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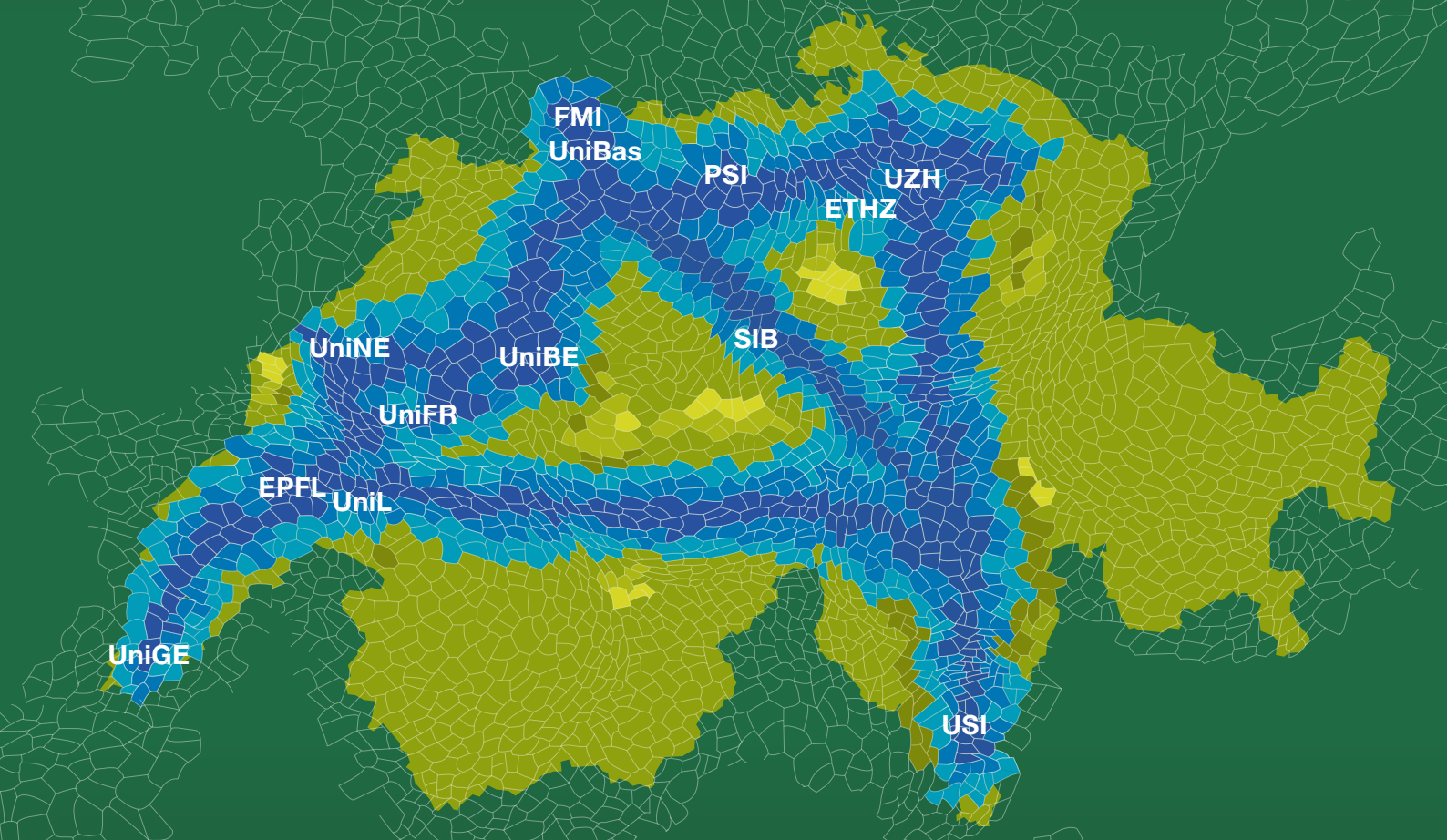

Systems biology in Switzerland

13 partners — one promising model

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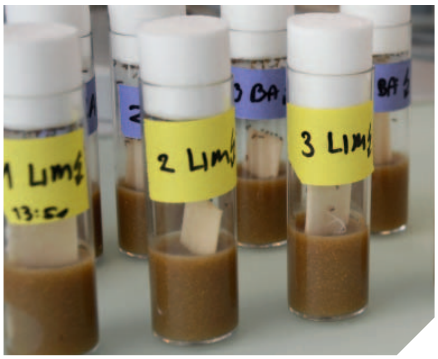

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SystemsX.ch
The Swiss Initiative in Systems Biology

Imprint

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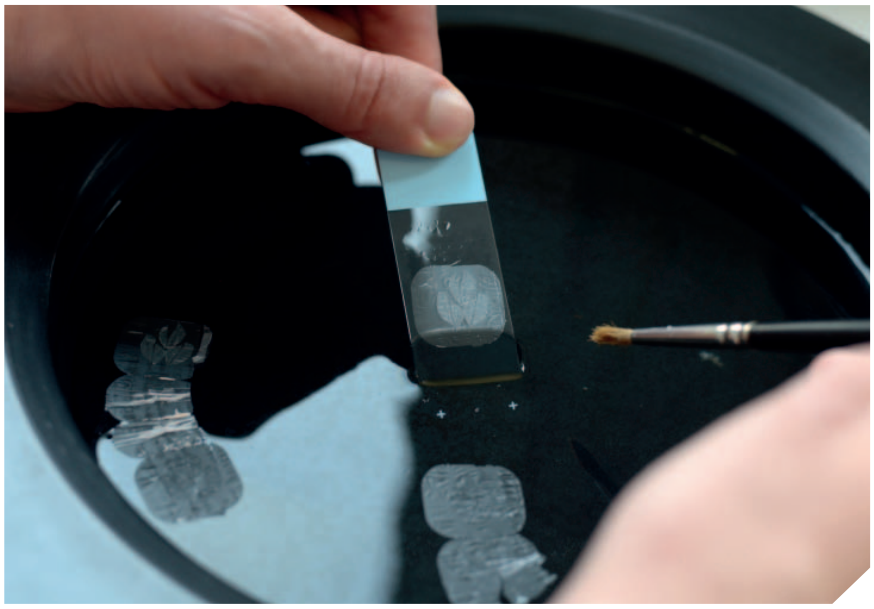
"SystemsX.ch will leave a lasting footprint in the research landscape."



SystemsX.ch is a national initiative conceived to connect biologists with other natural scientists, engineers, physicians and mathematicians on an interinstitutional level and across disciplines. The idea was put forward by the State Secretariat, led by Charles Kleiber, and implemented in the 2008–2011 Education, Research and Innovation (ERI) Message. Projects have since been suggested bottom-up by scientists, evaluated by the Swiss National Science Foundation and carried out jointly by Swiss universities and the Federal Institutes of Technology in Zurich and Lausanne.

The modeling of biological processes using a quantitative approach plays an important part in systems biology. In order to permanently anchor this novel mode of thought in the life sciences, one of the main focuses is the training of PhD students and the establishment of new professorships.

Taking stock after over six years, one can say that the outcome is very positive. SystemsX.ch has been extended until the end of 2016. During the initial phase of the initiative, systems biology approaches were successfully applied to basic research. The last phase, on the other hand, focuses on involving the medical field and transferring this new way of thinking to hospitals.

To date, the initiative has attracted numerous excellent scientists on all levels and has brought together investigators working in very diverse disciplines. A multitude of outstanding scientific publications have been released. And various collaborations have led to the development of new technologies, as well as to spin-offs and to various projects with industrial partners. The networking between scientists working in different fields in Swiss universities has also increased. Additionally, all Swiss universities have created new systems biology professorships, whereby the initiative will leave behind a lasting footprint.

With this in mind, SystemsX.ch can truly serve as a model for future scientific support programs.

Ralph Eichler
Chairman of the SystemsX.ch
Board of Directors (BoD)

Didier Trono (left) and Ruedi Aebersold have been involved in the successful establishment of systems biology in Switzerland since the very beginning of the initiative.

A conversation with Ruedi Aebersold and Didier Trono

"We again have the opportunity to create something momentous"

SystemsX.ch is drawing to a close. As of 2016, the initiative will no longer support new projects in the area of systems biology. Will this also spell the end of this new research approach? Ruedi Aebersold and Didier Trono, two longtime and active SystemsX.ch participants, take stock and venture a glimpse into a time after SystemsX.ch.

Would we have research in the area of systems biology in Switzerland if it were not for SystemsX.ch?

Aebersold: Almost certainly yes. After all, SystemsX.ch did not invent interdisciplinary and interinstitutional collaborations. As early as the end of the 1990s, scientists worldwide started looking for new ways to study biological processes in a systemic context, considering these to be complex molecular systems. They termed this approach systems biology. And it became obvious that new frameworks in the area of life sciences were necessary in order to be able to answer the truly important questions. By launching this research initiative, we were able to react to these needs early on.

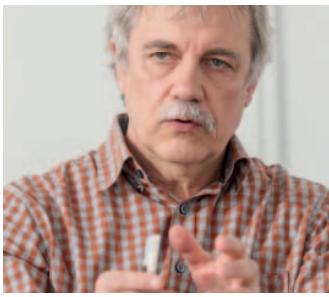
Trono: In order to be able to boost the pace at which this new mode of thinking could be implemented, a special impulse was needed. SystemsX.ch provided the funds to catalyze this transition by selectively promoting interdisciplinary and integrative approaches to biological projects. Therefore, the initiative has not fundamentally changed the orientation of Swiss research but has accelerated an extremely timely development.

Can other changes within this structural shift be attributed to SystemsX.ch?

Trono: Overall, one can say that SystemsX.ch helped bring together specialists working in very diverse fields who, under other circumstances, would hardly have cooperated as successfully. In this way, it was possible to shore up and anchor the reorientation towards systems biology all across the country.

Aebersold: Another accomplishment of this scientific initiative is definitely the implementation of comprehensive IT support. It was rapidly clear that the enormous amount of data generated by data-driven systems biology experiments called for interinstitutional IT infrastructure. Data management and programming would have



Matthias Scholer Heiner H. Schmitt Jr.

overburdened the individual laboratories. At the very beginning of the initiative, SystemsX.ch therefore initiated the SyBIT support project. SyBIT assists SystemsX.ch partners regarding many aspects of large data management and processing.

Has the research initiative thereby already reached its goal?
Aebersold: Implementing systems biology in the Swiss research community is a process. There is no actual finish line. It can be said that a considerable number of scientists in Switzerland have learned to tackle complex problems in the area of life sciences in interdisciplinary teams.

"SystemsX.ch has catalyzed a trend that can no longer be stopped."

It was never SystemsX.ch's goal to turn all bioscientists into systems biologists. After all, we are not a political movement trying to convert as many people as possible.

The initiative might not be a political movement, but an attractive source of funds ...
Aebersold: To some scientists, interdisciplinarity is a forward-looking way of performing research. Others do not appreciate this setup; and that is a good thing. There are sufficient other funding possibilities for different types of projects, be it the Swiss National Science Foundation (SNSF) or EU calls for proposals, for example.

What will remain of SystemsX.ch after the initiative runs out in a few years?
Trono: SystemsX.ch has catalyzed a trend that can no longer be stopped. Nowadays, a systemic approach is a must in most areas of research. Similarly to molecular biology forty years ago, systems biology is becoming a constituent of life sciences.

Aebersold: I too would be very surprised if, in 2016, scientists were to say "it was nice having funds for interdisciplinary projects, but now, let's go back to the traditional methods". I am convinced that most scientists will incorporate their experiences into future projects.

What consequences does the running out of the initiative have for the involved institutions?
Aebersold: This will hardly have an impact on the individual institutions, as all partners involved knew from the very beginning that SystemsX.ch will not endlessly support this area of research. They were not forced to build new laboratories that now need to be maintained either. In the future, each partner institution will have to decide how much importance to attach to systems biology, and how to finance such projects.

Trono: It was SystemsX.ch's mission to pass the impulse on to the partner institutions, to initiate changes and to train a first generation of systems biologists. This has already happened to a good extent, rendering additional earmarked funds and thus also SystemsX.ch unnecessary in the foreseeable future.

Is there room for improvement within the remaining time allotted to the initiative?
Trono: It is pointless to say that we should improve this or that at the end of such a long process. It is simply too late to make any fundamental changes. It is more constructive to find out which expectations were not fulfilled and for what reasons.

Which expectations have not been fulfilled?
Aebersold: The interactions with the private sector have been the least successful part of the initiative. In this area, substantial goals

"The main goal, i.e. to involve industry in sizeable and sustainable collaborations, was not reached."

had been set and promises made, but many were not fulfilled. It was indeed possible to promote certain collaborations between academia and the private sector, but the main goal, i.e. to involve industry in sizeable and sustainable collaborations, was not reached.

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Why was this not possible?

Aebersold: Industry requires time to integrate the systemic approach into their research too, but these companies work for profit and on short timelines that make fundamental transitions challenging. We are however observing that industry is increasingly looking for scientists who have been trained in systems approaches.

Trono: Industry simply has other perspectives and calculates in different time spans. For companies, the emphasis is on the return on investment, and it is not important whether it takes place in Shanghai, Singapore or Switzerland. Swiss industry does not feel an obligation to be committed to the Swiss research community. To attract partnerships with industry, Swiss science simply needs to be the best overall.

In its second phase, SystemsX.ch is supporting more projects relevant to medicine. Why now and not earlier?

Trono: At the start of the initiative, SystemsX.ch manifested little interest in genomics, even though this field was already prepared for medically-relevant systems-oriented investigations at that time.

Additionally, systems biology was defined too narrowly, with far too much emphasis on modeling and mathematical models. In the medical field however, many aspects cannot yet be modeled, which is why project proposals in this field hardly stood a chance when it came to funding.

"Switzerland can become a center of excellence for personalized health."

Aebersold: The project reviewers also went through a steep learning curve in this respect. One of the strengths of SystemsX.ch is that all funds must be submitted to peer review. The SNSF has constituted its own expert panel in order to guarantee the quality of the proposals. Many projects ultimately failed to convince this authority because they lacked the integration of mathematical models. However, it was possible to convince the assessors that modeling is not always feasible in the medical field. That is why the specifications were relaxed. Projects relevant to medicine increased as a consequence of this policy.

Can SystemsX.ch serve as a model for future country-wide research initiatives?

Aebersold: Probably not so much on the organizational level. But the basic idea behind the initiative, which is to recognize trends in an early stage, to assess them and to implement a focused nationwide program as needed, is very well adapted to a small country such as Switzerland. This is why we need to define a standardized mode of action we can resort to in similar situations.

Trono: Such a mechanism would be quite useful at the present time. We are both members of a task force entrusted with the analysis of the developments in the area of personalized health and the weighing of various scenarios regarding the future of Swiss research in this field. Much needs to be decided ad hoc.

Can you tell us more about this task force?

Aebersold: The concept of using systemic approaches in medical research as well is fascinating. The course of a disease in itself is extremely complex. Findings in the genetics field show that a disease is additionally strongly influenced by the patient's hereditary disposition. It is therefore feasible to optimize the therapy by developing individual treatment approaches, thus leading to personalized medicine, the establishment of which calls for a nationwide program and common objectives. This enterprise is much more complex than SystemsX.ch. It is not only about changing the way people work in the laboratory. We must succeed in radically changing the intellectual approach to medicine and medical research.

Trono: Switzerland can become a center of excellence for personalized health, not only from a research standpoint but also in terms of health maintenance and management. Our country indeed offers perfect conditions for this development, such as compulsory health insurance, high-quality health care, superior research, acceptance of the application of new technologies, et cetera. If we manage to bring together the various actors and to define common objectives, we can ambition to be amongst the world's very best in this area. We again have the opportunity to create something momentous.




SystemsX.ch's influence on partner institutions

A network that benefits all involved

More than 1000 scientists working in different institutions are involved in SystemsX.ch projects. Three of them explain how the initiative has influenced the research community in their region.

Prof. Susan Gasser, FMI, Basel

The initiative has stimulated more interdisciplinary work, and has had a major impact on our hiring practices, as we had to fill the gap between quantitative, computational and basic biomedical research. Apart from promoting collaborations and expanding the cooperation on infrastructure, being part of SystemsX.ch also made us take a closer look at how we could improve our research.

The five Basel-based Research, Technology and Development (RTD) Projects that were funded in 2009 had a big impact. For example, in the RTD Project Cell Plasticity, led by the Friedrich Miescher Institute for Biomedical Research (FMI), half of the primary investigators came from the University of Basel, while the other half came from the FMI. This project allowed us to establish next-generation sequencing, with the platform being hosted by the D-BSSE. Other benefits included the data analysis pipelines, many joint papers, a great set of postdocs, and a progress seminar that continues to serve as a sounding board for stem cell and epigenetic research.

So this truly interinstitutional effort has strengthened Basel as a research center. In total, roughly 30 Basel scientists were involved in SystemsX.ch networks, in addition to several postdocs and IPhD students.

With SystemsX.ch coming to an end in 2018, we will need to start looking for innovations that advance biomedical research. After all, science is all about new challenges, and we definitely want to be part of any upcoming effort to strengthen research in Switzerland.

Prof. Walter Senn, University of Bern

The number of projects supported by SystemsX.ch at the University of Bern is not particularly large. Nonetheless, this initiative has made a difference within our institution. In the area of plant growth, one Research, Technology and Development Project and a corresponding follow-up project have been approved. Additionally, an assistant professorship in computational biology has been created thanks to SystemsX.ch's support. Furthermore, the University of Bern has been, and still is, part of two RTD Projects in the area of systemic neurosciences, and has recently become involved in a large project investigating the tropical disease malaria.

On the whole, the initiative has led to many new connections with other universities. Furthermore, SystemsX.ch's Interdisciplinary PhD Projects stimulate collaborations within our own university. In our opinion, it would be reasonable to give projects in the medical field stronger support in the future, and we hope to be able to contribute to these exciting new projects.

Prof. Howard Riezman, University of Geneva

The overarching goal of SystemsX.ch was to establish a foundation for the discipline of Systems Biology in Switzerland, which is capable of comprehensively understanding living systems. To do this requires the generation of quantitative data on biological systems as well as the modeling of this data. This is done using physics and mathematics as well as sophisticated equipment, which allows for high throughput data collection.

SystemsX.ch has clearly been successful in stimulating quantitative biology in Geneva. On a personal note, I have participated in and witnessed the installation of facilities to quantitatively analyze lipids in cells and screens for studying lipid localization. These studies were done using quantitative high throughput imaging methods coupled with genetic techniques. These data-driven approaches have been productive and have uncovered new aspects of biology that were not readily predicted by previous data.

SystemsX.ch has also been successful in stimulating interactions, both between disciplines and between institutions in Switzerland. Clearly, our scientific culture has been widened, and we are ready for some of the challenges of the future. However, I think that the Lemanic region still needs structural changes to develop a more coherent systems biology program, which promotes interdisciplinary, quantitative biology to train young scientists in this growing discipline.

Simon Sprecher in his laboratory in the Department of Biology at the University of Fribourg.

The SynaptiX RTD Project

Looking into the mechanisms of forgetting

Within the scope of the SynaptiX RTD Project, scientists are investigating the process of forgetting on the neuronal, genetic and molecular levels. Experiments using fruit flies are to elucidate the function of individual neurons and substances. In the future, the results may form the basis for the development of drugs for ailments such as Alzheimer's disease.

Strawberries or bananas? The fruit fly has no trouble deciding which odor it prefers. Having learned that following the smell of bananas results in a light electric shock, the fly settles for strawberries.

This olfactory conditioning experiment is part of a first series of experiments performed within the scope of the SynaptiX RTD Project, headed by Simon Sprecher. This biology professor, working at the University of Fribourg, as well as four additional scientists and their teams are investigating the process of forgetting on the genetic, molecular and neuronal levels since May 2013.

Forgetting so as to learn something new

Simon Sprecher describes the initial situation: "We know where and how information is inscribed in the brain. However, we do not know how this information is stored or how it degrades." In order to be able to investigate the actual research subject, forgetting, the team is first looking into learning processes in fruit flies. At first glance, this might seem paradoxical. But learning and forgetting are tightly linked. "The capacity of the brain is limited. Forgetting helps make room for newly acquired knowledge", explains Sprecher. The areas of the brain responsible for learning processes are therefore most probably also involved in the process of forgetting.

Fruit flies as model organisms

The current conditioning experiments serve the purpose of understanding changes in the olfactory memory of animals. The fruit fly *(Drosophila melanogaster)* is well suited for these experiments for two reasons. On the one hand, this insect's brain has been extensively studied. On the other hand, its brain resembles that of humans in many respects. "On the molecular level, the ageing process in fruit flies, for instance, is the same as in humans", clarifies Sprecher. "An older fly learns more slowly than a younger one."

In order to be able to learn as much as possible about memory processes, Sprecher and his team vary the experiments. For example, fruit flies are trained to avoid the odor of bananas in a first step, then conditioned to differentiate between the smell of lemons and marzipan. The aim of this experimental setup is to determine the extent to which new knowledge erases previous experiences: will fruit flies still remember that they should avoid the banana odor? Or have they already forgotten what they learned earlier?

A microscope reveals modifications in the brain

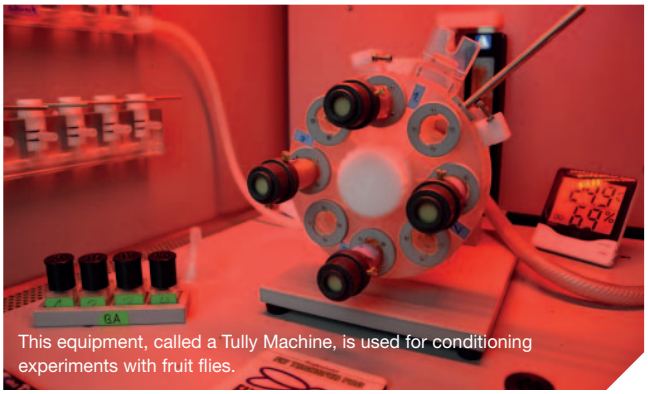
The scientists are most interested in the events taking place in the brain at the molecular level, rather than the behavior of the flies. In order to visualize these processes, Frank Scheffold, a physics professor at the University of Fribourg, has refined a high-resolution light microscope especially for this project. Now, it is even possible to observe processes taking place in the synapses, the links between neurons in the fly's brain.

The experiments using odorants cause alterations in Drosophila's so-called mushroom bodies, important in olfactory memory. Each fruit fly has two such mushroom bodies. They contain 2000 neurons and approximately 13,600 genes each. Only a fraction of these genes are involved in the learning process.

In order to determine which genes are important for learning, the scientists extract various neurons and perform further analysis using transcriptomics. This technique is used to measure which genes are switched on or off during a given process. A database of the presumably essential genes involved in the processes of learning and forgetting is thus generated during the course of the various experiments.

Tests using genetically modified fruit flies

As the project continues, the scientists will manipulate the genome of the fruit fly by switching certain genes on or off. "By modifying the genes, we want to find out where and how learning and forgetting occurs, and to identify the changes that take place when information is actively substituted", explains Sprecher. These experiments are planned for the next phases of the project which runs until 2017.



This equipment, called a Tully Machine, is used for conditioning experiments with fruit flies.

Providing the scientists can unravel the process of forgetting and can determine which substances in the brain are involved, this knowledge could form the basis for medical research and the development of drugs for ailments such as Alzheimer's disease, an increasingly relevant topic in an ageing society.

SynaptiX at a glance

Principal investigator: Prof. Simon Sprecher

Research groups:

- Prof. Simon Sprecher, Department of Biology, University of Fribourg – Quantitative behavioral experiments
- Prof. Alex Keene, Department of Biology, University of Nevada, Reno – Quantitative behavioral experiments
- Prof. Walter Senn, Computational Neuroscience, Department of Physiology, University of Bern – Theory of remembering and forgetting
- Dr. Rémy Bruggmann, Bioinformatics and Computational Biology, University of Bern – Transcriptomics
- Prof. Frank Scheffold, Department of Physics, University of Fribourg – Advancement of high resolution STORM microscopy

Total budget (2013–2017): CHF 4.065 million, including CHF 1.975 million from SystemsX.ch

Project type: Research, Technology and Development (RTD) Project

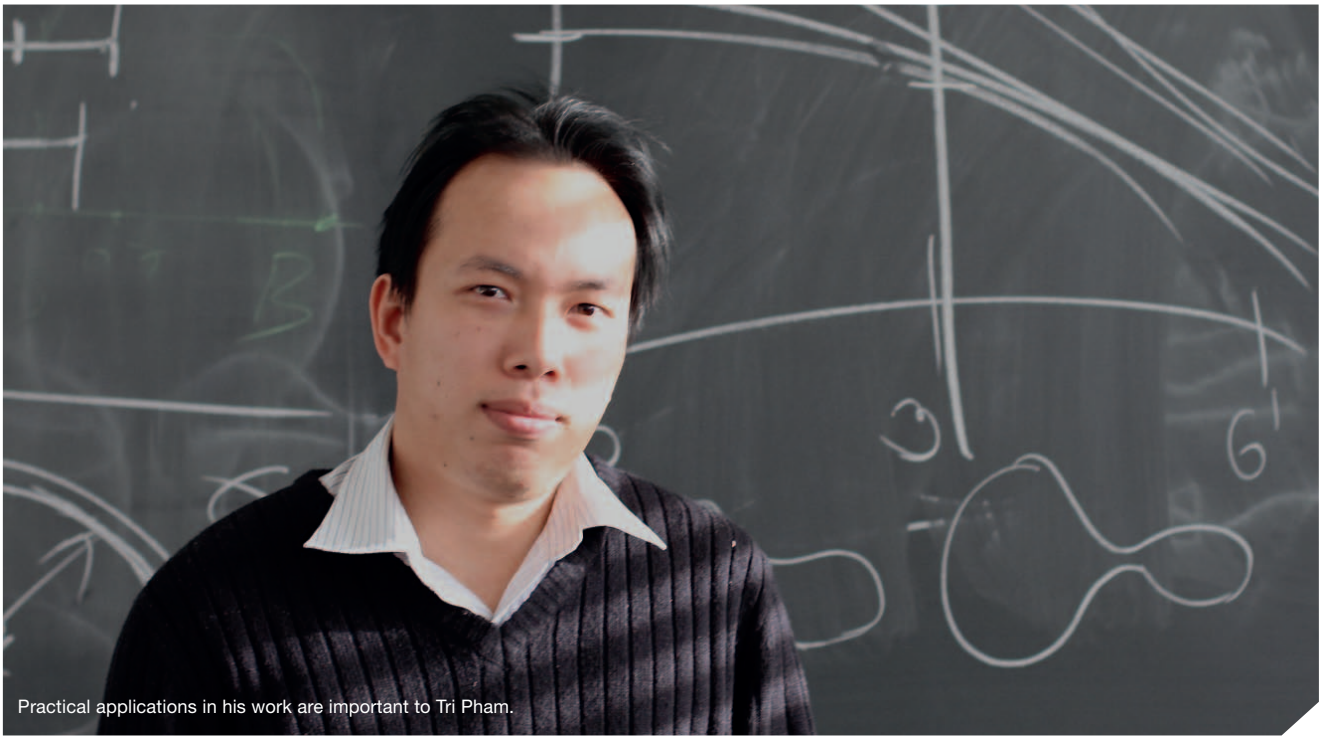
SynaptiX
Systems Biology of Forgetting

Matthias Scholer

Transition Postdoc Fellowship

Extreme interdisciplinarity

SystemsX.ch Transition Postdoc Fellowships aim to promote knowledge exchange between various disciplines. Within the framework of this project type, a mathematician specialized in aeronautics and cell biologists working at the University of Basel initiated a collaboration. The achievements of this exceptional team will benefit many researchers worldwide.



Practical applications in his work are important to Tri Pham.

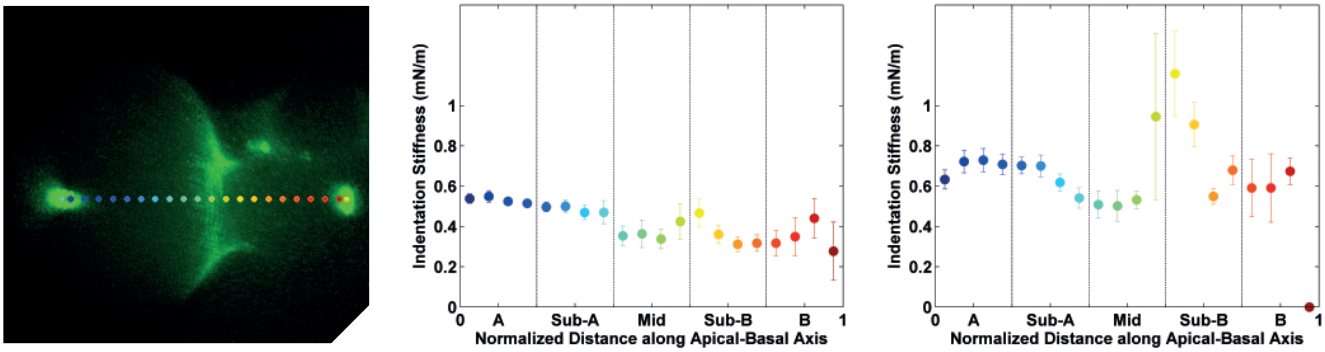
Cells and biological experiments were not Tri Thanh Pham's cup of tea when he took up his job at the Biozentrum in Basel in 2012. However, this native of Vietnam was well versed in airplanes, aerodynamics and satellite navigation. But why would an aeronautical and aerospace engineer want to work with cells? "Before I came to Basel, my work was extremely theoretical. I increasingly missed the link to practical applications", remembers Tri Pham. After his aeronautical space engineering studies in Australia, Tri did his PhD and further research in the field of chemical sciences. "When Professor Cabernard's laboratory in Basel was looking for a mathematician, I seized the opportunity to switch to a different field. The fact that I knew nothing about molecular biology was my biggest handicap", says the scientist.

However, he was determined to catch up in this area and for this purpose he was even willing to move down a rung on the career ladder: "If necessary, I would have agreed to work as a PhD student again, in order to familiarize myself with the new subject." However, Professor Clemens Cabernard, head of his current research group, conceived a better way to put to good use Tri Pham's broad mathematical knowledge in Basel. "At that time, the SystemsX.ch call for proposals for Transition Postdoc Fellowships was open. The general conditions were in accordance with our needs and we were thus able to welcome Tri as a postdoc into our group", remembers Cabernard.

Problems despite the use of standard methods

Two years have gone by since then. During this time, Tri Pham studied how cortical tension, cell membrane elasticity and inner pressure behave during cell division in so-called neuroblasts. These cells are embryonic precursors of various neural cells. Neuroblasts, like stem cells, divide to multiply or to produce differentiated cells. In this context, experts speak of asymmetric cell division because the cells divide in a physically asymmetric manner: "From the larger cell half arises a genetically identical replicate, whereas the smaller half leads to a differentiated sibling, which can further develop into a neuron, for instance", explains the scientific investigator.

The scientists have chosen the fruit fly *(Drosophila melanogaster)* as the test organism. This decision is based on the fact that "fruit fly cells are used worldwide and frequently in basic research". The scientists in Basel can therefore fall back on standardized investigation methods and they have the resources to manipulate the insect's genes. But ironically, Tri Pham was confronted with sizeable problems regarding the data collected using one of these standard techniques.



In the fluorescence microscopy image (left), the cleavage furrow is clearly visible. The uncorrected surface measurement data did not permit a similarly accentuated representation of the cell membrane indentation (middle). This was only possible after the coordinates had been precisely assigned (right). Illustration: Tri Thanh Pham, University of Basel

In search of the error

Tri Pham: "I first used dividing cells to measure various parameters involved in the characterization of the cell membrane and cell pressure. I then tried to correlate these results with the fluorescence microscopy image information." Fluorescence microscopy involves the yellow-green fluorescent staining of a cell structure defined by the investigator. The behavior of this structure is then monitored over a given amount of time.

In this way, Tri Pham tracked the distribution of myosin in the neuroblasts. This protein, also known as a motor protein, enables movements and deformations in a cell by temporarily binding to the intracellular network. During cell division, such a deformation leads to the so-called cleavage furrow.

The scientist describes the problem: "As expected, the images showed increased fluorescence along the cell division line, suggesting a high myosin concentration in this area. However, the surface measurement data did not permit a similarly accentuated reproduction of the cleavage furrow", explains the scientist (see illustration).

Where was the error? In a first step, Tri Pham looked for an answer in the statistical processing of his data, but was not successful.

Data washout due to imprecise localization

Tri Pham's aeronautical knowledge proved helpful during his further search for errors: "Using mathematical methods, I was able to show that the spatial mapping of a specific point measured on the cell surface is imprecise. This leads to the observed washout of the measurement data." A similar imprecise localization is observed in everyday life when a GPS satellite fails and a precise determination of one's own position using a navigation device is no longer possible.

Well acquainted with the mathematical derivations used to calculate the trajectory of flying objects, Tri Pham developed a complex program geared towards automatically correcting faulty deviations in the localization of the measured point. "Using this program, I revised my values and these immediately revealed a clearly delimited modification of cell membrane properties in the area of the cleavage furrow. The measured data now correlated with the fluorescence microscopy images", says the pleased scientist.

This success lays the groundwork for the exceedingly precise measurement of mechanical properties during asymmetric cell division. This has never been done before, and in conjunction with future developments could potentially resolve the question of how physical asymmetry is established during cell division.

Project leader Clemens Cabernard is therefore convinced that "completely new opportunities arise every so often, despite, or maybe because of this collaboration at the extreme end of interdisciplinarity".

The project at a glance

Project title: Cortical tension and stiffness during asymmetric cell division

Applicant: Dr. Tri Thanh Pham, University of Basel

Host research group: Prof. Clemens Cabernard, Biozentrum, University of Basel

Project duration: 2012–2014

Project type: Transition Postdoc Fellowship – young PhD graduates formulate their own interdisciplinary project application and switch to a complementary discipline that is new to them.

The development of the human brain

Tri Pham's work is part of a large-scale project in which Professor Clemens Cabernard and his team are studying various aspects of asymmetric cell division using neural stem cells. The knowledge gained from these studies should offer new insights into the development of the human brain. Cortical tension measurements are performed in collaboration with Professor Daniel Mueller's laboratory at the D-BSSE in Basel.

More information is available at:
www.biozentrum.unibas.ch > Research > Groups & Platforms > Clemens Cabernard

Christa Smith Frederike Asaël

The focus of the 10th call for proposals is on medical projects and collaborations with industry.

10th Call for proposals

Wanted: medical and clinical projects

The last SystemsX.ch call for large research and development projects is currently in progress. The focus is on projects specifically applying systems approaches to answer medically and clinically relevant questions.

Within the scope of the 10th call for proposals, SystemsX.ch has launched a new project category: Medical Research and Development Projects, so-called MRD Projects, are aimed at directing the results of systems biology research toward medical applications. This is the logical consequence of SystemsX.ch's encouragement strategy, explains the managing director, Daniel Vonder Mühll: "During the first half of the initiative, we succeeded in establishing systems approaches in basic research. Now is the time to find specific applications for the acquired knowledge."

MRD Projects can for instance focus on the in-depth analysis of the course of a disease or on the development of new technologies to improve the treatment or diagnosis of a disease. "In the long run, systems biology can only be of interest to industry and of relevance to society if such applications in the medical field and in clinical research are available", underlines Vonder Mühll.

Additionally, all MRD Projects must feature quantitative elements and include research groups working in different disciplines and institutions. Ideally, hospitals and the private sector are also involved in the projects.

Collaboration with industry

In a second category within the 10th call for proposals, SystemsX.ch will support academia-industry collaborations. Research proposals for Transfer Projects must include at least one partner each working in the academic and the private sectors. Proposals involving a hospital as well as systems approaches applied to medical or clinical problems will be privileged. Transfer Projects last at least 18 months. A successful project can however be extended to a maximum of 36 months, i.e. until the phasing-out period of the initiative.

Schedule for the 10th call for proposals

Scientists can submit project proposals for MRD as well as Transfer Projects until July 31. The project leaders of the most promising MRD proposals will subsequently be invited to present their projects to an expert panel of the Swiss National Science Foundation. A decision regarding the projects to be supported by SystemsX.ch until the end of the initiative in 2018 will be taken in November 2014. A total of 18.5 million Swiss francs are available for these MRD and Transfer Projects.

11th call for proposals in December

SystemsX.ch will launch its very last call for proposals in December 2014. The 11th and last call is intended to support projects performed by PhD students and postdocs, as well as collaborations with industrial partners.

Project categories in the 10th call for proposals

MRD Project: Medical Research and Development Project lasting three years.
Upper budget limit per project: CHF 2.5 million.

Transfer Project: Research collaboration between academia and the private sector. Applications for up to two years, with an optional one-year extension.
Upper budget limit per project: CHF 300,000.

The 10th SystemsX.ch call for proposals can be found at:
www.systemsx.ch > SystemsX.ch > Calls for Proposals

Heide Hess

ERASysAPP: Training and exchange

Systems biology training programs are just one click away

The European research network ERASysAPP has expanded the range of information and services available on its website. Besides an event calendar, the menu item “Training & Exchange” now also offers an overview of graduate teaching programs and educational portals pertaining to systems biology.

The extended range of services available on the ERASysAPP website helps budding systems biologists find appropriate teaching programs, classes and educational material. It includes an extensive list of European Masters and PhD programs. Some courses focus exclusively on systems biology, whereas in others, systems biology is just one subject in an interdisciplinary curriculum. Various filter options, including main focus, country and language priorities, simplify the search for an appropriate offer. Moreover, this website is not only for students looking for a training program. Organizations providing services can also apply to have their programs listed in the overview.

Additionally, a brief overview of various new educational portals is now available on the website. Young scientists can choose from a wide array of learning tools, from E-courses to video lectures. A special platform has also been developed to encourage the exchange of study materials between scientists. Presentations, publications or videos can now be made available to a broad audience and users can evaluate the quality of the contributions online.

More information is available at:
www.erasysapp.eu > Training & Exchange

Results of the first transnational call

The review of the 34 project proposals submitted within the first transnational ERASysAPP call for proposals is currently in progress. It will be decided this summer which projects will receive funds. The successful applicants will be able to commence their projects in the fall.

Daniel Vonder Mühll

Special Opportunities Fund

Flexible support for special projects

The Special Opportunities Fund has been set up for projects which do not fulfill the requirements of the conventional funding channels, yet contribute significantly to systems biology research in Switzerland. In addition to official calls for proposals, SystemsX.ch can offer certain projects flexible support thanks to this special fund. Novel technologies, urgently required for an existing project, can for instance be financed in this way.

All scientists working in a SystemsX.ch partner institution can apply for such support. Private companies involved in a project are however excluded from this offer. Funding can be applied for at all times. Requests are deliberately subject to just a few formal conditions, thereby allowing for varied project proposals.

In a streamlined but nonetheless demanding process, the SystemsX.ch Scientific Executive Board evaluates all proposals by peer-review. Relevance of the project for systems biology research in Switzerland is decisive for funding. Other important criteria include scientific and technical quality as well as balanced financing of the project by the involved partner institution, by SystemsX.ch and, where applicable, by third parties.

Further information regarding the Special Opportunities Fund and how to apply is available at: **www.systemsx.ch > Projects > Special Opportunities Fund**

Gabriella Mosca is developing a model of tissue growth in plant embryos.

Interdisciplinary PhD Project (IPhD)

The code of life

Plants make up approximately 99% of the Earth's biomass. They provide us with food, forage and fuel. It is therefore of great relevance that we understand plant growth and the impact of the environment on these processes. A physicist at the University of Bern is making a small but important contribution to this endeavor.

The walk to Gabriella Mosca's laboratory leads us through a wide variety of worlds within a very short time: through various greenhouses filled with tropical plants and butterflies, past fragrant rock gardens and along a number of laboratories with a view of the botanical gardens. A creaky wooden staircase eventually leads us to the attic of the Institute of Plant Sciences at the University of Bern, to Gabriella Mosca's work space. And here, the young scientist immediately takes us on yet another journey.

A virtual image of plant reality

Mosca's work environment involves mathematical codes used to produce a virtual image of plant reality on a screen. "This is the illustration of a part of the plant embryo. The behavior of these cells during the first hours and days of a plant's life takes center stage in my interdisciplinary PhD thesis", explains Mosca while rotating an oblong structure reminiscent of the tip of a pen on the screen (see illustration, page 15). The small multicolored boxes represent single cells in the so-called hypocotyl, the short section located between the root system and the cotyledons in a plant embryo. "These cells expand once they have absorbed water. This leads to growth in absence of cell division", explains the scientist. The particularity of this process is that the cells chiefly expand in a given direction.

This property can also be observed in other parts of the plant: "At the onset of germination, the roots always grow downwards, whereas the shoot concurrently moves upwards." This anisotropic growth involves extremely complex processes, with many questions at the molecular and mechanical levels remaining unanswered.

After the experiment is before the experiment

In order to understand plant growth on all levels, the scientists at the University of Bern are striving to bring together individual models to form a superordinate model integrating mechanics and genetics. Developing one part of this model is the goal of Gabriella Mosca's IPhD Project. "By the end of this year, I hope to have developed a mechanical model for a physically correct computer simulation of tissue growth in the hypocotyl." For this purpose, the scientist first performed experiments and measurements on the test material.

But when Mosca tried to process the collected data and to assemble it into a model using commercially available software, instabilities and errors cropped up.

Luckily, being a physicist, Gabriella Mosca had the skills to write her own computer program, an exceedingly complex and challenging task: “The growth of the hypocotyl is determined by various factors: pressure, mechanical properties of the cell wall and geometry of the cell. However, we do not yet know to what extent and at which point in time each factor influences growth.” This is a question that can be answered by comparing the developed model with data collected during the appropriate experiments.

She is passionate about mathematics

Mosca’s IPhD Project runs out at the end of the year, a good time to look back on the past years as a member of the SystemsX.ch community and on this interdisciplinary collaboration. “The experiences I gained performing the experiments at the beginning of my project will surely be of use in the future. The laboratory work taught me what needs to be taken into account when planning the experimental part of a project, but also what can go wrong in the process”, tells us the PhD student. Gabriella Mosca, being a theoretical physicist, has so far usually concentrated on theoretical approximations and analyses in her research work. “But I also realized that working concurrently in experimental and mathematical fields is too much for one person. I am passionate about mathematics and will focus my attention on this part of the work”, says Mosca.

But for now, Gabriella Mosca is looking forward to successfully completing her interdisciplinary PhD thesis and to being able to publish her results in a renowned journal. Thanks to this subproject, yet another piece of the puzzle which will allow systems biologists to simulate plant growth on the computer in the foreseeable future has been found.

The project at a glance

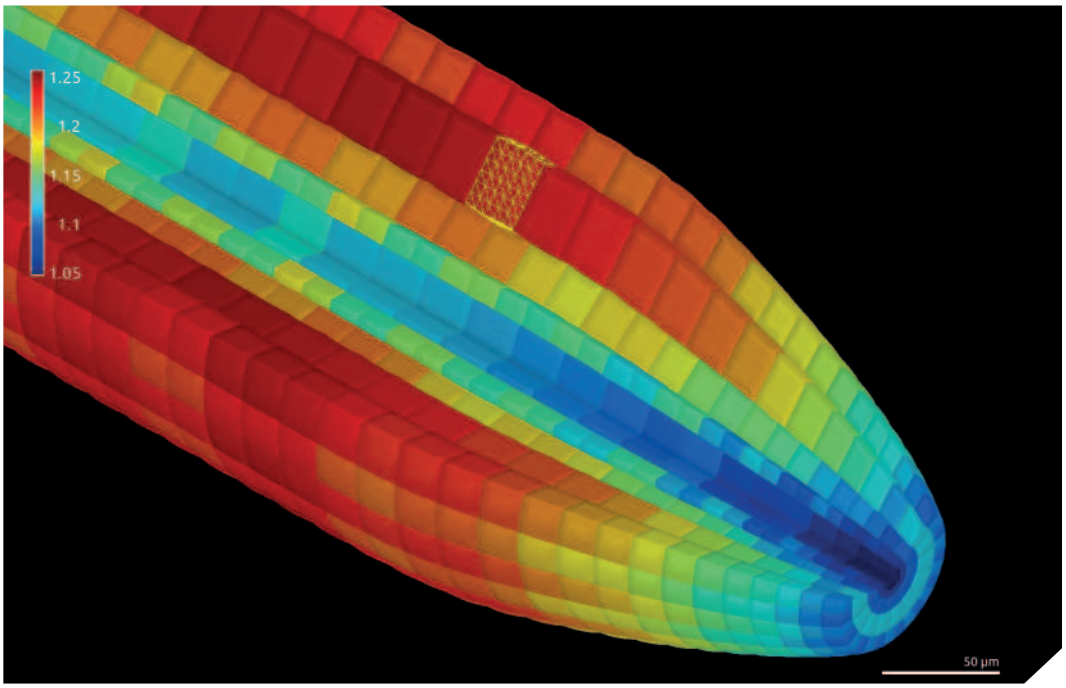
Project title: An Integrated Biophysical Model of Phototropism in the Arabidopsis Hypocotyl

PhD student: Gabriella Mosca, University of Bern

Advisors: Prof. Richard Smith, University of Bern;
Prof. Christian Fankhauser, University of Lausanne

Project duration: 2010–2014

Project type: Interdisciplinary PhD Project



The area of the hypocotyl was drawn schematically on the computer. The aim is now to simulate the growth of these cells as accurately as possible, using state-of-the-art computational methods for solid body simulations.
Illustration: Gabriella Mosca, University of Bern

Inken Heeb

Interdisciplinary, interinstitutional and international

“SystemsX.ch is a typical ‘child’ of its time”

Within the scope of his PhD studies at the ETH Zurich Institute for the History of Technology, Alban Frei has, for the past two years, been investigating systems biology research in Switzerland. SystemsX.ch is the main focus of his thesis. In his view, the research initiative illustrates the interdisciplinary and interinstitutional networking that takes place in a globalized information society.

Historical research today: Alban Frei at his computer.

Bookshelves are not historian Alban Frei’s idea of the perfect setting to have his picture taken. For him historical research is not about rummaging through old books. In fact, his work requires a computer and the internet, thus connecting him to the globally available knowledge.

The interconnected information society

For the past two years, Alban Frei has been studying research networks, with an emphasis on the history of the emergence of the systems biology initiative SystemsX.ch. An important feature of the initiative is its interdisciplinary and interinstitutional connections based on modern communication technologies. “It’s a research network on a real and on a non-material level”, says Frei, a PhD student in history of technology. “SystemsX.ch makes use of the fiber optic cables that connect the institutes from Bern to Lausanne and Zurich, thus bringing the researchers together on a scientific level.”

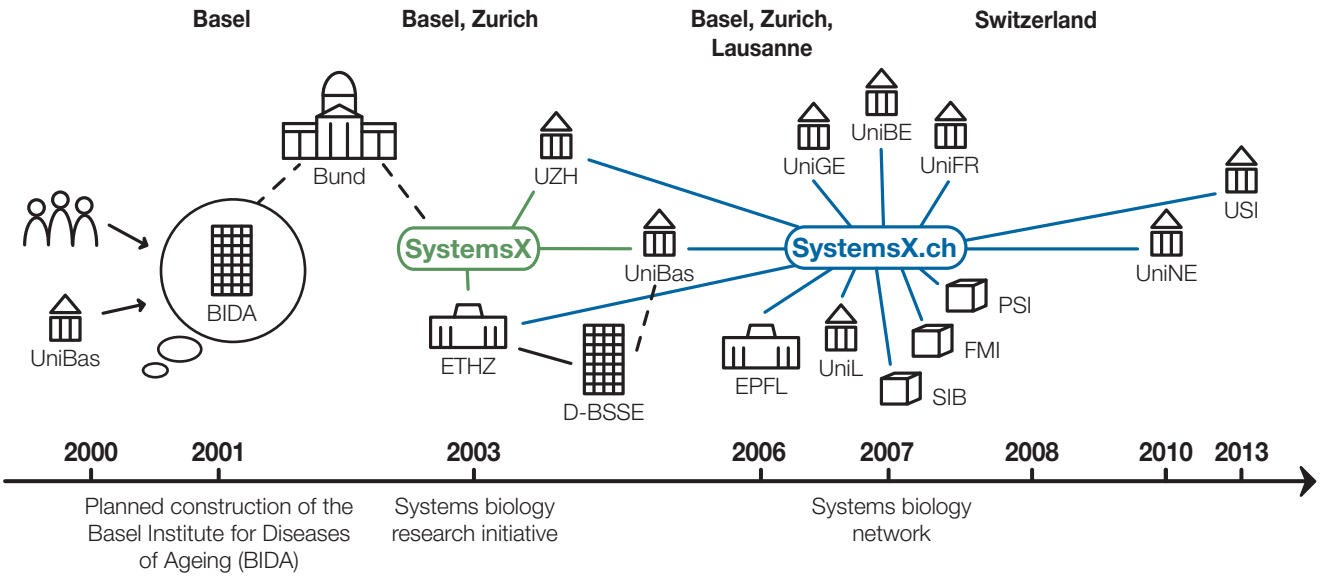
But there is more: the network also draws on computer sciences for research purposes, as systems biology is not only characterized by interdisciplinary collaboration but also by the collecting and analysis of large amounts of data in order to build models of biological processes. It is therefore logical that SyBIT, an IT and bioinformatics project, was developed as part of the initiative. SyBIT provides central services related to the handling of the digital flood of information.

SystemsX.ch acts like a catalyst

Interdisciplinary, interinstitutional and international. “These are characteristic words used to describe scientific practice in the 21st century. They equally describe the present state of SystemsX.ch”, explains Alban Frei. This research initiative, shaped by networks, is a typical “child” of the internet age and an epitome of the thought pattern typical of a globalized information society. SystemsX.ch acts like a catalyst. The initiative promotes networks between scientists while making them visible to others.

Economic and scientific changes

The initiative had to cover a considerable distance before reaching its present size. “The onset on the research policy and social levels took place in the late 1990s”, explains Frei. “Globalization pressure was increasing and was accompanied, in Switzerland, by a phase of economic uncertainty and reorganization in the area of life sciences.” The closing, in 1995, of the molecular biology research institute belonging to the F. Hoffmann-La Roche chemical



company in Basel and the merger between the chemical companies CIBA Geigy AG and Sandoz to create Novartis in 1996 are amongst the most far-reaching events of the time. In the year 2000, Roche also shut down its second Swiss research institute, the world-famous Institute for Immunology (BII). And, in 2002, Novartis transferred part of its research activities from Basel to the United States. "All these events provided the fertile political grounds for the establishment of an initiative in the promising field of post-genomic life sciences. Initially, its nucleus was the region around Basel, influenced by the pharmaceutical and medical branches."

The research initiative's nucleus

Owing to these changes, the idea for the foundation of the Basel Institute for Diseases of Ageing (BIDA) arose in Basel after the turn of the century. This institute was to strengthen the city as an economic and scientific location, and to pursue research in the field of applied life sciences. Ultimately, the BIDA did not come into being, but promoted the consensus for a life science initiative supported by the Swiss Confederation.

Against this background and during a collaboration of the Universities of Basel and Zurich with the ETH Zurich, a systems biology initiative, named SystemsX, was founded in 2003. In a first expansion phase, the EPF Lausanne joined the initiative in 2006. The Universities of Bern, Geneva, Lausanne and Fribourg as well as the Friedrich Miescher Institute for Biomedical Research, the Paul Scherrer Institute and the SIB Swiss Institute of Bioinformatics followed only one year later. Within a few years the cooperation between three universities had developed into a countrywide research initiative. This is also illustrated in the "ch" addition to the name, resulting in SystemsX.ch.

Systems biology as a national research focus

"It was a complex negotiation process between various people and institutions", reports Frei. But by 2007, SystemsX.ch had taken shape and was allocated 100 million Swiss francs for systems biology research between 2008 and 2012. Since then, SystemsX.ch has managed to establish itself as a broad-based initiative, and has in the meantime been extended until the end of 2016 and been endowed with an additional 120 million francs to support the research and education of budding systems biologists. Today, SystemsX.ch unites well over 1000 scientists across the country in approximately 150 projects carried out in 13 partner institutions and represents these in the EU-wide ERASysAPP systems biology network.

"The present size of the initiative speaks well for the significance of SystemsX.ch", says Alban Frei. Over the past years, SystemsX.ch has created new structures in the research sector and promoted the establishment of the systemic approach in life sciences. The format of the call for research projects, requiring interdisciplinary and interinstitutional collaboration, has proven successful and has thus given rise to a complex systems biology research network.

A PhD thesis on SystemsX.ch

Project: "Visible Networks. Research Policy and Life Sciences in the 21st Century" PhD thesis on the subject of systems biology research in Switzerland, with a particular focus on SystemsX.ch.

PhD student: Alban Frei at the ETH Zurich Institute for the History of Technology

Duration: 2012–2016

The first year was funded jointly through the SystemsX.ch Special Opportunities Fund and by the ETH Zurich. The following three years are supported by the Swiss National Science Foundation (SNSF).

Piero Martinoli is convinced that SystemsX.ch will further raise USI's profile. Photo: USI

Inken Heeb

Piero Martinoli, President of the Università della Svizzera italiana

"SystemsX.ch offers many opportunities for national and international collaboration"

Università della Svizzera italiana (USI) became a SystemsX.ch partner only at the end of 2013. With its main academic focus on the four faculties Architecture, Economics, Communication and Informatics, USI wasn't an obvious candidate to join the network. Piero Martinoli, President of USI, explains how both SystemsX.ch and USI will benefit from this new partnership.

Apart from its Informatics department, USI hasn't been very active in fields related to systems biology. Will this change in the future?

We have actually invested substantially in fields relevant to SystemsX.ch in recent years. Since 2010, the internationally renowned Institute for Research in Biomedicine (IRB) in Bellinzona has been affiliated with USI. Its main focus is on immunology, structural biology and molecular modeling. In addition, USI has recently built up a strong competence in computational sciences. Our Institute of Computational Science (ICS) collaborates with the Swiss National Supercomputing Centre (CSCS), with biological modeling one of our top priorities.

Which role does the IRB play in this context?

The collaboration between IRB and ICS in molecular modeling is developing rapidly and will be further strengthened by the creation of an assistant professorship in computational biology. Another outcome of this collaboration is the new SystemsX.ch IPhD Project, led by Santiago Fernandez Gonzalez (IRB) and Rolf Krause (ICS-USI), which was approved in the 2013 call.

Why did USI join SystemsX.ch at this advanced stage of the initiative?

The main reason is the only very recent development of systems biology-related research domains at USI, with the rapid growth of the computational sciences and the affiliation with the IRB.

Our interest in joining the initiative is not solely based on access to funding, but rather due to the manifold opportunities for collaboration at the national and international level that participation provides. We consider the partnership a long-term investment, in order to raise USI's profile in the fields related to systems biology.

What does USI expect from this new partnership?

We expect our research groups to profit from SystemsX.ch's extensive network to establish new, interdisciplinary collaborations. This is particularly important for USI, a small university, which simply cannot conduct research in all fields; our strategy is to focus on certain niches in which we strive to excel.

USI in a nutshell

Founded in 1996, USI is the only Italian-speaking university in Switzerland and outside Italy. It comprises four faculties: Architecture, Communication, Economics, and Informatics. The Institute for Research in Biomedicine (IRB) has been affiliated with USI since 2010.

Research at USI has steadily developed in recent years due to an increase in internal resources. The number of competitive research grants has gone up in the last 5 years by 50 percent to 17 million CHF, thanks especially to the rapid growth of research activities in informatics, computational sciences and biomedicine. Specifically, in the computational sciences domain, USI coordinates two large-scale collaborative programs with the Swiss Supercomputing Center.

Before 2017, USI plans to establish a new faculty of biomedical sciences, which will offer a master's degree in human medicine. The IRB will be integrated into this faculty. Currently, USI is awaiting the final decision on this project from the Cantonal Parliament of Ticino.

More information is available at:
www.usi.ch

Eavan Dorcey supports young scientists

Eavan Dorcey is the new SystemsX.ch scientific coordinator.

Eavan Dorcey, the new scientific coordinator for SystemsX.ch since the beginning of this year, is in charge of young scientists. Her tasks include the coordination of activities pertaining to postdoctoral and doctoral training as well as networking among young scientists. In collaboration with the SIB Swiss Institute of Bioinformatics, she has organized the Summer School in Kandersteg, and she is currently preparing a retreat to be held during winter 2014/15.

Eavan Dorcey grew up in Spain but is originally from Ireland. She holds a doctorate in biochemistry and molecular biology, and her professional know-how is an asset to her work. Furthermore, she has been familiar with SystemsX.ch since the time she was a postdoc at the University of Lausanne. She was then involved in the Plant Growth RTD Project. Later, Eavan worked as a project leader in the International Breast Cancer Study Group in Bern.

Through her work, Eavan Dorcey wishes to connect people and research projects, and to contribute to science by doing so. This was also her motivation to switch to SystemsX.ch.

We extend a warm welcome to Eavan Dorcey and look forward to a productive collaboration.

vdm

International SystemsX.ch Conference

The 2nd International SystemsX.ch Conference will be held on October 20–23, 2014. Over four days, the Swiss Tech Convention Center in Lausanne will be a meeting point for 450 systems biologists. The conference program includes five key topics: quantitative cell and developmental biology, functional genomics and gene regulation, systems genetics and medicine, theory and biophysical modeling, as well as single-cell biology.

Alongside talks by renowned international scientists, leading scientists from SystemsX.ch projects will present their current research. In addition, dedicated poster sessions and short talks will give young researchers a chance to exhibit their work to an international audience. There will be awards for the best poster in each of the five main categories. Sharing of knowledge and networking will also be possible during the conference dinner on October 22.

Important notice: Abstracts for posters or short talks may be submitted by all participants until August 1, 2014. *ih*

The EPF Lausanne inaugurated the Swiss Tech Convention Center in spring 2014. Picture: © EPFL - Visualization Richter. Dahl Rocha & Associés architectes SA et MIR

Further details and registration can be found at:
http://conference.systemsx.ch

2nd International SystemsX.ch Conference on Systems Biology

October 20 – 23, 2014
Swiss Tech Convention Center, Lausanne, Switzerland

Keynote Speakers

Michael Elowitz CALTECH, USA
Gene Myers MPI-CBG, Germany

International Speakers

Patrick Cramer LMU, Germany
Carl-Philipp Heisenberg IST, Austria
Tim Hughes University of Toronto, Canada
Frank Jülicher MPIPKS, Germany
Galit Lahav HMS, USA
Andrew Oates NIMR, UK
Dana Pe'er Columbia University, USA
Lars Steinmetz EMBL, Germany
Manuel Théry iRTSV, France
Tsvi Tlusty IAS, USA

http://conference.systemsx.ch

SystemsX.ch
The Swiss Initiative in Systems Biology

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Photo: Martin Oeggerli, supported by School of Life Sciences FHNW. Clonal evolution versus cancer stem cell theory, Homo sapiens, Magnification: 6'700:1, www.micronaut.ch