SystemsX
The Swiss Initiative in Systems Biology

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June 13th 2006

Center for Systems Bacterial Infections becomes Scientific Node of SystemsX

C-SBI
Center for
Systems Bacterial Infection

Basel. thm. The Partners' Meeting of SystemsX has declared the Center of Systems Bacterial Infections a new Scientific Node of SystemsX. The new Node is led by Prof. Guy Cornelius from the Biozentrum of the University of Basel. The goal of the Center of Systems Bacterial Infections (C-SBI) is to model the network of interactions between pathogenic bacteria and various cell types contributing to the onset of the inflammatory response which orchestrates our innate immunity.

A better understanding of these interactions may lead to new ways of preventing or treating not only infectious diseases but also diseases resulting from uncontrolled inflammation. Bacterial infections represent a matter of concern, worldwide. However, major scientific breakthroughs have recently revealed how pathogenic bacteria and mammalian hosts interact at the cellular and molecular level. On one hand, hosts have evolved a very efficient immune system, based on the tight collaboration between soluble factors and various specialized cell types including phagocytes, which leads to adapted inflammatory responses.

On the other hand, pathogenic bacteria have developed sophisticated nanoweapons which enable them to paralyze phagocytes and to invade non-phagocytic host cells by manipulating cellular control processes. These weapons also interfere with key intracellular signalling pathways that control inflammation such as, for instance, the activation of the transcription factor NF- K B. Due to genome completion of most microbial pathogens and of the human host as well as a variety of model host systems (mouse, rat, fly, and worm), the field of bacterial infection can now be addressed by Systems Biology approaches. The pathogen and the host can be described as two networks of cellular components that interact and adapt to each other.

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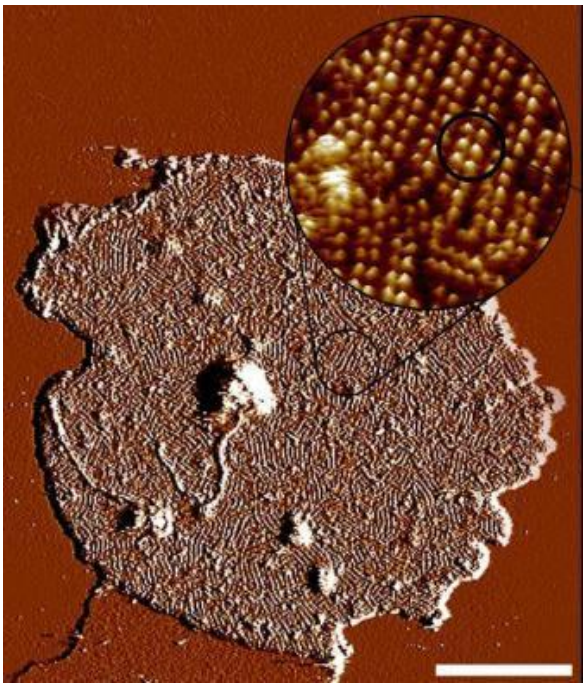
Center for Cellular Imaging and Nanoanalytics approved as SystemsX Glue Project

Basel. thm. The Center for Cellular Imaging and Nanoanalytics (CINA) was approved to be a Glue Project of SystemsX by the Partners' Meeting of SystemsX. Appointed Director is Prof. Andreas Engel from the Biozentrum of the University of Basel. CINA will be located in the building of the C-BSSE on Rosental Biopark in Basel. CINA's mission is to develop novel analytical tools to determine the proteome of single cells, to visualize single cells and their constituents at nanometre to atomic scale resolution, and to provide services supporting the scientific goals of SystemsX.

To assess the biological machinery involved in signal transmission and gene regulation in the cellular context, cryo-electron tomography of vitrified cells will be the method of choice to achieve Nanoscale resolution. This non-invasive three-dimensional imaging technique is a unique method to unravel the architecture of biological systems. CINA will establish the entire range of EM methods and will combine them with sample preparation automation and nanoanalytics.

Within two years automated 3D-EM for supramolecular complexes and membrane protein 2D crystals with nanometer to atomic resolution will be established. A high-end 300 kV field-emission EM with He-cooled sample holder and 8k x 8k CCD camera will be installed.



Rhodopsin packed disk membranes from murine retina.
Picture Koster/Baumeister.

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Center for Information Sciences and Databases is built up to a Glue Project of SystemsX

Basel. thm. The Center for Information Sciences and Databases (CISD) has started. Dr. Adrian Honegger was appointed by the Partners Meeting as Director of this SystemsX Glue Project. The CISD business plan has been submitted and is currently under review. Once approved, a team of life science and database engineering experts will be built up.

The mission of CISD is to establish and ensure simple, reliable access to data of high quality and consistency with sufficient context to enable and support knowledge generation across SystemsX scientific nodes. As a focused group of interdisciplinary experts, fluent in all domains, CISD is to provide an effective scientific service bridging the gap between applied biology and information technologies enabling cross-disciplinary research. Simple, scalable and consistent storage and management of information is a key to successful research and collaboration within SystemsX. For further information and positions look at http://www.systemsx.ch/about/platforms/cisd_openpositions.html.

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Center of Biosystems in Basel is seeking three Assistant Professors

Renato Paro, founding director of the C-BSSE.
Photo Flierl

Basel. thm. Renato Paro, the founding director of the Center of Biosystems of ETH Zurich in Basel, is seeking assistant professors. The Center is planned to have at least 15 professorships in different disciplines of life sciences, engineering and informatics. Negotiations with senior candidates for full professorships are on the way. In addition, C-BSSE seeks to fill three positions at the assistant professor level (tenure track). The candidate in the area of experimental quantitative cell biology should have a strong background in quantitative analyses of cellular processes. The one for the field of computational biology is expected to demonstrate potential to develop an innovative research program in computational biology targeted towards biosystems sciences and engineering. And the person for the area of synthetic biology/engineering of biological systems should bring along the ambition to develop an innovative research program in the rational engineering of complex biological systems.

Paro was appointed Professor for Biosystems at ETH Zurich by the ETH Council last March. His mission is to make the Center of Biosystems Science and Engineering (C-BSSE) in Basel a world wide known address in Systems Biology.

For open positions, see:
http://www.bsse.ethz.ch/box_feeder/Inserat_Assistant_Professors.pdf
Press release on the appointment of Renato Paro:
http://www.systemsx.ch/news/press.html.

Three new Systems Biology Centers in UK awarded £27M

Swindon (UK). BBSRC. Three new centres for integrative systems biology, representing an investment of £27M (CHF 60), have been announced on April 20th 2006, by the Biotechnology and Biological Sciences Research Council (BBSRC) in Great Britain. This follows the successful launch of three centres last year. The new centres will be located at the Universities of Edinburgh, Nottingham and Oxford and will bring together biologists, mathematicians and computer scientists. The funding includes £4.8M from the Engineering and Physical Sciences Research Council (EPSRC). The host universities are also making considerable investments in the centres, devoting dedicated space and contributing research posts and facilities.

The new centres focus specifically on: dynamic biological systems, such as biological clocks, the nature and behaviour of plant roots and signalling pathways in bacteria and yeasts. They will also have an 'outreach' function, stimulating systems biology research across the whole of biological science research.

University of Edinburgh

The University of Edinburgh is committed to a multidisciplinary approach that integrates the life sciences with the physical sciences. The Centre for Systems Biology at Edinburgh aims to model dynamic biological systems – focusing on RNA metabolism, the interferon pathway and circadian rhythms – and will bring together researchers from informatics, molecular plant sciences, medicine and cell and molecular biology among others. One of the professors involved is Andrew Millar.

University of Nottingham

The Centre for Plant Integrative Biology (CPIB) at the University of Nottingham will develop a 'virtual root' which will serve as an exemplar for using Integrated Systems Biology to model multicellular systems. The Nottingham Centre will integrate advanced experimental and imaging approaches with innovative mathematical, engineering and computer science research in conjunction with Rothamsted Research and several international collaborators. The CPIB will be directed by Professor Charlie Hodgman.

University of Oxford

The Oxford Integrative Systems Biology Centre will tackle a range of biological problems concerning network pathways. A major interdisciplinary initiative, the centre involves members of the Departments of Biochemistry, Pathology, Chemistry, Mathematics, Statistics, Engineering and Computation. The research will look at the language which single cell organisms use to control their behaviour. The aim of the project is to develop robust predictive models of these complex models. One of the professors involved is Judy Armitage.

Max-Planck-Center for Systems Biology in Dortmund

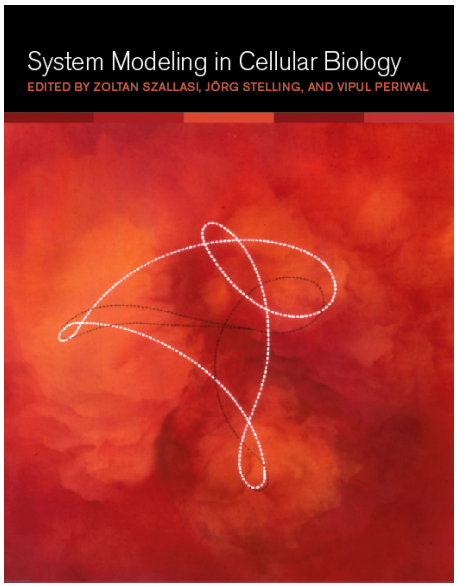
Dortmund. thm. In Dortmund, 20 Million Euro will be invested in a Center for Systems Biology. Another 19 Million Euro flow into a new Center for Chemical Genomics, and 8 Million Euro are reserved for a Center for Applied Proteomics. Until 2008, in total 47 Million Euro (73 Mio. CHF) will be invested into this so called innovation platform for the life sciences.

The funding comes from the state Nordrhein-Westfalen and from EU and is intended to build up new infrastructure. The running costs of the facilities have to be financed by the carriers. The new Center for Systems Biology will be set up in the buildings of the Max-Planck-Institute of Molecular Physiology in Dortmund, which is the carrier of this center. The Centers for Chemical Genomics and for applied Proteomics will be located on the area of the Technologiezentrum Dortmund. The carriers of these two centers are the Technologiezentrum Dortmund, the Ruhr-Universität Bochum and Unversität Dortmund. Close ties exist also to companies like Degussa.

The Center for Chemical Genomics focuses on target-oriented syntheses of small molecules, their collection in functional libraries and the development of new drugs. The Center for Applied Proteomics will develop new technologies in proteomics, glycoanalysis, proteinbiochips and bioinformatics.

A kick-off meeting of the Dortmund innovation platform for the life sciences takes place on June 23rd.
More information is available from Dr. Doris Schnabel, +49 231 9742 130, schnabel@tzdo.de

New Book on System Modelling



Zürich. thm. This book is worth a read. Jörg Stelling, Professor at the Institute of Computational Science of ETH Zurich, is one of the co-editors of «System Modeling in Cellular Biology. From Concepts to Nuts and Bolts». The book is highly recommendable also for non-computational scientists. It covers a comprehensive overview of system modeling for researchers from different disciplines. It presents key concepts like robustness and modularity, the best-known modeling approaches with their advantages and disadvantages, learns lessons from the application of mathematical models to the study of cellular biology. Especially rewarding are the introductory chapters on the general concepts of modelling, robustness and modularity in systems biology.

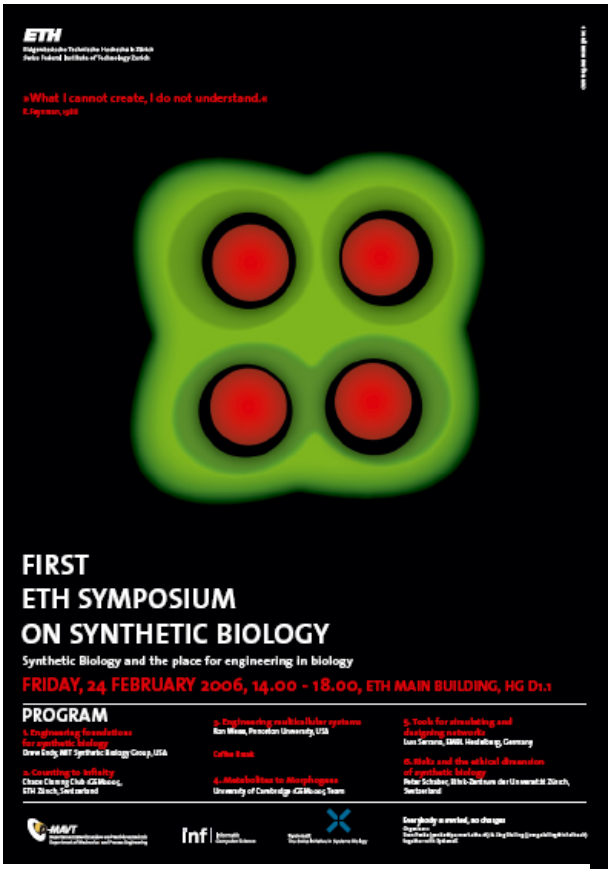
More Information: http://mitpress.mit.edu/catalog/item/default.asp?ttype=2&tid=10923

Synthetic Biology on the Rise

The first ETH Zürich Symposium on Synthetic Biology «Synthetic Biology and the place for engineering in biology» showed the high hopes of a new branch of biology, but did not neglect ethical and societal issues.

*By Sven Panke**

Synthetic Biology is a rapidly emerging novel discipline that tries to introduce a more comprehensive engineering perspective into the field of biotechnology. Biology has traditionally more revolved around the concepts of complexity and evolution, emphasizing the elements that are typically at odds with an engineering approach based on, for example, mono-functional and clearly characterized parts, standardized interfaces, hierarchical organization, and the separation of design and manufacturing. However, recent advances in genetic engineering, systems biology, and foundational technologies such as DNA synthesis are changing the picture and have encouraged a growing number of scientists to work on implementing an engineering approach into biotechnological research. Some of these efforts were discussed in the "First ETH Symposium on Synthetic Biology – the place for engineering in biology", that took place in the ETH main building on Feb. 24th, 2006.



The conference attracted about 100 people.

Poster by Ruedi Widmer

Reengineering viruses

Drew Endy, Assistant Professor at the MIT Bioengineering Division, presented for example his vision on re-engineering biological systems to e.g. eliminate sequences of obvious multiple functions. His group works on one of the simplest available biological systems, the *Escherichia coli* phage T7, and re-designed the first 10 kB of T7's genome. Encouragingly, the phage was fully functional after the redesign. Such ideas have also led to the set-up of a novel database at MIT – the Registry of Standard Biological Parts (http://parts.mit.edu). The idea is here to have a repository where thoroughly characterized DNA elements ("parts") that have been designed along a specific format can be deposited. Due to the formatting process, the re-combination of these parts to "devices" or even "systems" should be very much facilitated. Coupled to the idea of one part – one function, it might at some point be possible to design systems from these parts just as it is possible to assemble a car from standardized parts today.

Fascinating patterns

Ron Weiss, Assistant Professor at the Electrical Engineering Department of Princeton, discussed his work on engineering and re-building cell-cell communication, an instrumental part of any future engineering perspective in biotechnology that would involve cellular properties that vary in a pre-determined fashion over a cellular population. Rather than using classic examples such as mammalian cells, in which cell differentiation is common, his group is rebuilding the basics for such activities in bacteria. For example, by exploiting the homoserine lactone-based chemical signalling system from *Vibrio fisheri* in order to control the synthesis of a variety of fluorescent proteins along bacteria-produced chemical concentration gradients, he could produce a variety of fascinating patterns, reflecting the molecular events that lead to differentiation in higher organisms. Promisingly, at least some of these concepts should be transferable to exciting fields of applications, such as gene therapy.

UT Austin 2004 Synthetic Biology competition photo.

Courtesy Jeff Tabor and Randy Rettberg

Finally, the basis of engineering is mathematical modelling, and consequently synthetic biology will require a thorough modelling foundation. Some suitable tools for this purpose were presented by Luis Serrano from the European Molecular Biology Laboratory in Heidelberg. While at least some of the classical genetic engineering concepts appear to be transferable to re-designing systems on DNA level, the situation is more complicated on the protein level. For example, it is a lot more difficult to provide robust protein modules that function when coupled to a variety of different proteins than to successfully integrate transcription terminators at the end of any bacterial operon. However, again, a lot of progress has been made, for example in rationalizing the structure-function relationship in proteins which allows to manipulate protein function in a targeted, rational way rather than following evolutionary approaches. These advances have been made conveniently available in the program “FoldX” that has been developed in the Serrano-lab.

The biological design contest

An exciting approach to train people in the highly interdisciplinary area of Synthetic Biology is the international iGEM summer competition in Synthetic Biology. Here, undergraduate and graduate students from different disciplines get – after a short but intensive training in the basics of the different disciplines - together over the summer break and carry out their biological design project: from abstract system description and mathematical analysis via devices and parts down to DNA-sequence design and – sometimes – implication. The results of such design projects are then presented at a final get-together at the MIT in Boston. The two European teams that took part in the 2005 competition also presented their projects at the symposium: the team from Cambridge their project “Metabolites to Morphogens” and the ETH-team from the Chaos Cloning Club, who tried to design and implement a biological counter. Both projects demonstrated the enthusiasm that arises when people with different backgrounds get together and collaborate for a common goal, overcoming the different initial hurdles in order to deliver a re-

sult that is much better developed than any single discipline alone could ever have hoped for.

A new ethical dimension?

Finally, the envisioned possibilities of Synthetic Biology revive familiar discussions around the ethical implications of genetic engineering. If systems become so highly engineered that manipulations become indeed simple and easily predictable, would this not require new regulations? If techniques such as in vitro DNA synthesis might one day transfer the capabilities of reconstructing viruses to – basically – everybody, will this be a new quality of danger? Prof. Peter Schaber from the University of Zurich commented on these topics. In his view, Synthetic Biology does not represent a novel quality in the discussion around genetic engineering. Of course there are issues that need to be discussed and integrated into existing schemes of biosafety precautions, but from an ethical perspective Synthetic Biology does not represent a fundamentally new ethical dimension.

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*Sven Panke is Professor at the Institute of Process Engineering at ETH Zürich

Conference on Systems Biology of Mammalian Cells

Heidelberg. thm. From July 12 to 14, 2006, the first Conference on Systems Biology of Mammalian Cells (SBMC 2006) takes place. The Conference is organized by HepatoSys, the Federal German Competence Network in Systems Biology of hepatocytes http://www.systembiologie.de/.

Among the speakers are L.C. Cantley from Harvard Medical School in Boston, J. Ferrell, University of Stanford, R. Heinrich, Humboldt University in Berlin and B. Kholodenko**,** Thomas Jefferson University in Philadelphia.

The themes of the conference circle around cellular behavior and cell fate decisions as the result of the coordinated activation and deactivation of multiple signaling pathways. Following genomic sequencing - one of the challenges Systems Biologists are now facing - is to quantitatively understand the complex interactions which cause the purposeful behavior of mammalian cells through modeling. Goals are for example being able to explain the cross-talk of signaling pathways through mathematical models as well as understanding the process by which interactions between transcription factors and their target sequences result in cellular responses. A proper understanding of mammalian cell behavior requires the merging of disciplines and the collaboration of life scientists, mathematicians, physicists, chemists, engineers and computer scientists.

SBMC 2006 Conference on Systems Biology of Mammalian Cells

Please visit the SBMC web presence at www.sbmc06.de and download the SBMC Flyer to obtain further information regarding participation and registration.

Jobs, Jobs, Jobs…

Zurich. thm. There is a number of open positions for PH.D. students, postdocs, and technical and administrative staff at different Nodes and Glue Projects of SystemsX. All job advertisements are accessible through: http://www.systemsx.ch/openpositions/openpositions.html.

Remarks by the Editor

Zurich. thm. This is the sixth newsletter about SystemsX, the Swiss Initiative in Systems Biology. This newsletter appears sporadically to inform about what is going on in and around SystemsX. The circle of addressees is kept wide. Please, spread the newsletter further.

Anyone who wishes to be put on the list of addressees can subscribe by sending an email to thomas.mueller@systemsx.ch. By the same way anyone who does not want to receive this newsletter can be put off the list.

Best regards
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