The University Of Sheffield.

Automatic Control & Systems Engineering.

The 5th New-ACE Workshop

LIFE SCIENCES

APPLICATIONS OF CONTROL

18 – 19 March 2010
University of Sheffield

Chair: Daniel Coca

EPSRC
Engineering and Physical Sciences Research Council

New-ACE
newace.org.uk

Motivation

"The use of new technology and mathematics to study the systems of nature is one of the most significant scientific trends of the century. Driven by the need for more precise scientific understanding, advances in automated measurement are providing rich new sources of biological and physiological data. These data provide information to create mathematical models of increasing sophistication and realism—models that can emulate biological and physiological systems with sufficient accuracy to advance ourunderstanding of living systems and disease mechanisms.

New measurement and modelling methods set the stage for control and systems theory to play their rôle in seeking out the mechanisms and principles that regulate life. It is of inestimable importance for the future of control as a discipline that this rôle is performed in the correct manner.

If we handle the area wisely then living systems will present a seemingly boundless range of important new problems—just as physical and engineering systems have done in previous centuries. But there is a crucial difficulty. Faced with a bewildering array of choices in an unfamiliar area, how does a researcher select a worthwhile and fruitful problem?"

(P. Wellstead, E. Bullinger, D. Kalamatianos, O. Mason, M.Verwoerd, The role of control and system theory in systems biology, Annual Reviews in Control, Volume 32, Issue 1, April 2008, Pages 33-47.)

Background and Aims

The workshop is organized by **New-ACE**, an EPSRC funded Network for New Academics in Control Engineering, which was established to support early-stage academics, researchers and industrialists in control engineering and related subject areas.

The aim of this workshop (fifth in the series) is to highlight the importance of control and systems theory in understanding fundamental regulatory mechanisms in living organisms and to provide guidance, particularly to new academics in control engineering, on how to identify and exploit the huge research opportunities that exists in this area.

Technical Programme

Day 1 – Thursday 18th March 2010

Location: Mappin Hall, Sir Frederick Mappin Building (number 170 on the University Map)

11:00 – 12:50 :	**Arrival, Registration and Lunch**
12:50 – 13:00 :	**Welcome Message**
13:00 – 13:40 :	**Prof Frank Doyle,** University of California Santa Barbara *Controlling Noisy Oscillators to Achieve Robust Timekeeping*
13:50 – 14:30 :	**Prof Declan Bates,** University of Exeter *Uncovering the design principles underlying robust cAMP signalling in aggregating Dictyostelium cells: A Control Engineering approach*
14:40 – 16:00 :	**Posters and Coffee**
16:00 – 16:40 :	**Prof Peter Wellstead,** Hamilton Institute, National University of Ireland *The Role of Control and Systems Methods in Biology and Disease*
16:50 – 17:30 :	**Prof Kevin Warwick,** University of Reading *The Cyborg Experiments*
18:30 :	**Dinner (Venue TBA)**

Day 2 – Friday 19th March 2010

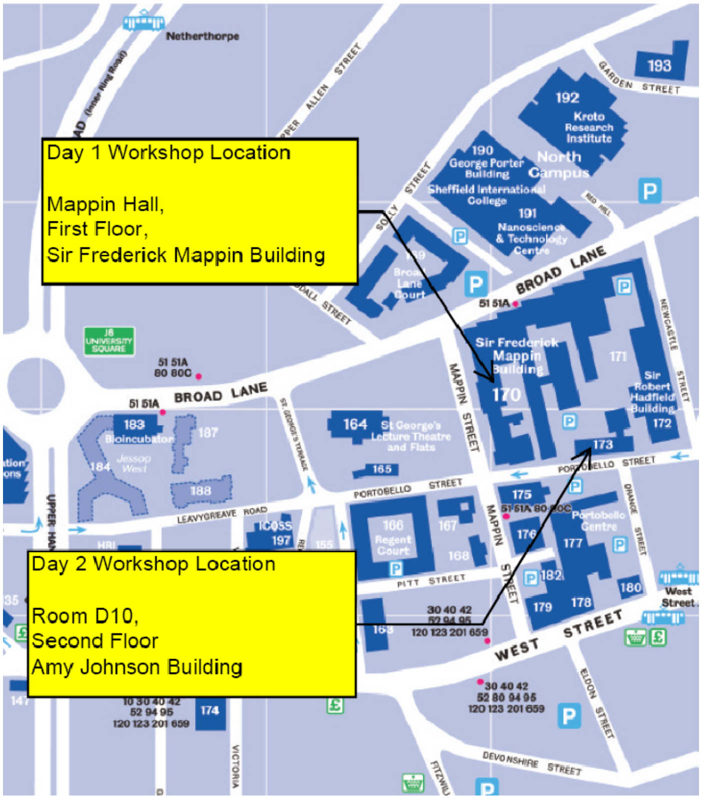
Location: Room D10, Amy Johnson Building (number 173 on the University Map)

09:00 – 09:40 :	**Prof. Mahdi Mahfouf,** University of Sheffield *From 'Parsimonious' Models to 'Pragmatic' Decision-Making and Control: Present and Future Perspectives of Research in Biomedicine*
09:50 – 10:30 :	**Dr. Hong Yue,** University of Strathclyde *Model-based Experimental Design for Biological Systems Modelling*
10:40 – 11:00 :	**Coffee break**
11:00 – 11:40 :	**Dr. Ying Zheng,** University of Sheffield *Understanding physiological constraints: a key to dynamic modelling of physiological systems*
11:50 – 12:30 :	**Dr. Chloe Heywood,** EPSRC *Funding Healthcare Research at the Engineering and Physical Sciences Research Council*
12:40 – 14:00 :	**Lunch**
14:00 – 14:40 :	**Dr. Eric Bullinger,** University of Liège *Control Engineering Challenges in Systems and Synthetic Biology*
14:50 – 15:30 :	**Dr. Daniel Coca,** University of Sheffield *Reverse-engineering Drosophila's Retinal Networks*
15:40-16:10 :	**Discussions**
16:10 :	**Closing Remarks and Departure**

HOW TO GET TO SHEFFIELD UNIVERSITY

http://www.shef.ac.uk/content/1/c6/06/04/93/CentralSheffield.pdf - Map of Central Sheffield

http://www.shef.ac.uk/content/1/c6/06/04/92/aug09-map-pdf.pdf - Map of Campus



Local transport

Supertram

Trams link the railway station and the city centre directly to the University. The tram stop is located at the back of the railway station. Trams from the station to the University run on the Blue route (destination "Malin Bridge").

Trams from the city centre to the University run on both the Blue route and the Yellow route (destination "Middlewood").

During the day, trams run every 10 minutes (15 minutes on Sundays) from 6.00am to midnight. Some departments are best accessed by alighting at the West Street stop, while for others it is best to use the University of Sheffield stop. Check which one is best to use before you start your journey.

Buses

Buses to the University are frequent and inexpensive. From the railway station and coach station you can take the number 40 directly to the University. Other buses from the city centre include the 51 and 52.

Park and Ride

The easiest way for car drivers to travel to the University is by Supertram Park and Ride. There are Park and Ride sites at Nunnery Square (off the Parkway), at Meadowhall Interchange (M1, junction 34) and Middlewood.

Taxis

There are taxi ranks at the railway station and beside the City Hall. The journey to the University should only take 5 minutes, but can take 15 minutes if traffic is heavy. Expect to pay about £5.

Speakers Biographies

Professor Frank Doyle, *University of California Santa Barbara*

Dr. FRANCIS J. DOYLE III is the Associate Dean for Research in the College of Engineering at UC, Santa Barbara and he is the Associate Director of the Army Institute for Collaborative Biotechnologies. He holds the Duncan and Suzanne Mellichamp Chair in Process Control in the Department of Chemical Engineering, as well as appointments in the Electrical Engineering Department, and the Biomolecular Science and Engineering Program. He received his B.S.E. from Princeton (1985), C.P.G.S. from Cambridge (1986), and Ph.D. from Caltech (1991), all in Chemical Engineering. Prior to his appointment at UCSB, he has held faculty appointments at Purdue University and the University of Delaware, and held visiting positions at DuPont, Weyerhaeuser, and Stuttgart University. He is the recipient of several research awards (including the NSF National Young Investigator, ONR Young Investigator, Humboldt Research Fellowship) as well as teaching awards (including the Purdue Potter Award, and the ASEE Ray Fahien Award). He is a Fellow of the IEEE, and a Fellow of IFAC. He served as the editor-in-chief of the IEEE Transactions on Control Systems Technology from 2004-2009, and currently holds Associate Editor positions with the Journal of Process Control, the SIAM Journal on Applied Dynamical Systems, and Royal Society's Interface. In 2005, he was awarded the Computing in Chemical Engineering Award from the American Institute of Chemical Engineers for his innovative work in systems biology. His research interests are in systems biology, network science, modeling and analysis of circadian rhythms, drug delivery for diabetes, model-based control, and control of particulate processes.

Professor Declan Bates, *University of Exeter*

Declan Bates was born in Clonmel, Co. Tipperary, Ireland in 1970 and educated at Powerstown National School and CBS High School, Clonmel. He received a B.Eng degree in Electronic Engineering and a Ph.D. degree in Robust Control Theory from the School of Electronic Engineering, Dublin City University, Ireland, in 1992 and 1996 respectively, before joining the Control and Instrumentation Research Group at Leicester University, where he was promoted to Professor of Control Engineering in 2009. His research is focused on the development and application of advanced design and analysis methods for complex dynamical systems. He has held visiting lecturer positions at the Technical University of Delft, Holland, and the University of Cranfield. He is a co-author, with Ian Postlethwaite, of Robust Multivariable Control of Aerospace Systems (Delft University Press, 2002). From 2004 to 2007, he was the Vice-Chairman of the GARTEUR FM-AG17 Action Group on Nonlinear Analysis and Synthesis Techniques in Aircraft Control, and an editor of the resulting research monograph , published by Springer-Verlag. In 2006, he established Systems Biology Lab, an interdisciplinary research laboratory within the Departments of Engineering and Biology at the University of Leicester. In 2007, he was invited to serve on BBSRC's Engineering and Biological Systems Research Committee, and he is currently a core member of BBSRC's Research Committee C on Technological and Methodological Development. From 2009 to 2012 he is a member of the Research Grants Review Committee of the International Human Frontier Science Program. In March 2010 he was appointed to a Chair in Biological Systems Engineering at the Centre for Systems Biology of the University of Exeter.

Professor Peter Wellstead, *Hamilton Institute NUI, Maynooth*

Peter Wellstead was trained in mechanical and electrical engineering at Marconi Instruments Ltd and Hatfield College of Technology. After postgraduate study at Warwick University, he held a CERN Technical Fellow, before joining the Control Systems Centre at the University of Manchester Institute of Science and Technology. In Manchester his activities were in adaptive control, system identification, mathematical modelling and their applications to industrial problems. During 2003 he was an E.T.S. Walton Visitor to Ireland and in 2004 became Science Foundation Ireland Research Professor of Systems Biology at the Hamilton Institute. In Ireland his mission has been to promote systems biology in the country and to develop a systems biology group within the Hamilton Institute. His research objective is to use systems methods to help understand of the causes and pathologies that drive Parkinson's disease.

Professor Kevin Warwick, *University of Reading*

Kevin Warwick is Professor of Cybernetics at the University of Reading, England, where he carries out research in artificial intelligence, control, robotics and biomedical engineering. He is a Chartered Engineer (CEng.) and is a Fellow of The Institution of Engineering & Technology (FIET). He is the youngest person ever to become a Fellow of the City & Guilds of London Institute (FCGI).

Kevin was born in Coventry, UK and left school to join British Telecom, at the age of 16. At 22 he took his first degree at Aston University, followed by a PhD and a research post at Imperial College, London. He subsequently held positions at Oxford, Newcastle and Warwick universities before being offered the Chair at Reading, at the age of 33. He has been awarded higher doctorates (DScs) both by Imperial College and the Czech Academy of Sciences, Prague. He was presented with The Future of Health technology Award from MIT (USA), was made an Honorary Member of the Academy of Sciences, St.Petersburg and received The Mountbatten Medal in 2008. In 2000 Kevin presented the Royal Institution Christmas Lectures, entitled "The Rise of The Robots".

Kevin carried out a series of pioneering experiments involving the neuro-surgical implantation of a device into the median nerves of his left arm in order to link his nervous system directly to a computer in order to assess the latest technology for use with the disabled. He was successful with the first extra-sensory (ultrasonic) input for a human and with the first purely electronic communication experiment between the nervous systems of two humans. His research has been discussed by the US White House Presidential Council on BioEthics, The European Commission FTP and led to him being widely referenced and featured in academic circles as well as appearing as cover stories in several magazines – e.g. Wired (USA), The Week (India). The Institute of Physics cites Kevin as one of only 7 scientists in the world due to the ethical impact of his work (**http://www.peep.ac.uk/content/614.0.html**), the others being Galileo, Einstein, Curie, Nobel, Oppenheimer and Rotblat.

His work is used as material in several advanced Level Physics courses in the UK and in many University courses including Harvard, Stanford, MIT & Tokyo. His implants are on display in the Science Museums in London and Naples. As a result, Kevin regularly gives invited Keynote presentations.

Kevin's research involves robotics and he was responsible (with Jim Wyatt) for Cybot, a robot exported around the world as part of a magazine "Real Robots" – this resulted in royalties totalling over £1M for Reading University. Robots designed and constructed by Kevin's group (Ian Kelly, Ben Hutt) have been on permanent interactive display in the Science Museums in London, Birmingham and Linz.

Kevin's recent research involves a collaborative project with the Oxford neurosurgeon, Tipu Aziz, using intelligent computer methods to predict the onset of Parkinsonian tremors such that they can be stopped by means of a deep brain implant. In 2007 this work was hailed in the Mail on Sunday as "the most significant recent advance in biomedical engineering".

He presently leads an ongoing EPSRC sponsored project in which a cultured neural network (using biological neurons) is trained to control a mobile robot platform. This work, which was reported on in a New Scientist feature article, is being used as an exercise for high school science studies in the UK. A Youtube video of this research has now been downloaded/viewed around 1 million times (**http://www.youtube.com/watch?v=1-0eZytv6Qk**).

Kevin was a member of the 2001 HEFCE (unit 29) panel on Electrical & Electronic Engineering, was Deputy Chairman for the same panel in the 2007/8 exercise and is a member of the EPSRC Peer College. He has produced over 500 publications on his research including more than 110 refereed journal articles and 25 books. Kevin received the EPSRC Millenium Award (2000) for his schools robot league project and is the youngest ever Fellow of the City and Guilds of London Institute. Kevin's research has featured in many TV and film documentaries, e.g. Inventions that changed the world (BBC2), Late Night with Conan O'Brien (NBC), Future Scope (RAI 1) and The Making of I Robot (Twentieth Century Fox/Channel 5). He has appeared 3 times on Tomorrow's World, 5 times in Time magazine, thrice in Newsweek and was selected by Channel 4 as one of the Top 6 UK Scientists for their 2001 series "Living Science". In 2002 he was chosen by the IEE as one of the top 10 UK Electrical Engineers. Kevin also appeared as one of 30 "great minds on the future" in the THES/Oxford University book – Predictions – with J.K.Galbraith, Umberto Eco and James Watson.

Professor Mahdi Mahfouf, *The University of Sheffield*

Mahdi Mahfouf has received the Degrees of MPhil (1987) and PhD (1991) in Control Systems Engineering from the University of Sheffield (UK). He was a Post-Doctoral Research Fellow (1992-1996) in the Sheffield University Department of Automatic Control and Systems Engineering. In January 1997 he was appointed as a Lecturer of Industrial Control in the Department of Mechanical Engineering, The University of Manchester. In October 1997 he re-joined the Sheffield University Department of Automatic Control and Systems Engineering, as a Lecturer in Systems and Control Engineering and was promoted to Senior Lecturer in 2000, Reader in 2003, and to a Personal Chair in Intelligent Systems Engineering in 2005. Professor Mahfouf has worked in the areas of Intelligent Control, Modelling and Optimisation in Biomedicine and Process Industries for more than 24 years and is the author of more than 180 papers in these subjects.

Dr Hong Yue, *University of Strathclyde*

Dr. Hong Yue is a lecturer at the Department of Electronic and Electrical Engineering, University of Strathclyde. Before taking this position in 2007, she was with Manchester Interdisciplinary Biocentre from 2005 to 2007, and University of Manchester Institute of Science and Technology from 2001 to 2004 as a research assistant. She is also affiliated with the Institute of Automation, Chinese Academy of Sciences. Dr. Yue's research interests include modelling and analysis of biological networks, process modelling and advanced control of industrial processes, and output shaping control of molecular weight distribution systems, etc. Her recent interest in systems biology is to integrate mathematical modelling and engineering analysis methods into quantitative investigation of complex dynamic behavior of gene regulatory systems.

Dr Ying Zheng, *University of Sheffield*

Ying Zheng received the BEng degree in Automatic Control and Systems Engineering with first class honours from the University of Sheffield in 1983, the degree of PhD in Control Systems Engineering from the University of Sheffield in 1988. Her main research interest is the development of mathematical modelling and system identification methodologies with applications to neuro-imaging and biophysical modelling of brain function.

Dr Chloe Heywood, *EPSRC*

Chloe Heywood works at the Engineering and Physical Sciences Research Council(EPSRC), the main UK government agency for funding research and training in engineering and the physical sciences. EPSRC invest more than £800 million a year in a broad range of subjects – from mathematics to materials science, and from information technology to structural engineering. Chloe's role at EPSRC is as medical engineering portfolio manager, helping tomanage a £100M portfolio of academic-led (or responsive mode) research projects. She is also a member of the Healthcare sector team, which aims to understand how the needs of industry may be met by academia and help to facilitate links between academia and users. She works closely with the Towards Next Generation Healthcare Programme at EPSRC who are responsible for delivering a managed programme of funding to improve the health of UK citizens.

Dr. Eric Bullinger, *University of Liège*

Eric Bullinger (http://www.montefiore.ulg.ac.be/~bullinger/) received his diploma and Ph.D. degree in electrical engineering from the ETH Zurich in 1995 and 2001, respectively. Since 2009, he is Francqui Assistant Professor at the University of Liège (http://www.ulg.ac.be) in Belgium, jointly at the Montefiore Institute (http://www.montefiore.ulg.ac.be), in the electrical and computer science department and the GIGA (http://www.giga.ulg.ac.be) biomedical research centre. Before, he held positions at the Industrial Control Centre of the University of Strathclyde, the Hamilton Institute of the National University of Ireland Maynooth and the Institute for Engineering Cybernetics of the University of Stuttgart, Germany. His theoretical research interests are system identification, observer design and robustness analysis. His main application area is systems biology, from data analysis over modelling to model analysis, and chairs the IET Systems and Synthetic Biology Network (http://kn.theiet.org/communities/biology/index.cfm).

Dr Daniel Coca, *University of Sheffield*

Daniel Coca received an M.Eng. degree in electrical engineering from the "Transilvania" University of Brasov, Romania, and the Ph.D. degree in Automatic Control and Systems Engineering from the University of Sheffield in 1993 and 1997 respectively. He was Postdoctoral Research Associate in the Department of Automatic Control and Systems Engineering Department at the University of Sheffield (1997-2002). In 2002 he was appointed Lecturer in the Department of Electrical Engineering and Electronics at the University of Liverpool. In June 2004, he re-joined the Department of Automatic Control and Systems Engineering at Sheffield University, where he is currently Reader. His research interests include identification and control of complex dynamical systems, bioimaging and biological data analysis using reconfigurable computers.

Speakers Abstracts

Professor Frank Doyle, *University of California Santa Barbara*

Controlling Noisy Oscillators to Achieve Robust Timekeeping

The generation of highly robust rhythms from the synchronization of large numbers of oscillators is is a recurring theme in biology. Of particular interest in this talk is the exquisite synchrony achieved in circadian oscillators in the brain, arising from a population of "sloppy" cellular timekeepers that are linked by local signaling cues. The details of the coupling mechanism will be presented, with an emphasis on phase metrics for modeling and analysis. Extensions of this work for other biological systems, including coral reproduction, will be described.

Professor Declan Bates*,* *University of Exeter*

Uncovering the design principles underlying robust cAMP signalling in aggregating Dictyostelium cells: A Control Engineering approach

Stable and robust oscillations in the concentration of adenosine-cyclic monophosphate (cAMP) are observed during the aggregation phase of starvation-induced development in Dictyostelium discoideum. In this talk, I will show how ideas and tools from control engineering can be used to improve our understanding of the molecular networks underlying this dynamic behaviour. In part one of the talk, I will use robustness analysis techniques to show that stochastic fluctuations in the molecular interactions play an important role in preserving the stabilty of the oscillations in the face of variations in the kinetics of the intracellular network. I will also show that dynamic interactions between different intracellular modules, as well as synchronisation of the aggregating cells through the diffusion of extracellular cAMP, are additional key factors in ensuring robustness of the oscillatory waves of cAMP observed in Dictyostelium cell cultures. In part two of the talk, I will show that the ligand/receptor interaction network employed to relay external cAMP signals in aggregating Dictyostelium cells exhibits generic structural characteristics which are highly conserved in nature. Using elementary analysis tools from linear control theory, It will be shown that the network parameters for the ligand bound cell receptors which are distributed on the outer shell of Dictyostelium cells are highly optimised, in the sense that the response speed is the fastest possible while ensuring that no overshoot occurs for step changes in external signals. Finally, I show that the response of the network to external signals is extremely robust to variations in the relevant kinetic parameters of the network, the cell volume and the number of receptors present on the surface of the cell.

Professor Peter Wellstead, *Hamilton Institute NUI, Maynooth*

Control and systems methods in biology and researching neurodegenerative disease

Life science is undergoing a fundamental change from a world of qualitative phenomenological descriptions, to one in which mathematics will be used to provide a quantitative unified basis for understanding the behaviour of living systems. For two decades, this move toward a quantitative basis for biology has been dominated by static bioinformatic studies of high throughput genomic/proteomic data. But perceptions are evolving and there is now an acceptance that bioinformatic models cannot describe the subtle temporal processes that characterise all living objects. As a consequence, dynamical system modelling is increasingly employed to capture the time dependent behaviour of cellular systems, tissue and organisms. These models are most commonly used to simulate biological processes *in-silico*, with the aim that they will inform *in-vivo* and *in-vitro* experimentation.

In-silico simulation is only a partial step – dynamical control systems analysis is essential if we are to understand how living systems perform and (more importantly) how they fail. Using Parkinson's disease as the target application, this talk will elaborate on how modelling and dynamical systems analysis methods familiar to control systems specialists can be used to extract information about the mechanisms that regulate and determine disease. In particular, I will illustrate how biochemical system modelling, combined with control system analysis, can provide a unifying basis for the study of this fatal long-term neurodegenerative disease who's causes are unknown and for which there is no known cure.

Professor Kevin Warwick, *University of Reading*

The Cyborg Experiments

In this presentation a look is taken at how the use of implant and electrode technology can be employed to create biological brains for robots, to enable human enhancement and to diminish the effects of certain neural illnesses. In all cases the end result is to increase the range of abilities of the recipients. An indication is given of a number of areas in which such technology has already had a profound effect, a key element being the need for a clear interface linking a biological brain directly with computer technology. The emphasis is clearly placed on practical scientific studies that have been and are being undertaken and reported on. The area of focus is notably the use of electrode technology, where a connection is made directly with the cerebral cortex and/or nervous system. The presentation will consider the future in which robots have biological, or part-biological, brains and in which neural implants link the human nervous system bi-directionally with technology and the internet.

Professor Mahdi Mahfouf, *The University of Sheffield*

From 'Parsimonious' Models to 'Pragmatic' Decision-Making and Control: Present and Future Perspectives of Research in Biomedicine

The link between the mathematics of control theory and drug strategies was discovered and published more than 40 years ago (1969 to be precise). In fact, such synergy between control and medicine is so natural that it was waiting to be discovered rather than concocted as a story which would make sense. It is hardly surprising then that the clinicians I worked with over the years were found to be receptive and amenable to control designs which were not necessarily 'transparent' or at least not as transparent as those designs which employ fuzzy logic based linguistics for example, provided that the notions of 'cost-function', 'control stability', pole-positions, etc. were explained to them beforehand. Perhaps, it is slightly surprising then that the last area of science related to control engineering is 'clinical medicine 'where I can suggest unashamedly that it is where the biggest challenges to any theoretical results in control theory perhaps lie. While this bold change of attitude vis-à-vis drawing engineering and clinical medicine closer together is very much welcome by researchers like myself, one needs to be reminded that the catalyst behind this (somewhat) belated progress is very much linked to 'safety'. Indeed, similarly to any other industry clinical medicine had to be convinced that control (and modelling) and signal processing are effective but perhaps most importantly safe, although I still believe that safety and effectiveness somehow go hand in hand.

While I will have to agree with Professor Karl J. Astrom who argues that 'control engineering' remains very much the 'hidden technology', I will also argue that there is no nicer and more emphatic way of demonstrating the usefulness of feedback control, modelling, or signal processing than on the most beautiful machine ever built which is the human machine. This latter embodies all the challenges known to 'system's theory', i.e. non-linearities, complex and ill-defined interactions, long and varying time-delays, sudden disturbances, inter and intra dynamics variability, and uncertainties due to external disturbances as well as measurements all in one setting. On the subject of measurement, clinical medicine is perhaps the one area where Galileo's principle of 'measuring everything that is measurable and making available all the variables which have not been measured so far' will prove most difficult to apply.

More often than not, when I describe results of clinical trials to an audience I always begin with a message that says that this is no simulation but real-life drama. The same patient who undergoes several clinical trials, seemingly under similar conditions, may produce different results. This is typical of trials under closed-loop control conditions where the same controller can lead to different transients and steady-state behaviour. The audience indeed appreciates that one is more likely to obtain consistent behaviour if one dealt with engines rather than humans . Perhaps what fascinates the audience first and foremost is the multi-disciplinary nature of bioengineering research as it calls upon expertise in science and engineering. This is simply its raison d'etre.

It is in this spirit that I feel particularly privileged to have been given the opportunity to present the research work that I and members of my Research Group in the Sheffield University Department of Automatic Control and Systems Engineering have been involved with over a time-period that spans more than 3 decades and which concerns three (3) main areas, in particular, Muscle Relaxation and Anaesthesia, Cardiac and General Intensive Care Medicine, and Operator Breakdown in Safety Critical Environments. The systems-engineering paradigms relating to modelling, optimisation and control called upon to solve some of the intricate challenges usually thrown at us by the above systems will be described and simulations as well as real-time results will be presented and analysed hence illustrating lessons learnt. Furthermore, a perspective into future challenges relating to the above areas, in particular, and to research in Biomedicine, in general, will be addressed in this talk.

Dr Hong Yue, *University of Strathclyde*

Model-based Experimental Design for Biological Systems Modelling

Experimental design is an essential tool of mathematical modelling, especially for parameter identification of biological regulatory networks in which experiments to generate data is expensive and complex, as a consequence the time series data are often sparse, noise and short. The purpose of model-based experimental design is to maximise the information gathered for quantitative model identification whilst minimising the experimental efforts. The quality of conventional optimal experimental design largely depends on the accuracy of model parameter estimation, which is often either unavailable or poorly estimated at the stage of design. Robust experimental design algorithms have thus been proposed when model parametric uncertainties need to be addressed during the design process. In this talk, some of our recent progresses in optimal and robust experimental design are presented with discussions on design criteria, formulation of optimization problems, computational procedures and the links with global sensitivity analysis.

Dr Ying Zheng, *University of Sheffield*

Understanding physiological constraints: a key to dynamic modelling of physiological systems

As system engineers and mathematical modellers, our ability to 'identify' mathematical models of physiological systems can be greatly enhanced by our understanding of the mechanisms underlying such systems. I will use our recent modelling work to demonstrate that by applying the appropriate constraints we are able to establish physiologically plausible models linking neural activity to cerebral blood flow and volume. Furthermore these models can be used to not only explain the observed experimental data but also generate hypotheses for further research.

Dr Chloe Heywood, *EPSRC*

Funding Healthcare Research at the Engineering and Physical Sciences Research Council

Dr. Eric Bullinger, *University of Liège*

Control Engineering Challenges in Systems and Synthetic Biology

Systems biology and particularly synthetic biology are new relatively new research areas, driven by the availability of large scale biological data and novel experimental possibilities. In this presentation, I will give an overview of control structures identified in biological systems as well as of opportunities for control theoretical methodologies in this field. Finally, I will share my vision of synthetic biology beyond Lego, and its need for systems and control as a key component.

Dr Daniel Coca, *University of Sheffield*

Reverse-engineering Drosophila's retinal networks

Vision is the most important sense of many living organisms. Even in the dimmest habitats animals have functional eyes, which allow them to extract useful optical information from the environment and to respond rapidly and appropriately to changing events and conditions. The anatomical structure, molecular signalling cascades and ultimately the performance of an organism's visual system, measured in terms of speed, sensitivity, dynamic range and robustness, has been tuned to suit its lifestyle by the content of the photic stimuli as well as other environmental factors. The signal-processing capability of fly photoreceptors is prodigious, outperforming human engineered image sensors in many respects. They are exquisitely sensitive, being able to respond to single photon events. Weak input signals embedded in noise can be selectively amplified and filtered to provide efficient and reliable sensing of physiologically relevant stimuli. A fascinating functional attribute of photoreceptors is their ability to light adapt, i.e. adjust the amplification gain, according to both past and on-going light events, using many layers of positive- and negative-feedback control. This allows them to operate over a wide environmental range. They can reliably respond to the absorption of single photons under dark-adapted conditions, but can also adjust the gain to operate in bright daylight conditions. This talk aims to demonstrate how tools and techniques borrowed from control and systems engineering can be used to derive and analyse detailed mathematical models of the early vision system, allowing us to understand the role of different molecular components that are instrumental in converting light into electrical signals as well as the adaptation rules which enable fly photoreceptors to operate reliably over a wide environmental range.