

# X-Letter

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## SystemsX.ch is put to the test

The experts of the Swiss National Science Foundation (SNSF) have reviewed the progress of SystemsX.ch. After a detailed evaluation, the panel concluded that SystemsX.ch must continue at the previous level of funding. This continuity guarantees the development of the previously generated potential and strengthens the position of systems biology in the university landscape of Switzerland.



Critical scrutiny exercised at the Mid-Term Reviews.

Photo: VDM

By Daniel Vonder Mühl

When the initiative SystemsX.ch was set up four years ago, everyone was aware that the whole project was an experiment. Whether it would succeed or not – given the political, scientific and time-demanding framework conditions – was written in the stars. It was therefore agreed that the Swiss National Science Foundation (SNSF) would carry out a critical mid-term review of the initiative in 2010 in order to make a recommendation to the State Secretariat for Education and Research (SER) as to whether SystemsX.ch would enter a second phase, as if so, how?

### National Science Foundation calls upon a panel

The SNSF is an independent body responsible for overseeing the quality assurance of the overall initiative, as well as the RTD and IPhD projects. To this end, the body called

upon its own systems biology panel of 12 international experts and 6 Swiss research councillors together.

The thus constituted panel of experts met at Irchel campus of the University of Zurich from 20th–22nd October 2010 to conduct the mid-term review. SystemX.ch’s 2010 Scientific Interim Report provided the panel with a documentary basis that included reports of the 15 RTD, 26 IPhD and 16 IPP projects, as well as an overview of the initiative as such. In December 2009 the experts had also received the multi-year plan 2012–2016.

Following a presentation from Prof. Ruedi Aebersold, Chairman of the Scientific Executive Board of SystemsX.ch, about the current state of the initiative and its future plans, the project managers informed the panel of the status of the RTDs that had been approved by the SNSF in 2008. The experts

### Have the modelers lost sight of the ball?

Prof. Dr. Dieter Imboden, President of the Research Council of the Swiss National Science Foundation (SNF).

The assessment from the review panel concludes that SystemsX.ch is on the right track. Amongst the praise, however, I also read that successes on the theoretical side lag behind those on the practical side. As a former theoretical physicist, I ask myself why this is so. A falling behind in modeling may be one reason; another is probably to be found in the very nature of natural science. Research findings are usually stimulated by experiments, but understood only by a mathematical description, and then, finally, awarded the distinction of a law or rule. In simple systems, new experimental findings and their explanatory theory often arose almost simultaneously. By contrast, superconductivity took almost half a century to proceed from its discovery by K. Onnes (1911) to its theoretical description (BCS theory, 1957). No wonder, then, that a far more complex structure such as a cell, or even only a single enzyme, challenges the modelers. Here’s hoping that they haven’t lost sight of the ball and will completely overrun SystemsX.ch in the near future!

were then able to interview the heads of projects for more details and also acquired a deeper insight about the individual works in the poster exhibition.

### Praise and criticism

The panel was therefore able to base its assessment on various sources. The experts shared their first impression with the SystemsX.ch Management at the end of the event. The written report-with which SystemsX.ch can be very satisfied-arrived a month later.

The main points contained therein are:

- SystemsX.ch unites many of the best scientists in its 80 projects, which comprise over 300 research groups from 12 institutions, and most RTDs have a good balance between biologists and non-biologists.
- Methodological developments and data collections are excellent, important progress has also been achieved in the modeling.
- The RTD projects provide multiple possibilities to approximately 170 doctoral candidates to cooperate with other disciplines.
- The topics of the 40 IPHD projects are innovative.

- The panel was impressed with the poster exhibition, which had led to high-quality discussions with the doctoral students.

But there were also some critical remarks:

- Quantitative modeling, data mining and physical interpretations are not yet exhausted (see Editorial in this issue).
- Individual sub-projects are poorly integrated within some RTDs.
- SystemsX.ch should also develop new theoretical tools.
- All of the eight RTDs evaluated are dominated by biologists.
- With few exceptions, there is little collaboration with big business and SMEs. The level of the originally advised privately funded contributions to SystemsX.ch has therefore not been reached.
- The visibility at the international level is still low, but will certainly grow.

### Making more of existing potential

Finally, the SNSF's expert panel make the following recommendations:

- More professorships are needed in

the theoretical and quantitative areas.

- Various large and small projects need to be initiated to develop the theoretical framework conditions.
- Now that a critical number of non-biologists are involved in systems biology, they should increasingly take on leadership roles.
- International and multi-disciplinary summer courses should be organized for PhD students and postdocs to increase their skills, as well as the visibility of the initiative.
- To increase cooperation with the industry, one possibility would be to bundle projects and patents.
- International conferences hosted by SystemsX.ch would increase international perception.

Given the progress made, the panel concludes that SystemsX.ch must continue until 2016, and at the previous level of funding (25 million per year). Only then can the potential generated in the first phase be developed. This second phase is to strengthen the researchers so that systems biology becomes a long-term component of the university landscape in Switzerland.

## Two days of "All-SystemsX.ch"

Around 200 scientists from various disciplines attended the 2010 "All-SystemsX.ch" conference on 1st/2nd of November, hosted this time by the University of Geneva. Over the two-day event, heads of the RTD and IPHD projects presented short summaries and the current status of their work.

At the poster exhibition participants were able to gain an overview of the current research of SystemsX.ch students. This offered the possibility for lively discussions where participants were able to exchange valuable information and ideas. Most of the 55 posters on display had been entered for the traditional competition. After detailed examination and assessment the SystemsX.ch Educational Board declared Simon Blanchoud (EPFL) the winner for his poster entitled "Temporal and spatial quantification of embryos made easy". Fisun Hamaratoglu (UBas) won second place

and Johannes Friedrich (UniBe) came third.

The physical well-being was also taken care of and personal exchanges in a relaxed atmosphere were made possible when SystemsX.ch invited all

participants to a cosy dinner in Restaurant La Cave on the first evening. The stunning interior of the premises and the excellent food enchanted the guests and contributed to a lively atmosphere.

msc



Around 200 scientists attended the All-SystemsX.ch-Day.

Photo: msc

# Joint FEBS & SystemsX.ch Advanced Lecture Course

By Piera Cicchetti (SystemsX.ch),  
Hannes Link (ETHZ), Berend Snijder (UZH)  
and Eduardo Sabido (ETHZ)

From Feb 26th through March 4th, 2011, the Hotel Grauer Bär in scenic downtown Innsbruck, was overrun with 150 students, postdocs and senior scientists convening for the intense and instructive FEBS-SystemsX.ch Advanced Lecture Course on Systems Biology, "From Molecules to Function". FEBS, the Federation of European Biochemical Societies, draws its main income from its two major scientific journals, FEBS Journal and FEBS Letters, and is well known for its support of prestigious educational events such as this training course, which was co-organized and supported this year by SystemsX.ch.

Prof. Uwe Sauer of the Institute of Molecular Systems Biology, (IMSB) ETH Zürich, participated as a main organizer and teacher of the course and was extremely pleased with the outcome, noting "Every 2 years I am impressed by the intensity of student engagement during this demanding course with close PI-student inter-

actions and poster sessions extending beyond 23:00. With particular pleasure I note this year that the participants ranked three SystemsX.ch related lectures amongst the top five of the 20 overall lectures. Likewise, the blackboard tutorial by Prof. Dagmar Iber (ETH Zürich) received an excellent rating, and one of five poster prizes (from



Karl Kochanowski, Eduard Sabido and Hannes Link (from l. to r.) came from Zürich to Innsbruck.

100 posters) went to a SystemsX.ch participant." One of these prize winners, Karl Kochanowski, gave a student's perspective: "The course was very well organized and structured, allowing us to get in touch with lecturers and fellow students. The course was kicked off by one-day pre-courses covering

a wide range of topics. I attended the course 'Mathematical Biochemistry' held by Prof. David Fell. It was a pleasure to learn about the principles of modeling of metabolism and linear programming from one of the pioneers of the field. The next days comprised morning sessions with three plenary lectures followed by parallel tutorials and subsequent results lectures. In place of an extended lunch break, was the possibility of a two hour ski session. Science resumed with late afternoon and evening blackboard tutorials and computer practicals. After dinner, short presentations by students were followed by late-night poster sessions which I particularly enjoyed: it was a revealing experience to talk to other students with very diverse backgrounds - from mathematics to cell biology, and I got very interesting and thoughtful feedback for my poster. But obviously the course was not about science only: besides skiing, going sledding at night together with all other participants was absolutely great, and the after-hour discussions at the hotel bar were a lot of fun."

## Selected Highlights:

### COPASI – a modeling platform

During a full-day pre-course schedule, with four parallel offerings, Dr. Sven Sahle, (BioQuant, University of Heidelberg), used the glycolysis pathway as a sample model to introduce the COPASI software, a complete biochemical network simulator, which allows the definition not only of the reactions to be modeled, but also user-defined rate equations, compartments and reagents.

### Targeted proteomics

In a morning lecture, Prof. Ruedi Aebersold (IMSB, ETH Zurich), introduced a new proteomic approach called Selective Reaction Monitoring (SRM) as an accurate, sensitive, and reproducible quantitative proteomics technique for systems biology. SRM is a targeted mass spectrometric approach in which the user can monitor several proteins of interest in different

samples and get a consistent quantitative dataset suitable for mathematical model analysis.

### Genetic clocks from engineered oscillators

Dr. Jeff Hasty (University of California, San Diego) surveyed the field of synthetic biology, as an alternative approach to deal with nature's innate complexity, focusing specifically on oscillatory systems. By coupling synthetic molecular oscillatory systems with components of bacterial quorum sensing Hasty has produced very robust oscillatory systems that allow the fine-tuning of the period of the oscillations by controlling the environmental conditions (a highlight of the talk was a first demonstration of the development of an "array of biosensors": a 24 mm x 12 mm chip containing 14,000 cell growth chambers.

### Spatial organization in growth factor signaling

Prof. Phillippe Bastiaens (MPI, Dortmund) is interested in how cells work over many orders of magnitudes of size: for instance, how cell structure and function on the micrometer scale originate from the collective behavior (dynamics) of proteins at the nanometer scale, which he models computationally using 2D cellular automata and the principles of stigmergy which describes how a well defined minimalistic rule set governing the behavior of agents can - via reinforcement or feedback - lead to the spontaneous emergence of apparently highly organized systems.

### Evolutionary Design

SystemsX.ch student, Laura Falter, said: "In general the Session 'Evolutionary design' was my personal highlight.

All the presenters illustrated their remarkable work and key findings in a very clear, captivating way. The biological questions they asked and the novel approaches they were using to answer those questions were extremely inspiring for my own work." Dr. Frank Bruggeman from the Netherlands Institute for Systems Biology in Amsterdam spoke about the origins of cell-to-cell heterogeneity and stochastic transcription dynamics, while Prof. Bas Teusink from the same institute addressed the topic of reverse engineer-

ing and how biological systems are constructed in the light of evolution. Prof. Matthias Heinemann (Univ. Groningen/IMSB, ETH Zurich) spoke about the adaptation of bacteria to nutrients and growth on substrates despite the lack of sensors for these substances. Using a simplified mechanistic model of central metabolism, he showed that adaptation to nutrients emerges from dynamic interactions in metabolism.

#### Industry Perspectives

Dr. Joseph Lehar from Novartis NIBR

in Boston raised the question whether synergetic effects can elucidate biology and explained how combinatorial drug therapy may overcome resistance to monotherapy. Dr. Birgit Schöberl from Merrimack Pharmaceuticals, Cambridge, MA discussed the application of engineering principles to the development of novel cancer therapies using antibodies and gave insight into the research perspective of industry, and the availability of job opportunities for modelers.

## SystemsX.ch PhD Retreat 2010

By Andreas Kühbacher  
SystemsX.ch's second student retreat took place from 30th September to 1st October 2010 in Murten. The relaxed atmosphere before and during the welcome speech, delivered by the organizer, Dr. Franziska Biellmann, made it easy for the participants to enter into a receptive mood.

The program started with an interesting presentation from Prof. Nouria Hernandez (University of Lausanne). She was followed by guest speaker Prof. Wolfram Weckwerth from the University of Vienna, who gave an insight into his work. Two poster sessions gave participants the chance to gain an overview of the various projects being carried out under the SystemsX.ch initiative. This introductory part of the program was rounded

off with a series of short presentations, which were presented by Prof. Jörg Stelling (ETH Zurich).

On a guided tour students and guest speakers learned how the medieval town of Murten had been founded under the Zähringer family, and thereafter developed under the influence of both German and French-speaking peoples over hundreds of years. In addition to the tour of the city, which is still is bilingual today, a welcome meal break afforded good opportunities for students to talk in a relaxed atmosphere among themselves and with guest speakers. The students benefited from the experience of the invited scientists, who in turn, showed great interest in the PhD student's own work and projects.

The retreat made an exciting exchange possible between international students from a range of scientific backgrounds. The retreat also revealed how very diverse biological problems can be solved with systems biological approaches.

### Register now ...

... for the 2011 **SystemsX.ch PhD Retreat, August 19th–22nd** in Kandersteg. **Deadline is April 30th.** Students should present an overview of their project from the logistical/technical/practical side, focusing on productive aspects or obstacles being faced. Prof. **Susan Gasser**, Director, FMI Basel will give a welcome address.

<http://www.systemsx.ch/events>

## How does an embryo make organs with a precise size?

Nature has ensured that the proportions of our limbs are respected, whether we are meant to be tall or short. One of the puzzling questions in developmental biology is how growth and patterning of tissues is controlled. Addressing this issue also helps to understand how the lack of coordination between growth of the tissue and specialization of its constituent cells leads to malformations. A team led by Marcos Gonzalez-Gaitan, Professor



The fruit fly was used as an experimental organism.

Photo: UniGe

at the University of Geneva, has discovered a growth control mechanism that regulates the size of the tissue. The scientists unveil how molecular actors named morphogens determine the dynamics of proliferation in developing organs. The authors of this study, published in the March 4th edition of Science, are currently investigating whether such a "growth rule" could explain some conditions leading to tumor development.

## Register now! SystemsX.ch/SIB Summer School 2011 in Kandersteg

By Piera Cicchetti and Patricia Palagi  
Modern biological science is able to generate enormous quantities of complex data, often through multiple sources. Efficient and accurate analysis of such data can only be accomplished through appropriate computational methods.

Systems Biology, with its aim of integrating complex measurements to understand the functioning of biological systems, is expected to make heavy use of these data, and, in particular, of their analysis within network paradigms. Working together, bioinformaticians and systems biologists can develop advanced approaches to extract knowledge from the data, and thereby drive the creation of hypotheses and models that have the potential to open new avenues of understanding for biology at the systems level.

To foster the development of this exciting and promising interdisciplinary understanding and collaboration, SystemsX.ch and SIB have joined forces to organise a PhD Summer School entitled, "From Data to Models in Bio-

logical Systems". The objective of this course is to teach PhD students how to integrate, manage and analyse experimental data using advanced bioinformatic tools. Topics covered include the visualization of complex



Kandersteg offers an idyllic location.

biological interactions and the application of modeling to predict network processes.

Theoretical approaches and their practical application covered during the week will be of interest to both systems biology and bioinformatics PhD students who wish to become competent in the application of

computational approaches to address biology at the systems level.

The summer school will take place in Kandersteg, a charming, small village in the Bernese Oberland (Swiss Alps). The beautiful and remote setting, along with the challenging program, were chosen to promote and enhance the communication and interaction amongst teachers and students. Lectures, hands-on sessions and round-table discussions will provide the necessary environment to generate lively and informative discussions. The following professors will participate in the school: Sven Bergman (University of Lausanne and SIB), Nicolas Le Novère, (EMBL-Heidelberg) Sean O'Donoghue (EMBL-EBI), Dagmar Iber, (ETH Zurich and SIB), Bas Teusink, (VU University of Amsterdam), Daryl Shanley, (University of Newcastle), Susan Gasser and Michael Stadler (FMI Basel).

Registrations **until April 30th** at:

<http://www.isb-sib.ch/education/sib-phd-training-network/phd-summer-school-2011.html>

## New Bridge 2 Industry Projects (BIP)

The Scientific Executive Board of SystemsX.ch has approved the 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 CHF 120 000. The approved BIPs are listed below:

Title	Gene co-regulation network inference and visualization based on novel bicluster maps	Novel data acquisition and mining strategies based on fast separations and high resolution mass spectrometry for simultaneous qualitative and quantitative analysis of xenobiotic and endogenous metabolites	Identification of synaptic core pathways as targets for autism treatment	High content screening by digital holographic imaging	Development of kinetic models of RNA-dependent silencing
Collaboration between	Prof. Dr. Wilhelm Grissem ETH Zurich and Nebion AG	Prof. Gérard Hopfgartner University of Geneva and AB Sciex	Prof. Peter Scheiffele University of Basel and Hoffmann-La Roche	Dr. Gerardo Turcatti EPF Lausanne and Lyncée Tec SA	Prof. Mihaela Zavolan University of Basel / SIB and Novartis Institute
Keywords	Biclustering, gene expression regulation networks, transcriptome analysis	High resolution mass spectrometry, MS acquisition workflow, metabolism, metabolomics, MS data mining	Autism, synapse, mouse models, pharmacological treatment, neural development	Digital holographic microscopy (DHM), label-free, imaging, screening, high content screening (HCS), high content analysis (HCA), cellular assays, toxicity assays, cell viability, small molecules, chemical interference, siRNA, gene knockdown	RNAi, miRNA, siRNA, gene silencing, kinetic model
Approved	2010	2010	2010	2010	2010

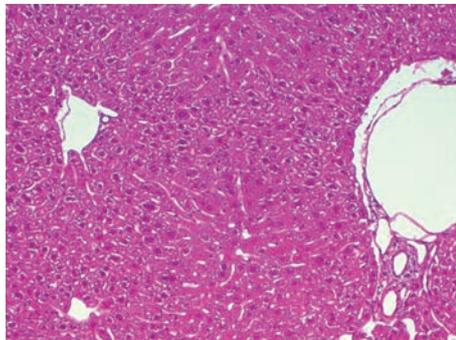
# For **millions of people** their liver metabolism no longer responds to insulin. How this happens is the subject of study from the **scientists of the “LiverX”-Team** – Sugar is just not always sweet ...

By Matthias Scholer

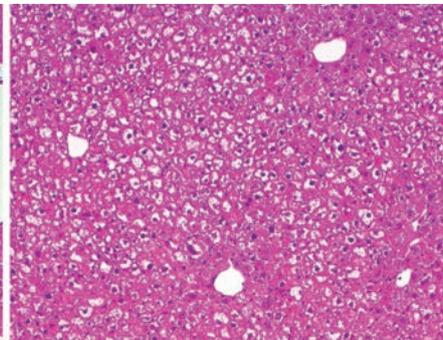
Now that we have consumed a delightful butter croissant with honey or a sumptuous serving of pasta, the thus incorporated carbohydrate are absorbed in the intestines and broken down into sugar. This then passes into the bloodstream and leads to a corresponding rise in blood sugar concentration. Faced with this increase, the pancreas responds by

quence, they suffer from diabetes. Fully 90% of sufferers have a so-called type II diabetes. With Type II, in contrast to Type I, enough of the insulin hormone is produced but has little or no effect on the metabolism of liver cells. For this reason, type II diabetes is also spoken of as an insulin resistance condition. “In this context, resistance does not mean that the hormone can-

the signal transmission to the metabolic network is disturbed. And it’s precisely these fractures in signal transmission that we want to define and explore,” explains Krek. For this, the researchers are employing the latest technology and complex mathematical models. “We’re focusing on the quantitative measurement of the various components involved in signal transmission and their spatial arrangement,” says the scientist about the aim of the measurements.



Normal diet (healthy liver).



High-fat diet (fatty liver).

releasing the hormone insulin. “Among other things, the insulin binds to the liver cells that then turn their metabolism around by 180 degrees” says Prof. Wilhelm Krek, director of the RTD project LiverX. Because, “the liver ensures that the body has enough sugar to produce energy, day and night”. Thanks to the blood sugar, the energy that the tissues need is available ‘on tap’. “The liver cells hold the blood sugar level constant. If the level sinks, the liver cells produce sugar or reduce the stored sugar, the so-called glycogen. If the body is fed sugar after eating, however, the liver cells turn round the metabolism and store it,” summarizes cell biologist Krek when asked about the regulatory processes in the liver. Thanks to a sophisticated interplay of energy supply and storage, the liver can keep blood sugar levels constant during the day-night rhythm.

## Disturbed signal transmission

For more than 220 million people worldwide, however, this mechanism has broken down and, as a conse-

not latch onto the receptor. But with these patients it takes a multiple of the normal hormone levels to activate even approximately-metabolic conversion in the liver cells”. This is why diabetic patients have to inject the missing insulin as soon as their blood sugar levels rise too high.

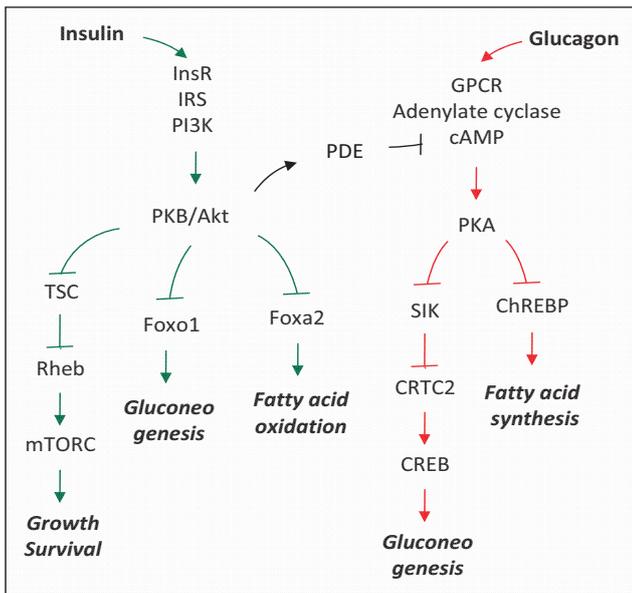
In recent decades many scientists have devoted themselves to the study of this disease process. This has already led to a wealth of findings. So, why is the LiverX team still keenly interested in the pathogenesis of insulin resistance in diabetes type II? “We want to find out why a healthy liver cell responds to insulin and an insulin-resistant cell doesn’t,” is how the cell biologist sums up the main objective of the project. Because, to date, research results give no uniformly consistent answer to this question.

What is undisputed is that the binding of the hormone to the receptor triggers a signaling network in liver cells. Finally, it is this signal that activates the liver-specific metabolic network. “In diabetes patients,

## Of mice and men

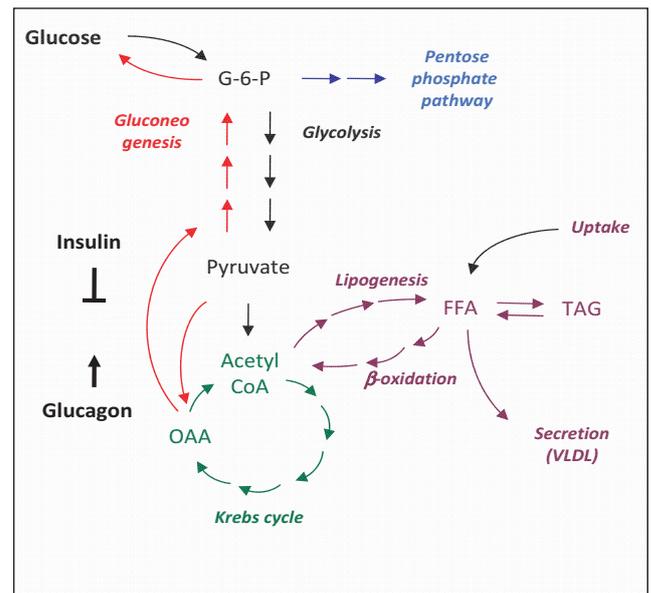
These analyses are first carried out in healthy liver cells, not in human tissues, but in mouse liver cells. These rodents are ideal for investigations. On the one hand, the knowledge thus gained enables the team to approximate processes in human cells. On the other, it is a simple affair to study the influence of circadian rhythms and food intake on the metabolic processes of the mice under controlled conditions. “And,” Krek goes on to explain, “we can deliberately ensure an oversupply of energy in order to provoke obesity within a mouse population. Obesity causes diabetes type II in animals, too, and gives us the means to compare the molecular processes, as well as healthy and insulin-resistant cells.” When the researchers find a difference between two cell populations that could be responsible for the defective signaling, they leave the molecular world of mouse cells. “Our goal isn’t to cure diabetes in mice. Once we have a hot lead, we investigate whether we can find the same difference between healthy and insulin-resistant human liver cells. Only then do we continue to examine the point in question,” says Krek. Because the researchers do not want to waste unnecessary time. “We don’t want to spend years defining the fractured points in the signal transmission in mice, only to find out, somewhere down the line, that only a small number of these plays a role in

### Glucagon-insulin signaling network



Damaged Area

### Metabolic networks



human biology,” says Wilhelm Krek, explaining the team’s methods. After all, the medical relevance of the research results plays a central role in LiverX. “In a first step we want to understand the mechanism of insulin resistance at the molecular level. This will create the basis to consider new approaches in the treatment of diabetes,” predicts the

cell biologist, giving an insight into the future.

First, however, the team is focusing on the defects in signal transmission. And head of project Krek is satisfied with the current state of LiverX. “The project has only been running for a little over two years. We’ve been able to adapt our methods of measuring to the

demands and the corresponding examinations are on schedule. Although we haven’t yet been able to define a specific breaking point, we are optimistic about the future”.

We can therefore hope that sugar will be sweet for everyone in the foreseeable future.

## The “LiverX”-Team

- **Wilhelm Krek** (ETH Zurich) is head of the LiverX project. His own area of expertise is in the analyses of signal networks and gene expression programs that are steered by hormones and nutritional components.
- **Markus Stoffel** (ETH Zurich) is a recognized expert on metabolic imbalances. His work concentrates on the identification of gene patterns that bring about insulin resistance.
- **Matthias Peter** (ETH Zurich) brings his experience of the quantitative analysis of metabolic pathways in microfluid systems to the team.
- **Joachim Buhmann** (ETH Zurich) deals with the computer simulations of the modeling of hormonally-driven dynamic processes in liver cells.
- **Giatgen Spinas** (University Hospital Zurich) and **Markus Heim** (University Hospital Basle) contribute to the project with their years of experience in endocrinology, diabetes and hepatology.

### «LiverX» – at a glance



**LiverX**  
Systems Biology  
of Hepatic Insulin  
Resistance

Principal Investigator	Prof. Wilhelm Krek (ETHZ)
Involved research groups	Prof. Peter Bühlmann (ETHZ), Prof. Ruedi Aebersold (ETHZ), Prof. Joachim Buhmann (ETHZ), Prof. Markus Heim (University Hospital Basel), Prof. Luke Lee (University of California), Prof. Holger Moch (University Hospital Zurich), Prof. Matthias Peter (ETHZ), Prof. Volker Roth (University of Basel), Prof. Markus Rudin (ETHZ), Prof. Uwe Sauer (ETHZ), Prof. Giatgen Spinas (University Hospital Zurich), Prof. Jörg Stelling (ETHZ), Prof. Markus Stoffel (ETHZ), Dr. Nicola Zamboni (ETHZ)
Number of research groups	15
Researchers: Administrators	39 : 1
Biologists: Non-biologists	1.2 : 1
Total budget (2008–2011)	CHF 13 100 000, of which CHF 6 155 000 from SystemsX.ch

## The Scientific Advisory Board has met – in addition to a lot of praise, there were also suggestions for improvements.

By Piera Cicchetti

Last November, while the All-SystemsX.ch-Day 2010 talks took place in the auditorium at the University of Geneva, the members of the Scientific Advisory Board (SAB) of SystemsX.ch convened upstairs to review the progress of SystemsX.ch projects during the past year. Over the course of two days, SAB members Fotis Kafatos, (chair), Eugene Butcher, Marvin Cassman, and Albert Osterhaus listened to presentations by SystemsX.ch PIs as well as PhD students and questioned them afterwards in depth. The SAB was highly engaged, interested not only in the scientific content of the research, but also in the practical aspects of the communication and coordination necessary for encouraging, supporting and managing the interdisciplinary projects. They offered insights from their experiences and knowledge of other programs, providing valuable feedback and new perspectives.

The report goes on to state the essential role of modeling and quantitative analysis for systems biology, cautioning: “SystemsX.ch” will fully succeed only if Systems Biology spreads across the higher education system, including doctoral training, teaching and development of cross-disciplinary programs. SystemsX.ch is currently one of the leading entities pursuing Systems Biology in Europe, and should aim to be the continental leader... we entirely agree with the emphasis in the SNSF review on the need to recruit and incorporate more modellers... We strongly recommend active recruiting and training of modellers, and in collaboration with the partner universities, bringing Systems Biology more intensively into the curriculum.”

The SAB report focused particularly on the doctoral education program. Currently, SystemsX.ch funds approximately 200 PhD students, as part of Research, Technology, Development

systems biology.

The report notes: “The SAB is aware that the high quality but dispersed nature of the autonomous Swiss University Systems inherently reduces the possibility of developing a coherent PhD Training Programme in Systems Biology across the entire country. However, the Federal system also presents an opportunity: visionary cantonal initiatives can be used to experiment and try out novel approaches, which, if successful, potentially can spread across the country. We recommend this approach as an effective and far-reaching strategy for Switzerland, their universities and for the SystemsX.ch. Success in this effort could trigger broader developments in science and the economy throughout the Confederation and potentially elsewhere in Europe.”

In addition to the issue of education, the SAB made particular note of the presentation of Dr. Peter Kunszt, the Project Manager of SyBIT, the Systems Biology IT project of SystemsX.ch.

The report states: “Dr. Kunszt has made extraordinary progress in overcoming the challenges of providing an infrastructure that can integrate data collection and meaningful sharing of different forms of data between dispersed groups, and is working effectively with dispersed RTD’s to solve problems in a coherent and unifying manner. The program he has implemented is unique to our knowledge, and should serve as a model for integrating systems biology and other data-intensive interdisciplinary programs in other countries, and indeed at an international level.”

In sum, the SAB was impressed with the progress of the SystemsX.ch initiative and its potential to not only advance systems biology nationally and internationally but also to serve as a positive model with far reaching significance for the country and beyond. The SAB will meet again in October 2011 at the International SystemsX.ch Conference on Systems Biology in Basel.



Members of the Scientific Advisory Board at the All-SystemsX.ch-Day 2010.

Photo: msc

In their report, they note: “SystemsX.ch has requested a total funding of CHF 125 Mio for the period 2012-2016 at the same level as for the previous 4-year term. It is the SAB’s opinion that this funding level is not only appropriate to the exciting programs that have been established in the first 4 year term, but also essential to allow maturation of the internationally recognized SystemsX.ch network into a self-sustaining systems biology community, within the Swiss national research environment”.

(RTD) projects and 40 Interdisciplinary PhD (IPhD) students. While very impressed by the PhD student presentations, finding the projects and the students themselves outstanding, the SAB was disappointed in the lack of identity of the students with SystemsX.ch and its goals, stating, “their (the students) sense of being engaged and committed to systems biology is not as strong as expected or needed.” Various measures were suggested to develop a more focused and committed SystemsX.ch graduate program in

# SystemsX.ch Management Office

## Many thanks, Natalia!



At last year's All-SystemsX.ch day Natalia Emery Trindade took leave of the All-SystemsX.ch management office. She had worked in the communication's team from December 2008. A milestone of Natalia's work was, without a doubt, the SystemsX.ch brochure. After Thomas Mueller's departure, she took over the editorship of the independent X-letters, the care of the homepage, the paper

monitoring of the Lecture Series and the organization of various SystemsX.ch events.

With her language skills and creative abilities Natalia brought an enriching component into the corridors of SystemsX.ch. We take this opportunity to thank Natalia for the many splashes of color and her dedication, and to wish her all the best for her future career.

## Welcome Piera Cicchetti

Piera Cicchetti joined the SystemsX.ch management office as Scientific Coordinator in November. Piera monitors the scientific aspects of SystemsX.ch projects, is responsible for the development of the graduate program and is involved in building external collaborations.

She grew up in New York, and received a B.A. in Economics from the University of Chicago. Piera earned her PhD in Life Sciences from the Rockefeller University while in David Baltimore's lab and received an Alexander von Humboldt Fellowship for post-doctoral research at the Institute for Genetics, University of Cologne.

She took time off for her children but found her way back to the bench as Instructor in Microbiology and Molecular Genetics at Harvard Medical School. She returned to Europe for family reasons, and is very excited by the challenges presented by the SystemsX.ch initiative.

According to Piera, "SystemsX.ch has the potential to transform scientific research in Switzerland. By encouraging synergistic interdisciplinary academic collaborations in life science across the country, as well as building bridges to industry, the SystemsX.ch initiative in Systems Biology may serve as a general

model for cooperation and collaboration in research."



## Welcome on board, Birgit Conzelmann!



**Dear Birgit, you've been part of the SystemsX.ch team since February.**

**Are you enjoying your work?**

I find it very exciting. As I don't have a scientific background, a lot of it's still a bit strange. But I'm enjoying the challenge. It's great to work independently and be part of a dynamic team.

**What is your professional background?**

After my translator's diploma I worked for a number of banks. Among other tasks, I also looked after the Intranet. This awakened my interest and that's why I focused on HTML and continued to expand my programming skills at a small web agency.

**What is your job description at SystemsX.ch?**

My main responsibilities lie in internal communication, the website and the introduction of new media - for me this position offers an optimal combination of language and the Web.

**What do you do in your free time?**

If I'm not diving, I'm cheering on my favorite team.

**FCB or FCZ?**

Neither! My heart beats for Xamax, Eintracht Frankfurt, and Schwenninger ERC, probably a team no one here's ever heard of!

## Pfizer Research Award 2011 for SystemsX.ch researchers

In early February three researchers working on the SystemsX.ch RTD project "Neurochoice", were awarded the coveted Pfizer Research Prize. For the past 20 years the prize has been awarded to honor outstanding scientists for their research at Swiss research institutes and hospitals.

Professor Fritjof Helmchen and Dr. Benjamin F. Grewe of the University of Zurich received the prize for their work "Observation of neuronal net-



Dr. Benjamin F. Grewe and Professor Fritjof Helmchen (UniZH) at the awards ceremony.

work activity by fast laser-scanning". In this work, the researchers developed a novel two-photon microscope with a special laser scanners. This allows scientists to measure neuronal network activity in the brain with more than ten times higher time resolution than before. Moreover, the position of the laser beam can be modified within a few millionths of a second. This means that greatly improved and more comprehensive studies of the activity patterns in the normal brain are possible on a relevant time scale. Any disturbances in information processing in a diseased brain can therefore also be studied.

The only female winner, Dr. Kelly R. Tan from the University of Geneva, received the Pfizer Special Prize for her work on "Benzodiazepine dependence", published in "Nature" (February 2010). Benzodiazepines are often prescribed in daily practice for their sedative effects. Used over a long period of time, however, they may lead to dependence. Kelly Tan and her team were able to show that certain



Dr. Kelly Tan (UniGe) is delighted with this year's special prize.

benzodiazepines bind to the same receptors in the brain as other drugs, that are known to lead to dependency (e.g. cocaine, nicotine, etc.) and therefore to the addictive reactions. These findings can serve to develop a new generation of benzodiazepines, which do not bind to these receptors and can thus be prescribed without risk of dependence. BC

## TOR, PI3K and Akt – 20 years on

By Anita Soltermann  
Signal transduction, given its temporal, spatial and functional complexity, is a particularly important topic in Systems Biology research. The PI3K-Akt-TOR signaling pathway is of special interest. It plays a central role in development and aging, and is implicated in many diseases including cancer and diabetes. PI3K, Akt and TOR were all discovered approximately 20 years ago. Researchers at the University of Basel and the Friedrich Miescher Institute played an important role in these discoveries and the development of the field.

The Basel Signaling Alliance is organizing a symposium to

highlight the enormous progress that has been achieved in this field within the past years and to identify future perspectives. The two-day conference from September 11th-13th, 2011, includes topics ranging from basic research to applied therapies. A focus will be translational cancer research. The speakers are world-renowned basic researchers, clinicians and leaders from the pharmaceutical industry. Besides the lecture sessions, a poster session for young researchers will be organized, and a poster prize will be awarded.

Further information:  
[www.torandmore.org](http://www.torandmore.org)


**Basel  
Signaling Alliance**

**TOR, PI3K and Akt -  
20 Years On**



[www.torandmore.org](http://www.torandmore.org)

September 11 - 13, 2011  
Biozentrum / Biomedicine, Basel  
Switzerland

**Confirmed Speakers:**  
Robert Abraham  
Kari Alitalo  
Mariano Barbacid  
Joan Brugge  
Lewis Cantley  
Julian Downward  
Napoleone Ferrara  
Michael Hall  
Douglas Hanahan  
Carl-Henrik Heldin  
Brian Hemmings  
Tak Mak  
Ramon Parsons  
Linda Partridge  
Anne Ridley  
David Sabatini  
William Sellers  
Kevan Shokat  
Nahum Sonenberg  
Matthias Wymann



**Organizers:**  
Gerhard Christofori, Michael Hall, Brian Hemmings, Matthias Wymann

## 8th International Workshop on **Computational Systems Biology** (WCSB) in Zurich, June 6th–8th, 2011

By Heinz Koepl  
WCSB will bring together the different research communities involved in computational systems biology research, e.g. experimental biology, bioinformatics, machine learning, signal processing, theoretical computer science, mathematics, statistics and theoretical physics. This 8th edition of the workshop is hosted by Professor Heinz Koepl and his newly-established

Biomolecular Signaling and Control Group of ETH Zurich ([www.bison.ethz.ch](http://www.bison.ethz.ch)). SystemsX.ch supports the workshop and strongly encourages all those involved in this initiative to take the chance of presenting results of SystemsX.ch projects. The workshop features invited and contributed talks, as well as poster sessions. Full-paper submissions and submitted abstracts will be available in the to-be-published

workshop proceedings. The organizing committee is pleased to announce internationally renowned speakers, including Ruedi Aebersold (ETH Zurich), Michael Stumpf (Imperial College London) and Ilya Shmulevich (ISB Seattle). Moreover, representatives of the pharmaceutical industry have agreed to present their efforts in computational research.

More at: [www.wcsb2011.ethz.ch](http://www.wcsb2011.ethz.ch)

## 1st **International SystemsX.ch** Conference on Systems Biology

The first International SystemsX.ch Conference on Systems Biology, will be held at the Congress Center, Basel,



Basle will be the venue of the Systems Biologists meeting in October.

Photo: Andreas Gerth

October 24th–26th, 2011. This conference will be the first in a series which is intended to provide an international venue for bringing together top Systems Biology researchers from Switzerland and worldwide. The conference will be divided into four major sections: Modeling, Novel Technologies in Systems Biology, Synthetic Biology and Medically Relevant Systems Biology. Each section will take about half a day and generally include three speakers from outside Switzerland and one SystemsX.ch speaker. Three additional speakers per section will be chosen from the submitted abstracts to present short talks, and two SystemsX.ch IPHD students per section will have the opportunity to give brief presentations of their work. There will be ample time for poster sessions and prizes for best posters will be awarded. An organized evening social event will be offered to encourage the participants to convene in a relaxed atmosphere and get to know each other better.

### Speakers Basel

#### Medically Relevant Systems Biology

Vamsi Mootha

Ari Helenius

Markus Stoffel

#### Modeling of Complex Systems

Uri Alon

Enrico Cohen

Boris Kholodenko

Felix Naef

#### Synthetic Biology

Jay Keasling

Christopher Voigt

Martin Fussenegger

Petra Schwille

#### Novel Technologies in Systems Biology

Tony Hyman

Nevan Krogan

Markus R. Wenk

Sebastian Maerkl

Please visit the conference website for details about registration.

<http://conference.systemsx.ch>

### Conferences and Events

Jun 6 <sup>th</sup> –8 <sup>th</sup> , 2011	8 <sup>th</sup> Int. Workshop on Computational Systems Biology	Zurich, Switzerland
Aug 14 <sup>th</sup> –19 <sup>th</sup> , 2011	SystemsX.ch/SIB Summer School	Kandersteg, Switzerland
Aug 19 <sup>th</sup> –22 <sup>th</sup> , 2011	3 <sup>rd</sup> SystemsX.ch Student Retreat	Kandersteg, Switzerland
Aug 28 <sup>th</sup> –Sept 1 <sup>st</sup> , 2011	12 <sup>th</sup> International Conference on Systems Biology	Heidelberg, Germany
Sept 11 <sup>th</sup> –13 <sup>th</sup> , 2011	TOR, PI3K and Akt – 20 Years On	Basel, Switzerland
Oct 24 <sup>th</sup> –26 <sup>th</sup> , 2011	1 <sup>st</sup> Int. SystemsX.ch Conference on Systems Biology	Basel, Switzerland

## PIs Spring Meeting at PSI

As in other years, heads of all RTD projects, so-called principal investigators (PIs) are meeting up twice in 2011. Instead of the customary half-day in Berne for their spring meeting, this year they were invited to the Paul Scherrer Institute (PSI) on 30<sup>th</sup> March. Among other points on the agenda was a detailed plan for the period 2012–2016 and the Financial Report for 2010.

In the afternoon, Professor Gebhard Schertler (PSI) presented a brief summary of PSI's Department of Biology and Chemistry (<http://bio.web.psi.ch/>) and Rafael Abela provided information on the status of the new X-ray free-electron laser, (SwissFEL, <http://www.psi.ch/swissfel/>), to be built over the next few years and due to be operative in 2016. After a short break, the partici-

pants were guided through the Swiss Light Source (SLS, <http://www.psi.ch/media/swiss-light-source-sls>), which is used in many different ways by researchers.

The informative and interesting visit at PSI showed project leaders which highly-developed technologies the PSI User Lab provides for questions pertinent to Systems Biology. BC

PIs gained an overview of SLS (from left to right): Fritjof Helmchen (Neurochoice), Piera Cicchetti (SystemsX.ch), Philipp Berger (PSI), Gebhard Schertler (PSI), Cris Kuhlemeier (Plant Growth), Friso van der Veen (PSI), Bart Deplanke (CycliX)



## 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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