SystemsX.ch Newsletter #22
October 2010

X-Letter 22

«SystemsX.ch scientists at PSI have access to one of the **best infrastructures in analytical Structural Biology**»

Since the beginning of the year Gebhard Schertler is Head of the Biology and Chemistry Department at the Paul Scherrer Institute. The membrane protein structure specialist was formerly Senior Scientist and Group Leader at the Laboratory of Molecular Biology, MRC, in Cambridge. Schertler is convinced that the **newly established fully-automated platform at PSI** offers scientists in Switzerland and abroad **one of the most attractive facilities to examine biological structures**.

The Paul Scherrer Institute at Villigen Photo: PSI

Interview with Prof. Gebhard Schertler, Head of the Laboratory of Biomolecular Research, PSI.
By Matthias Scholer

Does biomolecular research at PSI have tradition?

The Biomolecular Research lab has been a sub-division of PSI's Biology and Chemistry Department for around ten years. The main focus of the roughly 40 people who work here is the structural and functional analysis of complex biological systems. My own focus within the group is on eukaryotic membrane protein systems and we have determined a number of G Protein-Coupled Receptor (GPCR) structures. Proximity to the Swiss Light Source (SLS), one of the best syn-

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Harnessing unused potential at the Paul Scherrer Institute (PSI)
Prof. Ralph Eichler, President of ETH Zurich and Chairman of the SystemsX.ch Board of Directors.

Scientific progress occurs either by virtue of a theoretical toying with ideas, which are then experimentally verified, or by unexpected measurement results. Progess also happens, however, as new technologies for measuring or new vizualising methods become available.

A technological surge is currently underway, especially in biology, bringing with it an ensuing wealth of quantitative results that require powerful computing for their analyses.

Now that the Paul Scherrer Institute (PSI) runs its expensive installations for external as well as its own research groups, it will attract more users from the field of biology.

The biology department at PSI helps interested researchers to use the installations in an optimal way. Examples of this collaboration can be found in the present issue of X-Letter.

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chrotrons in the world, has driven the automatization of structural determination a long way in recent years.

And how far has automatization come?
In principle we can carry out all steps of a targeted protein production in a highly automated way, from a single and/or from several genes all the way up to cristallization. In addition, our modern and efficient applications of technologies enable us to make a detailed biophysical characterization of the examined proteins at every stage. Access to our biophysical instruments and to the screening facility at the synchrotron opens up additional possibilities and thus represents an important advantage over other laboratories from a scientific point of view. So users of the platform acquire a clear advantage for competitive publications.

Who uses this platform?
Up until now it mainly served our internal research projects. But we're in the middle of a reorganization and that is about to change. At the beginning of September, Richard Kammerer from the University of Manchester joined us at PSI to take over the supervision of the platform. One of his main tasks will be to establish and then implement a concept that allows it to be run at full capacity. In addition he'll be working together with the scientists involved in any given project already in the planning phase to determine the feasibility of a planned experiment as well as its projected time and costs.

So outside research groups will be able to use your services?
Absolutely! Once the platform has been extended it is to be available, in equal parts, to internal, collaborating and external scientists. What we will be looking for is a combination of shorter and longer experiments in order to ensure that the platform is continuously running at full capacity. This is the basic condition that an automated system functions optimally.

Costs are to be covered by external users. What will happen to the takings?
Our goal is not to cover the operational costs in their entirety. Rather, the financial contributions will flow back into the further development of the platform, since PSI won't be making any further funding available. This means that, in future, if we want to increase the number of staff in order to increase capacity, then we'll have to finance it ourselves.

Where can you see an interface between PSI and SystemsX.ch researchers?
SystemsX.ch is very interested in the identification and quantification of protein-protein networks. The main junctional point of these networks will be defined in the near future. In my opinion it will then be interesting to delineate the structure of these complexes. As not every SystemsX.ch team has access to all methods of protein structure determination we see ourselves as a port of call to find an entrance into the structural components. Over many years, with huge investment and the necessary expertise we've succeeded in building a sophisticated test installation. It wouldn't be possible for another laboratory to reach this level of perfection any time soon. What's more, in future SystemsX.ch researchers will have access to a world-class infrastructure in structural biology at PSI – a convenient location whether they come from Zurich, Bern, Basel or Lausanne.

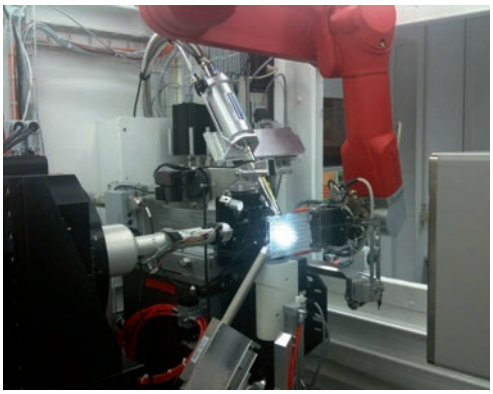
Gebhard Schertler aims to strengthen collaboration with SystemsX.ch. Photo: msc

From genes to protein structures: thanks to a **highly automated technology platform** at the Paul Scherrer Institute.

by Dr. Guido Capitani
Project Leader Bioinformatics and Protein Crystallography,
Laboratory for Biomolecular Research (PSI)

One of the main goals of current biology research at PSI is to better understand the structure, function and dynamics of proteins and their interactions in biological systems. The matter has acquired more urgency in recent years. The results of protein-protein interactions gained from research in proteomics and systems biology must now be examined in greater detail to characterize their structure and function.

Shared technologies and methods to clarify structure.
The Biomolecular Research Laboratory (BMR, *http://lbr.web.psi.ch/*) and the Swiss Light Source (SLS, *http://sls.web.psi.ch*) at the Paul Scherrer Institute (PSI) have jointly established a highly automated technology platform with three major goals: protein production, biophysical characterization of proteins, including complex membrane proteins, like G Protein-Coupled Receptors (GPCRs), and structure determination. The latter is carried out using electron microscopy,



Automated *in-situ* X-ray diffraction screening of protein crystals at the SLS. Photo: PSI

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small-angle X-ray scattering, and X-ray crystallography. In the near future scientists will be able to avail themselves of an X-ray free electron laser, (SwissFEL Project, *http://www.psi.ch/swissfel/*), currently under construction at PSI. The platform at PSI thus provides a valuable tool for the systems biology community and for other biologists interested in the structure, function and interactions of biomolecules in the cell. BMR is already interacting with a number of pharmaceutical partners to study the activation mechanism of GPCRs.

BMR@PSI: research on protein structure and function

At BMR researchers are extensively studying proteins and protein complexes. In order to examine the proteins in their native–or quasi-native–environment, both *in vivo* and *in vitro* characterization methodologies are employed. These include, among others, biochemical functional analysis in isolated systems, as well as imaging techniques on living cells.

A crucial prerequisite in understanding function on a molecular level is to know the atomic structure of the macromolecule being investigated. For this, proteins are made visible by using X-ray structure analysis, SAXS and EM. To obtain high resolution protein structures, however, it is necessary to produce protein crystals.

State-of-the-art technologies are used for protein production, as well as for biochemical and biophysical analysis. Robotics, which can rapidly carry out an automated structure determination, are now in use to determine protein crystallization. For this work, the researchers collaborate closely with the Macromolecular Crystallography (MX) group working with SLS. Thanks to access to one of the most advanced synchrotrons in the world scientists can rapidly collect high-quality diffraction data from protein solutions or crystals. A third of the capacity of the PSI technology platform is dedicated to in-house projects, a third is for collaborative projects and a further third is now offered–a new service–to external research groups.

With regard to SwissFEL, which will be operational at PSI in the near future, BMR has already started to produce suitable protein samples. SwissFEL will make a finely detailed analysis of the structure and dynamics of various materials possible thanks to high-energy, short X-ray pulses. This will be instrumental above all in advancing material sciences and in exploring the constituents of live organisms.

The above-mentioned procedures will now be described in more detail.

From gene to protein

Starting with a gene it should always be possible to produce a sufficient quantity of protein within three months. Adapted bacterial, yeast, and insect or mammalian cell expression systems are set on to a micro-titer plate, which makes an efficient and parallel cloning possible. Special acid amino sequences are added to the ends of recombined proteins in order to isolate the proteins in a single step or to verify their presence with antibodies.

Multi-protein complexes, made of a number of different proteins, are obtained using an automated platform for simultaneous protein expression recently developed in PSI's own laboratory. This procedure enables the production of isotopically-labelled protein samples, which can be examined with nuclear magnetic resonance spectroscopy (NMR). The purified, recombinant proteins are then subjected to biochem-

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MAIN RESEARCH LINES AT BMR

Molecular cell biology

The formation of lymphatic and blood vessels in multicellular organisms is steered by growth and differentiation factors, above all by Vascular Endothelial Growth Factors (VEGF). Our group investigates how these molecules activate their receptors by examining the three-dimensional structures of the complexes they form with the receptors.

Protein-protein interactions

The interaction between proteins is one of the fundamental processes of life. We focus on examining these interactions using protein crystallography in combination with biochemical and biophysical methods. We especially concentrate on the interactions of proteins that dynamically regulate the skeleton of the cell.

G Protein-Coupled Receptors

From the extremely important class of G Protein-Coupled Receptors (GPCRs) we have succeeded in determining the structure of the visual pigment rhodopsin using electron microscopy and protein X-ray crystallography. Recently, we have also elucidated the structure of the receptor of the stress hormone adrenaline, which regulates heartbeat and plays an important role in asthma treatment.

Structure and function of membrane proteins

While ionic channels, transporters and GPCRs are membrane proteins with different functions, they all mediate communication across cellular membranes. With the help of protein X-ray crystallography, small-angle X-ray scattering, as well as biochemical and biophysical methods, we want to solve their structures and understand the underlying molecular mechanisms.

Structural bioinformatics

Computer programs enable scientists to obtain information from experimentally determined protein structures, thus adding to the interpretation and the design of new experiments. We analyze protein-protein interfaces, as well as cellular processes triggered by the binding of specific substances to GPCRs on the cell membrane.

Nano structures for bioanalysis

The function of membrane proteins reconstituted in free-standing lipid bilayers can be examined using electrochemical methods. Our goal is to find a versatile testing system for kinetic examinations of membrane proteins.

Most of these projects, above all those involving GPCRs, can contribute to finding new ways of treating diseases.

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The SLS, one of the most advanced synchrotrons world-wide. Photo: PSI

ical and biophysical characterization and crystallization screening.

High-quality crystals

High-quality crystals of the proteins to be investigated are an important prerequisite for high-resolution structural X-ray analysis. The best indication of the conditions under which such crystals form is provided by a robot, which automatically assays the crystals produced by another robot in minute volumes. The crystallization conditions continue to be optimized at SLS until protein crystals suitable for high-quality data collection are obtained. The method is especially suited to projects like multi-protein complexes or membrane proteins.

The BMR-SLS technology platform

A comprehensive infrastructure for the production and analysis of protein has been established at PSI. The investigative pipeline covers all steps; from project design, expression vector cloning, protein expression and purification, all the way to the biophysical characterization and structural analysis of proteins. The platform allows scientists to produce the purest and biologically most active samples of every appropriate protein to the nearest milligram.

By screening a wide range of parameters (e.g., gene sequences, expression vectors, etc.) in a 96-well plate format, high-yield expression conditions can be determined quickly and efficiently for most targets, including multi-gene complexes. At BMR a number of different preparation and investigative methods are currently being used. Tecan Freedom Evo II, a liquid-handling robot is being deployed for cloning and expression/solubility screening; several automated Äkta FPLC serve to purify protein; and various analytical devices are in use to characterize purified protein solutions. Methods such as isothermal titration calorimetry and fluorescence spectroscopy stand ready to quantify protein interactions. Multi-angle laser light scattering makes the quantitive examination of the genesis of large protein complexes possible. Moreover, circular dichroism spectroscopy can quickly assess whether the proteins are properly folded and so-called thermal shift assays determine the stability of the proteins.

BMR high-throughput platform for protein production. Photo: PSI

For protein crystallography the MX group operates two high performance undulator beam lines, as well as a state-of-the-art bending magnet beam line.

The elements that make up this infrastructure makes PSI attractive to leading research groups from academe and industry from around the world.

Also dynamic analysis in the future

Thanks to various beam lines, biological material, from atomic to cellular, can be imaged on the SLS. Together with BMR, the MX group is also developing a system that can transport minute amounts of solutions. These are then subjected to the SAXS beam line analysis of proteins and protein complexes. This facility will be extended in the future to allow for a dynamic analysis of protein-protein interactions and for studying rapid structural changes in proteins under changing conditions.

In addition to its ambitious expansion of the infrastructure, the MX research group is focusing on the development of crystallographic methods, such as micro-crystallography, optical spectroscopy of molecules in crystals, as well as diffraction methods for counting pixel detectors. The MX group also supports non-crystallographic research groups in their structural biology projects.

New Interdisciplinary PhDs (IPhDs)

Recently, the Swiss National Fond approved a futher installment for Interdisciplinary Doctorates. The students, who will be supervised by mentors specialized in different disciplines, are still to be announced. Information on the new IPhDs is given below.

An integrated biophysical model of phototropism in the *Arabidopsis* hypocotyl

Mentors
Prof. Richard Smith
University of Bern
Prof. Christian Fankhauser
University of Lausanne

Detection and prediction of neural structures in fluorescence images using correlative light/ electron microscopy

Mentors
Prof. Thomas Vetter
University of Basel
Dr. Thomas Oertner
Friedrich Miescher Institute

Ensemble modeling of the Notch/p53 interactions in keratinocytes and experimental validation

Mentors
Dr. Heinz Wolfgang Koeppl
EPF Lausanne
Prof. Gian-Paolo Dotto
University of Lausanne

Imaging the interactions between transcription factors and DNA

Mentors
Prof. Demetri Psaltis
Prof. Bart Deplancke
EPF Lausanne

Metabolic network governing energy supply and carbon sources in Plasmodium falciparum

Mentors
Prof.Dominique Soldati-Favre
University of Geneva
Prof. Vassily Hatzimanikatis
EPF Lausanne

Nanoscale imaging of synaptic connectivity in the *Drosophila* larva

Mentors
Prof. Simon Sprecher
Prof. Frank Scheffold
University of Fribourg

Quantifying the activity contribution of individual matrix metalloproteinases

Mentors
Prof. Christian Heinis
EPF Lausanne
Dr. Hermann Wegner
University of Basel

Simultaneous determination of protein levels and their exposure to mechanical stress in the wing imaginal disc of Drosophila

Mentors
Dr. Christof Aegerter
Prof. Konrad Basler
University of Zurich

Single cell microfluidic imaging for spatial mapping and quantification of gene expression in an *in vivo* model of bone adaptation

Mentors
Prof. Ralph Müller
Prof. Petra Dittrich
ETH Zurich

Systems biology of angiogenesis; modeling of vessel formation in cultured endothelial cells

Mentors
Prof. Kurt Ballmer-Hofer
Paul Scherrer Institut
Prof. Petros Koumoutsakos
ETH Zurich

Systems modeling of metabolic networks in polyaromatic compound degrading bacteria

Mentors
Prof. Jan Roelof van der Meer
University of Lausanne
Prof. Vassily Hatzimanikatis
EPF Lausanne

The in silico limb: Building a dynamic spatial model for morpho-regulatory signaling interactions during vertebrate organogenesis

Mentors
Prof. Rolf Zeller
University of Basel
Prof. Dagmar Iber
ETH Zurich

Tissue engineering of a quantifiable 3D *in vitro* human blood vessel model

Mentors
Prof. Matthias Lutolf
EPF Lausanne
Prof. Jürgen Brugger
University of Zurich

New Bridge 2 Industry Projects (BIP)

The Scientific Executive Board of SystemsX.ch has approved following new «Bridge 2 Industry Projects». These are one year projects designed to get an academic and industry partner to carry out a project together. Funding can be up to CHF120'000. The approved BIPs are listed below:

Title	Identification of synaptic core pathways as targets for autism treatment	Rule-based models for drug-target identification: the TOR pathway as a case study	Development and application of CHIP-LC-MS technology for systems biology research	Development of a high precision cellular nanoinjection technology: a demonstration with *HeLa cells*	Simulation and Visualization of Crowding and Combinatorial Signaling
Colaboration between	**Prof. Peter Scheiffele** University of Basel and **Hoffmann - La Roche**	**Dr. Heinz Koeppl** EPF Lausanne and **Novartis Institute**	**Dr. Bernd Wollscheid** ETH Zurich and **Agilent Technologies**	**Dr. Tomaso Zambelli** and **Prof. Julia Vorholt** ETH Zurich and **Cytosurge LLC**	**Dr. Heinz Koeppl** ETH Zurich and **ScienceVisuals Sarl**
Keywords	Neuroscience, Autism, Synapse, Mouse models, Pharmacological treatment, Neural development	Computational systems biology, Drug-target identification, Pathway perturbations, Signal transduction	Strategic Partnership, CHIP-LC-MS technology development, Systems Biology, Proteomics	Nanobiotechnology, Single-cell injection, Metabolites, Microengineering, Nanofluidics	Stochastic processes, computational systems biology, spatial simulation, computer graphics, virtual reality
Approved	2009	2009	2010	2010	2010

Title	Systems-level analysis of *RAS*-driven tumor metabolism across growth conditions – 2D plastic to 3D to xenografts to tumors
Colaboration between	**Prof. Uwe Sauer** ETH Zurich and **Agios Pharmaceuticals**
Keywords	Oncology, Metabolomics, *In vitro* / *in vivo* cancer models, Ras tumors Metabotyping
Approved	2010

New Interdisciplinary Pilot Project (IPP)

The Scientific Executive Board of SystemsX.ch has approved following new Interdisciplinary Pilot Project. This high-risk research project will run for one year.

Title	Multidimensional genome organization: correlating 5C and SIM
Co-applicants	**Prof. Susan Gasser** Friedrich Miescher Institute **Dr. Andrzej Stasiak** University of Lausanne
Approved	2010

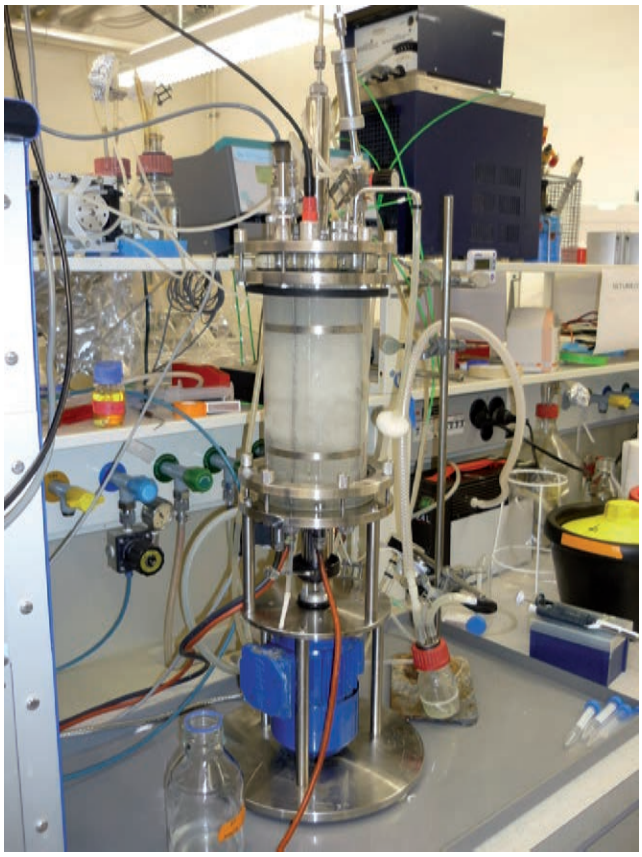
How does the alcohol get into the beer? By feeding sugar to yeast cells. Scientists working on **«YeastX»** are attempting to fathom the **regulatory processes** that unfold in the cell when the sugar is added – thereby developing a **fundamental modeling concept** to elucidate molecular biological phenomena.

Matthias Scholer

«In the meantime we can measure so many things but we're having difficulty keeping up with understanding,» is how Uwe Sauer and Jörg Stelling sum up one of the main problems that Systems Biology research faces. And these two scientists know whereof they speak. After all, together with their respective teams at ETH Zurich, they have been investigating metabolic processes in yeast cells for many years. «Many Systems Biology projects are aimed at finding an answer to a specific question. But as a result, two fundamental mistakes are often made. Either strong simplification is accepted in the development of the corresponding model. Or research begins by collecting as much quantitative data as possible, which one subsequently attempts to integrate into a model. But this simply doesn't work,» explains Sauer. Because biological phenomena have one thing in common; they are devilishly complex, highly dynamic and overlapping. Conceptional models are wholly inadequate to understand such a system. «When one is dealing with biological phenomena a certain mathematical formalism is indispensable. A theoretical analysis of the problem is especially called for in the preliminary phase of the research when more than one explanation for a mechanism exists or where we have bigger knowledge gaps,» expounds Stelling.

Efficiency in research

Developing a model before commencing on an experiment brings another benefit: the subsequent research becomes more efficient. «We've got biologists who understand the problem, analysts who can carry out exact measurements, and theoreticians who can develop models for any given problem,» is how Sauer sums up the situation. This is why the individual parts of a project have to be coordinated. «If you develop a model and have to wait two years for the measuring data or you carry out measurements over a month and then have to wait a year for the matching model it's frustrating for everyone involved,» muses Sauer. If, on the other hand, the focus is on the design of the experiment already in the planning phase of the project, the results then fit the model and make efficient research possible.



Fully operating bioreactor – the basis for the «BIG Y» experiment. Photo: YeastX

Yeast metabolism as a basic model

The SystemsX.ch project YeastX therefore aims to develop, on the theoretical side, a generic basic method. «We're trying to elaborate a modeling approach that can be adapted to many systems biological problems,» explains Sauer. Yeast serves the scientists as a model system, as this organism quickly allows them to put the necessary experiments into effect. Moreover, the results can later be transferred and applied to higher cells.

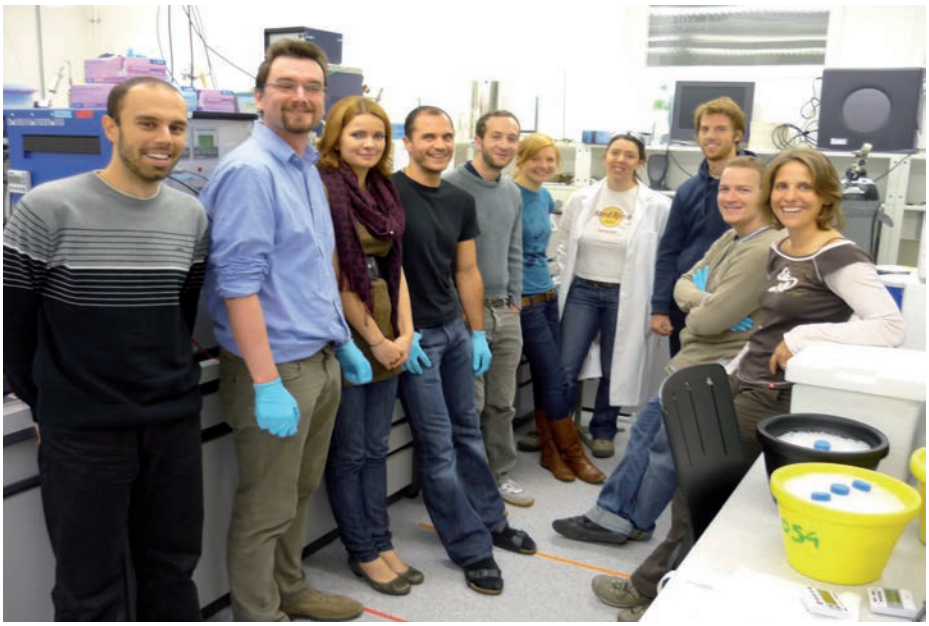
YeastX teams are concentrating on the nitrogen and glucose metabolism of yeast cells. «With their numerous networked interactions, the metabolic pathways represent the complexity of biological systems,» says Sauer concerning the choice of the research direction.

Even though it has been known for a long time that yeast cells begin alcohol production depending on the glucose concentration in their environment, the molecular interaction between the genes, proteins and metabolites that are involved is still not well understood. «Respected scientists have been working on this problem for the past fifty years. But up until now we have failed to understand in detail how, for instance, the cell measures the level of sugar and how it implements the signal that it triggers,» says Uwe Sauer. «Until now we have been looking at metabolic chains on a molecular level. While the results this has yielded have helped us to understand many process-

es quantitatively and schematically, we're reaching the limits of how far this methodology can take us.»

Uncertainty and restrictions

The complexity of metabolism poses two fundamental problems for researchers. On the one hand, the possibility of using experimental methods is restricted. On the other, great uncertainty exists when it comes to putting anything forward as a hypothesis on the processes of the signal chains. One consequence of this is that a number of models have to be developed for each problem, which must then be verified in experiments. In order to circumvent this cumbersome procedure, YeastX scientists divide the metabolic pathways into small segments, for which they then determine the most likely hypothesis. «This raises clear expectations, such as the dynamics of signal transmission. In turn, this can then be experimentally investigated,» says Stelling. Should the researchers succeed in developing a conceptional modeling approach for the regulatory phenomena under investigation, the approach can be applied to many other unanswered system biological questions. Sauer adds, «Whether it's glucose metabolism or organ development. Most biological processes are triggered initially by a signal that the cell then reacts to.» If researchers in the near future can discover, in detail, how a yeast cell measures the glucose concentration in its environment and then starts to produce alcohol, it would be of great interest, and not only to brewers.



The unflagging navvy of the dynamic multiomics experiment («BIG Y») Photo: YeastX

The «YeastX» Team:

The RTD project «YeastX» includes five project heads, each with a different area of responsibility:

- **Uwe Sauer** heads the YeastX project. His team develops new computer supported, quantitative measuring methods to analyze metabolic processes in yeast.
- **Jörg Stelling** is a researcher in bioinformatics at ETH Zurich. His focus in on computer simulations of metabolic pathways and the modeling of dynamic processes in cells and signal transduction.
- **Michael Hall** is a researcher at the Biozentrum of the University of Basel. YeastX benefits from his profound knowledge in the area of signal transmission.
- **John Lygeros** (ETH Zurich) brings his wide experience of control technique from the modeling of complex dynamic systems to the project.
- **Ruedi Aebersold** (ETH Zurich) has worked in the area of quantitative proteomics for many years and his fund of knowledge flows into the project.

«YeastX – Towards an Understanding of Nutrient Signaling and Metabolic Operation» at a glance

YeastX
Towards an Understanding of Nutrient Signaling and Metabolic Operation

Principal Investigator	Prof. Uwe Sauer (ETH Zurich)
Involved research groups	Prof. Ruedi Aebersold (ETHZ), Prof. Joachim Buhmann (ETHZ),
	Dr. Matthias Heinemann (ETHZ), Prof. John Lygeros (ETHZ),
	Prof. Matthias Peter (ETHZ), Dr. Bernd Rinn (D-BSSE), Prof. Jörg Stelling (ETHZ),
	Prof. Andreas Wagner (University of Zurich), Prof. Mike Hall (University of Basel)
Number of research groups	10
Researchers : Administration	30 : 0,5
Biologists : Non-biologists	50 : 50
Total budget (2008-2011)	12'371'000, thereof 5'984'000 CHF from SystemsX.ch

«Systems Biology of Development»
A conference on the Monte Verità indicates the **success and international impact of SystemsX.ch**

by Ernst Hafen and Silvia Gluderer (ETHZ)

«This was a fantastic meeting and an excellent opportunity to bring together theorists and experimentalists who are looking at problems of pattern formation and morphogenesis. We can now use new tools to develop an increasingly physicochemical and systems-level understanding of classical experimental models, such as a the blastoderm stage fly embryo. On the other hand, we realize the need to formulate new theories, computational tools, and experimental approaches to deal with the truly multi-scale nature of tissue and organogenesis,» observes Stas Shvartsman (Lewis Sigler Institute, Princeton) on the conference which took place from 16th-20th August 2010 on the Monte Verità in Ascona.

Audience at the conference room (auditorium). Photo: E. Hafen

Ernst Hafen, Professor at ETH Zurich and head of WingX, and Cris Kuhlemeier, Professor at the University of Bern and head of Plant Growth co-organized this conference. Their aim was to offer a platform to discuss, on the one hand, approaches to investigate biological mechanisms of the development from egg to multicellular organisms and, on the other, to present first results from the two Research, Technology and Development projects (RTDs), WingX and Plant Growth, to an international audience. Over the four days of the conference participants exchanged the latest results, methods, technologies, models and problems regarding the Systems Biology of development processes.

Focus on processes of development

The reasons for focussing on systems biological approaches to analyze developmental biology questions were the following: (i) The development from egg to organism that evolution has shaped over hundreds of millions of years. (ii) In the past 30 years, excellent genetic data has become available for some model organisms (e.g., *Drosophila* and *Arabidopsis*) that provide a unique basis for a systems biological approach. These reasons not only convinced an international panel of experts to recommend the funding of the two RTDs, Plant Growth and WingX, in 2008 but also convinced EMBO, the ETH conference center «Centro Stefano Franscini» (CSF) and SystemsX.ch, to support a Systems Biology conference in 2010 focussing on development processes. Konrad Basler (University of Zurich), Markus Affolter (University of Basel) and Michael Levine (University of California, Berkeley, USA) worked together as co-organizers on the agenda of the scientific program. They succeeded in attracting distinguished national and international researchers to speak.

Cris Kuhlemeier (right) at poster session. Photo: E. Hafen

Scott Fraser, California Institute of Technology, USA.

Participants from all over the world

On 16th August, 120 scientists from diverse disciplines, such as developmental biology, genetics, mathematics, informatics, physics and engineering, met up on the Monte Verità. Around a third of the participants were women. Roughly 20% of participants were from Switzerland, 20% from Germany and 17% from outside Europe (USA, Japan, Israel, etc.). About half of participants worked in animal research and the other half in plant research systems. The model organisms under scrutiny were *Drosophila melanogaster* (fruit fly) and *Arabidopsis thaliana* (mouse ear cress); both organisms were strongly represented in the subject matter of the conference. The two poster sessions and over 40 presentations enjoyed high participation and lively scientific exchanges took place. Michael Levine opened the conference with a genomic analysis of the transcriptional precision in the *Drosophila em-*

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Two award-winning professors

Christian Lüscher.

Christian Lüscher from the University of Geneva is one of two winners of this year's Cloëtta Prize. This prize has been awarded every year since 1974 to honor Swiss and foreign scientists for outstanding achievements in medical research. Lüscher receives the prize for his research into cell mechanisms in cases of drug dependency and addiction. Among other work, the scientist is a member of the SystemsX.ch RTD project, «Neurochoice». msc

Ruedi Aebersold.

Ruedi Aebersold receives this year's «Herbert A. Sober Lectureship» prize. This prize is awarded for exceptional work that enables new methods and technologies to be developed in the fields of biochemical and molecular-biological research.

Aebersold is a pioneer in proteomics and professor of Molecular Systems Biology at ETH Zurich and the University of Zurich. He is also Chairman of SEB at SystemsX.ch and head of the RTD project «PhosphoNetX». msc

Two award-winning PhD students

This year's «Young Bioinformatician Award» goes to Aitana Morton de Lachapelle. The 27 year-old PhD student works in Professor Sven Bergmann's «Computional Biology» group at the University of Lausanne. De Lachapelle is honored for her work into the investigation of cellular processes regarding the determination of their function.

The prize money of CHF 10,000 is awarded every year by the Swiss Institute for Bioinformatics (SIB) to a young researcher whose work focuses on computer assisted analyses of biological processes and structures.

SIB honored another PhD student: the 27 year-old Rajesh Ramaswamy received the «Best Graduate Paper Award 2010».

This prize, endowed with CHF 5,000, is awarded every year to a young researcher whose work makes an outstanding contribution to bioinformatics and computer assisted biology. Ramaswamy works in the MOSAIC group under the supervision of Professor Ivo Sbalzarini at ETH Zurich. The winning paper is entitled: «A new class of highly efficient exact stochastic simulation algorithms for chemical reaction networks».msc

Aitana Morton de Lachapelle and Rajesh Ramaswamy.

SystemsX.ch must continue 2012-2016

«The SNSF considers that the continuation of SystemsX.ch for the next four-year period is undisputed». This is the conclusion reached by the committee of the Swiss National Science Foundation (SNSF) on the assessment of the four-year research plan submitted by SystemsX.ch for the period 2012–2016. The State Secretariat for Education and Research (SER) commissioned the SNSF to assess the planning application from SystemsX.ch. The Research Council of SNSF records that a withdrawal at the end of 2011 is out of the question, as the time to put in place structural measures to safeguard the promotion of young researchers would be too short.

The committee recommends that SystemsX.ch receive targeted support in the next phase of structural arrangements, the promotion of young researchers, and collaboration with industry. msc.

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Monte Verità Conference

bryo, and Magnus Nordborg (Gregor Mendel Institute, Vienna) closed the meeting three days later with a presentation on the system genetics of *Arabidopsis*. Further highlights came from Veronica Grieneisen (John Innes Center, Norwich, UK) who presented experimental and theoretical data on the role played by the plant hormone Auxin in the genesis of the interlocked leaf cells of *Arabidopsis* or the presentation from Damian Brunner (EMBL, Heidelberg) who showed how the pulsating behavior of cell clusters, found with the help of the latest video-microscopy, contributes to the dorsal fusion of the epidermis in the *Drosophila embryo*.

Highly positive reactions

As the following statement from Sven Bergmann (Lausanne) makes clear, the connection between plant and animal systems, as well as bringing together technology, theory and population genetics was felt to be unique and groundbreaking. «In particular I enjoyed having participants both from WingX and Plant Growth. Both RTD projects face similar challenges in modeling a growing tissue, so it made perfect sense to learn from each and exchange experiences from the different organisms. The external speakers gave excellent talks – and having Systems Genetics at the end was a real highlight fitting very much with my vision of future modeling that also integrates the variability of phenotypes and genotypes in the biological processes we are studying.»

Owing to the high level of positive feedback the organizers are considering a follow-up conference in two years' time.

Quick, precise and comprehensive

Precise measurements within minutes–that is the main goal of a new collaboration between AB SCIEX and the Institute of Molecular Systems Biology at ETH Zurich, partially within the framework of the two SystemsX.ch RTD projects, YeastX and LiverX.

Two ETH researchers, Nicola Zamboni and Uwe Sauer, are working on this project that represents a quantum leap in the study of metabolomics. They are being supported in their work by AB SCIEX, the leading manufacturer of analytical systems. The basis of Zamboni's and Sauer's work is the mass spectrometer «QTRAP 5500», an apparatus already used in the areas of proteomics and lipidomics. This massive, one-piece measuring platform has a linear accelerator of the latest generation, which enables extremely rapid as well as very sensitive measurements to be made. It also comprises a flexible measuring system. The first aim of the project is to employ synergistically the manifold measuring possibilities of this spectrometer, together with newly developed separating techniques and bioinformatics, to set new standards in the analysis of metabolites.

The «QTRAP 5500» spectrometer. Photo AB SCIEX

The long-term aim is to develop a standardized and generalized method that could be used in future in research facilities all over the world. The initiators are convinced that their work will provide the basis for a more efficient exploration of complex biological systems. msc

Farewell to Franziska Biellmann

Franziska Biellmann came to work for SystemsX.ch in September 2007. Over the past three years the management office has profited from her specialized knowledge in biology and her language skills as a native English speaker, as well as from her versatility and flexibility. In particular, she took care of the PhD participants and the financial administration of the SystemsX.ch projects. Wherever a helping hand was needed, Franziska was there. We thank Franziska for her commitment and wish her all the best in her new job, which she will take up in October 2010. SystemsX.ch wishes you much enjoyment and fulfilment, Franziska! VDM

Franziska Biellmann.

Conferences and Events

October 10-15, 2010	International Conference on Systems Biology	Edinburgh, UK
November 1-2, 2010	All-SystemsX.ch-Day 2010	Geneva, Switzerland
November 24-26, 2010	Int. Conference on Biological Science and Engineering	Venice, Italy
December 5-7, 2010	3rd World Congress of Regenerative Medicine & Stem Cells	Shanghai, China
January 15-20, 2011	Mycobacteria: Physiology, Metabolism and Pathogenesis	Vancouver, Canada
February 21-26, 2011	Neurodegenerative Diseases	Taos/New Mexico, USA
March 6-11, 2011	Stem Cells, Cancer and Metastasis	Keystone, Colorado, USA

Glossary of SystemsX.ch

Research, Technology and Development Project (RTD project): SystemsX.ch's flagship project, multi-year duration.

Interdisciplinary Pilot Project (IPP): Research involving risks. One-year duration.

Interdisciplinary Doctorate (IPhD): Duration of 3 to 4 years.

Board of Directors (BoD): SystemsX.ch's highest steering body composed of the presidents, rectors and directors of all participating institutions.

Scientific Executive Board (SEB): Operative committee composed of scientists from the participating institutions.

SystemsX.ch
The Swiss Initiative in Systems Biology

IMPRESSUM

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