SystemsX.ch
The Swiss Initiative in Systems Biology

Newsletter #11
June 18th 2007

New Scientific Executive Board for SystemsX.ch elected

SystemsX.ch has a new operational board. The Scientific Executive Board is composed of scientists from all SystemsX.ch Partners and Systems Biology relevant disciplines.

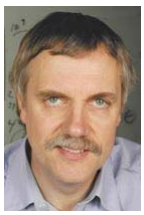
Zurich. thm/AK. SystemsX.ch is getting implemented. As an important step, the Partners decided at their meetings of April 12, 2007 and May 30, 2007 on the structure, the authorities, the duties and the composition of the new Scientific Executive Board (SEB). The board will replace the extended Executive Committee, with its main responsibility being the scientific strategic planning and operation of SystemsX.ch. All partners of SystemsX.ch and all disciplines relevant to Systems Biology are represented with at least one member. Managing Director Dani Vonder Mühll is member of the SEB without voting rights, and up to four guest scientists from industry may join.

The SEB will define and implement the over all strategic goals and operate SystemsX.ch. This involves in particular, in cooperation with the Swiss National Science Foundation (SNSF), definition and publication of calls for project proposals, but also to establish, manage and communicate facilitation of associated specifically tasked committees. The SNSF has been mandated to review and monitor all SystemsX.ch proposals from 2008 onwards.

Eight SEB members, presented below, have been elected. The election of a maximum of four further scientists will take place in July.

The Members of the Scientific Executive Board

Ruedi Aebersold (Chair)



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Ruedi Aebersold is one of the pioneers in the field of proteomics. He is known for developing a series of methods that have found wide application in analytical protein chemistry and proteomics. Aebersold and his team of researchers use protein profiles to differentiate cells in different states. This is expected to lead to new diagnostic markers and a more complete understanding of cell physiology.

Ron Appel

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Ron Appel is head of the Proteome Informatics Group of the Swiss Institute of Bioinformatics. The group is focusing its activities on the development of software tools and databases for proteomics. Besides proteome imaging and protein characterization, Ron Appel is involved in the servicing of the world-known ExPASy proteomics Web site and the SWISS-2DPAGE proteomics database.

Konrad Basler

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Konrad Basler is working on intercellular communication. Despite the countless instances of cell signalling, animals use a surprisingly small repertoire of signalling molecules. The goal of his research is to understand how these signalling proteins control growth and pattern building. Because these systems are highly conserved, Basler's group contributes to the general understanding of development.

Luke Lee

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Luke Lee's major research goal is the development of tools in nano- and micrometer dimensions to quantitatively describe processes in biological cells. His lab recently succeeded in building an artificial insect eye the size of a pin consisting of 8500 lenses and light channels. Other research fields are large scale single cell analysis, and culture tools for the intricate in-vivo networks that give rise to life.

Walter Senn

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Walter Senn is interested in how functions, such as memory or perception, emerge from the interaction of neurons in the cortex. His research covers models of neurons, synaptic plasticity, and learning. He develops models of neurons and networks which may explain behavior. One describes how attentional signals modulate the responses in sensory cortices, and how this can improve perception.

Vassily Hatzimanikatis

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Vassily Hatzimanikatis' main subject of research is computational biotechnology. He focuses on the development of mathematical and computational methods for the analysis of cell-wide genomic and proteomic information, and the identification of regulatory networks in cellular processes. He is also interested in the design of cellular and metabolic engineering applications.

Wolfgang Meier

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Wolfgang Meier is an expert in the interactions between synthetic polymers carrying anchor groups and model colloids like liposomes. Applications of this research are in cosmetic gels and wound healing dressings. Another topic focuses on polymerization processes in hollow particles with dimensions in the submicrometer range. These can be used in liquid crystals or in drug release systems.

Amalio Telenti

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Amalio Telentis research topic is the genetics of human susceptibility to HIV infection. Humans are not equal in this respect. There are individuals that remain seronegative despite of multiple exposures to HIV-infected partners, and others, so called «long-term progressors», who stay healthy much longer than expected. His laboratory studies the genetic variants that are associated with these differences in susceptibility.

The Decoding of Cell Fate

Deciphering the logic behind differentiation is the bold goal of the SystemsX Node «Center for Cell Plasticity and Stem Cell Biology» (C-CPHD) in Basel. Node Coordinator Susan Gasser explains how this shall be accomplished.

C-CPHD coordinator Susan Gasser is convinced that there are « basic circuits» which govern cell phenotypes. *Foto FMI*

Basel. How an unattractive larva transforms into a beautiful butterfly, or a single cell after fertilisation develops into a human being are still biological enigmas. Every day, our body fabricates on demand a whole arsenal of short-lived blood cells that arise from progenitor stem cells. Other types of cells, like neurons in the brain, develop once and remain functional for a lifetime.

By Thomas Müller

A phenomenon called cell plasticity allows animals such as salamanders and frogs to miraculously rebuild lost body parts. Plants can even be regenerated artificially from a single cell. Mammalian and human cells lack these abilities, but why? The same mechanisms hold the key, not only to normal function, but also when dysfunction occurs resulting in diseases such as cancer.

A lot is already known about these processes of differentiation and cell plasticity, but what is missing is «the logic behind it», as Susan Gasser puts it. Gasser, whose main job is directing the Friedrich Miescher Institute, part of the Novartis Research Foundation, is the coordinator of the new SystemsX Scientific Node «Center for Cell Plasticity and Stem Cell Biology» (C-CPHD) of the University of Basel. To decipher the logic behind differentiation and cell plasticity processes is the bold goal of C-CPHD.

Going beyond genetics

For a cell to maintain its identity through division, the process must faithfully reproduce this vital information. This cell memory which is embedded in the structure of the chromatin in the cell nucleus, where the DNA strand is coiled around proteins called histones. These proteins bear a range of covalent modifications that appear and disappear in a controlled manner. These changes are part of the mechanisms controlling genome expression. Working alongside histone modifications are transcription factors, proteins that bind specific sites in promoters to turn genes on and off. Epigenetics (=beyond genetics) is the science that analyses these mechanisms. Some of the factors that regulate epigenetic marks are themselves controlled by developmentally regulated genes; others are influenced by the environment of the cell – usually by other cells which send signals to the neighboring cell nucleus.

The working hypothesis of the C-CPHD is that there are «basic circuits» which govern the specification of gene expression by transcription factors and epigenetic marks as cells assume a differentiated cell phenotype. The confidence behind this belief in common principles is based on genetic evidence showing that master regulatory factors

often provoke a different outcome in different cells yet presumably act through common mechanisms. Similarly evolutionary evidence shows that conserved tasks can be ascribed to homologous factors in different species. It appears that nature has produced an economical multifunctional design, and the discovery and mathematical description of these circuits in computational models is the main goal of C-CPHD.

Building up Modelling Manpower

The construction of these models will be the task of the computational section of C-CPHD around Erik van Nimwegen and Mihaela Zavolan, both Professors at the Biozentrum of University of Basel. Two further computational scientists are to be hired at FMI and University of Basel to reinforce this core group. Collaboration is also foreseen with new recruits in computational biology coming soon to the Department of Biosystems Science and Engineering (DBSSE) of ETHZ.

C-CPHD intends to build up a coherent set of experimental systems in which differentiation and cell plasticity will be analysed and compared in three different mouse cell types: hematopoietic stem cells, neuronal cells and epithelial changes during tumor metastasis. The data will be generated in a way that is comparable within the three systems, and also with other similar data gathered elsewhere in the world. Susan Gasser sees the C-CPHD in a good position to achieve this outcome, «because FMI has been involved in the development of some of the techniques and is represented on the advisory boards which will set the standards for Europe and the US».

The data will be generated from gene expression analysis and genome-wide mapping of DNA and histone marks, and from a new method known under the buzzword «Deep Sequencing». «This technique opens a new door that should allow us to analyze very little amounts of DNA of highly complex composition in very a small number of cells –eventually one cell», says Gasser. C-CPHD is planning to buy the 700K CHF equipment in conjunction with the DBSSE, where it is intended to be installed in 2008.

A contribution from Roche?

There is however a somewhat delicate issue; at present there are two products on the market: the 454-sequencing system recently acquired by Roche, and one from Solexa (now Illumina). «It is not clear which is the most appropriate instrument for our applications », Susan Gasser says with a smile, «if it is the 454 sequencer, this may be a suitable object for a contribution from Roche».

Susan Gasser is so convinced of the project that FMI has agreed to carry half of the additional costs that C-CPHD will create at the University and FMI, supplying match funds up to CHF 1.5 M per year. As trade of, FMI gets access to the technology platforms (Glue Projects) of SystemsX; one of them (CINA), to be built also in the building of DBSSE nearby.

C-CPHD at a glance

Type of SystemsX Project:	Scientific Node
Coordinator:	Susan Gasser, FMI
Deputy coordinators:	Gerhard Christofori, DKBW University Basel. Georges Holländer, DKBW University Basel.
Participating institutions:	Friedrich Miescher Institute, Biozentrum University of Basel, Department Clinical-Biological Sciences University of Basel, Novartis Institute for Biomedical Research Basel, Institut Suisse de Recherches Experimentales sur le Cancer (ISREC), Department of Biosystems Science and Engineering (D-BSSE).
Number of research groups:	12 (2007), 15 (from 2010)
Over all budget:	CHF 7.8 Mio/year until 2009, 8.6 Mio/year from 2010-2012
For SysX requested funds:	3.0 M/year until 2009, 3.5 M/year from 2010-2012. FMI covers up to 1.5 M of the requested funds.

Struggle for more and saver Research Funds

Science politics is scheduled in the small chamber of the Swiss parliament. *Foto by Parlamentsdienste*

Berne. Tomorrow, June 19, in the small chamber (Ständerat) of the Swiss parliament, an interesting, and for SystemsX.ch relevant, decision is scheduled. The Ständerat is deciding whether or not the federal budget for Education, Research and Innovation, some 21,2 Billion CHF, will be guaranteed for the next four years (2008-2011).

Up to now, the parliament approved a «four year plan» in research and education, but the real bugdets are allocated in one year terms. In the past, the credits promised in the four year plans have been regularly cut significantly, leading to a dislocating stop and go progression for scientific institutions in Switzerland over the last decade.

It is anticipated that this routine will continue in the coming years with the Swiss Government already announcing in February that, for the bugdet year 2008, the Education, Research and Innovation sector would be cut by some 300 Million CHF.

This is why Fritz Schiesser, Ständerat from the Canton Glarus and President of the Swiss National Science Foundation is demanding a law which excludes all the science relevant federal credits from subsequent cuttings for the period of 2008-2011. There is some chance that the proposal will win a majority in the chamber. In the commission which prepared the debate, the proposal lost by only 7 to 5 votes.

Another point in the debate will be, whether the Federal Government will be forced to increase the overall budget for education, research and innovation by eight instead of the proposed six percent compared to the period 2004-2007. The Nationalrat last year favored an eight-percent increase, but in the responsible commission of the Ständerat the majority voted 6:2 against it. Observers expect the Ständerat to again turn down the motion.

Thomas Müller

Interested readers can watch the debate online and in realtime here. The debate is scheduled for tomorrow, Tuesday, June 19, 8 a.m.

Come all to the All-SystemsX.ch-Day

Zurich. AK. On September 17, 2007, the first All-SystemsX.ch-Day will take place at EPF Lausanne. The event is organized by SystemsX.ch and will consist of two parts. In a first part, ongoing research in Systems Biology and specifically on SystemsX Glue Projects and Scientific Nodes will be presented. In the second part, workshops will be organized to coordinate the setting up of teams to apply for new Glue Projects and Scientific Nodes. In addition, an excursion to the new LHC-accelerator of CERN, is planned for Sept. 16, 2007. The All-SystemsX.ch-Day is open to all people interested in Systems Biology.

More information and an application form here.

Scientific Advisory Board meets in November

Zurich. AK. The yearly meeting of the SystemsX Scientific Advisory Board will take place on November 26-28, 2007. The SAB is responsible for the critical review of the SystemsX scientific research, development plans, and their implementation. It also provides advice on general strategic and operational issues of SystemsX.

The SAB is composed of top scientific leaders with an interest in Systems Biology. Current members of the SAB are: Marvin Cassman (chair, San Francisco), Eugene Butcher (Stanford), Leroy Hood (ISB Seattle), Hiroaki Kitano (Sony Tokyo), Stanislas Leibler (Rockefeller), and Jasper Rine (Berkeley).

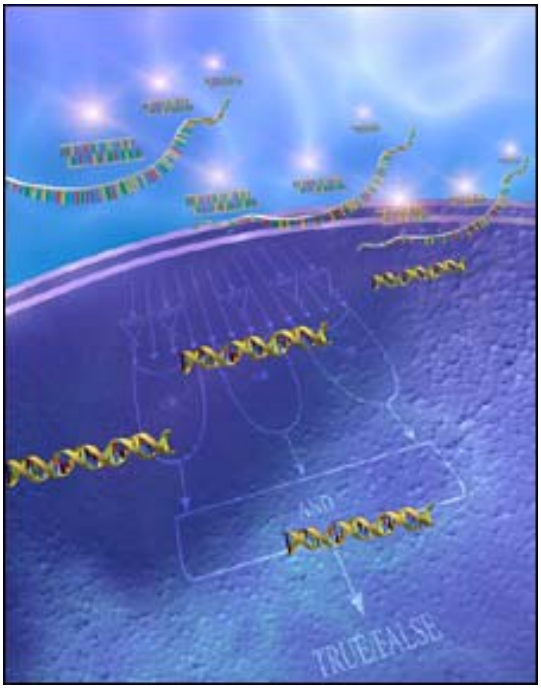
Helmholtz goes Systems Biology

Berlin. thm. The Helmholtz Association of German Research Centres is launching a systems biology initiative. The project will receive up to 24 million euros. The initiative will create a network comprising Helmholtz Centres, universities and other external partners, who will invest similar sums from their own funds. The long-term goal of the initiative is to shed light on the causes of complex disorders and diseases and develop new approaches for their treatment. The network will provide training opportunities for young scientists and technology platforms for all participating partners.

Prof. Dr. Roland Eils, head of the Theoretical Bioinformatics Division at the DKFZ, will head the initiative, which will initially involve the following Helmholtz Centres: the German Cancer Research Centre, the GSF - National Research Centre for Environment and Health, the Max Delbrück Centre for Molecular Medicine Berlin-Buch, Research Centre Jülich, Forschungszentrum Karlsruhe, the Helmholtz Centre for Infection Research, and the Helmholtz Centre for Environmental Research - UFZ.

More information:
Press release Helmholtz Gemeinschaft

Biocomputers Made in your Body



The graphic art shows implantable devices that monitor the activities of cells. *Courtesy Benenson*

Cambrigde/Princeton. thm. Researchers at Harvard University and Princeton University have made a crucial step towards building biological and implantable computers that can monitor the activities and characteristics of human cells. The information provided by these «molecular doctors», constructed entirely of DNA, RNA, and proteins, could eventually direct therapies specifically to diseased cells or tissues, according to a press release on a paper published in Nature Biotechnology.

«Each human cell already has all of the tools required to build these biocomputers on its own,» says Harvard's Yaakov (Kobi) Benenson, a Bauer Fellow in the Faculty of Arts and Sciences' Center for Systems Biology. «All that must be provided is a genetic blueprint of the machine and our own biology will do the rest. Your cells will

literally build these biocomputers for you.» Evaluating Boolean logic equations inside cells, these molecular automata will detect anything from the presence of a mutated gene to the general activity of genes within the cell.

Benenson and his colleagues claim in their Nature Biotechnology paper that biocomputers can work in human kidney cells in culture. Research into the system's ability to monitor and interact with intracellular cues such as mutations and abnormal gene levels is still in progress.

Benenson and colleagues including Ron Weiss, associate professor of electrical engineering at Princeton, have also developed a conceptual framework by which various phenotypes could be represented logically. A biocomputer's calculations, while mathematically simple, could allow researchers to build biosensors or medicine delivery systems capable of singling out very specific types or groups of cells in the human body.

More information
See press release by Harvard University.

$30 Million for Princeton Systems Neuroscience

Princeton. thm. James S. McDonnell III and John F. McDonnell have made a $30 million gift to Princeton University to establish the McDonnell Center for Systems Neuroscience. Teaching and research conducted by the center, which will be housed within the Princeton Neuroscience Institute, will investigate how the brain acquires, modifies and stores information during cognitive processes.

The Princeton Neuroscience Institute, co-directed by Jonathan Cohen, the Eugene Higgins Professor of Psychology, and David Tank, the Henry L. Hillman Professor in Molecular Biology, was launched in 2005. The institute is expected to expand basic knowledge about the brain, gaining insights that could lead to breakthroughs in treating diseases such as schizophrenia and epilepsy. It is also making significant contributions to development, and use of, new imaging and microscopy technologies as well as biochemical and genetic tools.

The McDonnell gift will fund the application of advanced technology in systems neuroscience and establish an endowment to support the highly trained specialists needed to run it. It will also set up an endowed fund for innovation in systems neuroscience, create a new faculty position and four graduate fellowships, and provide for a new systems neuroscience teaching laboratory.

More information:
Press release by Princeton University

Venter patent on «Synthetic Life» challenged

ETC Groups' view of synthetic biology.

Ottawa/Zurich. thm. The ETC Group, an activist group with a (very) critical eye on green biotechnology, nanotechnology, and now synthetic biology announced a challenge a to a patent by the J. Craig Venter Institute on «synthetic life». The ETC press release states that the US patent application claims exclusive ownership of a set of essential genes, and any synthetic «free-living organism that can grow and replicate» made by using these genes.

J. Craig Venter institute did not comment on the issue so far. But it is known that scientists at the Venter Institute are working on new methodologies to synthesize large segments of DNA to eventually enable the construction of whole artificial chromosomes. By removing 101 of 482 genes from the bacterium Mycoplasma genitalium they identified that 381 is the minimum number of genes required for this particular organism to survive.

The leader of the synthetic biology group at J. Craig Venter Institute is nobel laureate Hamilton O. Smith, who will

speak at the Synthetic Biology conference 3.0 on June 25 at ETH Zurich.

The ETC Group announced its attendance at the conference where it wants to call upon scientists to join in a global dialogue on synthetic biology.

More information:
Press release by ETC Group
BBC News story on the subject
Synthetic Biology 3.0 conference

Upcoming events

Date	Location	Topic
June 24-27 2007	ETH Zurich, Switzerland	Synthetic Biology 3.0, ETH Zurich
June 25-29 2007	Porto Heli, Greece	5th Pathways, Networks and Systems Conference
July 12-14 2007	Nashville, Tennesse, USA	Building a Better Mouse II at Vanderbilt University
June 26-27 2007	Barcelona, Spain	International Symposium on Bioinformatics in Europe
September 6 2007	Kuala Lumpur, Malaysia	International Conference on Mathematical Biology 2007 (ICMB07)
September 10-12 2007	The New Forest, UK	Seventh International Conference on Modelling in Medicine and Biology
September 13-14 2007	Buxton, Derbyshire, UK	17th New Phytologist Symposium Systems Biology and the Biology of Systems: how, if at all, are they related?
September 9-12 2007	Stuttgart, Germany	2nd Conference Foundations of Systems Biology in Engineering (FOSBE 2007)
September 16-17 2007	EPF Lausanne	All-SystemsX.ch-Day
October 1-6, 2007	Long Beach, California	International Conference on Systems Biology (ICSB-2007)
October 11-13 2007	Jeju-do, Korea	Frontiers in the Convergence of Bioscience and Information Technologies (FBIT 2007)
November 27-29 2007	Zurich/Basel	Scientific Advisory Board Meeting
January 4-8 2008	Big Island, Hawaii	From Molecules to Cells to Organisms Pacific Symposium on Biocomputing conference

Recent Publications from SystemsX Scientists

Publications from Glue Projects and Scientific Nodes, which have been released since the beginning of the year. The compilation is based on self-declaration.

CENTER FOR CELLULAR IMAGING AND NANOANALYTICS

The contrast-imaging function for tilted specimens.
Philippsen A, Engel HA, Engel A
Ultramicroscopy. 107; 202-12.

Collaborative EM image processing with the IPLT image processing library and toolbox.
Philippsen A &, Engel A et al
J Struct Biol. 157; 28-37.

Controlled 2D crystallization of membrane proteins using methyl-beta-cyclodextrin.
Signorell GA & Rémigy HW et al.
J Struct Biol. 157; 321-8.

CENTER FOR MODEL ORGANISM PROTEOMES

A high-quality catalog of the Drosophila melanogaster proteome.
Brunner E & Aebersold R et al.
Nat Biotechnol (5):576-583.

A Proteome Catalog of Drosophila melanogaster: An essential resource for targeted quantitative proteomics;
Ahrens AH & Basler K.et al.
FLY 2007 in press.

COMPETENCE CENTER FOR SYSTEMS PHYSIOLOGY AND METABOLIC DISEASES

Insulin receptor substrates 1 and 2 but not Shc can activate the insulin receptor independent of insulin and induce proliferation in CHO-IR cells
M. Niessen & G. A. Spinas et al.
Exp. Cell Research 313; 2007; 805-815.

Superiority of Small Islets in Human Islet Transplantation
R. Lehmann & G.A. Spinas et el.
Diabetes, 56; 594-603.

An integrated mass spectrometric and computational framework for the analysis of protein interaction networks
O. Rinner & R. Aebersold et al.
Nature Biotechology, 25, 345-352.

Reproducible isolation of distinct, overlapping segments of the phosphoproteome
B. Bodenmiller & R. Aebersold et al.
Nature Methods, 4, 231-237.

CENTER OF SYSTEMS BACTERIAL INFECTIONS

YscU recognizes translocators as export substrates of the Yersinia injectisome.
Sorg I. & Cornelis G.R. et al.
The EMBO Journal advance online publication 17 May 2007

Escape from Immune Surveillance by Capnocytophaga canimorsus
Shin H. & Cornelis G.R. et al.
J Infect Dis 195:375-386.

INSTITUTE OF MOLECULAR SYSTEMS BIOLOGY

Computational prediction of proteotypic peptides for quantitative proteomics
Mallick P, Kuster B and Aebersold R et al.
Nat Biotechnol 25(1):125-131.

Overlapping Segments of the Phospho-Proteome.
Bodenmiller B &, Aebersold R et al.
Nat Methods, 4(3):231-237.

Development and validation of a spectral library searching method for peptide identification from MS/MS
Lam H & Aebersold R et al.
Proteomics 7(5):655-667.

An integrated mass spectrometic and computational framework for the analysis of protein interaction networks.
Rinner O & Aebersold R et al.
Nat Biotechnol (3):345-352.

Absolute quantification of specific proteins in complex mixtures using visible isotope-coded affinity tags.
Lu Y & Gelb MH.
Methods Mol Biol 359:159-176.

Using stable isotope tagging and mass spectrometry to characterize protein complexes and to detect changes in their composition.
Ranish JA, Brand M, Aebersold R.
Methods Mol Biol 359:17-35.

Tandem Mass Spectrometry Protein Identification on a PC Grid.
Zosso D & Schwede T. et al.
Stud Health Technol Inform 126:3-12

Solid-phase extraction of N-linked glycopeptides.
Tian Y & Zhang H. et al.
Nat Protoc 2(2):334-339.

An integrated chemical, mass spectrometric and computational strategy for (quantitative) phosphoproteomics: Application to Drosophila melanogaster Kc167 Cells.
Bodenmiller B. & Aebersold R. et al.
Mol BioSystems 3(4):275-286.

Reproducible isolation of distinct, overlapping segments of the phosphoproteome.
Bodenmiller B & Aebersold R. et al.
Nat Methods 4(3):231-237.

Efficient classification of complete parameter regions based on semidefinite programming.
Kuepfer L, Sauer U, Parrilo PA.
BMC Bioinformatics. 2007 Jan 15;8(1):12.

Comparison of pancreas juice proteins from cancer versus pancreatitis using quantitative proteomic analysis.
Chen R & Brentnall TA et al.
Pancreas 34(1):70-79.

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