come from the Technical University of Denmark (DTU) where he was an Associate Professor in the Biochemical Microreactors Group at the Department of Micro and Nanotechnology. Nicolas did both his Diploma Degree in Mechanical Engineering and his Doctorate Degree in Microtechnology at ETH Zurich in the Department of Mechanical and Process Engineering. For his doctorate he designed and realized a micromachined pipetting device for the rapid handling of (sub)microlitre volumes in collaboration with Roche Diagnostics Division and Hamilton Bonaduz, Switzerland. In 2001, he joined Klavs Jensen in the Department of Chemical Engineering at MIT, where he was working on miniaturized bioreactors in collaboration with DuPont. He was also responsible for the evaluation and definition of a Laser Micromachining System. His research interests are in Bioprocess Microfluidics. Please feel free to contact him on 020 7679 4418 or email him at [n.szita@ucl.ac.uk](mailto:n.szita@ucl.ac.uk).

The MBI® Training Programme is run by the Department and comprises a series of UCL-accredited short courses in bioprocessing, designed specifically for industrialists. They can be taken as stand-alone modules or can be combined for certificate, diploma or Masters qualifications. To date 1,000 modules have been taught to over 700 international delegates, and more than 200 companies have participated.

## Department wins LDA support for MBI®

The LDA is the Mayor's agency responsible for driving London's sustainable economic growth – it works to ensure that London remains a global success story. To help it deliver this it works closely with partners from industry, public and voluntary sectors. Work is prioritised by four themes: Regenerating London, Supporting People, Encouraging Business and Marketing.

We are delighted that the LDA has decided to support the following initiatives.

**The London Development Agency MBI® Voucher Scheme:** to grow bioprocess leadership in the region; the LDA will, over the next three years, provide vouchers (worth 75% of module fees) to employees of London-based SMEs to undertake an MBI® module of their choice. These vouchers are worth in excess of £1,000 each and will be available on a first-come-first-served basis. For further information please email [mbi-training@ucl.ac.uk](mailto:mbi-training@ucl.ac.uk).

**The London Development Agency/UCL MBI® Diploma Competition:** this competition will be open to employees of SMEs based in London. It will cover all course fees associated with obtaining a UCL post-graduate Diploma in Bioprocessing via the MBI® route. This prize has a value in excess of £15,000 and will provide the recipient and their company with a wide range of scientific and industry insights and benefits associated with this pioneering course from a world-leading Department. A senior level panel led by Prof. Mike Hoare (UCL) will assess entries and a winner will be announced in July 2007. Details of how to enter the competition will be available shortly.

If you would like to express an interest, please contact Dr Karen Smith at [karen.smith@ucl.ac.uk](mailto:karen.smith@ucl.ac.uk).

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A G E N C Y

WORKING FOR THE MAYOR OF LONDON

# New training initiative from BioProcess UK for MBI® support

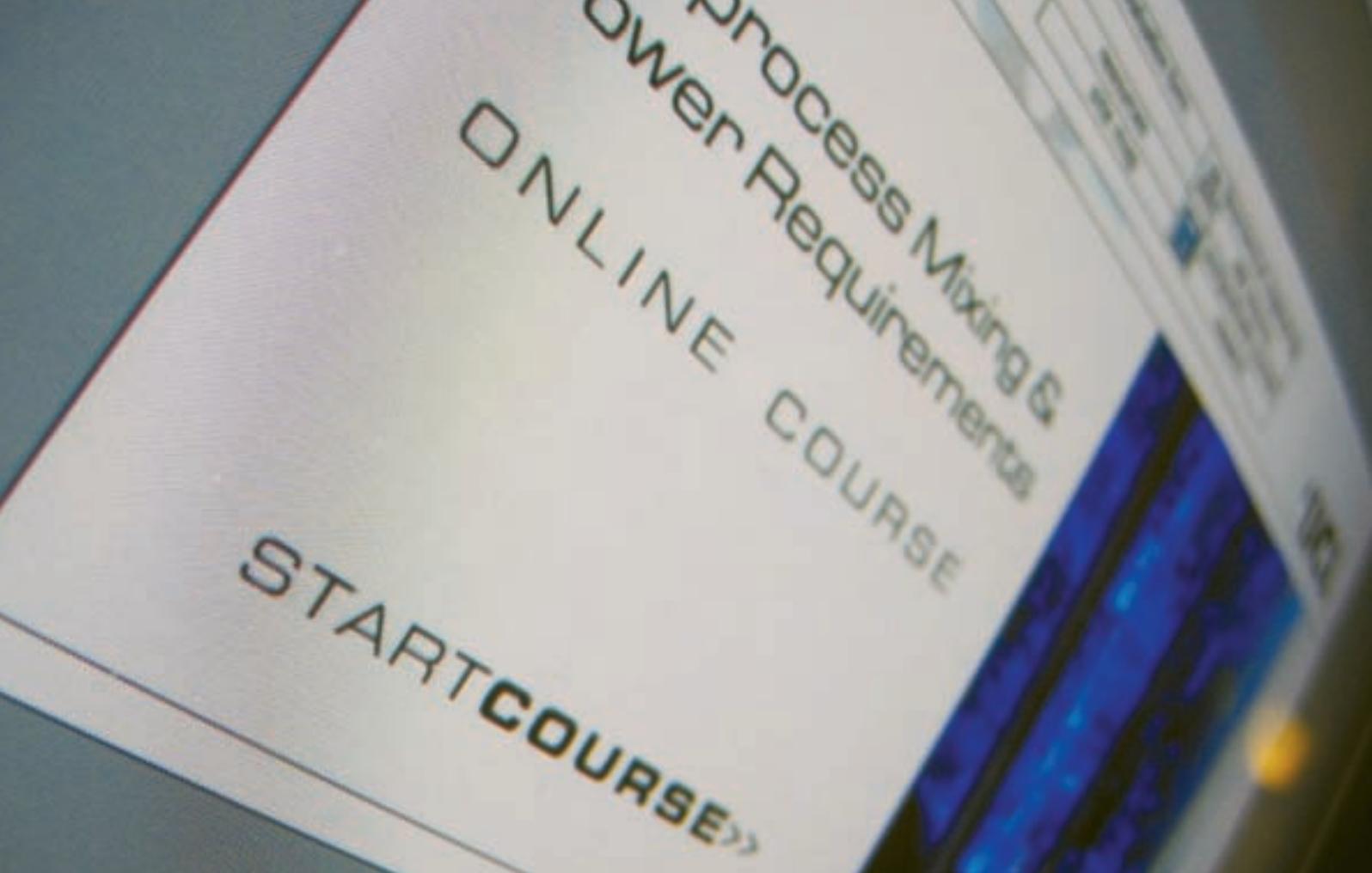
Thanks to the generous support of the South Eastern Health Technologies Alliance (SEHTA), BioProcess UK has been able to offer a limited number of free delegate places on MBI® modules to small-to-medium sized companies within the South East of England Development Agency (SEEDA) region.

Dr Tony Bradshaw, Director of BioProcess UK, said, “Such initiatives are key to developing bioprocess leaders of the future and strengthening bioprocessing capabilities in the South East”. Several eligible companies have taken advantage of the offer including Avidex, Capsant, Emergent, iQur and ReNeuron.



*Tim Hughes of Genentech leading a 'real-life' Validation case study exploring major processing difficulties in the production of biological product.*





## Providing interactive online learning for the Bioprocessing industries

As the world's largest provider of trained biochemical engineers for the bioprocess industries we've helped literally thousands of delegates from hundreds of companies get the training in bioprocessing that they need to get on in their careers via our traditional 'on site' MBI® modules.

We are delighted to announce the launch of our first four e-learning modules:

- Bioproducts Recovery and Loss: A study of recovery of fermentation broths using centrifuges or membrane filters
- Successful Biomaterial Transfer, Pumping and Flow to Chromatography Columns
- Successful Bioreactor Temperature Management
- Successful Bioreactor Mixing

"Each module is designed to help delegates reach their goals working either from home or in their own workplace. The modules have been developed in collaboration with MDC and with the support of Scottish Enterprise, and each has been tested extensively at UCL to ensure ease of use and quality of content. We believe the modules represent a significant innovation in the bioprocess leadership space and we hope that individuals and companies find them valuable training tools!" Dr Karen Smith, Director of Bioprocess Leadership.

Please contact [mbi-training@ucl.ac.uk](mailto:mbi-training@ucl.ac.uk) for further details.

# Major research initiatives

The MBI® training programmes provide a crucial knowledge transfer route for advanced bioprocessing research. For information on UCL's bioprocessing research activities, see [www.ucl.ac.uk/biochemeng/research](http://www.ucl.ac.uk/biochemeng/research)

## Regenerative Medicine Bioprocessing (ReMeBio) Group win major DTI funding

*Dr Chris Mason*

The UCL Advanced Centre for Biochemical Engineering, Plasticell Ltd and the National Institute for Biological Standards and Control (NIBSC) have received £1.1 million in funding from the Department of Trade and Industry's Technology Programme in a major boost for stem cell research in the UK.

The funding is for a collaborative project to develop robotics to automate stem cell research. This new technology will greatly increase the number of experiments stem cell researchers can conduct simultaneously. Currently, a single scientist can only conduct a handful of experiments at one time. The aim of the project is to enable thousands of experiments to be conducted in parallel using far smaller quantities of materials (ultra scale-down). London-based biotechnology company Plasticell Ltd is developing drugs to regenerate tissues of the body. By collaborating with the Advanced Centre for Biochemical Engineering, the firm will be able to automate its novel stem cell platform technology, CombiCult™. The consortium also includes the NIBSC which will provide advanced imaging methods.

The robotic equipment to be utilised in the project will enable researchers to test the effects of thousands of different factors and combinations of factors – such as growth, nutrients, hormones, or physical conditions – on how stem cells differentiate, or how they give rise to tissue cells like lung, heart, brain cells which can be used clinically. Plasticell calls this technology Combinatorial Cell Culture™.

Minister for Science and Innovation, Malcolm Wicks, said: “The UK is an acknowledged leader in the field of stem cell research and we want to ensure that the UK remains at the forefront. That's why we're supporting the Plasticell consortium on this project, which provides a great opportunity to harness the UK's world-class expertise and use it to boost our economy and, potentially, our health. Stem cell research has tremendous potential to tackle some of the most devastating diseases. It could benefit patients with conditions such as Parkinson's disease, juvenile diabetes and heart disease.”

*Chris is a Senior Lecturer and Fellow of the Royal College of Surgeons. See page 11 for the Stem Cell and Regenerative Medicine Bioprocessing MBI® course.*





## The Innovative Manufacturing Research Centre (IMRC) for Bioprocessing

*Professor Nigel Titchener-Hooker*

It is acknowledged across the global biopharmaceutical industry (human proteins, genes and vaccines produced by recombinant methods) that time to market must be significantly reduced for these very expensive medicines. Reducing development costs will allow product costs to be lower in a highly competitive global climate. This would allow broader markets to be created and gains to be achieved for more than a minority of patients. The purpose of the EPSRC-funded IMRC Bioprocessing programme which commenced in 2002 with ten industry partners and twelve academics both within UCL and beyond, is to create experimental and design methods to change fundamentally the way in which such bioprocesses are developed for the manufacture of next-generation biopharmaceuticals. The MBI Programme provides a major knowledge transfer forum for these activities especially the Effective Biopharmaceutical Development and Manufacture and the Primary Recovery and Chromatography modules.

The IMRC methods allow bioprocessing options to be studied at the early stages of the biopharmaceutical development pathway in parallel to preclinical and clinical trials and when only small quantities of test material are available for study. By working with industrial partners we can test the capabilities of the IMRC tools on their own systems and provide feedback for their verification or refinement. The maximum value of IMRC tools will be realised if early prediction of robust and reliable bioprocesses allows speed to market to be gained at the stage of large scale bioprocess development. Each day lost at this stage leads to irretrievable loss of over £1 million to a company engaged in developing a major biopharmaceutical product with its limited period of exclusivity and high profitability.

*Nigel is Professor of Biochemical Engineering, Director of Engineering Doctorate Programme (EngD), Director of IMRC and Co-Director of The Advanced Centre for Biochemical Engineering. For further information see [www.ucl.ac.uk/biochemeng/industry/imrc](http://www.ucl.ac.uk/biochemeng/industry/imrc)*

*This ultra-scale down device has been successfully used with IMRC company partners to predict full-scale processing of sheer sensitive biological material.*

## The Bioconversion-Chemistry-Engineering Interface Programme (BiCE)

Professor Gary Lye

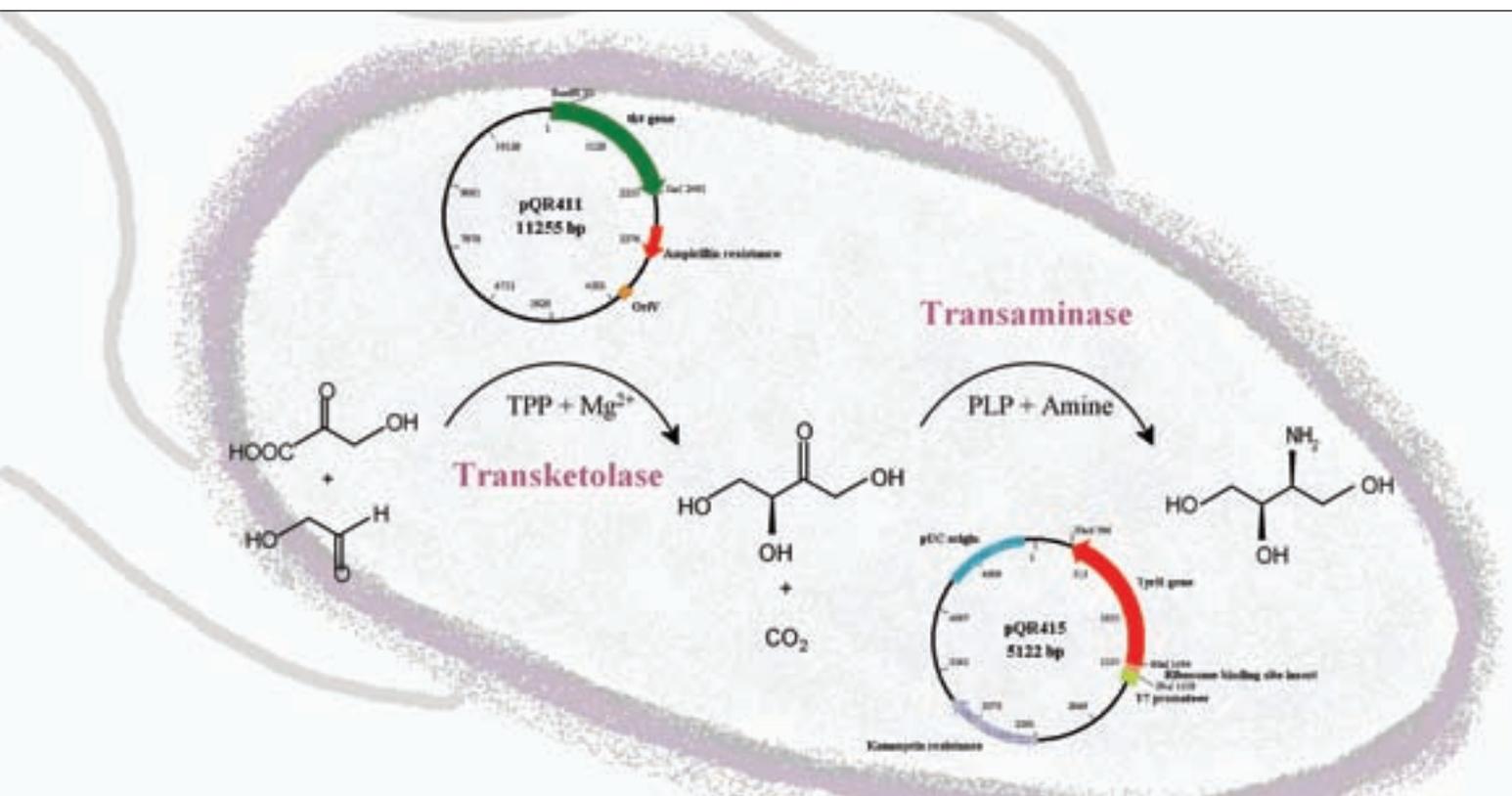
The Bioconversion-Chemistry-Engineering Interface Programme (BiCE) brings together a group of researchers interested in the development of the next generation of complex pharmaceuticals. The EPSRC-funded BiCE programme has two immediate objectives: (i) accelerating the speed of process selection and optimization; (ii) integration of biocatalysis with chemistry. It will achieve this via:

- Chemistry studies examining the integration of chemistry and biocatalysis.
- Metabolic engineering for creation of *de novo* synthetic pathways.
- Directed evolution to test new approaches to protein improvement and assess its potential against new targets.
- Microscale processing to test miniaturised processes and collect relevant process data in parallel experimentation.
- Modelling to set targets for catalyst, biocatalyst and process improvement.

There are innovative elements in each of the five parts bringing new tools forward for testing. Real savings in process development time will come via parallel operation, use of informatics, modelling and defined libraries. The integration of these elements into a framework for rapid design and process evaluation will be a key deliverable. The concepts and tools will be tested with a three-step conversion involving carbon-carbon bond formation to create a ketodiols, amination to create an aminodiols and selective oxidation for further elaboration. Catalytic and enzymatic methods are available at UCL for each of these steps.

Gary is Professor of Biochemical Engineering. He is Chair of the IChemE Biochemical Engineering Subject Group. For further information on BiCE see [www.ucl.ac.uk/biochemeng/industry/bice](http://www.ucl.ac.uk/biochemeng/industry/bice). All MBI® courses benefit from this activity especially Rapid Fermentation Process Design (next running on 29 – 31 October 2007) and Challenges and Opportunities in Biocatalysis (next running on 12 – 14 November 2007).

*E. coli* provides a reliable host for the *de novo* engineering of metabolic routes to the production of chiral amino alcohols.





# Mammalian Cell Processes module

*Dr Farlan Veraitch*

A very successful Mammalian Cell Processes module was run on 4 – 6 December 2006, which attracted 18 international delegates and a range of high- quality speakers from companies such as Covance, GSK, Lonza and Merck & Co. Through a series of lectures and interactive problem solving case studies, they addressed the following issues:

- The underlying technology of mammalian cell process development.
- The jump from research to development.
- The early process decisions and how they affect later development.
- The impact of the product itself upon the process.
- Economic evaluation and the business challenges.
- The impact of cell physiology and metabolic engineering.



*Steve Froud of Lonza Biologics leading a case study 'From Development to Production' that considers the inherent tensions for the development of a manufacturing process using mammalian cells for both early trials and future in-market supply. This module will next be run on 3 – 5 December 2007.*

# Stem Cell & Regenerative Medicine Bioprocessing module

In February, Farlan Veraitch and Chris Mason led a number of MBI® delegates through their innovative module on Stem Cell & Regenerative Medicine Bioprocessing.

Achieving consistency and high efficiency is critical when using stem cells for regenerative medicine or drug evaluation and this is true for both discovery and development studies. To achieve it there is a need to understand the effect of the whole bioprocess sequence from cell sourcing and purification, through expansion, differentiation and implantation into the patient.

Through a series of lectures and problem-solving case studies, stem cells (embryonic, fetal and adult), adult cells and tissue engineered constructs were discussed.

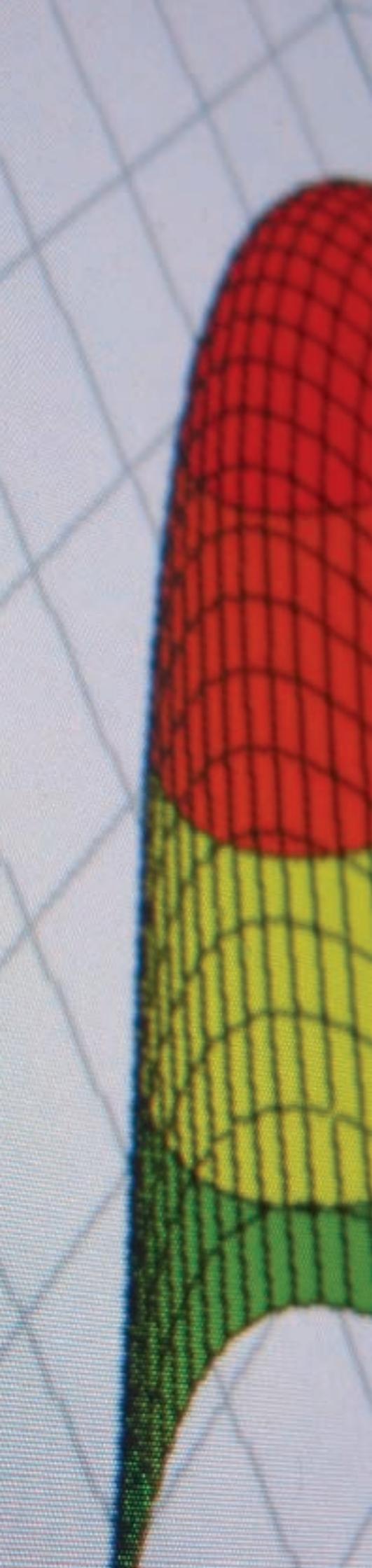
Topics included:

- Stem cell derivation, characterisation and banking.
- Stem cell expansion.
- Cell therapies.
- Tissue engineering – three dimensional constructs.

The list of expert speakers was impressive and included: Julie Daniels, Moorfields Eye Hospital; Paul Kemp, Intercytex; Mark Lewis, Eastman Dental Institute; Sheila MacNeil, CellTran; Nick Medcalf, Smith & Nephew; Stephen Minger, KCL; Kenny Pollock, ReNeuron; Angela Scott, Angel Biotechnology and Glyn Stacey, UK Stem Cell Bank.

This module will next be run on 18 – 20 February 2008.





# New Design of Experiments for Bioprocess Optimisation module: teddy bears, catapults and Ishikawa

*An exciting BBSRC-supported collaboration between the Department and PRISMTC is described by Craig Gershater.*

What do Teddy Bears, catapults and Ishikawa (this is not a motorbike!) have to do with doing better science? The answer lies in a new course being offered by the ACBE (Advanced Centre for Biochemical Engineering) under the MBI<sup>®</sup> banner, 'Design of Experiments (DoE) for Bioprocess Optimisation'. Every graduate emerging from university with a hard-won science or engineering degree may well feel that they are fully equipped to carry out test-tube-rattlingly-good experiments. Certainly we can recognise that scientists of recent and more mature standing now have access to staggeringly powerful technologies, what is becoming increasingly apparent is that, no matter how breathtakingly sophisticated the laboratory toys are, the data they generate are really only as good as the experimental design to which they have been assigned. Staff at UCL have come to realise that they are uniquely positioned to offer a new course on a topic that will transform the way scientists will come to look at their experimental systems and radically increase the efficiency of experimental data acquisition as well as information and knowledge generation.

This approach to experimentation has been under discussion in UCL for some time, and scientists within the ACBE have been actively investigating these techniques within research projects; the time has now come to offer DoE training as a full external three-day training course. To facilitate the delivery of this exciting new venture, staff have formed a powerful alliance with industrially-based scientists who have been practitioners of these techniques over many years. Craig Gershater has over 30 years of industrial bioprocess development experience and is CEO of Cambridge Bioprocess Management Ltd. He has been delivering lectures on various MBI<sup>®</sup> courses over many years and has employed these types of DoE techniques for over 15 years. Ian Macpherson is a statistician also with over 30 years of industrial experience and is MD of PRISM Training and Consultancy, a company offering statistical training, software and experimental design support to the science-based industries. Together Craig and Ian offer close to 70 years' expertise and have a profound understanding of the issues emerging from the application of these techniques as well as the immense impact the application of these techniques can have on any type of experimental system. Prof. Gary Lye

and Dr Frank Baganz have worked very closely with Ian and Craig over many years and will act as the cornerstone for the delivery of this course. In addition recognised experts from academia and industry (e.g. Protherics and Xenova) will be presenting on the course on the various DoE and related systems that have already been applied at the sharp end of research objective attainment.

The intention is to provide front line scientists and research managers with a sound introduction to the techniques so that all participants should be able to leave the course and immediately carry out vastly more efficient experiments. The development of this course is funded by the BBSRC and benefits in particular from the EPSRC-funded BiCE (page 9 and IMRC (page 8) programmes. The intention is that this is the first of perhaps other courses taking in more advanced ideas and techniques designed to equip the Bioprocess business and related sectors with some of the most powerful experimental design and data analysis approaches. Despite the fact that Biotechnology may be regarded as one the most advanced sciences in terms of technologies and potential, the truth may also be that we biotechnologists are lagging behind other research-based industries in the application of these types of industrial approaches – hence the UCL initiative.

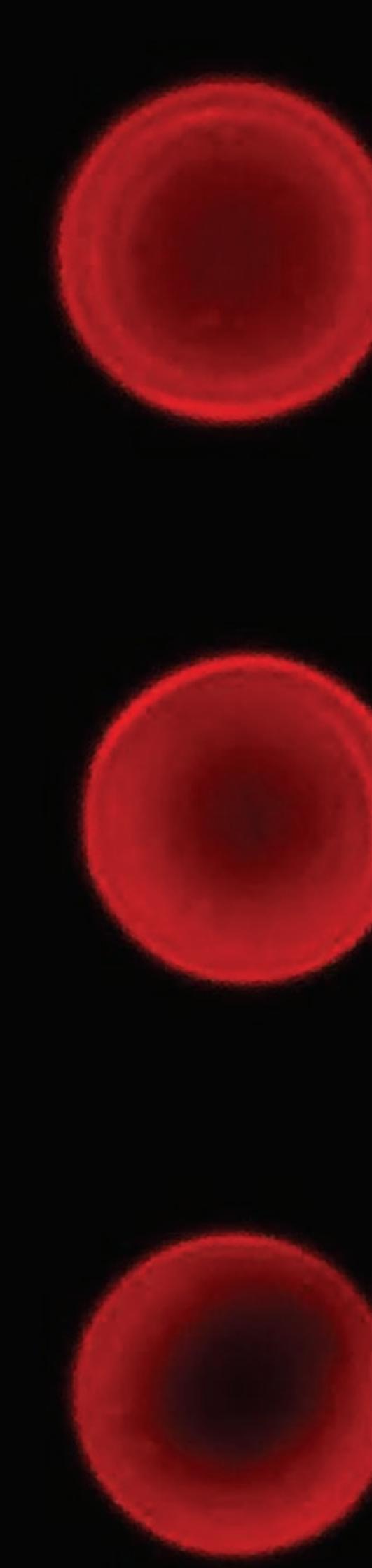
So, to get back to the question about Teddy Bears etc., the reader is directed to obtain the answer from Gary or his colleagues. One thing should perhaps be apparent, the course is intended to be fun as well as hugely rewarding – in every sense.

By the end of the module attendees will be able to:

- Generate appropriate experimental designs within fixed research budgets and timescales.
- Ensure analytical methods can be validated and provide reliable data for process evaluation.
- Rapidly screen and optimise different fermentation media and operating conditions.
- Obtain the highest yield of active product throughout their downstream process sequence.

We are now taking reservations for the 19 – 21 May 2008 course as the 2007 course is already full.





## Work with us

The UCL Advanced Centre for Biochemical Engineering actively encourages and fosters long-term research partnerships between its academics and sponsors for mutual benefit. We facilitate interaction in a range of ways e.g. sponsor visits, industrial advisory boards, Bioprocess Briefings, industrial placements for graduate students and the MBI® Programme and over 60 industrial and academic experts contribute to our MBI activities.

We also believe that the foundation of our education and training programmes, is laid in schools. Our main interaction with schools and their students is via our Headstart courses, as well as visits by school parties and individuals, sponsored through the Nuffield Scheme, for example. The Department is happy to speak at school conferences and we have a range of teaching aids and literature available.

Prospective students to the Department will find active and highly-motivated cohorts throughout all our programmes at undergraduate, masters, doctoral and post-experience levels. These are underpinned by international-class research and by exceptionally strong industrial links. The Department has pioneered parallel training on innovation and enterprise to fit our graduates for a fast moving world. The Department is the EPSRC Engineering Doctoral Training Centre for Bioprocess Leadership (EngD) and has a special enhanced Masters degree. It is active in the Young Entrepreneurs Scheme (YES) and is a partner with the London Business School in a Government selected Centre for Scientific Enterprise.

We take great pride in the success of our alumni; they are responsible for major advances such as processes for a first Hepatitis A vaccine and for a first medicine for the major killer, septic shock. The Department is increasingly concerned with keeping in touch with its alumni and has recently set up a new web page to more rapidly disseminate news and for alumni to update contact information. This can be found at [www.ucl.ac.uk/biochemeng](http://www.ucl.ac.uk/biochemeng)



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# MBI<sup>®</sup> course dates 2007–8

Principles of Fermentation Processes

1 – 3 October 2007

Rapid Fermentation Process Design: From Development to Manufacture

29 – 31 October 2007

Challenges & Opportunities in Biocatalysis

12 – 14 November 2007

Mammalian Cell Processes

3 – 5 December 2007

Primary Recovery

28 – 31 January 2008

Chromatography

4 – 7 February 2008

Stem Cell and Regenerative Medicine Bioprocessing

18 – 20 February 2008

Validation of Bioprocesses

21 – 24 April 2008

Effective Biopharmaceutical Development & Manufacture

12 – 14 May 2008

Design of Experiments for Bioprocess Optimisation

19 – 21 May 2008

Bioprocess Design & Economic Evaluation

2 – 5 June 2008

Bioprocess Facility Design

23 – 26 June 2008

For more information,  
send an email to  
[mbi-training@ucl.ac.uk](mailto:mbi-training@ucl.ac.uk)

 modular training for  
the bioprocess industries