SystemsX.ch Newsletter #16
November 2008

X-Letter 16

HAPPY BIRTHDAY SIB

At the tenth anniversary of SIB, director Ron Appel sang an aria from Franz Lehar. **03**

PLANT SYSTEMS BIOLOGY

Fathoming the plants nature in models and reality is Chris Kuhlemeier's aim. **04**

SYSTEMS THINKING

Systemsbiology and Systemstheory are surprisingly far apart from each other. **06**

In a poster session 32 project were presented. Photo Thomas Müller

The **All-SystemsX.ch-Day** in Basel was a success. New project ideas were presented and a poster price was awarded.

Thomas Müller

Basel. The second All-SystemsX.ch-Day was a premiere at the same time. It took place within the framework of the «Life Sciences Week» in Basel and attracted 350 visitors interested by Systems Biology and SystemsX.ch in the Montreal Hall of the Congress Centre in Basel. The veteran of drosophila research, Walter Gehring, of University of Basel's Biocentre also made a brief appearance; some of his students are involved in SystemsX.ch. The exchanges between the participants were lively, the meeting even took on something like a family atmosphere.

This time, a happily large number of 70 scientists from the pharmaceutical industry, biotechnology, and IT-companies found their way to SystemsX.ch. Perhaps a synergy effect with the technology fair «Life Sciences» which welcomed the impressive number of 2600 visitors. Dominique Michel and Richard Quaderer from Lonza in Visp are interested in ways to produce small molecules, today

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Union of Wills instead of Partnership of Convenience

Thomas Müller,
Head of Communications,
SystemsX.ch

For me, it was a lesson in research policy. Six years ago, all began with an ETH Life Sciences Institute in Basel supported by Basel politicians and «federal Bern», today SystemsX.ch is Switzerland's largest research initiative.

SystemsX.ch is a construct typical of the Swiss Confederation. Cultures and interests of two ETH, six cantonal universities and three research institutions must be brought together – a difficult task since conflicts of objectives, which arise from competition for research subventions and the obligation to cooperate being side-by-side, must be sorted out by the joint steering bodies.

However, for the political establishment and the public at large, this does not matter. They are only interested in high-level scientific output. This can only be achieved if SystemsX.ch, like Switzerland, understands itself as a confederation of wills and not as a mere partnership of convenience to keep the subsidy pot.

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synthesized through organic chemical methods, by a (systemic) biological process. Pasquale Di Cesare of IBM Switzerland is impressed by the interdisciplinarity of Systems Biology in Switzerland. He came to get acquainted with the research conducted by potential clients of IBM. And Dieter Scholer, member of the University of Basel Council with an intimate knowledge of the life sciences scene in Basel, is delighted by the «overwhelming enthusiasm» with which the SystemsX.ch scientists get down to work. Hans-Peter Wessels, director of the business promotion department of Basel-City and Basel-Land and future state secretary of the Basel-City canton, praises SystemsX.ch as a model initiative to advance biology. SystemsX.ch's network approach to address biological problems is exemplary, he says.

And the winner is…

Rajesh Ramaswamy from India won the main poster award. Photo thm

In the afternoon, a series of researchers presented new project ideas and Peter Meier-Abt, vice-rector of the University of Basel, handed over the prize for the best poster to the PhD student Rajesh Ramaswamy (ETH Zurich) for his illustration of protein recycling in the cell membrane.

The second call for proposals for research projects targets technology, genomics and biomedicine.

Zurich. SystemsX.ch, the Swiss initiative in Systems Biology, has launched its second call for proposals for large research projects. The research volume will exceed 50 million francs. SystemsX.ch will support between five and seven Research, Technology and Development Projects (RTD) with a contribution of up to 6 million francs over four years.

Altogether, SystemsX.ch has up to 28 million francs at its disposal. The institutions of scientists supported are required to contribute the same amount, bringing the total research volume to between 50 and 60 million francs. This round of research promotion focuses on the development of future-oriented technology for Systems Biology and on projects at the interface of biomedical research. The deadline for submitting proposals is January 15, 2009.

Risks wanted

To foster the development of Systems Biology in Switzerland, SystemsX.ch attaches a great importance to supporting young researchers willing to take risks. Thus, SystemsX.ch finances about a dozen doctoral theses of young researchers every year. The interdisciplinary doctorates (IPhD) are supervised by two professors from two different disciplines. In addition, SystemsX.ch finances about 10 high-risk projects (interdisciplinary pilot projects, IPP) under the condition, here too, that two research groups from two different disciplines work together. In contrast to the doctoral thesis, risks may be taken while this is usually not encouraged by the research promotion agencies. RTDs and IPhds are evaluated by an international Review Panel of the Swiss Research Fund, whereas IPPs are subject to approval by the SystemsX.ch's Scientific Executive Board. thm

Big medically focussed projects have better chances. Photo Christian Flierl

An IT-Manager for SystemsX.ch

Zurich. SystemsX.ch is getting a centrally controlled IT structure. The objective of the Systems Biology IT Project, abbreviated SyBIT, is to provide the data and storage hungry Research, Technology and Development Projects with adequate hardware and software support.

For this challenging position, SystemsX.ch is looking for a IT and bioinformatics specialist to build a coherent structure adapted to the researchers' needs. Among the existing resources, he will have access to the Center for Information Sciences and Databases in the Department of Systems Biology and Engineering of the ETH Zurich in Basel and to the services of Vital-IT, the informatics initiative in the Life Sciences of West-Switzerland.

This exciting position requires a taste for interdisciplinarity, interpersonal communication, different university cultures as well as some IT-experience. thm

Founded by pioneers, born in misery, today world class. Swiss Institute of Bioinformatics celebrated its 10th anniversary with a congress and a banquet.

Ron Appel, director of SIB, and Laure Verbregue sing a duet from Franz Lehár's operetta «The Merry Widow» at the banquet. Photo Fred Merz/SIB

Thomas Müller

Bern. The evening was already advanced as Ron Appel, director of the Swiss Institute of Bioinformatics, went back up on the stage, accompanied this time by Laure Verbregue. And then the surprise! Director Appel morphed into a tenor incarnating Count Danilo Danilowitsch and sang the duet «Lippen schweigen, ‹s'flüstern die Geigen» (from Franz Lehár's «The Merry Widow») with the soprano Laure Verbregue in the role of Hanna Glawari.

The SIB Jazz band which, a few minutes before, had come out brilliantly by playing amino acid sequences transposed in melodies and harmonies, proved to be equally at ease in the operetta genre.

With large volume and impeccable intonation, tenor Appel and soprano Verbregue brought the audience to a boiling point. The guests, more than 350, gave them a rousing standing ovation and shouted for an encore, and since it had been so beautiful, they sang the duet once more.

The birthday ceremony, which took place on the 24 September at the Kultur-Casino in Bern, had begun in due form with a scientific congress featuring Werner Arber, Nobel laureate. In the evening, at the banquet, Mauro Dell'Ambroglio, state secretary for education, and research, recalled and praised the institute's path full of obstacles to world class.

Without informatics, rien ne va plus

The story begins in the mid 1980s as total belief in the explaining capacity of genes still prevailed. But, in Geneva, a small conspirator group of young researchers would not give up their conviction that the real actors of lives were the proteins, and not the genes which in fact would contain only the script and by no means everything of crucial importance. The members of this rebel group included amongst others Ron Appel and the biochemist Amos Bairoch who now conducts the biggest group at the SIB. «At that time, we were considered as failures who were fooling around on computers», recalls Bairoch. Today, without computer scientists, rien ne va plus. They channel the data streams produced by the other biologists and assist them in extracting new insights in biology from them. This is one of the reasons, and not the least, why the SIB is a partner of SystemsX.ch, the Swiss initiative in Systems Biology. In addition, SIB researchers participate in many SystemsX.ch projects.

A Service Network

Like SystemsX.ch, the SIB constitutes a network of research groups. Some are implanted directly on the site of the SIB, but most are affiliated in another Swiss university or research institution. In this way, the institute counts about 300 researchers. Its task is to provide services and support to the national and international research community in the natural sciences through databases, software applications, web servers, and coordination and service centres as well as education and research in the field of bioinformatics.

The plant, the unknown. To fathom its secret, that is the objective of the SystemsX.ch project «Plant Growth in a Changing Environment».

Thomas Müller

Bern. A plant is very different from us. It keeps growing until it dies. It cannot run away, and for this reason, it has developed defense mechanisms completely different from those of mobile multicellular organisms. The plants are the most successful products of evolution, at least in terms of mass, representing 99% of the biosphere. They are frugal, they need nothing, but light, air, water and a few minerals. And last, but not least, we human beings live from the plants and breathe the oxygen they produce.

«The genes cannot ignore physics.»

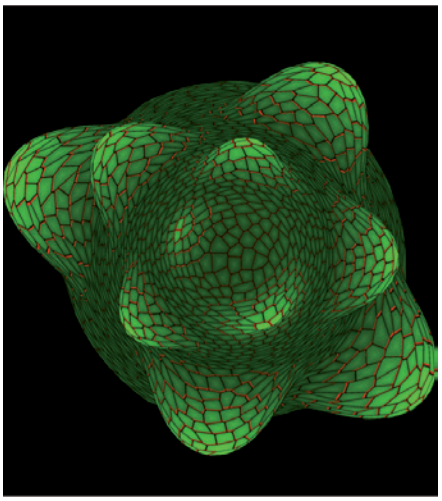
Plants are among the «creatures» mentioned in the Swiss Constitution which confers them a certain dignity. How do they function in fact? How do they grow and develop in an ever-changing environment? How does nature, this engineer, manage to create a cell wall which is, at the same time, scaffold, support, protection envelope, filter, pressure container and many more other things, all this growing at the same time? In comparison, our «functional tissue» is a simplistic affair.

Modellers refute biologists

These are the questions among others addressed by 18 research groups in the whole of Switzerland within the framework of the SystemsX.ch project «Plant Growth in a Changing Environment». «We intend to study the nature of the plant at many systemic levels», explains the director of the project, Cris Kuhlemeier, professor at the University of Bern and director of the Institute of Phytobiology affiliated at this university.

In this project, computer simulation will play a central role. Kuhlemeier explains his expectations with the following example: how does a plant trigger the construction of a leaf? Under the cold light of mathematical formulas generated by modellers, the explanation attempts, so dear to the «classical» biologists, were found to be insufficient. Kuhlemeier explains his strategy: «We expect to make other discoveries also in other fields through the interplay between computer simulations and practical experiments». The project «Plant Growth» will involve other systemic levels such as the plant cell and the plant as a whole in its environment.

Cris Kuhlemeier presents his experiment subject, the thale cress. Photo Thomas Müller



Computer simulation of a meristem, the highest point of a shoot. Photo Richard Smith

To reduce the number of variables, «Plant Growth» limits itself to the biologists' preferred plant, the thale cress, (arabidopsis thaliana) which has a short generation cycle and a small genome composed of only five chromosomes.

The objective, is it to develop a virtual plant, an «iPlant» so to say? «That's the latest hype, but it does not mean very much», he says. However this name cannot be so wrong as it is the name of an American research project pursuing similar goals.

From architecture to construction

Kuhlemeier is keen to know how a plant organ, whether a leaf or a flower, is actually constructed. Just as the architect's plan does not say very much about how masons, carpenters, joiners, painters, plasterers and plumbers will construct a house, so the genetic construction plant does not allow to understand how the plant is constructed. «Thus, we want to know how a plant sets scaffolds for itself, generates the cell wall and determines the angel at which the shoots and the stems will grow upwards to the sky. One thing is certain: it is not written in the genes that many plants arrange their leaves at an angle of 137,5 degrees».

Mechanics and statics will thus play an important role in «Plant Growth». «The genes cannot ignore physics» remarks Kuhlemeier with a smile. Thus, the forces involved in the construction of the plant are to be measured, and this on the living subject for the first time. For this task, the project will collaborate with the firm Femto-Tools which constructs the necessary sensors (s. box: «Delicate Force Measurements on Shoots and Stems»).

«We will try to link our plant models to the climate models»

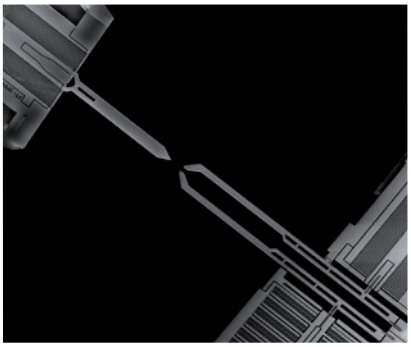
The global aspects will be addressed in a second phase. Kuhlemeier's dream is to give the plant the place they deserve in the climate discussion. «Often, plants play only a minor role in this discussion whereas they are much more important than the animals in the composition of the atmosphere» explains Kuhlemeier, somewhat worked up.

Naturally, it is about extrapolating from one plant-model to the whole biosphere. Nevertheless, a good model could give us a good idea of what is going on at the global level. «That's why we will try to link our plant models to the climate models of the atmosphere physicists». At the moment, their models take only the atmosphere and the oceans into account. «Plant Growth» intends to inject a bit of life into them.

Delicate Force Measurements on Shoots and Stems

Zurich. Femtotools, that is the name of the company which provides assistance in measuring the forces involved in cell growth or cell division. Counting four employees, the company is a spin-off of ETH professor Bradley Nelson. that specializes in the development of sensors capable of measuring tiny forces. They can measure forces as small as those exerted by a grain of dust of one tenth of a milligram on a piece of paper.

As sensors, it uses a flexible piece of silicon embedded directly in a chip. With this technology, the company hopes to fill the «measurement gap» between the large scanning microscopes and the usual meters. «With our participation in «Plant Growth», we want to demonstrate that our sensors can be used not only in engineering, but also in biology», with these words, the company director, Felix Beyeler, describes the reason for the company's participation to «Plant Growth». thm



A silicon force sensor with pincers to grab objects of a size between 0.001 and 0.1 mm. Photo Femtotools

«Plant Growth in a Changing Environment» at a glance

Plant Growth
in a Changing
Environment

Principal investigaor:	Prof. Cris Kuhlemeier, University of Bern
Participating institutions:	University of Bern, University of Zurich, ETH Zurich, University of Basel, University of Fribourg, University of Genf, EPF Lausanne, University of Neuchâtel, University of Lausanne, Swiss Institut of Bioinformtics
Industriy partners:	Femtotools GmbH, Zurich.
Number of research groups:	18
ressearcher / administrators:	74 / 1
Ratio biologists - non-biologists =	3:1
Total budget (2008-2011):	14, 778 342 Mio. Fr.
from SystemsX.ch:	5, 87 Mio. Fr.

When the part becomes the environment and the whole a system. Systems Biology in the view of a systems theoretician.

Stéphane Vézina*

Heidelberg. «Systems biology» is a worldwide academic hype. A bit intriguing. The word «system» has become banal, you can hardly buy anything but systems: bed, office, shelf, energy, and even coffin systems. But what is a system? The philosopher and theologian Augustinus of Hippo (354 - 430) was probably in the same situation as he wrote this about a similarly puzzling triviality: «What is time? If nobody asks me, I know it. But I should explain it to you, I do not know».

Taken in general, the system concept is extremely rich and complex. The theory which concerns itself with systems goes back to the 1920's. Systems theory originated through cybernetics and information theory (Shannon, Weaver) and was further developed in systemic sociological theories such as Niklas Luhmann's theory. Other forms are e. g. the «chaos theory», the «autopoeisis theory» of the biologists Humberto Maturana and Francisco Varela or the theory of complex systems, as developed in the 1990's at the Santa Fé Institute (Stuart Kauffman).

In a control center of a traffic management system, automobiles are not part of the system, but its environment. Photo Siemens

Less than the sum of its parts

But strangely enough, Systems Biology remains largely untouched by such developments. Systems theories are mentioned in books about Systems Biology, it is true, but they hardly play a role. For example, a new introduction states: «The core fundamental concepts of Systems Biology ... remain pretty much the same as in the time of Aristotle.» («Systems Biology: Principles, Methods and Concepts» (ed. Konopka, 2006, S. 1)! It relies on a more or less intuitive comprehension of the concept «system», for example with the old saying: «The whole is more than the sum of its parts».

But this is only one aspect among many other aspects. Water is composed of hydrogen and oxygen. The whole, water, has qualities which the parts - hydrogen and oxygen, both gases - do not have. On the other hand, the parts have qualities which the whole does not have: Hydrogen is extremely inflammable, and oxygen fuels fire, but fire goes out when you pour water on it. Thus the whole is also less than the sum of its parts.

Moreover, the parts do not exist isolated to be integrated unchanged in a whole. A melody is composed of individual notes. However it can be played on a recorder or on a double bass, or transposed it into any key, you will recognize it. You hear only the relation between the notes. Time also plays a role. The notes are played one after the other, but if you should be able to recognize the melody, the notes already played and the notes not yet played must be there somehow even though, at the moment, another note is being played. They are there and not there at the same time. In addition, any musician knows that the whole melody must be in the first note, otherwise it falls apart.

Exploring such intriguing phenomena is the objective of the General Systems Theory. In a first step, it has replaced the traditional distinction whole/parts by the distinction system/environment. The advantages of such a reformulation spring to mind, any system - a biological too - develops in an environment and must sustain itself in it. The focus has now moved to the dynamic processes involved in system development.

Part becomes environment

As the first surprising consequence of this reformulation, that which is intuitively considered part of the system is now banished into its environment. So one would think society is a system composed of human beings. Wrong, says sociologist and systems thinker

Niklas Luhman, for the immediately obvious reason that human beings as biological entities do not constitute a social system. As all-encompassing social system, society develops and sustains itself through the communications between human beings who are part of the environment of society, he says.

Then, the system is not composed of parts any more, but rather it develops out of events occurring when parts out of its environment come into relation with one another, that means in the social system when human beings come into relation with one another and produce communications. The system

Society does not consist of humans but of communication between humans.

uses such events to construct itself in the form of structures, processes, etc.. In society, sub-systems such as the legal system, the economic system, the political system, develop and sustain themselves out of communications in this manner.

As events, the elements of the system are without duration and are thus fundamentally unstable. For example, in a communication, in a conversation, each word does not have any duration, hardly pronounced, it must leave its place for the next word. It is one of many events in a process which emerge and disappear in the same moment. But the elements must disappear, otherwise the system, already with a few elements, would attain an incontrollable complexity leading to chaos. What a commotion would arise if the words and sentences in a conversation would not die away, but remain audible! Thus, the system can achieve a certain stability only if its elements do not have any duration and are unstable; on the other hand, it must develop structures which can link certain emerging and passing elements-events over time distances. In a communication, in a conversation, this is achieved by memory that preserves certain spoken words and brings them into a meaningful statement.

Through the continuous instantaneous disintegration of its elements, the system gains a large degree a freedom and ability to adjust to its environment. It can allow events to happen in a limitless number, under the condition that they die away immediately. Under these innumerable possibilities, it selects the events relevant and important for its existence and transposes them into structures.

Death is a trick of life

The organism is the prototype of the system. It too constructs itself out of events, biochemical reactions between substances in its environment which occur and immediately end, but trigger other reactions to ensure that the chain of reactions-events is not interrupted. It develops structures and processes which prevail over the trend to immediate dissolution and allow a selection under the innumerable events, thus giving the system stability. It can allow innumerable events, immediately dying away, to happen and can in this way develop very complex forms of life. Death is a trick of life to create more life.

* Stéphane Vézina has studied philosophy and sociology and works as scientific translator.

Markus Stoffel discovers Diabetes Drug Target. Roche mulls using it.

Zurich/Basel. The collaboration between Roche and the Competence Center for Systems Physiology and Metabolic Diseases has produced the first drug target candidate. The target is a membrane protein of insulin-producing beta-cells in the pancreas which die in cases of diabetes Type 2.

This has been confirmed by Markus Stoffel from the Molecular Systems Biology Institute of ETH Zurich who identified the target. At the moment, the ETH Zurich is filing the patent applications, and for this reason, the «identity» of the target may not be disclosed.

Roche might license the patent, declares Cristiano Migliorini, Roche's project coordinator. The pharmaceutical firm has already identified the protein as a target for another disease. That's why it was possible to conduct the pharmacological animal experiments for the target only one year after its identification. If the feasibility study is completed successfully, the first clinical studies could follow in 2011 already.

«That's lightning-fast for testing a new concept», rejoices René Imhof, director of Roche Research in Basel and a pemanent guest of SystemsX.ch's Scientific Executive Board. thm

NEWS

ERC-Grants to SysX.ch Members

Brussels. Three members of the SystemsX.ch's Scientific Executive Board are among the beneficiaries of the first phase of the Advanced Grants by the European Research Council: Ruedi Aebersold, ETH Zurich, Konrad Basler, Zurich University, Denis Duboule, EPF Lausanne. The Swiss researchers have obtained eight of the 78 grants. thm

A Genome for $5000

Mountain View. 5000$, that is the amount which the Californian company Complete Genomics will charge next year for commercial sequencing of a human genome. In 2009, the company expects to sequence about 1000 genomes, in 2010 some 20000, and in the next five years in cooperation with partners, one million. The Institute of Systems Biology in Seattle (ISB) is one of the partners. thm

Systems Biologist will head BBSRC

London. Douglas Kell, director of the Manchester Centre of Systems Biology will be the new CEO of the Biotechnology and Biological Sciences Research Council (BBSRC) in UK. thm

With Systems Biology against Infectious Diseases

Bethesda. In the United-States, the National Institutes of Health are betting on Systems Biology to combat infectious diseases. Four research institutes will receive up to $ 68.7 million over five the next years. SARS, tuberculosis and influenza are targeted. thm

Natalia Emery Trindade joins the SystemsX.ch Management Team

Natalia Emery joins SystemsX.ch .

Zurich. Natalia Emery Trindade joins the SystemsX.ch Management Office team as the new communications staff member. She will start on December 1, 2008, will implement the existing communications concept, and will produce the forthcoming SystemsX.ch X-Letters and X-Flashes. Natalia Emery holds a Bachelor's degree in Portuguese and French. On top of that she speaks English, German, Spanish and Italian fluently. Furthermore she will receive her certificate of studies in Art and Electronic Media from the Zurich University of the Arts next January. She is also completing a journalism and news writing course at the London School of Journalism via a correspondence course. A part of her time will be devoted to general administrative tasks. Natalia Emery Trindade is a German and Brazilian citizen and lives in Zurich

Thomas Müller, head of communications at SystemsX.ch and SystemsX is leaving SystemsX.ch at the end of the year. Müller elaborated the communications concept of SystemsX.ch, and developed together with Ruedi Widmer Grafik the «corporate identity» of SystemsX.ch, the website, the newsletter (X-Letter) and the email news service (X-Flash). He will have edited 16 Newsletters and wrote many of the articles. In December 2007, a media conference made SystemsX.ch known to a broader public.

From January 1, 2009, Thomas Müller will head the science section of the Neue Zürcher Zeitung. thm

Thomas Müller leaves for NZZ.

Yeast Biologists seek for Common Language for Common Problems

Zurich. The systems biologists who seek to model metabolic activities or even whole cells study often the same problems, but they use different software and terminologies in their research, rendering any collaboration difficult if not impossible. That's why a group of modellers, yeast biologists, have joined their efforts to develop a common, clear and coherent nomenclature of reactions and reaction partners.

From SystemsX.ch, Uwe Sauer and Matthias Heinemann of the Institute of Molecular Systems Biology of the ETH Zurich have taken part in this initiative. «No big science, but a necessary organizational step which the yeast specialists have first taken, indicating the direction to follow». thm

Nat Biot. 2008 Oct;26(10):1155-60.

Conferences and Events

Nov 15 - 18, 2008	4th EMBO Conference	Heidelberg
Nov 27, 2008	Swisscore: Swiss Science Briefing on SystemsX.ch	Brüssel
Dec 04, 2008	Partnering Event on Bioinformatics and Proteomics	Genf
Dec 7-10, 2008	Drug Discovery Design Methods & Applications Workshop	Hyderabad
March 23 - 25, 2009	BioSysBio	Cambridge, UK
March 25, 2009	SystemsX.ch Industry Day	Basel
April 16 - 19, 2009	The 3rd International Biocuration Conference	Berlin
Aug 09 - 12, 2009	FOSBE 2009	Denver, USA
Aug 30-Sep 4, 2009	ICSB 2009	Stanford, USA
Dec 11-12, 2009	Latest Advances in Drug Discovery Modelling & Informatics	Hyderabad

The Glossary of SystemsX.ch

Research, Technology and Development Project (RTD project): SystemsX.ch's flagship project, multi-year duration, budgets of 1.4 to 6 mio. CHF per year.

Interdisciplinary Pilot Project (IPP): Research involving risks. One-year duration. About 120'000 per year.

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

IMPRINT

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