ICSU bio-unions satellite symposium

Multi-Scale Systems Biology

28th-29th July 2013, Chicheley Hall, United Kingdom

Chicheley Hall, Chicheley, Newport Pagnell, Buckinghamshire, MK16 9JJ, United Kingdom

http://physiomeproject.org/meetings/

ICSU bio-unions satellite symposium

Multi-Scale Systems Biology

The International Council for Science's first collaborative Bio-unions Symposium is a satellite conference of the 2013 IUPS Congress, and will bring together, at the Royal Society's stately Chicheley Hall, scientists working on all aspects of systems biology.

The meeting will bring together representatives of the ICSU Bio-Unions to develop a roadmap for the development of multi-scale systems biology that addresses the diverse needs of these unions, as well as the wider systems biology community.

SPEAKERS

Emer. Prof Denis Noble (IUPS President/University of Oxford)	**Dr Bernard de Bono** (UCL/Auckland Bioengineering Institute)	**Prof Peter Hunter** (IUPS/Auckland Bioengineering Institute)
Prof Pingfan Rao (IUFoST)	**Prof Ibrahim Elmadfa** (IUNS President)	**Prof Malcolm Gordon** (IUPS/UCLA)
Dr Elhanan Borenstein (IUMS/University of Washington)	**Prof Nils Christian Stenseth** (IUBS President/University of Oslo)	**Prof Janet Thornton** (EBI)
Prof Stig Omholt (NTNU)	**Prof Charlie Hodgman** (University of Nottingham)	**Dr Hiroaki Kitano** (SONY)
Dr Adriano Henney (Virtual Liver Network)		**Prof Hans Westerhoff** (IUBMB/ Manchester Centre for Integrative Systems Biology)

The National Institutes of Health's definition states that systems biology is an approach in biomedical research to understand the larger picture — be it at the level of the organism, tissue, or cell — by putting its pieces together. It's in stark contrast to decades of reductionist biology, which involves taking the pieces apart.

ATTENDEE INFORMATION

- Please print and bring a copy of your registration confirmation

Accommodation

- For attendees with accommodation included within their registration, a room has been booked for you in the main house at Chicheley as per your specifications.

  Check in: after 2pm on Saturday 27th July

  Check out: Monday 29th July

Meals

- All meals will be provided**, beginning with dinner on Saturday 27th and ending with lunch on Monday the 29th.

** For Day Registration attendees, please make your way to and from Chicheley Hall each day.

Lunch and refreshments will be provided on Sunday 28th and Monday 29th.

Your registration also includes dinner on Sunday 28th.

Saturday, 27th July

Time	
2pm onwards	**Arrival at Chicheley Hall**
7-9pm	**A casual dinner buffet will be available**

Symposium Programme

Day 1: Sunday, 28 July

Time	
7.30am	**Breakfast**
9- 9.30am	**Welcome: Introduction and goals for the meeting** Andrew McCulloch and Peter Hunter
9.30-10am	**A systems biological view of Evolutionary Biology: all in the interactions** Denis Noble (IUPS President)
10-10.30am	**An overview of the VPH/Physiome activities** Peter Hunter (IUPS)
10.30-11am	**The Virtual Liver: A multidisciplinary, multiscale challenge for systems biology** Adriano Henney
11-12pm	**Discussion**
12-1.30pm	**Lunch**
1.30-2pm	**Articulating physiology knowledge about tissues for drug discovery** Bernard de Bono
2-2.30pm	**Bridging the genotype-phenotype gap: what does it take?** Stig Omholt
2.30-3pm	**Recent advances in plant physiomics** Charlie Hodgman
3-4pm	**Discussion**
4-6.30pm	**Poster Presentations**
6.30pm	**Dinner**

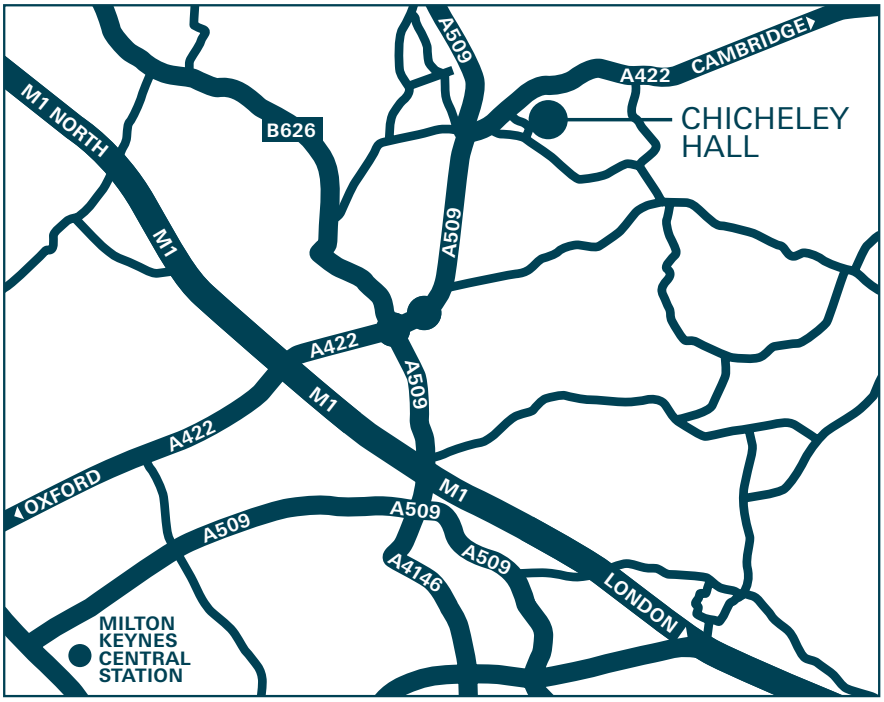
Symposium Programme

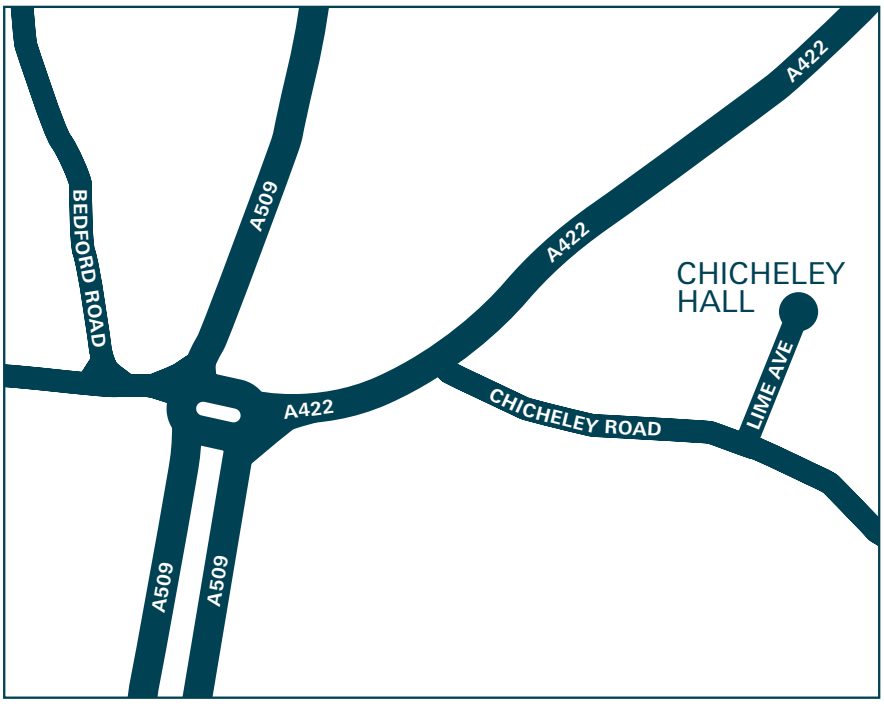
Day 2: Monday, 29th July

Time	
7.30am	**Breakfast**
9 - 9.30am	**Mapping metabolic systems biology** Hans Westerhoff (IUBMB)
9.30-10am	**HD-Physiology Project -A Japanese Flagship Physiological Modeling Project** Hiroaki Kitano
10-10.30am	**A hidden system for superoxide disposal** Pingfan Rao (IUFoST)
10.30-11am	**The role of antioxidants in the immune function** Ibrahim Elmadfa (IUNS President)
11-12pm	**Discussion**
12-1pm	**Lunch**
1-1.30pm	**Comparative and evolutionary systems biology: examples from an endless frontier** Malcolm Gordon (IUPS)
1.30-2pm	**Towards a Predictive Systems-Level Model of the Human Microbiome** Elhanan Borenstein (IUMS)
2-2.30pm	**The interplay between ecology and evolution in host-vector-pathogen systems: Yersinia pestis as an example** Nils Christian Stenseth (IUBS President)
2.30-3pm	**Bioinformatics at EBI: fulfilling the work of Systems Biology** Janet Thornton (EBI)
3-4pm	**Discussion**

Chicheley Hall

Home of the Kavli Royal Society International Centre





Address:

Chicheley Hall,
Chicheley,
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Telephone:

01234 868650

By train:

Chicheley Hall is located just 15 minutes by car from Milton Keynes Central Station. Trains run frequently from London Euston Station with the journey time just 30 minutes on the fast train. The station also has rail links to other major cities including Manchester, Liverpool, Birmingham and Glasgow.

By car:

From London and the M25, proceed north along the M1 until junction 14.

Exit onto the slip road (M1 J14). At the roundabout, take the third exit onto London Road A509 towards Wellingborough and Kettering.

Stay on this road, passing over two roundabouts. After a long, straight mile of dual carriageway, take the third exit onto A422 towards Bedford.

After leaving the roundabout turn right down Chicheley Road (before the pub on the left), then turn left through the gates to Chicheley Hall.

Satellite navigation:

If using a satellite navigation system please note that you will be advised to use Hall Lane, the former access to Chicheley Hall.

The correct access is via the main entrance on Chicheley Road, the next road along from Hall Lane.

CELEBRATE 350 YEARS

SPEAKER INFORMATION

Bernard de Bono

Articulating physiology knowledge about tissues for drug discovery

Histology information management relies on complex knowledge derived from morphological tissue analyses. These approaches have not significantly facilitated the general integration of tissue- and molecular-level knowledge across the board in support of a systematic classification of tissue function, as well as the coherent multi-scale study of physiology. Our work aims to support directly these integrative goals in general, and to achieve drug discovery objectives in particular.

Bernard de Bono, MD PhD, leads on the development of semantic interoperability infrastructure and standards for biomedical resources. In particular, he is developing the requisite computational infrastructure for the ontology-based annotation, sharing and inferencing of physiology-related semantic metadata to bridge resources generated by the Innovative Medicines Initiative and Virtual Physiological Human communities. In addition, de Bono has developed the ApiNATOMY approach to ontology visualisation in support of more effective knowledge management by the physiology and pharmaceutical research communities. De Bono holds PI positions at the Auckland Bioengineering Institute and University College London.

Elhanan Borenstein

Towards a Predictive Systems-Level Model of the Human Microbiome

The human microbiome represents a vastly complex ecosystem that is tightly linked to many host-related processes and that directly impact human health. To date, however, most studies have focused on characterizing the composition of the microbiome in health and in disease and on comparative analyses, and relatively little effort has been directed at studying and modeling the microbiome as an integrated and comprehensive biological system. In this talk, I will highlight the pressing need for the development of predictive system-level models of the microbiome and discuss potential computational frameworks for metagenomic-based modeling of this microbial system. I will describe several preliminary attempts at constructing such models at the cellular, ecological and supra-organismal levels, accounting for the complex web of interactions in the microbiome. I will further review routes for integrating various modeling approaches and for obtaining a multi-scale modeling framework. Finally, I will discuss exciting future clinical and ecological applications and research avenues facilitated by such models of the microbiome, including designer microbiomes and ecosystomics.

Elhanan Borenstein is an assistant professor of Genome Sciences at the University of Washington, with an adjunct position in the Department of Computer Science and engineering and an external professor position at the Santa Fe Institute for complexity science. He received his PhD in computer science from Tel-Aviv University, Israel, and held a joint postdoctoral fellowship at the Department of Biology in Stanford and at the Santa Fe Institute. Dr. Borenstein uses computational and mathematical models, complex network analysis, and a systems biology approach to address a diverse set of central questions in evolutionary and systems biology. He studies the metabolic networks of microbes and microbiomes to identify the environmental and genetic factors that determine their organization, function, and evolution. Applying these methods to study the human microbiome, he aims to develop a better systems-level predictive understanding of the microbiome and its role in human health. Dr. Borenstein is the recipient of various awards including, most recently, the Alfred P. Sloan Fellowship and the 2012 NIH New Innovator Award.

Ibrahim Elmadfa

The role of antioxidants in the immune function

Antioxidants are essential to the body's function to cope with the constant burden of highly reactive molecules and free radicals arising from exogenous as well as endogenous sources.
However, while reactive oxygen and nitrogen species (ROS and RNS) can be detrimental to body structures like fatty acids and proteins and impair their functions, they are also part of physiological processes. Most importantly, they are used to kill pathogens during the respiratory burst. Damage to the radical-generating immune cells is prevented by antioxidants that are needed in adequate amounts to enable efficient defence. Radicals are also involved in the synthesis of eicosanoids, important regulators of immune responses especially of the inflammatory kind. Moreover, ROS and nitric oxide (NO) play a role in cell signal transduction. As inducers of transcription factors like NFkB or AP-1, they regulate the synthesis of proinflammatory cytokines. An imbalance in the oxidative system, known as oxidative stress, disrupts these processes making a tight control of oxidative balance necessary for optimal immune function. Indeed, many non-communicable diseases linked to oxidative stress are characterised by chronic low-grade inflammation.
Considering the involvement of free radicals in the generation and progression of inflammatory processes, antioxidants can be used in the therapy as modulators of the immune answer. There is good evidence of the beneficial effects of nutritional antioxidants such as vitamins C and E and secondary plant compounds on diseases like rheumatoid arthritis and inflammatory bowel disease.
A good status of antioxidants down-regulating inflammatory processes can also contribute to longevity and better health in later life.
However, due to the complex interactions between single antioxidants and their involvement in various processes, supplementation particularly with high doses requires great care. Especially in healthy persons, a well-balanced diet rich in vegetables, fruits and whole grain cereals is the best source of antioxidants.

President of the International Union of Nutritional Science (IUNS), President of Austrian Nutrition Society
Professional appointments:
1990 - 2011 Professor for Human Nutrition and director of the Institute of Nutritional Sciences, University of Vienna
1980 – 1990: Professor for Human Nutrition at the University of Giessen, Germany
Expertise: Scientific advisor to the European Commission and member of Steering Committee on Nutrition, Diet and Healthy Lifestyle of EU commission (DG Sanco);
The Austrian MOH as member of the Codex Alimentarius Austriacus Committee (Dietetic Foods, Novel Foods, Upper Safe Level of nutrients),The WHO as member of Nutrition Guidance Expert Advisory Group (NUGAG) and the International Advisory Council of theGlobal Non-communicable Disease Network (NCDnet).
Editor-in-Chief, Annals of Nutrition and Metabolism and Forum Nutrition (2000-2011); Author and co-author of over 400 original papers , 24 books. Coordinator and author of the Austrian Nutrition Report 1998, 2003, 2008, 2012 and the European Nutrition and Health Report 2004 and 2009.

Malcolm Gordon

Comparative and evolutionary systems biology: examples from an endless frontier

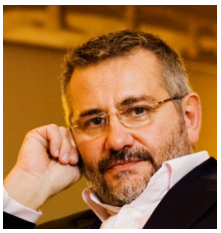
Much of contemporary systems biology is directed toward exploring the rich connections between molecular and cell biology, epigenetics and the many fields of omics. My emphasis will be on aspects of the comparably rich connections that can be developed between systems approaches broadly defined and comparative organismic and evolutionary biology. My personal research interests in these latter areas currently emphasize biophysical, biomechanical and bioengineering questions involving locomotion in some evolutionarily highly derived bony fishes.
Combining current understanding of evolutionary processes with relatively simple robotic models makes it possible, for the first time, to analytically evaluate major functional trade-offs in the design and operation of morphologically convergent (homoplastic) fishes belonging to distantly related clades. We can perform experiments that nature cannot. I illustrate this with recent results of a study of wake dynamics in two types of mackerel, a scombrid true mackerel and a carangid jack mackerel. An unexpected side development from earlier stages of this work has been an influence on aspects of automobile design.

Malcolm Gordon is a faculty member in the Department of Ecology and Evolutionary Biology at the University of California, Los Angeles (UCLA). His primary research subjects are bony fishes and amphibians (anurans). His topical research interests have centered on functional adaptations of animals to challenging environmental conditions in their natural habitats. Early work emphasized biochemistry and physiology; current activities are biophysical and biomechanical. He is a founding faculty member for the UCLA doctoral program in Environmental Science and Engineering and for the Institute of the Environment and Sustainability.

Adriano Henney

The Virtual Liver: A Multidisciplinary, Multilevel Challenge for Systems biology

The liver is the central metabolic organ in human physiology, with functions that are fundamentally important to the detoxification of xenobiotics, the maintenance of homeostasis of numerous blood metabolites, and the production of mediators of the acute phase response. Liver toxicity, whether actual or implied is the reason for the failure of many promising novel medicines that consequently never reach the market, and diseases such as atherosclerosis, diabetes, and fatty liver diseases, that are a major burden on current health resources, are directly linked to functional and structural disorders of the liver. In this lecture I shall present the concepts and approaches underpinning one of the most exciting and ambitious modelling projects in the field of systems biology and systems medicine. This major multidisciplinary research program is aimed at developing a whole-organ model of the human liver, representing its central physiological functions under normal and pathological conditions. The model will be composed of a larger battery of interconnected sub-models representing liver anatomy and physiology, integrating processes across hierarchical levels in space, time, and structural organization. The talk will offer an outline of the general architecture of the liver model and present the first steps taken to reach this ambitious goal.



Dr Henney has a PhD in Medicine and many years academic research experience in cardiovascular disease in laboratories in London, Cambridge and Oxford. His interests have focused predominantly on atherosclerosis, with studies ranging from pathology, through molecular and cellular biology to molecular genetics. In 1997, he was recruited by Zeneca Pharmaceuticals from a Senior Fellowship position leading his own molecular genetics group in Oxford, to lead the exploration of new therapeutic approaches in atherosclerosis, specifically focusing on his research interests in vascular biology. Following moves within AstraZeneca he became responsible for exploring strategic improvements to the company's approaches to pharmaceutical target identification, and the reduction of attrition in early development, directing projects across research sites and across functional project teams in the US, Sweden and the UK. This resulted in the creation of a new multidisciplinary department that focused on pathway mapping, modelling and simulation supporting projects across Research and Development, which evolved to establish the practice of Systems Biology, prototyping the application of mechanistic disease modelling approaches to the discovery of innovative new medicines. Since leaving AstraZeneca, Dr Henney has continued his interest in Systems Biology, Synthetic Biology and Systems Medicine through his company, Obsidian Biomedical Consulting Ltd. He now directs a major €50M German national flagship programme: the Virtual Liver Network.

Charlie Hodgman

Recent advances in plant physiomics

Following an outline of key aspects of plant anatomy and physiology, there will be a brief description of modelling approaches used to represent aspects of the plant physiome. Recent technological developments will be introduced including non-destructive fluorescent sensors of hormone levels, advanced image analysis techniques and novel multiscale modelling frameworks. Their application will then be described in three examples, specifically the hormone-dilution hypothesis of primary root growth, a biological tip-switch in root responses to gravity signals, and the role of multicellular mechanics in the emergence of lateral roots.

Charlie Hodgman has spent over 30 years at the interface between biology, mathematics and computer science to address biological issues in both industrial and academic settings. In 2004, he moved from GlaxoSmithKline to the University of Nottingham to take up the Chair in Bioinformatics and Systems Biology and in 2007 became the founding director of the Centre for Plant Integrative Biology (http://cpib.ac.uk/). Since then, the majority of his research effort has focussed on root biology (in Arabidopsis and rice) and fruit ripening (in tomatoes).

Peter Hunter

An overview of VPH/Physiome activities

Multi-scale models of organs and organ systems, based on model encoding standards, are being developed under the umbrella of the Physiome Project of the International Union of Physiological Sciences (IUPS) and the Virtual Physiological Human (VPH) project funded by the European Commission. These computational physiology models deal with multiple physical processes (coupled tissue mechanics, electrical activity, fluid flow, etc) and multiple spatial and temporal scales. They are intended both to help understand physiological function and to provide a basis for diagnosing and treating pathologies in a clinical setting. A long term goal of the project is to use computational modeling to analyze integrative biological function in terms of underlying structure and molecular mechanisms. Web-accessible databases, based on the standards, have been established for models and model-related data at the cell, tissue, organ and organ system levels. This talk will discuss recent developments in the VPH/Physiome Project.

References:

1. Hunter, P.J. and Borg, T.K. Integration from proteins to organs: The Physiome Project. Nature Reviews Molecular and Cell Biology. 4, 237-243, 2003.
2. Hunter, P.J. and Nielsen, P.M.F. A strategy for integrative computational physiology. Physiology. 20,316-325, 2005.
3. Hunter, P.J. Modeling living systems: the IUPS/EMBS Physiome Project. Proceedings of the IEEE. 94:678-691, 2006.
4. Bassingthwaighte, J., Hunter, P.J. Noble, D. The Cardiac Physiome: perspectives for the future. Experimental Physiology, 94(5):597-605, 2009.
5. De Bono, B. and Hunter, P.J. Integrating knowledge representation and quantitative modelling in physiology. Biotechnol. J. 7:958-972, 2012. DOI 10.1002/biot.201100304
6. Coveney, P.V. , Diaz-Zuccarini, V., Graf, N., Hunter, P., Kohl, P., Tegner, J. and Viceconti, M. Integrative approaches to computational biomedicine. Interface Focus. 2013 3 20130003; doi:10.1098/rsfs.2013.0003
7. Hunter, P.J., et al. Discussion: A vision and strategy for the virtual physiological human: 2012 update. Interface Focus. 2013 3 20130004; doi:10.1098/rsfs.2013.0004

Peter Hunter completed his Engineering and Masters of Engineering degrees at The University of Auckland before undertaking his DPhil (PhD) in Physiology at the University of Oxford where he researched finite element modeling of ventricular mechanics. Since then his major research interests have been around modelling various aspects of the human body using specially developed computational algorithms and an anatomically and biophysically based approach which incorporates the detailed anatomical and microstructural measurements and material properties into the continuum models.
As recent Co-Chair of the Physiome Committee of the International Union of Physiological Sciences, Peter is helping to lead the world in the use of computational methods for understanding the integrated physiological function of the body in terms of the structure and function of tissues, cells and proteins. Alongside his role as Director of the Auckland Bioengineering Institute and Professor of Engineering Science at The University of Auckland, Peter is also Director of Computational Physiology at Oxford University and he holds honorary or visiting Professorships at a number of universities around the world. Peter is also on the scientific advisory boards of a number of research institutes in Europe, the US and the Asia-Pacific region.

Hiroaki Kitano

HD-Physiology Project -A Japanese Flagship Physiological Modeling Project

Modeling of large-scale multi-layer physiological modeling is one of the grand challenge in biology and medicine. HD-Physiology Project is a Japanese flagship project intent to develop technical foundations for virtual patients. Current focus are integration of a whole body ADME/PK model and heart model that are grounded onto sub-cellular signaling networks and metabolic networks as well as protein structure conformation changes at even lower level. The project proposed and promoted the Garuda Platform that enables multiple software to smoothly operate to form a consistent workflow by assuring high-level of interoperability. CellDesigner and PhysioDesigner are two major software enable multi-layer modeling. Multiple models from various research groups are now being integrated to develop a consistent and large-scale model of virtual patients. We also attempt to use genetic variations to differentiate different computational outcome of the model reflecting possible use of personal genome data in clinical situation in future. Such a platform combined with a range of software tools and experimental approaches can be used to facilitate drug discovery and clinical decision-making. This talk describes overall objectives and achievement of the project and envisions future developments.

Hiroaki Kitano is a President and CEO at Sony Computer Science Laboratories, Inc., Tokyo, a President at The Systems Biology Institute, Tokyo, and a Professor at Okinawa Institute of Science and Technology Graduate University, Okinawa. He received a B.A. in physics from the International Christian University, Tokyo, and a Ph.D. in computer science from Kyoto University. Since 1988, he has been a visiting researcher at the Center for Machine Translation at Carnegie Mellon University. His research career includes a Project Director at Kitano Symbiotic Systems Project, ERATO, Japan Science and Technology Corporation. Kitano received The Computers and Thought Award from the International Joint Conferences on Artificial Intelligence in 1993, Prix Ars Electronica 2000, Design Award 2001(Japan Inter-Design Forum), Good Design Award 2001, and Nature's 2009 Japan Mid-career Award for Creative Mentoring in Science.

Denis Noble

A systems biological view of Evolutionary Biology: all in the interactions.

It is becoming clear that variation in organisms can be created by many different processes, including the gradual mutation idea of the Modern Synthesis, but also including larger changes through natural genome engineering, various forms of inheritance of acquired characteristics, symbiogenesis, genetic assimilation. Indeed, evolution itself must have evolved. The question how these mechanisms relate to each other is a fascinating new area for systems biology.

References:
Noble, D. (2011) Neo-Darwinism, the Modern Synthesis, and Selfish Genes: are they of use in physiology?, *Journal of Physiology* **589**, 1007-1015.
Noble, D. (2013) Physiology is rocking the foundations of evolutionary biology *Experimental Physiology*. doi: 10.1113/expphysiol.2012.071134

Denis Noble is Emeritus Professor of Cardiovascular Physiology in the University of Oxford and Director of Computational Physiology. He is author of *The Music of Life* (OUP 2006) and is President of the International Union of Physiological Sciences. His work using computational biology to reveal the mechanisms of genetic buffering in organisms has led him to question some of the central tenets of the Modern Synthesis.

Stig Omholt

Bridging the genotype-phenotype gap: what does it take?

The genotype–phenotype map (GP map) concept applies to any time point in the ontogeny of a living system. It is the outcome of very complex dynamics that include environmental effects, and bridging the genotype–phenotype gap is synonymous with understanding these dynamics. The context for this understanding is physiology, and the disciplinary goals of physiology do indeed demand the physiological community to seek this understanding. This task is beyond reach without use of mathematical models that bind together genetic and phenotypic data in a causally cohesive way. Bridging the genotype–phenotype gap also demands that large-scale biological ('omics') data and associated bioinformatics resources be more effectively integrated with computational physiology than is currently the case. A third major element is the need for developing a phenomics technology way beyond current state of the art that is solidly grounded on biophysically based mathematical descriptions of physiology.

Stig W. Omholt is Research Professor in the Faculty of Medicine at the Norwegian University of Science and Technology (NTNU) and Director of its new cross-campus biotechnology programme 'NTNU Biotechnology – the Confluence of Life Sciences, Mathematical Sciences and Engineering'. His current research interests include the etiology of hypertension, aspects of the astroglia–neuron interaction in the brain, model-guided drug targeting, experimental evolution, life-history biology, and the linking of genetics with systems dynamics and multiscale modelling.

Pingfan Rao

A Hidden System for Superoxide Disposal

Superoxide is widely implicated in stress, diseases and aging as a metabolic waste. It is macroscopically self-evident that harmless wastes requires a system including processes of collection, transportation, storage and treatment for an efficient and effective disposal, and harmful wastes demand even much more sophisticated one. As a detrimental metabolic waste, superoxide is never known to be accommodated with such a disposal system except the neutralization by various antioxidant mechanisms, which is random rather than systematical. We encountered this hidden system by complete accident when we found that the topical application of TAT-SOD, an intracellular superoxide quenching enzyme on certain facial parts could instantly mitigate rhinitis. It reminded us of acupuncture meridians which are mysterious channels linking different parts of the body to pass the effect from one site to another, and prompted us to correlate the mysterious meridians with the intracellular superoxide anion. **1**. To visualize the channels possibly involving intracellular superoxide, rats were injected with DCFH-DA, an intracellular reactive oxygen species (ROSs) indicator at the tail vein. As a result, their fascial lines on the inner side of the frontal abdominal wall including the linea alba emitted intense fluorescent light,

forming a pattern which could be superimposed on the classic human meridians chart, indicating that ROSs are transported along a connective tissue of fascia. **2.** The ROSs was confirmed to be superoxide in a controlled clinical trial, in which substituting acupuncture with topical application of TAT-SOD cream achieved a comparable effect on weight loss. **3.** The biological function of the superoxide channel was illustrated by the investigation of the effect of severing the linea alba of a rat on its hepatic metabolic function. Rats with the linea alba severed awoke from choral hydrate anaesthesia in 3 hours in comparison with 20 minutes for the control group, due to a decreased choral hydrate metabolism caused by the failure of diffusing the hepatic superoxide through the linea alba. The reconnection of the two ends of the severed linea alba with a wire shortened the awaking time to 23 minutes, indicating the electronic nature of the transportation along the linea alba. It was further demonstrated that the passage of the hepatic superoxide to the linea alba was carried out by the thin film between the hepatic falciform ligament and the linea alba. The film emitted the green fluorescent light when the rat was injected with DCFH-DA, and the disruption of the film changed the electric current pattern along the linea alba. **4.** Furthermore, the hepatic superoxide was found to be conducted through the bile duct wall to the intestine wall through DCFH-DA intracellular superoxide visualization of living rats, which suggests that the connective tissue is not the only channel for superoxide transportation and the intestine may possibly be a site for superoxide treatment. Those results indicate the existence of a superoxide disposal system implicating connective tissues such as fascia, falciform ligament and bile duct as transportation channels, and reveal its vital physiological role of electrically diffusing superoxide anions as a prerequisite of the normal function of the visceral organs. To understand the whole picture of this hidden system, a formidable task lies ahead to elucidate how intracellular or mitochondrial superoxide is conducted from tissue cells to the fascia, and what cells inside fascia and in the bile duct and intestine wall are transporting superoxide, and where and how superoxide is stored and what the eventual fate of the diffused superoxide is.

Pingfan Rao, Ph.D., received BEng in food technology from Fuzhou University of China in 1982, MSc in food science from Hiroshima University in 1986, and PhD in biochemistry from Osaka University of Japan in 1989. He is currently Professor and founding Director of CAS.SIBS-Zhejiang Gongshang University Joint Center for Food and Nutrition Research, and a Professor of Fuzhou University of China.
He is President (2012-14) of the International Union of Food Science and Technology, a fellow of International Academy of Food Science and Technology, Vice President of the Chinese Institute of Food Science and Technology. His research focuses primarily on identifying and characterizing bioactive proteins and expression and scale production of recombinant enzymes, protein derivatives as the active ingredients of tradition Chinese medicine and food, new methodology for cell separation and superoxide channels.

Nils Christian Stenseth

The interplay between ecology and evolution in host-vector-pathogen systems: *Yersinia pestis* as an example

The presentation will start with a summary of how ecology and evolution mutually affect each other in a feedback loop. Then the ecology and evolution of the *Yersinia pestis*-ssytem will be discussed (including both statistical and mathematical modeling) – modeling work being used as a basis for understanding how climate variation might affect this system as well as how the ecological dynamics might affect the evolution of virulence. Examples will be taken from Central Asia, the Caucuses and China.

Besides being an active scientist I am also a public advocate for science, actively participating in the discussions of how best to structure and strenghten the scientific community. I am an elected member of the Norwegian Academy of Science and the Letters, DNVA; currently I'm the president of that Academy. I am also an elected member/fellow of several other academies, including the Royal Norwegian Society of Science and Letters, DKNVS, Academia Europaea, French Académie des Sciences and the Finnish Society of Sciences and Letters. I have been awarded honorary doctorates (Doctor Honoris Causa) at the University of Antwerpen, Belgium (2001) and at the École Normale Supéreure, Lyon, France (2011). I am Chevalier (Knight) in the French National Order of the Legion of Honour.

I am a Core Member, Research Professor and the Chair of CEES. In addition, I am a Chief Scientist at the Institute of Marine Research.

My research interests span a broad spectrum of ecological and evolutionary topics, most of which are rooted in population biology. Before the early 1990s, much of my work was purely theoretical. Later, I have adopted the research strategy of 'asking' available data what the underlying ecological or evolutionary process might most likely be - all within a theoretical perspective. I strongly favour comparative studies - by comparing similar features between different (but comparable) systems, we typically learn more than we otherwise would have done. Variations in population densities in time and space - and the underlying demographic processes - have been a main interest of mine over the years. An important example is the interdependent relation between density-dependent and density-independent processes, where the ecological effect of climate is an important example of the latter.

Janet Thornton

Bioinformatics at EBI: Fulfilling the Work of Systems Biology

The life sciences are now, more than ever, a big data science. Life sciences are firmly embedded as an "eScience". One of the major bottlenecks in systems biology is the handling, management and interoperability of data. I will introduce EBI - and describe how we are approaching some of these challenges.

After graduating in Physics from Nottingham University in 1967, Janet studied for her Ph.D. in Biophysics at the National Institute for Medical Research, Mill Hill, London. Her research is focused on understanding the structure , function and evolution of proteins using computational approaches. In October 2001 Janet became Director of EMBL – EBI. In 1999 Janet was elected a Fellow of the Royal Society and a Member of EMBO in 2000; in 2002 she was appointed Extraordinary Fellow, Churchill College, Cambridge and Honorary Professor, University of Cambridge and in 2003 she was elected a Foreign Associate Member of the U.S. National Academy of Sciences. In 2012 she was appointed a Dame Commander of the British Empire.

Hans Westerhoff

Mapping metabolic systems biology: from molecule to man

By organizing the plethora of biomedical information into a new type of dynamic framework, more of the information that is acquired will work towards the understanding of health and disease. The basis of this framework will be a molecule-based, structured and dynamic model of the human. I will discuss the potential that Recon2, the March 2013 consensus reconstruction of genome-wide human metabolism, may already offer. The furture may include the generation of millions of metabolic maps, one for each sequenced individual. Individualized n=1 medicine should become possible, acknowledging the individuality of genome, nutrition, lifestyle and ambition. Feeding real-time information about the state of the individual's body into the map should liven it up to include a more dynamic predicting of one's well-being.
Indeed, the map of recon2 should be made more dynamic than it is, requiring more dynamic modeling. It should also move up the scale, differ between organs as well as individuals, and between induction states. I will discuss our attempts to do this around the issue of glutathione-mediated drug detoxification and biomarkers thereof.

Hans Westerhoff is a long time researcher of how dynamic interactions between components of biological systems generate function. After a PhD at the University of Amsterdam and stays at the University of Padova, at the US National Institute of Health and at the Netherlands Cancer Institute, he is now Professor of Systems Biology and Director of the Manchester Centre for Integrative Systems Biology, of the Manchester Doctoral Training Centre for Systems Biology. He is also Professor of Microbial Physiology at the VU University of Amsterdam and of Synthetic Systems Biology at the University of Amsterdam. He is among the drivers of ITFoM and the Infrastructure of Systems Biology Europe (ISBE).

Thank you to our contributors for their support: