

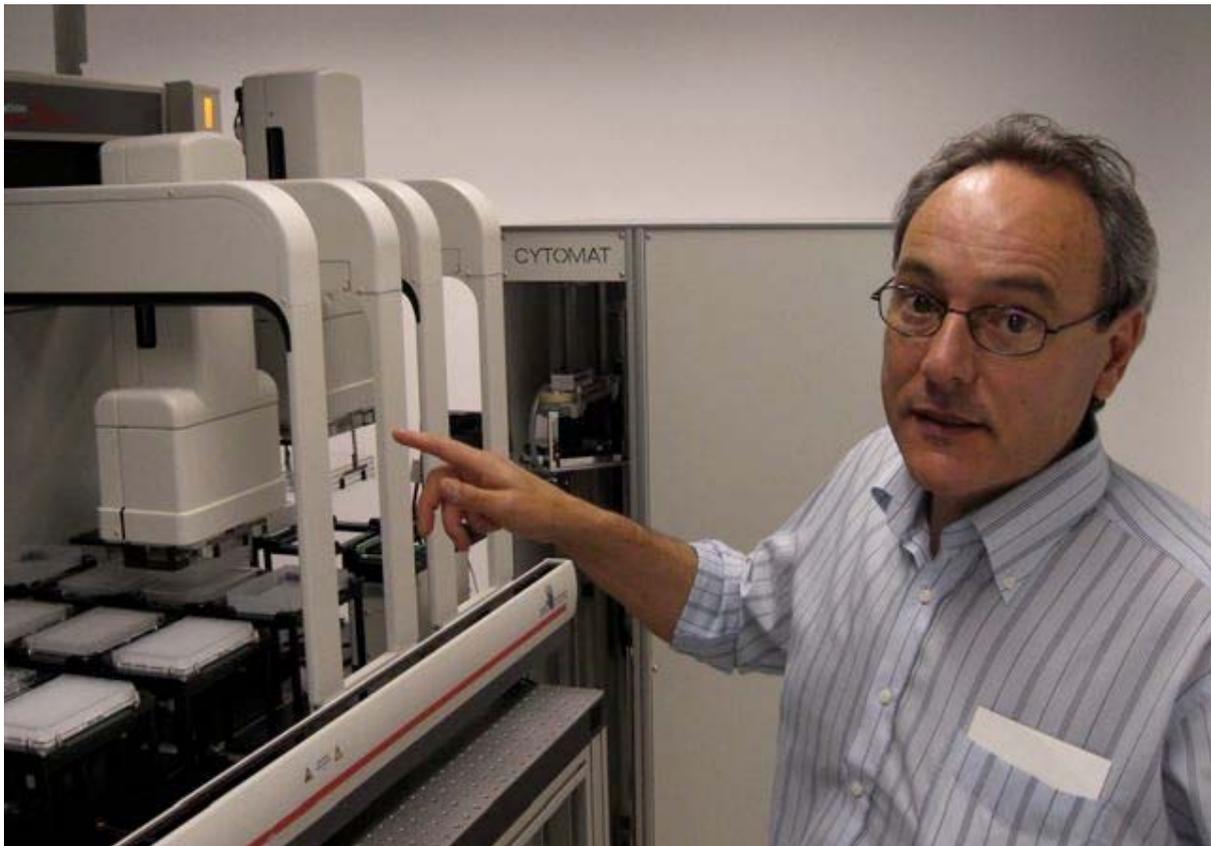


Newsletter #10 May 21th 2007

SystemsX.ch
The Swiss Initiative in Systems Biology

First SystemsX Glue Project at EPFL starts

The Biomolecular Screening Facility is the first SystemsX Glue Project at EPF Lausanne. As Director Gerardo Turcatti explains his plans, common ground with the High-Throughput Cell-Based Screening Centre at ETH Zurich becomes obvious, but also some differences.



Gerardo Turcatti explains the works of his integrated platform for siRNA screenings.

Foto Thomas Müller

ETH Lausanne. Everything blinks, and there is the smell of recently unpacked equipment, as Gerardo Turcatti guides through the facilities of the Biomolecular Screening Facility (BSF), the first Glue Project of SystemsX at ETH Lausanne. Engineer Pierre-Olivier Regamey is just adjusting the four-meter long, brand new high-end fluidic handling device for automated high-throughput screening assays. BSF offers assistance and

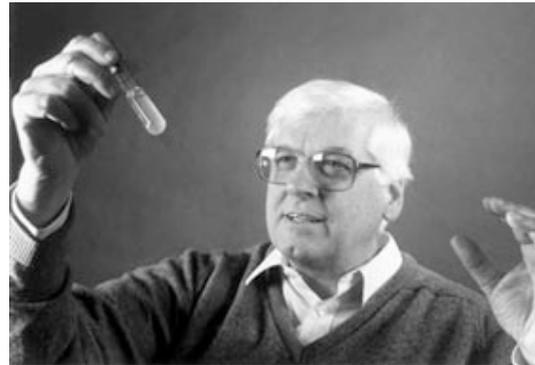
performs cellular and biochemical assays for screening siRNAs and chemical collections with emphasis on the essential areas of assay development, automation, as well as information and compound management. «The operational start for automated large siRNA screening campaigns is planned after this summer», says Turcatti.

Continuation page 2

Nobelist Hamilton O. Smith at Synthetic Biology 3.0

Zurich. The third international conference of Synthetic Biology will be held this year from June 24 to 26 at the Swiss Federal Institute of Technology (ETH) in Zurich. The conference topics will revolve around the technological and conceptual challenges on our way to the engineering of pro- and eukaryotic systems to an unprecedented extent. How can we practically achieve these manipulations on a system scale? What could be suitable system boundaries to introduce a suitable hierarchy of abstraction? How can the required context-insensitivity of parts we implement? What are the most exciting applications? And fundamentally – can systems biology provide the detailed knowledge that is required to enable such sophisticated bioengineering?

Synthetic Biology experts, including the keynote speakers George Church (Harvard), Tom Knight (MIT), and Nobelist Hamilton Smith (J. Craig Venter Institute), from all over the world and exponents of related fields will discuss their latest research on the ETH Höggerberg campus. There will also be workshops for those who are new to Synthetic Biology. We look forward to an inspiring conference



Hamilton O. Smith sequenced 1995 the first bacterial genome.

and to welcoming our guests to Zurich. The potential to revolutionize current bioengineering techniques by utilising the methods of the natural sciences and engineering has attracted a large number of researchers over the last couple of years, and made the “Synthetic Biology” conference series an exciting meeting place for the international bioengineering community. The previous conferences [SB1.0](#) (at MIT) and [SB2.0](#) (at UC Berkeley) conveyed this spirit very well.
Sven Panke

For more information see <http://www.syntheticbiology3.ethz.ch/index.htm>

Continuation from page 1

BSF started as an EPFL project two years ago and was co-opted recently by SystemsX, primarily because of the rising need for screening facilities in SystemsX, especially in the realm of RNAi. Actually, there are two similar screening facilities in SystemsX. The High-Throughput Cell-Based Screening Centre (HT-CBSC) at ETH Zurich Glue Project appears to duplicate some of the efforts of the Glue Project BSF.

«We are complementary, not competing facilities», says Turcatti, and explains that the build up of the facilities is coordinated. Gabor Csúcs, head of the Glue Project at ETH Zurich agrees, and both underlines for instance the fact that two siRNA libraries for mouse and human (so called druggable genomes) will be purchased jointly. Daniel Vonder Mühl, managing director of SystemsX.ch, sees this as a logic next step. Instead of

competing against each other, duplicating equipment and technology within the same nation, complementary collaboration and increasing capacity will allow Switzerland to be among the world leaders. Therefore, the two projects are planned to apply as one Glue Project at two main locations (Lausanne and Zurich) for SystemsX.ch from 2008 onward.

Gerardo Turcatti is a man with a lot of experience in industry. A chemist by training, he has worked his entire scientific career in Life Sciences multidisciplinary environments. After developing a new high throughput DNA sequencing technology and instrumentation in a company he co-founded (Manteia S.A.), he worked for a couple more years as a consultant for transferring the technology and also for other pharmaceutical and biotech companies. «With time I realised that I needed a lab around me». Just at this time

What is siRNA?

thm. siRNA- assay can be regarded as the most important new technology in (Systems) Biology in the last five years (Nobel Prize in medicine 2006). Small interfering RNA (siRNA) is a class of 20-25 nucleotide-long double-stranded RNA molecules that play a variety of roles in biology. Most notably, siRNA is involved in the RNA interference (RNAi) pathway, where the siRNA interferes with the expression of a specific gene. In addition to their role in the RNAi pathway, siRNAs can be used in functional genomics assays to deliberately switch genes in cells off and on. This is why siRNA became essential for biomedical research and drug development.

came the request by EPFL to build up BSF.

«Technology is the key, especially in Systems Biology», Turcatti says. The ability to develop new technologies and methodological approaches can give you the edge required to run at the forefront of Systems Biology, otherwise this is unlikely. So, Turcatti and his crew of four want to be more than just another «user lab». Innovation is a priority, as the telomerase project, that he is doing with a group at the Swiss Institute of Cancer Research (Isrec, now also a part of EPFL), shows. Telomerase is an enzyme that is involved in some cancer types. Turcatti and his team have recently developed and validated a new automated high throughput assay for the screening of inhibitors of telomerase activity, which does not rely on a post DNA amplification step as most of the reported methods.

This leads to the next question: what to screen against? Turcatti is convinced that academic research institutions have to begin to build up their own compound libraries of small chemical molecules by initiating or joining Chemical Biology networks. The aim is not necessarily to discover and develop new drugs, a task that will stay in the realm of pharmaceutical industry which has much more compounds at their hands, rather Turcatti thinks that in academic institutions

the search for, in a wider sense, bio active molecules is becoming more and more – especially in Systems Biology.

Turcatti's industrial origins become obvious, when it comes to information management of data. Here, Turcatti is building up his own system, because «I realised that nobody I asked is happy with the expensive commercially available systems». The BSF is currently developing its own system in collaboration with Luc Patiny, computer-scientist at the EPFL. At this time however, Turcatti is not convinced about sharing all the details of the tools with the community, he would prefer the BSF keeping the control of future developments.

«Zurich» has another philosophy in this respect. Gabor Csúcs clearly prefers the «open source» approach, where in principle everybody is free to improve a certain technology or software. «In this way it is easier to build networks with other players like EMBL», says Csúcs. Despite this difference, both are convinced that a solution which suits everybody will be found soon.

Adrian Honegger, head of CISD, the central data management agency in SystemsX, stresses the point that it is of utmost importance that the final data generated at the Glue Projects at EPFL and ETHZ have to be standardised and consistently annotated. «If this is not guaranteed, it makes no sense to access the data from a SystemsX wide computational framework», Honegger insists.

So, not everything has fallen into place, yet. Because both Glue Projects see themselves still as an EPFL- respectively ETHZ- and a SystemsX facility at the same time, at least in principle conflicts about access can occur. This is why Turcatti envisages the installation of a steering committee to decide on such issues. For Honegger, the implementation of the two Glue Projects at the borders of Lake Geneva and Lake Zurich and their subsequent fusion is «the litmus test whether SystemsX is developing into some kind of funding agency or becomes a truly collaborative Systems Biology research initiative». *Thomas Müller*

Deep Proteomics at ESF-Workshop

At the European Science Foundation exploratory workshop “Model Organism Proteomics” in Zurich, 26 European Systems Biology researchers from nine countries met and discussed the current status of the field and plans for the formulation of future research proposals.



Concentrated work. Foto Sabine Schrimpf

Zurich. At a workshop, organised by SystemsX scientists, a future application in proteomics to the European Framework Program FP7 was set. The participants generated an application outline for a project about «enabling time resolved deep proteomics». The core technique they agreed upon was proteotypic peptides (PTPs), a concept that has been pioneered by the SystemsX Glue Project Model Organism Proteomes (see article «A high quality catalogue...» in this Newsletter).

The exploratory workshop on Model Organism Proteomics was organized at the University of Zurich by Sabine Schrimpf, Erich Brunner, and Ruedi Aebersold of the Center for Model Organism Proteomes (C-MOP). C-MOP is a Glue Project of SystemsX, and is also supported by the University Research Priority Project “Systemsbiology”, and the

ETH Zurich. The exploratory workshop held in April was supported by a grant from the European Science Foundation (ESF).

Twenty-six European researchers from nine countries specializing in the different disciplines of systems biology and proteomics were invited to discuss the current status of the field and plans for the formulation of future research proposals. The focus was on proteome annotation, databases / data mining, and the use of proteome maps. Nine presentations on these topics yielded the basis for the following discussion sessions.

Around the core technique there was, on the one hand, developmental input from separation science and mass spectrometry for accurate quantitative measurement and kinetics. On the other hand there were application and biological questions based on the expertise of the workshop participants.

The benefits of such a consortium for the analysis of different organisms is the establishment of the synergies necessary to study evolutionary aspects and integrate the acquired data into existing data repositories. Such a network of collaborations certainly strengthens the influence of the European research community in the field of systems biology worldwide. *Sabine Schrimpf, Erich Brunner and Ruedi Aebersold*

Gosau Course makes Systems Biology work

Gosau. As the largest European training course in systems biology, the 2nd FEBS Advanced Lecture Course on «Systems Biology: From Molecules to Life», took place in Gosau, Austria, on March 10-16, 2007. Supported among others by SystemsX and organized by Edda Klipp (MPI Berlin), Anneke Koster (Univ. Amsterdam), Karl Kuchler (Vienna Biocenter), Uwe Sauer (ETH Zurich), and Hans Westerhoff (Univ. Manchester), 120 international masters and PhD students,

and postdocs, about 30 PIs and more than 30 teachers gathered in a secluded mountain resort to focus for a week on systems biology.

Framed by the two key note lectures on «Making Systems Biology work» by Leroy Hood and «Systems Biology at last: ageing» by Tom Kirkwood, the course had a strong teaching mission by bringing together experimentalists and computer scientists. Three key elements were the multiple interactive blackboard lectures,

computer practicals, and poster session, with feedback sessions for each group of presenters. The general lectures followed the unusual format of only 3-4 main speakers per day with each 20-60 min of didactic lectures, 40 min tutorials on the subject, and 20 min research highlights.

This format was greatly appreciated by the students. Opportunities for informal interactions with experts and teachers, as well as for networking among the participants, were used extensively during meals, on the ski slopes during the free afternoons or over drinks. *Uwe Sauer*

First CC-SPMD Minisymposium a Big Success

ETH Hönggerberg. The Minisymposium entitled «Keeping the Balance - New Insights into Energy Homeostasis» was a big success. This first symposium organized by graduate students of the Competence Center for Systems Physiology and Metabolic Diseases (CC-SPMD) offered both exciting science and a pleasant atmosphere. It took place on March 15th 2007 at ETH Hönggerberg.

Four experts from very different fields gave their own perspective of energy homeostasis: David Carling (Imperial College, London), Jeroen Jeneson

(Eindhoven), Jim Kaput (UC Davis) and Steve Oliver (Univ. Manchester). The topics covered, ranging from mouse cell biology over nutrigenomics to yeast functional genomics, were quite broad, but complemented each other well.

«I was rather surprised to see the combination of speakers, but it turned out to be both a entertaining and scientifically fascinating afternoon», summarized Prof. Carling the day. The event also included a reception and poster session where CC-SPMD students had the opportunity to present their work. *Jennifer Ewald*

A high-quality Catalog of the Fruitfly Proteome



Zurich. thm. 63% of the predicted proteome of the fruitfly has been cataloged by a large group of SystemsX scientists. Erich

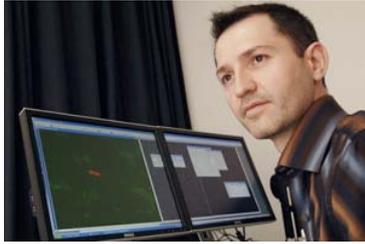
Brunner, Sonali Mohanty, and Christian Ahrens from the SystemsX Glue Project «Center for Model Organism Proteoms» at University of Zurich and Ruedi Aebersold from the Institute of Molecular Systems Biology at ETH Zurich (a structural SystemsX Scientific Node) will publish their work in the June edition of «Nature Biotechnology».

The catalog contains 9124 proteins and represents the largest high quality proteomics dataset (some terabytes) to date. Whether the undetected genes are expressed at levels below the threshold of detection or whether they are represent incorrect predictions of the genome, remains to be established. The directed shotgun approach holds great promise for pharmaceutical applications, write the authors. One fifth of the identified proteins are transmembrane proteins and about one tenth are secreted.

More information:

[Press release University of Zurich](#)
[The paper in nature biotechnology](#)

Cells use noise to make cell-fate decisions



Dallas. thm. A kind of biochemical noise is helping cells transform from one state into another,

says a Science paper by et al. at UT Southwestern Medical Center. Conventional thinking has been that the random nature of the fluctuations in the chemical composition in cells interferes

with the reliable operation of biological systems.

The study, published in Science however states that the amplitude of this «noise» correlates with the triggering of cell differentiation. To determine the biological role for noise, the scientists analyzed a «genetic circuit» that controls the transformation of bacteria (*Bacillus subtilis*) from one state to another.

More information:
See [press release](#).
See [abstract](#).

Stoffel wins another prestigious Diabetes prize



Zurich. thm. Markus Stoffel, ETH-Professor at the Institut for Molecular Systems Biology (IMSB) has won for his research one of the six Scholar Awards of the Juvenile Diabetes Research

Foundation International (JDRF). The largest world wide foundation for Type-1-Diabetes Research supports Stoffel for five years with \$250'000 annually. Last year, Stoffel received the «Outstanding Scientific Achievement Award» of the American Diabetes Association.

Christian Wolfrum elected member of CC-SPMD



Zurich. UH. Dr. Christian Wolfrum, ETH Institute for Molecular Systems Biology, has been elected as a new CC-SPMD member. Wolfrum's group focuses on elucidating the molecular

mechanisms underlying the altered preadipocyte and adipocyte biology in different models of obesity, type 2 diabetes and associated metabolic disorders, with special emphasis on gene expression, posttranslational modifications and lipid composition of the cell.

Upcoming events

Date	Location	Topic
June 4-21 2007	Gothenburg, Sweden	2nd International Course in Yeast Systems Biology
June 5-7 2007	Richmond, Virginia	Summit on Systems Biology Integrative basic, clinical and translational research
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, Tennessee, USA	Building a Better Mouse II at Vanderbilt University
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)
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)
January 4-8 2008	Big Island, Hawaii	From Molecules to Cells to Organisms Pacific Symposium on Biocomputing conference

Imprint

Publisher

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