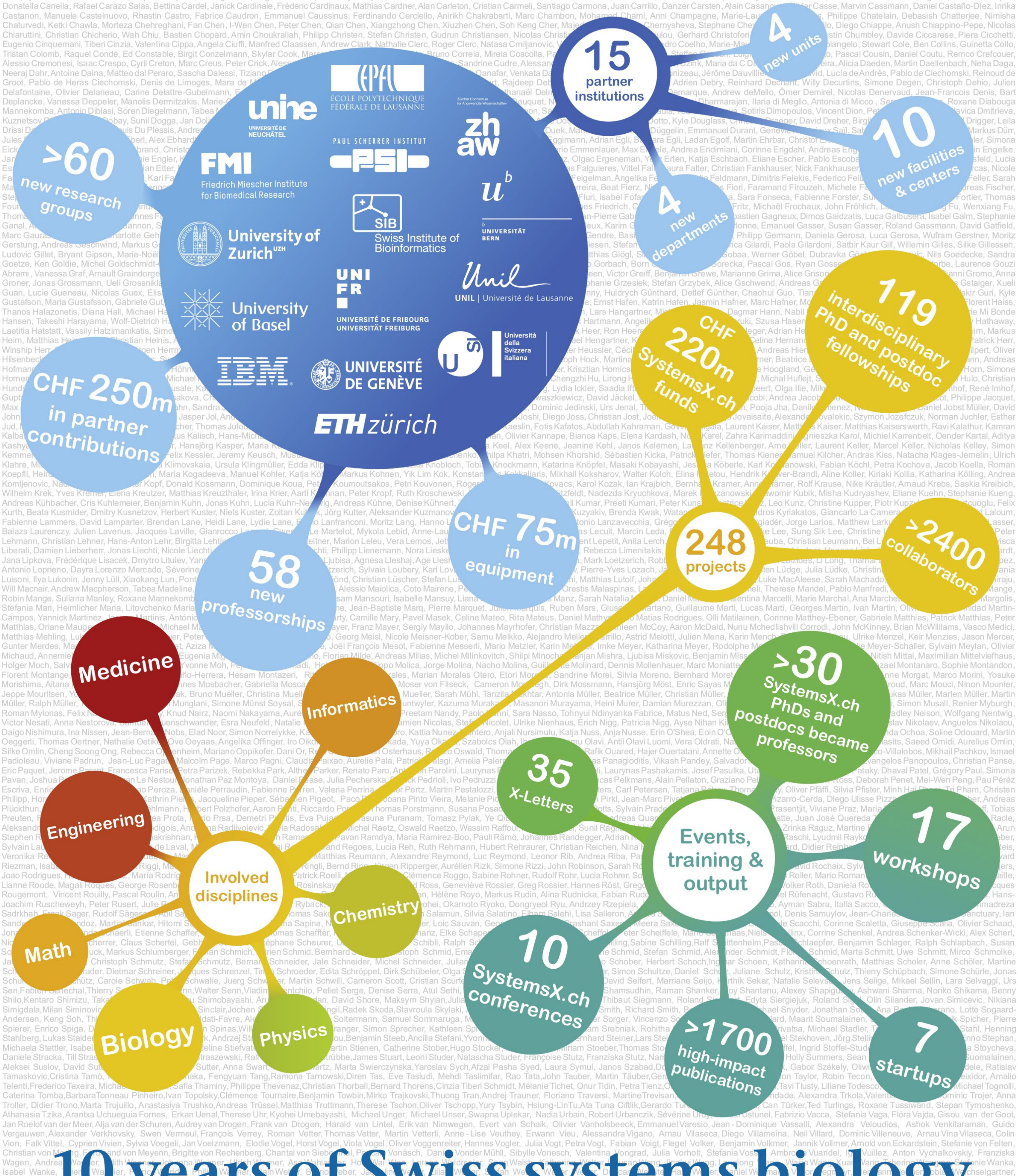
X-Letter 35



10 years of Swiss systems biology

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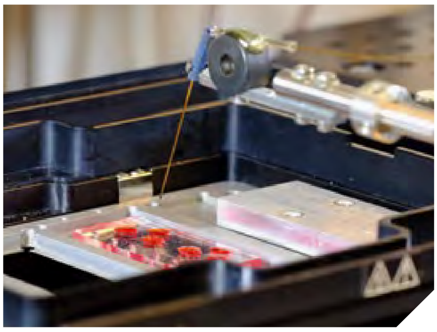

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SystemsX.ch
The Swiss Initiative in Systems Biology

Imprint

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Cover: Facts and figures of the SystemsX.ch initiative. Illustration: Dagmar Bocakova

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"Thank you for being a part of it!"

Reading this last X-Letter, you will see that SystemsX.ch has experienced many highlights, big and small, over the past 10 years. One of the overarching achievements is surely the long-term anchoring of the systems approach in Swiss life science research. This has helped transform biology into a quantitative science, with which we can make predictions about the behavior of complex biological systems.

One of the most recent high points was the SystemsX.ch documentary film, "The Human Body," which succeeded in giving the public an insight into this type of interdisciplinary research. Further highlights are set out in this X-Letter, for example in the interview with René Imhof and the personal statements from some of the involved scientists, who describe the initiative's impact from their personal point of view.

As part of the comprehensive evaluation of SystemsX.ch's impact, we commissioned a bibliometric analysis, carried out by Leiden University (Netherlands). The link to their report is shown on page 23.

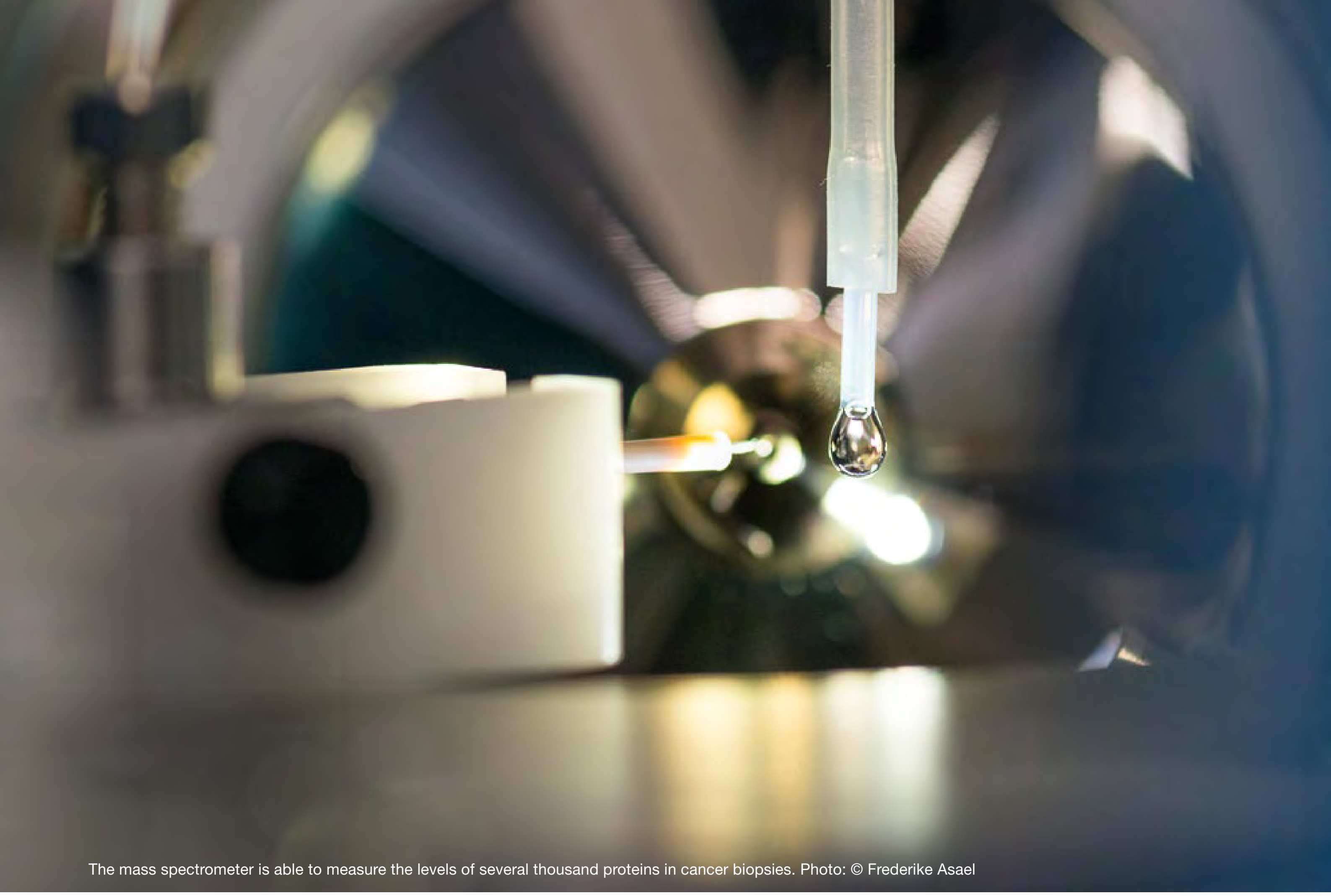
We would like to thank all those who made SystemsX.ch possible. First and foremost, the State Secretariat for Education, Research and Innovation and the Swiss National Science Foundation (SNSF). Without the support of the SNSF, which provided indispensable expertise in the project selection process as well as the scientific and financial reporting, SystemsX.ch would not exist in the form it takes today.

Our thanks also go out to our international partners, who enabled collaboration between international and Swiss research groups to flourish, thus broadening the SystemsX.ch network. For example, the German Federal Ministry of Education and Research, which contributed the funds for the German groups within SystemsX.ch consortia with minimal bureaucracy.

Special thanks are also due to the members of the SystemsX.ch boards. In particular, we would like to thank the chairmen of the Board of Directors, Ralph Eichler and Detlef Günther, as well as the chairmen of the Scientific Executive Board, Ruedi Aebersold and Lucas Pelkmans.

And last but not least, we would like to thank our collaborators at the 15 partner institutions, particularly all of the researchers involved, who, over the past 10 years, have made the Swiss Initiative in Systems Biology what it was: a great adventure with many highlights. Thank you for being a part of it!

Daniel Vonder Mühll,
SystemsX.ch Managing Director 2007–2017


The mass spectrometer is able to measure the levels of several thousand proteins in cancer biopsies. Photo: © Frederike Asael

An insight into the technological developments within the SystemsX.ch initiative

Technological innovation drives creative scientific breakthroughs

Progress in systems biology often goes hand in hand with novel technological achievements. This is why SystemsX.ch has supported projects that incorporate the development of new technologies from the outset. Since then, a number of high-impact innovations have emerged from within the SystemsX.ch community.

Novel technologies and approaches are of vital importance for new discoveries in the field of systems biology. The ability to analyze a single cell, and to characterize not only its genes but also its proteins and lipids, is increasingly crucial for research projects in the life sciences. The new technologies developed by SystemsX.ch researchers, from omics to novel devices, push the boundaries of biological research, allowing unprecedented insight into the inner workings of single cells, tissues and organs. New imaging techniques allow researchers to look at the tiniest constituents of life from a new perspective, and algorithms help perform quantitative analyses much faster than ever before. Here we describe some of the most groundbreaking innovations to have emerged from SystemsX.ch-funded research.

Quantitative omics analysis for cancer research

A spectacular example of technological innovation is the PCT-SWATH mass spectrometry technology which was developed by Ruedi Aebersold's group at ETH Zurich as part of the RTD Project PhosphoNetX. This new omics method for quantitative analysis of biological samples was subsequently employed in the follow-up project PhosphoNet PPM, which focused on developing better prediction strategies for prostate cancer. The method measures the precise levels of several thousand proteins in very small cancer biopsies. The resulting proteomic maps can be analyzed, re-analyzed and compared in order to identify proteins of interest and accurately quantify them across multiple samples.

The highly innovative PCT-SWATH technology forms the core of the International Centre for the Proteome of Human Cancer (ProCan) in Sydney, Australia, which opened in 2016. The analysis of about 70,000 samples of different types of cancer at the facility will enable doctors to pinpoint the best currently available treatment to fit a patient's individual diagnosis, avoiding the administration of invasive treatments that are unlikely to effectively treat the disease.

From proteomic maps to single cells

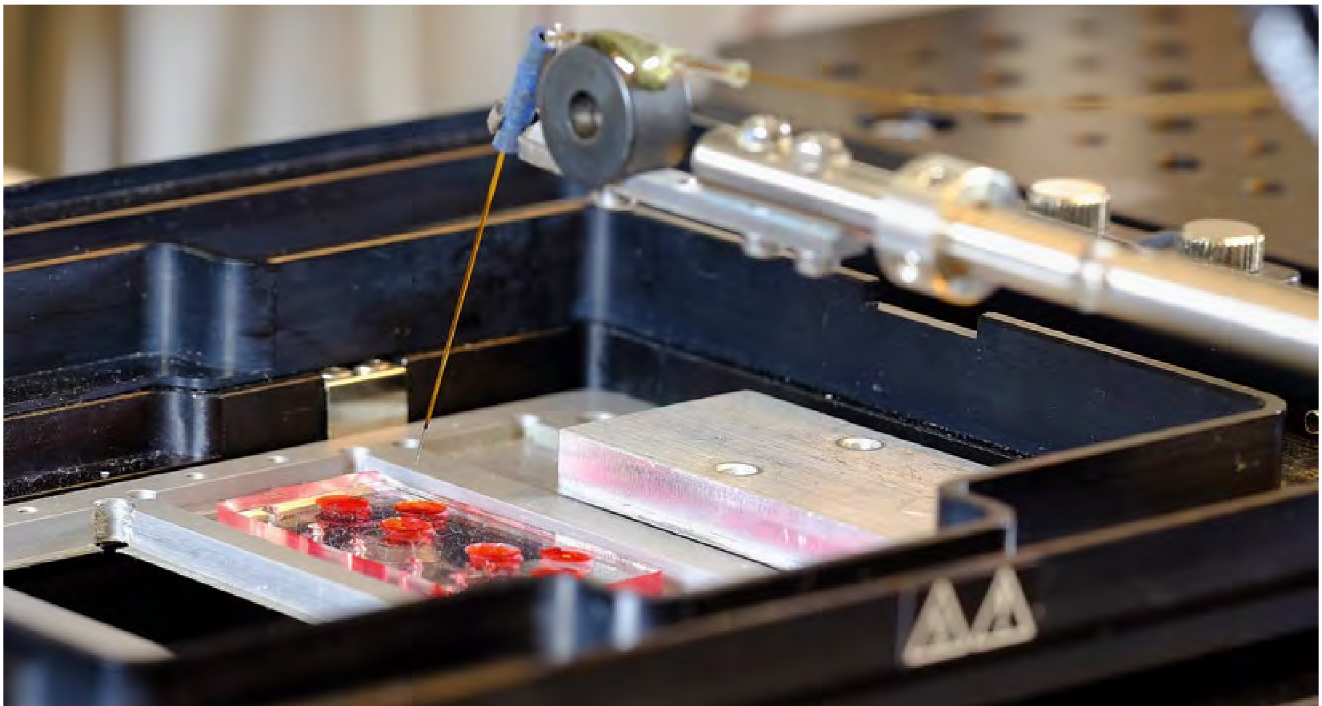
Another pioneering omics approach to have emerged from the PhosphoNet PPM project was developed by Bernd Bodenmiller's group at the University of Zurich. The CyTOF mass cytometry imaging technology has significantly advanced the field of spatial proteomics. This technology enables the large-scale study of proteins directly in tissues, with subcellular resolution. With the latest developments of the technology, the quantities of over 100 types of molecules can be measured simultaneously in a single cell. In combination with computational methods developed by Manfred Claassen's group at ETH Zurich, this method is currently being used to elucidate the cellular characteristics and mechanisms influencing cancer development.

With mounting evidence of the importance of single-cell analysis for understanding complex biological systems, the CyTOF technology is not the only new development to address the need to look more closely at individual cells. The groundbreaking Single-Cell Visual Proteomics analysis technique was developed in Thomas Braun's team as part of the CINA RTD Project, led by Henning Stahlberg at the University of Basel. This patented method gently breaks up a cell membrane in a matter of seconds and sends the unharmed cell components to be analyzed by a series of modules that can filter certain proteins out of the cell's cytosol or prepare the entire cytosol for visualization. In the latter case, the entire contents of a single, hand-picked cell are deposited on an electron microscopy grid and subsequently imaged by the world's most advanced cryogenic transmission electron microscope. With the aid of this state-of-the-art technology, scientists can study disease processes or test the efficacy of drugs at the single-cell level.

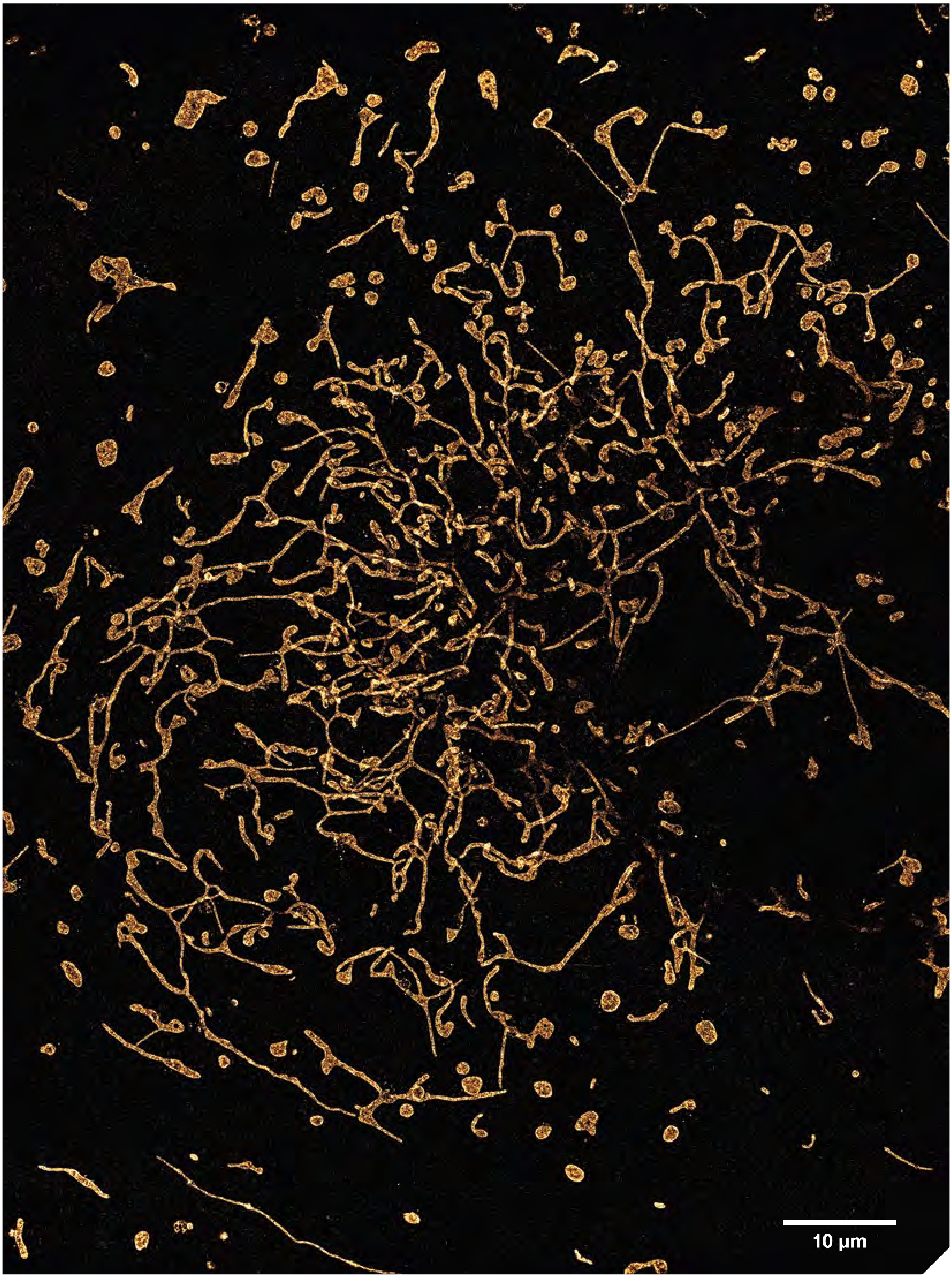
Life in high resolution

The Single-Cell Visual Proteomics technology is just one of the innovations developed by the CINA team. Another is the imaging platform set up for the visualization and manipulation of single cells and their constituents at nanoresolutions. Different types of optical and electron microscopes were combined to enable the high-resolution characterization of the 2D or 3D structures of biological samples.

For Kyle M. Douglass, a former Transition Postdoc Fellow at EPF Lausanne, high-resolution microscopy was just the starting point. He managed to resolve the issue of the highly constrained field of view in single-molecule microscopy techniques, going on to develop a super-resolution microscopy technique. With this newly-developed method, called Flat Illumination for Field-Independent imaging (FIFI), researchers are now able to image multiple cells at once at a remarkable single-molecule resolution. Several labs at EPFL have started using this high-throughput, super-resolution microscopy method, allowing them to answer questions in structural and systems biology that could not be attempted before.

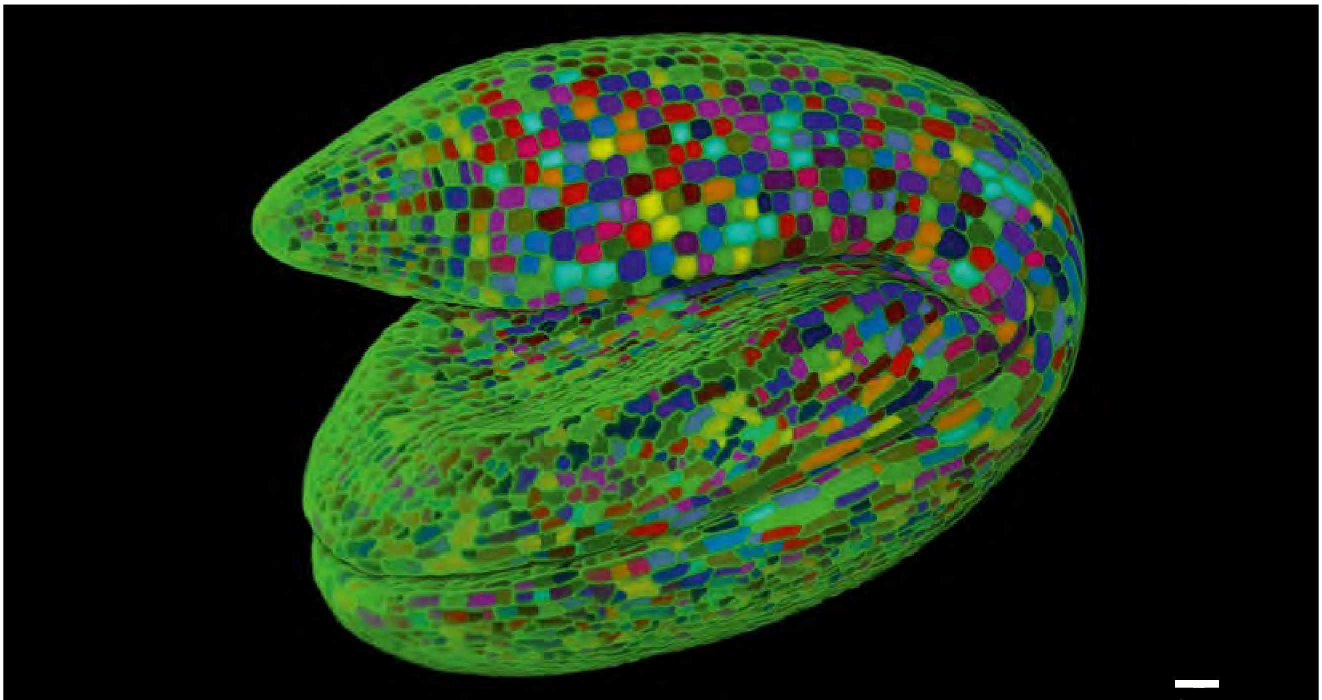


As part of the Single-Cell Visual Proteomics analysis, individual cells are lysed and sucked up by a microcapillary. The cell components are then prepared for visualization and analyzed at the single-protein level.



Mitochondrial membrane protein TOM20, labeled and imaged with a super-resolution microscopy technique that is capable of imaging single fluorescent molecules. Image: © Kyle M. Douglass

The range of developments that resulted from the RTD Projects Plant Growth 1 and 2, led by Cris Kuhlemeier from the University of Bern, also includes new microscopy techniques. One of the new methods, called Cellular Force Microscopy (CFM), was developed as a collaboration between the Nelson, Kuhlemeier, Grossniklaus and Smith labs. This is a micro-indentation technique that measures cell stiffness by applying a small probe connected to a force sensor. The recorded force and displacement of the sensor are used to determine a sample's stiffness; the higher the force required to indent to the same depth, the stiffer a sample is. In plant cells, the stiffness measured in this way reflects both the turgor pressure and cell wall elasticity – both essential characteristics for understanding cell wall mechanics. The main advantage of CFM is its wide measurement range. The system is also highly flexible and can be used in combination with optical microscopes.



A mature embryo of *Arabidopsis thaliana,* segmented into cells with MorphoGraphX. Image: George Bassel

In a further technological breakthrough, Sarah Robinson and the Plant Growth team recently published details of a new open-source device that can be used to track mechanical properties of plant cells in 3D. This new method, called the Automated Confocal Micro-Extensometer (ACME), improves on earlier techniques by going beyond quantifying cell wall properties. It can infer the mechanical characteristics of samples at the cellular level based on changes undergone by the tissue during the application of a known force or deformation. This technology will help uncover the mechanisms behind cellular expansion and morphology in different plants and tissues.

Computational tools for the wider research community

Needless to say, all of these new technological instruments go hand in hand with the creation of new computational tools, be it algorithms, computer models or databases. But some of the most valuable developments to have emerged from SystemsX.ch projects do not involve any new hardware, instead comprising computational support for systems biology research. Also as part of the Plant Growth project, in collaboration with four other SystemsX.ch projects, the MorphoGraphX software is an open-source application for the visualization and analysis of 4D biological datasets (three spatial dimensions plus time). The application was developed by Richard Smith and collaborators and is available at www.morphographx.org. Labs around the globe use it to quantify cellular parameters and reconstruct 3D structures from sets of images obtained at different depths.

A further example is the website metanetx.org, which was developed as part of the MetaNetX RTD Project, led by Jörg Stelling (D-BSSE, ETH Zurich), and is aimed at understanding metabolism. It is a user-friendly portal for accessing, analyzing and manipulating genome-scale metabolic networks and biochemical pathways. Researchers worldwide have open access to this platform and can use it to develop high-quality models of cellular metabolic processes within hours. This is interesting for research in several areas, including microbial and human metabolism, where understanding interactions by modelling the metabolic processes could make it easier to control the human microbiome.

A lasting impact

The technological developments presented here are just a handful of the many that have arisen from SystemsX.ch projects over the past 10 years. They span a wide range of applications, technologies and biological scales, but they all have one thing in common: they are widening the horizon of systems biology research, making it possible for scientists to look at life as it has never been seen before. And although SystemsX.ch is coming to an end, these technologies and their progeny will continue to drive discoveries in systems biology research for years to come.

René Imhof appraises SystemsX.ch from an expert viewpoint

SystemsX.ch leaves its mark

Hardly anyone knows SystemsX.ch better than René Imhof. The former Director of Research at Roche has accompanied the initiative from its beginnings as a project idea right through to this year's impact analysis. While Imhof is extremely satisfied with the scientific outcomes of the initiative, he also identifies certain weaknesses from which future research initiatives can profit and learn.


René Imhof was an early advocate of systems biology.

René Imhof, when did you first come into contact with SystemsX.ch?

In 2002, I belonged to a small group of experts consisting of the Vice Director of Research at the University of Basel, the President of ETH Zurich and the Rector of the University of Zurich. Our task was to evaluate how Switzerland could be given new impetus as a globally competitive center for research and education. This issue was raised by the then Secretary of State for Education, Research and Innovation. We identified the potential of systems biology as a pioneering discipline and recommended that it be specifically promoted in Switzerland.

What influence has the initiative had on the Swiss research landscape?

SystemsX.ch has fundamentally changed our approach to biological research. Classical molecular biology, with its focus on individual molecules, has been expanded into the systems domain. The focus is now on biological networks in order to understand the interplay between different molecular components.

Additionally, scientists from various disciplines now work together in a goal-oriented manner. Only in this way can we address new scientific problems that require technological progress and interdisciplinary collaboration.

What were your greatest highlights of the initiative?

I would like to mention just three of the many highlights here. One is certainly the sheer number of scientific publications. From the roughly 250 SystemsX.ch projects, more than 1,700 articles have already emerged that fulfill the strict selection criteria of the most prestigious journals including Nature, Science and Cell. The frequency of citations is on average twice as high – and for some research groups even four times as high – as the world average. Such an impressive outcome leaves me as a researcher awestruck. This is a great indicator of the initiative's scientific brilliance.

Secondly, SystemsX.ch played an important part in boosting innovation in Switzerland. The initiative has served as a catalyst for business ideas and startups. So far seven startups have emerged from SystemsX.ch research projects.

And the third highlight?

This is on one hand the constructive, efficient cooperation between the management, evaluation and coordination committees such as the Board of Directors, Scientific Executive Board, Swiss National Science Foundation and the Management Office. On the other hand, the initiative was given coherent federal support, specifically when it came to funding. The federal government, along with the cantonal universities and research institutions involved, provided over 400 million Swiss francs to fund the initiative. Without such extensive cooperation across all levels, SystemsX.ch would never have been so successful.

Can this Switzerland-wide team spirit also be felt at the level of the research community?

Definitely. Not only have we seen an increase in collaboration across the most diverse disciplines, but around half of the 43 large-scale projects also involved increased cooperation between the French- and German-speaking regions of Switzerland. Today many of the networks and collaborations even extend beyond national boundaries.

Does this mean that Swiss systems biology now has a lead role on the international stage?

Absolutely. Let me illustrate this in two ways. Firstly, SystemsX.ch publications have been cited more than 800 times by both Harvard University and the Max Planck Society. An extremely high citation frequency can also be observed at other world-renowned institutions. Secondly, the European Research Council has now awarded more than 70 long-term project grants to former or current SystemsX.ch project leaders. These are both clear indications that the scientific excellence of SystemsX.ch is world-class.

We've now heard a lot about the initiative's successes. Which of its aspects are you critical of?

The ambitious goal of recreating biological processes in simulations with the help of quantitative data could not be implemented at the high level that was hoped. However, this does not surprise me very much, since complex biological systems require huge datasets on different hierarchical levels. This is also a problem in the field of meteorology, for example, where complex forecasting models very soon reach their limits.

Are there other aspects you feel were not as successful as hoped?

When it comes to interdisciplinary collaboration, I feel that the fields of chemistry and medicine didn't participate as actively as they could have. With few exceptions chemistry seems to me to remain too attached to classical molecular biology. And the medical sector was only brought on board relatively late, in 2015, with the launch of the Medical Research and Development Projects.

Furthermore, the private sector was somewhat reluctant to commit wholeheartedly to systems biology research collaboration. Nevertheless, there have been several partnerships with industry that have produced very promising results and technological innovations.

Let's look towards the future. Do you think SystemsX.ch has managed to establish systems biology in Switzerland for the long term?

SystemsX.ch will not leave any Potemkin villages behind. Of that I am convinced. Thanks to this initiative more than 60 new research groups have sprung up across the country. 12 of the 15 cooperating institutions have set up new departments, research units or competence centers in the field of systems biology. One notable example is the foundation of ETH Zurich's Department of Biosystems Science and Engineering (D-BSSE) in Basel, in which both half-cantons invested substantially.

Also, the need for highly professional IT support for systems biology research was recognized very early on. Four competence centers in addition to the SIB Swiss Institute of Bioinformatics have been set up for this purpose. Across Switzerland nine PhD and just as many Master's programs with a focus on systems biology have been integrated into university curricula. And last but not least, more than 1,000 postdocs and PhD students have been trained within the SystemsX.ch projects themselves. This is why I am not in the slightest bit worried about the sustainability question.

Could this infrastructure also be used for further development in other fields of research?

Yes, as a matter of fact, the foundations built for systems biology research could help in the establishment of other initiatives. These might include areas from systems physiology and pathophysiology to systems health and medicine.

So, has the investment in systems biology paid off?

Definitely! Swiss universities seized the opportunity to build new departments or realign existing ones, create and fill professorships in systems biology and invest in technology development. Our research community will continue to benefit from these investments for a long time to come.

About René Imhof

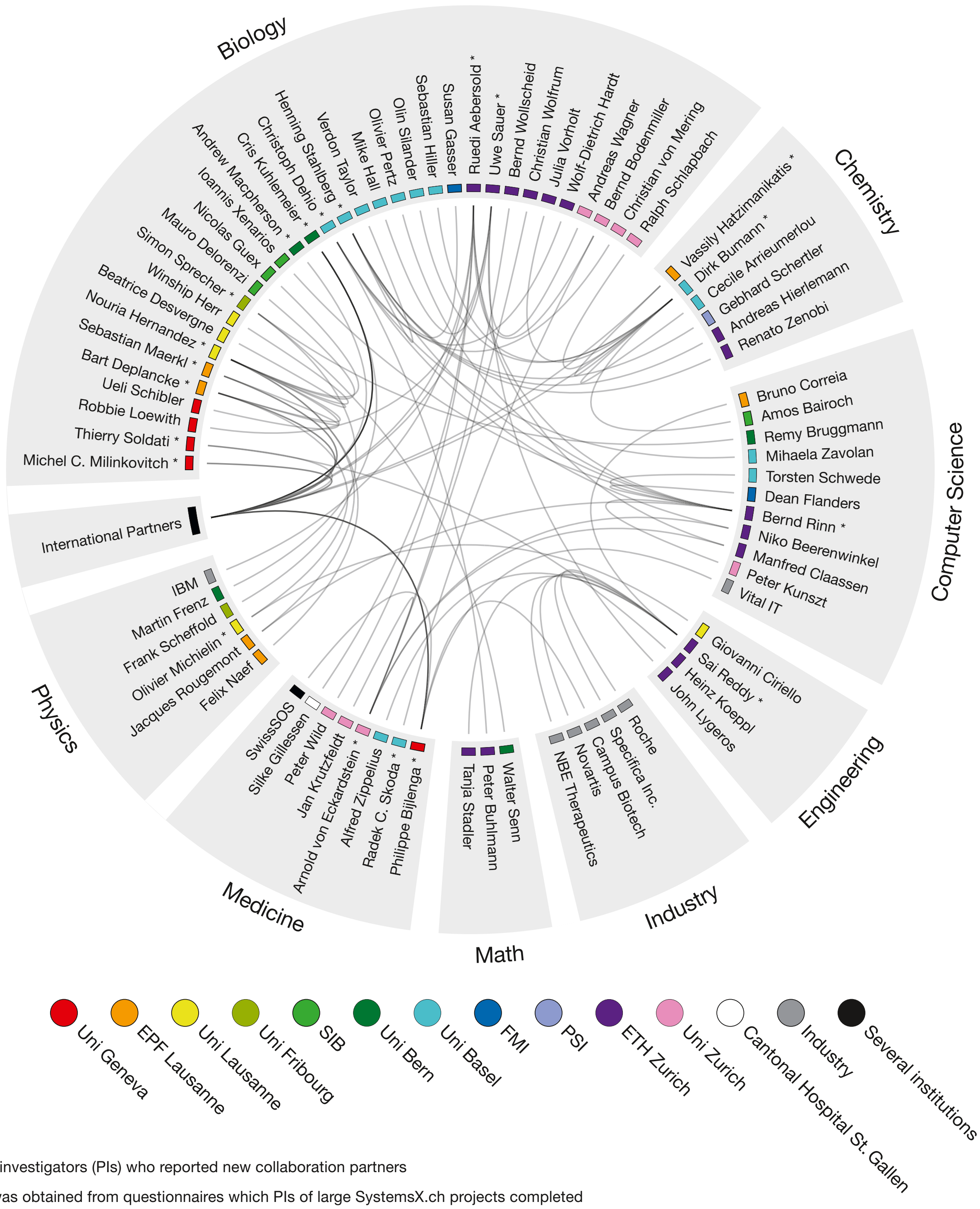
René Imhof studied chemistry at ETH Zurich. In 1976 he joined the company F. Hoffmann-La Roche and followed a steep career path there. He eventually became Director of Pharmaceutical Research in Basel and Global Head of Scientific and Talent Relations. At the same time, René Imhof was involved in various committees in different research areas at the university level. These included the Boards of Directors of the University of Basel and of SystemsX.ch as well as the Scientific Executive Board of SystemsX.ch. He is still active on the Board of Trustees of the Swiss National Science Foundation, to which he was elected by the Swiss federal government.

Christa Smith

New collaborations arising from SystemsX.ch projects

Switzerland-wide collaboration network

With the combination of tailored funding measures and community-building efforts, SystemsX.ch sped up the development of a Switzerland-wide collaboration network and facilitated the integration of new disciplines into systems biology. This graphic shows newly-developed interdisciplinary, interinstitutional collaborations between Swiss research groups resulting from large-scale SystemsX.ch projects.



* Principal investigators (PIs) who reported new collaboration partners

The data was obtained from questionnaires which PIs of large SystemsX.ch projects completed in 2016 as part of the SystemsX.ch self-evaluation. Disciplines were defined based on the topics of the PIs' doctoral theses. Graphic: Sam Hertig

Matthias Scholer Christa Smith

Industry collaboration

The key to successful public-private partnerships

Some of SystemsX.ch's initial objectives were only partially reached. For instance, the number of collaborative projects between industry and academia fell short of expectations. We asked some of the scientists who managed to bridge the gap between academia and industry which factors were pivotal in their success.

To the management boards of SystemsX.ch, it was always clear that in order for systems biology to get a foothold in clinical research, sustainable knowledge transfer between academia and private institutions such as industry or SMEs, as well as hospitals, would be needed. SystemsX.ch created the necessary framework for this, including special events, Transfer Projects involving private partners, and the focus on medical and clinical research in the second phase. Despite the fact that the number of fruitful collaborations fell short of expectations, a number of highly promising projects have emerged.

IBM and the University Hospital Zurich (USZ) are collaborating successfully thanks to SystemsX.ch: (from left) María Rodríguez Martínez (IBM), Elina Koletou (IPhD student) and Peter Wild (USZ).

Set the rules of play in advance

One such project is Elina Koletou's Interdisciplinary PhD (IPhD), which is aimed at developing a computational method for the reliable diagnosis of prostate cancer malignancy. The doctoral student has two advisors, Peter Wild, senior consultant at the Institute of Pathology and Molecular Pathology at the University Hospital Zurich (USZ), and María Rodríguez Martínez from IBM Research – Zurich. If you ask the two supervisors what factors are vital for successful collaboration, they are in agreement: clear protocols on intellectual property issues are crucial. There need to be detailed regulations on who gets to use which data in which ways, and also what to do with any profit, should a product emerge from the research project. Or, as Peter Wild puts it, "all players need to be on an even playing field."

A learning curve on both sides

According to the experts, other factors vital for success include the formulation of common goals, good communication between researchers, and proactive project leaders. "The division of tasks is well defined in our project, and both sides are able to benefit equally from each other's specialist knowledge," says Rodríguez Martínez. In this way, IBM provides expertise in machine learning and artificial intelligence, while the USZ is able to contribute expert medical knowledge as well as an extensive collection of prostate cancer tissue sections. The remarkable thing about these samples is the fact that they have been taken from a number of different sites in each diseased gland. "This allows us to examine different levels of malignancy in the same patient," explains Wild. This is in turn ideal for the researchers at IBM. "The cohort is an exceptional opportunity for us to validate our newly-developed method for classifying prostate cancer," says Rodríguez Martínez. A win-win situation in which both parties can profit from the steep learning curve.

Successful collaboration needs time

As well as the collaboration between IBM and USZ, there have been other projects demonstrating successful cooperation between partners in academia and industry. One researcher who is involved in several such projects is Bernd Bodenmiller. The systems biologist from the University of Zurich is principal investigator of the Transfer Project "Foes or Friends?" in collaboration with Roche.

According to Bodenmiller, there is another key ingredient to success. "To be able to work together effectively, you need to get to know each other on a personal as well as a scientific level. This includes understanding each other's scientific interests and how things work in industry," highlights the scientist. Factors such as speaking a common scientific language, having a shared vision and establishing a basis of trust also play an important role in cementing a good collaboration. And there is no getting around it: these things take time – something that was likely in short supply over the course of the Transfer Projects, which ran for a maximum of three years.

Realizations such as these have been collected and summarized in a self-evaluation of the SystemsX.ch initiative as part of a detailed impact analysis which will be published in 2018. The findings should help optimize future large-scale research schemes.

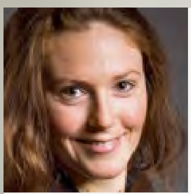
A close-knit research community

Some personal highlights

SystemsX.ch community members describe the initiative's most important achievements from their personal point of view, and what was particularly beneficial for them.

"The initiative has fundamentally changed the way we do research. I can't imagine going back to the way we did it before."

Gisou van der Goot, EPF Lausanne

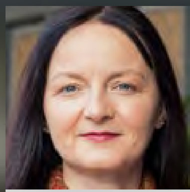


"SystemsX.ch events enabled me to build up a network within the systems biology community covering a wide range of disciplines and expertise. It will be essential to keep this community alive after the initiative ends."

Marion Betizeau, former Transition Postdoc Fellow, University of Zurich

"By bringing together cell biologists, geneticists, physicists, computer scientists and mathematicians, we can now answer questions that were previously off-limits, opening new avenues of research."

Michel Milinkovitch, University of Geneva



"The SystemsX.ch projects laid the foundation for personalized medicine by actively promoting a systems approach to medical research questions."

Karin Metzner, University Hospital Zurich

"The IPhD Projects were a great way of exploring interdisciplinary research, not only for the students but also for the host groups – in our case it even led to collaborations on several other projects."

Jan Roelof van der Meer, University of Lausanne

"I received a unique learning opportunity in a multidisciplinary research environment, which is sure to help me achieve my career goal of establishing my own research group."

Weijia Wang, Transition Postdoc Fellow, ETH Zurich

“The TPdF projects were a great instrument that allowed researchers to delve into a new discipline. I’m sure future research initiatives will benefit from this tested project type.”

Mihaela Zavolan, Biozentrum, University of Basel

“SystemsX.ch made it easier for scientists in the healthcare industry to connect with an established network of academic partners, increasing private-public collaboration.”

Hans Widmer, Novartis Institutes for BioMedical Research

“Through the partnership model, a national, interdisciplinary network has been created that has helped catapult Swiss systems biology groups to the forefront of global research.”

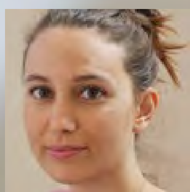
Christian Mazza, University of Fribourg

“The sheer quality and quantity of scientific publications to have emerged from the initiative is outstanding, and shows that Switzerland has been at the forefront of systems biology for the past 10 years.”

Lucas Pelkmans, Chairman of the SystemsX.ch Scientific Executive Board, University of Zurich

“Our Cell Plasticity RTD Project helped pave the way for the use of next-generation sequencing by academia in Basel. This crucial technology facility will be sustained by the University of Basel and the ETH Zurich’s D-BSSE even after SystemsX.ch ends.”

Susan Gasser, Friedrich Miescher Institute for Biomedical Research



“My IPhD Project made me part of a community of students who shared the same interests, ambitions, and, most importantly, faced similar challenges in their new interdisciplinary environments.”

Sunniva Förster, former IPhD student, University of Bern

Diversity of systems biology research

From lipids to malaria and gut bacteria

Systems biology provides the key to unlocking a great many scientific problems, as illustrated by the breadth and success of the SystemsX.ch projects. The involved researchers have used the systems approach to achieve a fundamental and comprehensive understanding of the behavior of the most diverse biological systems.

Intestinal bacteria, infectious diseases, cancer; basic research, medical applications or the development of innovative technologies. However diverse the research questions may be, they all have a common denominator: it is only thanks to a systems biology approach that many of today's open questions in biology can be answered. Out of the roughly 250 projects involving almost 2000 scientists, we have chosen to present a number of successful examples that reflect the variety of research topics in systems biology.

When useful fat turns into mortal enemy

LipidX was one of the very first SystemsX.ch projects. This Research, Technology and Development (RTD) Project produced a number of promising offshoots and technical innovations.

As the name suggests, the LipidX project is all about lipids. These natural products, which include fats, waxes and steroids, had previously been the focus of relatively few research projects. This is surprising, as lipids form one of the major components of a cell and are vital to the human body. They play a particularly important role in the cell membrane, where changes in the lipid composition can lead to illness.

At the metabolic level, too, lipids are crucial factors in health and disease. Changes in lipid metabolism can lead to obesity or metabolic syndrome, regarded as the precursor to type 2 diabetes. Furthermore, a disruption in the breakdown of fat at the cellular level can trigger lysosomal storage disease, in which the metabolism no longer functions properly. An accumulation of cholesterol – also a lipid – has been implicated in the development of arteriosclerosis. And last but not least, changes in lipid distribution have been observed in diseases such as Alzheimer's, Huntington's and cancer.

Based on the success of LipidX, the SystemsX.ch and Swiss National Science Foundation review panels granted the project a further four years' funding in 2012. "We were able to build on the findings from the first phase and show that the systematic characterization of fatty acids and their metabolic products presents an important source of biological information," says project leader Gisou van der Goot of EPF Lausanne. Among other findings, the LipidX team succeeded in establishing how the lipid composition of the cell membrane changes in relation to its environment. In addition, a lipid mass spectrometry platform has been set up at EPFL, facilitating the rapid quantification and characterization of lipids.

As part of a further project www.swisslipids.org was created – a unique database that contains the details of more than 400,000 known and theoretical lipid structures, enriched with expert-curated information on their metabolism, protein interactions and occurrence in cells, tissues and organs. The platform has the potential to become one of the leading resources in lipidomics research. The further development and maintenance of SwissLipids beyond the lifetime of SystemsX.ch is supported by the SIB Swiss Institute of Bioinformatics, ensuring the long-term sustainability of this valuable resource.

Getting under the skin

Chameleons communicate their emotions by changing the color of their skin. The researchers working on the EpiPhysX RTD Project wanted to find out how this color changing works. They discovered nanoscopic crystals within some of the chameleon's skin cells, which can produce different colors through the interference of light. This incredibly sophisticated system may one day be em-

Fat cells are not intrinsically bad: they store energy and supply building materials for new body tissue. Image: computer illustration, GruppoCreativo

Chameleons change their color by manipulating light interference in their skin, the same physical process that is responsible for the shimmering colors of soap bubbles. Photo: © Michel Milinkovitch

ployed in the textile or cosmetic industries. Even the defense industry is interested in the discovery in order to develop invisible objects. On top of investigating how a chameleon changes color, the EpiPhysX team has also demonstrated that hairs, feathers and scales all share a common evolutionary origin which evolved in a primitive reptile over 300 million years ago.

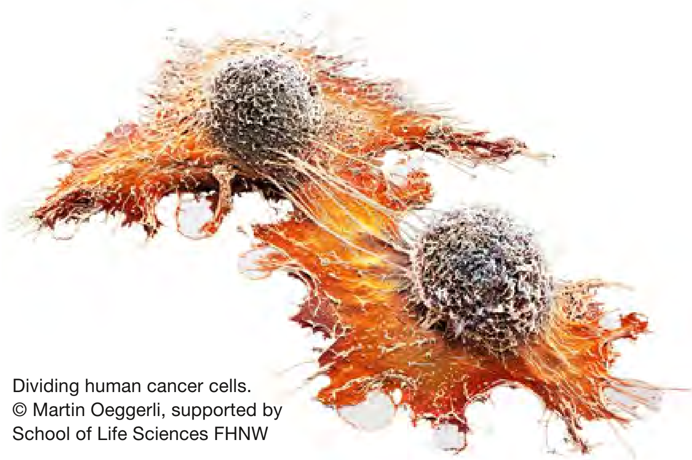
To help make these incredible discoveries, the research team developed the R2OBBIE-3D robot, which is able to scan objects up to 1.5 meters long, allowing the close examination of the skin of chameleons, snakes or even crocodiles. The device is so precise that even details such as the color or shape of individual skin cells can be measured. This novel scanning robot is already garnering interest in the field of forensic science, where it may be employed to examine injuries resulting from violent crimes in order to more precisely ascertain what took place.

The project leader Michel Milinkovitch is convinced of the reasons behind the project's success. "The EpiPhysX project shows that the integration of biology with physics and mathematics in everyday research is crucial if we are to understand biological complexity."

Disrupting cancer cell communication permanently

Cancer research forms the focus of a number of SystemsX.ch projects. This includes the MERIC RTD Project headed by Niko Beerenwinkel of ETH Zurich. The MERIC team is trying to find out how cancer cells are able to develop resistance to targeted therapy so rapidly – a problem that can have fatal consequences for patients, particularly those suffering from inoperable cancers.

Cancer drugs are supposed to disrupt a cancer's intracellular communication and thus put a stop to the cells' reproduction. However, these degenerate cells manage to find new ways of re-establishing communication within a short time, rendering the drugs ineffectual. To combat this phenomenon, known as evasive resistance, the MERIC team is examining the involved molecular processes and networks in detail. The first step involved characterizing the DNA, RNA and proteins, including their phosphorylation statuses, that are present in cancer cells at different stages of liver cancer.



Dividing human cancer cells. © Martin Oeggerli, supported by School of Life Sciences FHNW

The first potential therapeutic targets have already been identified. "The findings obtained by the systems-biology-level analyses will first be tested in functional, proof-of-concept experiments and then translated into a clinical setting," explains Beerenwinkel. These approaches will go well beyond the framework and duration of the SystemsX.ch grant. But the future of this promising project has already been safeguarded with the award of an ERC Synergy Grant totaling 11.2 million Euros, allowing the groundbreaking research to continue seamlessly.

Malaria pathogen in the liver stage.
Image: Volker Heussler, University of Bern

Defeating malaria – one of the most widespread infectious diseases

It is not only cancer that researchers hope to tackle using a systems biology approach. There are also projects dedicated to finding new treatment options for infectious diseases such as tuberculosis, HIV and malaria.

Malaria was widespread in Western Europe right up into the 20th century. Thanks to preventive measures, good diagnostics and effective medical treatment, the disease was repressed. In more southerly latitudes, however, malaria still represents a substantial problem due to the rise in drug-resistant parasites and limited access to effective medical interventions. The MalarX RTD Project, led by Vassily Hatzimanikatis at EPF Lausanne, is aimed at making a decisive contribution to the eradication of the disease.

In order to do this, the researchers need to develop completely new therapeutic approaches that take the malaria parasite's particular life cycle into account. After a mosquito bite the pathogen migrates from the bloodstream into the liver of the host organism, where it lodges. After multiplying and maturing in the liver tissue the parasites migrate back into the bloodstream where they infect red blood cells and reproduce again. It is during this infectious stage that the parasite is transmitted to the next host via mosquito bites.

Previous attempts to fight malaria were focused on eliminating the pathogen in the blood. But this approach is not always successful, as new generations continuously arise in the liver. This is why the MalarX researchers are looking into the molecular interactions between pathogen and host in the liver. The data they collect is fed into a comprehensive mathematical model, which should help them find new and more efficient ways of eliminating the parasite for good.

The MalarX team is already one step closer to achieving this goal. The scientists have identified two enzymes in the parasite that are essential to its survival and transmission. They have even gone so far as to find a substance that blocks both of these enzymes in laboratory experiments. "We must now translate these findings into a therapeutic approach that is appropriate for use in the countries most affected by malaria," says Hatzimanikatis.

Getting to know our intestinal bacteria

It is estimated that each of us carries about one kilogram of intestinal bacteria around inside us. These microorganisms can be divided into at least a thousand different species. Not only do they play an important role in digestion, but they also synthesize vitamins and neutralize toxins.

However, it is not always possible to live in harmony with one's gut bacteria, not least when the body's immune system attacks the microorganisms. This is what happens in inflammatory bowel disease (IBD), which is estimated to affect one in every 1,000 people.

The Medical Research and Development (MRD) Project GutX aims to find new approaches in the treatment of IBD. This requires a deeper understanding of the interactions between the gut bacteria themselves, and also between the bacteria and their host. As principal investigator Andrew Macpherson from Inselspital Bern explains, "we're trying to understand how the exchange of molecules between different types of intestinal bacteria and the body affects our health." To this end, the scientists are measuring a large number of different biochemical substances in the contents of the intestine and examining how these substances are passed onto the host. The data will be integrated into a model that will then simulate these processes in a healthy and diseased organism.

This is a completely novel approach. Until now, research was limited to cataloging the individual species of bacteria in the gut. Therefore, hardly anything is known about the complex interactions taking place in the intestine. With this systems approach, Macpherson and his collaborators are hoping to gain a comprehensive picture of the roles of individual gut bacteria as well as their interactions. In the long term, these findings will help us actively regulate our intestinal system when something goes wrong, and positively influence our health.

The bacteria in our bowels play an important role in our health.
Image: computer illustration, GruppoCreativo

Christa Smith

A diverse array of scientific and soft-skill events

Event highlights

The final international SystemsX.ch conference took place in September 2017. Around 200 researchers from a broad range of fields attended this last major event, using the opportunity to exchange ideas and network with fellow scientists. The smaller events organized by SystemsX.ch were no less successful: the retreats and postdoc workshops were always fully booked, and feedback from participants was overwhelmingly positive.

The 3rd and final international conference represented the conclusion of SystemsX.ch.

Over the past 10 years, SystemsX.ch has organized around 30 events and supported almost 100 further events organized by members of the community. The aims of these events included the establishment of a Switzerland-wide network of systems biologists as well as the support of young scientists, who regularly took part in the SystemsX.ch conferences and workshops.

A central component of each conference was the poster session, which always encouraged lively discussions and exchange. At the 3rd and final international conference in Zurich, over 140 PhD students and postdocs presented their latest research. Onur Tidin (EPFL), poster prize winner in the single-cell biology category, explained what distinguished the initiative's events. "The SystemsX.ch conferences were great thanks to their diversity – not only in the topics covered and disciplines involved but also in the cultures represented by the participants."

This diversity was also evident in the SystemsX.ch retreats and workshops. For these events, SystemsX.ch decided to shift the emphasis away from the science itself, and instead focus on strengthening soft skills. The events addressed the human aspects of doing science, in order to influence and support both participants' current scientific work as well as their future careers. Topics such as conflict management, presentation skills, and leadership and communication made these workshops very popular with young scientists. "The soft-skill workshops were unique and provided me with multiple opportunities, not only to expand my presentation skills but also to connect with my peers," explained Elad Noor (ETHZ) after attending a SystemsX.ch retreat. Anil Kumar (PSI) attended one of the postdoc workshops to prepare for his future role as a research group leader. "Through application-oriented theory and team exercises, we learned how to motivate, engage and activate others in a group, in order to harness the maximum potential of each and every team member," he said. Özlem Ipek (EPFL) also found the SystemsX.ch workshops very beneficial, saying, "I now have a much clearer idea of how to effectively set goals and deadlines and be a proactive leader."

For all those who have not yet had the chance to take part in a SystemsX.ch workshop or retreat, one more such event is planned for 2018. More information will be available via the SystemsX.ch newsletter and website.

Özlem and Anil at the 2016 Postdoc Workshop on Leadership and Management Skills.

Young entrepreneurs

From research project to startup

More than half of the roughly 2000 researchers working in SystemsX.ch projects were postdocs and PhD students. After deepening their expert knowledge in an interdisciplinary context, a number of these young researchers went on to develop promising startup ideas that now have to survive in the competitive market. Here, we present three of them.

Mario Emmenlauer wants to put the biologist in the driver's seat for image analysis. Photo: © Mario Emmenlauer

Automated image analysis and simplified image processing for biologists – this is Mario Emmenlauer's business idea in a nutshell. With this, the bioinformatician has his finger on the pulse of current biological research. Up until now, working with image analysis software was time consuming and complicated. Big data image analysis required the manual setup of a number of complex tools. Often, the analysis could only be performed with the help of an IT specialist, while the biologist could do no more than assist them from the sidelines.

Emmenlauer has experienced this first-hand. "It starts with setting the measurement parameters, which are based on highly complex algorithms," he says. As a postdoc in the Research, Technology and Development (RTD) Project InfectX, he had the task of finding new ways of analyzing millions of images generated during the project efficiently and reproducibly. "For me it was clear that such a challenge could only be overcome with a solid software solution," says the bioinformatician.

High-level image processing for non-experts

When the RTD Project InfectX came to an end in 2013, Mario Emmenlauer had already made substantial progress towards automating image analysis, and was able to seamlessly integrate his know-how into the follow-up project TargetInfectX. The conclusion of this RTD in early 2017 represented an important crossroads for Emmenlauer's career. He then went on to establish the Munich-based company BioDataAnalysis GmbH in order to make his software more widely available for biological research. Thanks to the BioDataAnalysis CellAnalyzer, biologists will soon be able to process images unaided, without requiring an IT specialist. At the same time, the software will learn how to identify cell structures independently through machine learning. The researcher initially assigns a category to each type of cell structure with a click of the mouse. "Once the software is able to recognize a cell nucleus, it looks through the data and automatically marks all of the cell nuclei it finds," explains Emmenlauer. The results then need to be verified by the researcher just once, and any errors corrected. The program records these corrections and thus avoids making the same erroneous interpretations in subsequent steps, improving accuracy. "With our CellAnalyzer, even non-experts will be able to carry out high-level image processing," remarks Emmenlauer, who is resolutely working towards the goal of his software being used at top universities worldwide within five years. "I am convinced that the BioDataAnalysis CellAnalyzer has the potential to revolutionize image analysis in biology."

BioDataAnalysis GmbH
Intuitive image analysis and data mining

More information can be found at: **www.biodataanalysis.de**

Matthias Scholer


The microfluidic device, developed by Ata Tuna Ciftlik, makes tumor sample diagnostics faster and more accurate. Photo: © Ata Tuna Ciftlik

Eighteen employees with an average age of 30, nine languages, two interns and a diverse range of specialisms mixed with dynamics and passion – this is how the Lunaphore team looks today. The Lausanne-based Lunaphore Technologies SA is undoubtedly the most advanced of all the startups in which SystemsX.ch has played a vital part. The success story started with the funding of Ata Tuna Ciftlik's Interdisciplinary PhD Project (IPhD) through the initiative. "Thanks to my IPhD, I was able to lay the foundations of our business accomplishments," recalls Ciftlik, the company's founder and CEO. During his time at EPF Lausanne, the engineer and mathematician, who had previously never worked in biological research, developed a microfluidic device.

Harnessing microfluidics

The core technology of the device is a microfluidic chip. This is traversed by a number of microcapillaries with a diameter of a thousandth of a millimeter. "There is an inlet on one side of the chip through which the capillaries can be filled with liquid. On the other side is an outlet through which the liquid is sucked out again," explains Ciftlik. In the center there is a chamber, the real core of the device. Here, samples can be examined by means of immunohistochemistry (IHC), a method widely used in medicine and biology for visualizing cellular components. To do this, specific antibodies that bind to the components of interest in the sample material are added to a liquid reagent. With the help of different dyes, the bound antibodies can then be localized and quantified.

The novel aspect of Ciftlik's technology, which goes by the name of Fast Fluidic Exchange Technology, or FFeX for short, is the fast delivery and high flux of the antibodies to the tissue sample relative to other available methods. Additionally, not only does the microsystem allow the tissue sample to be brought into contact with the reagent for a precisely defined time period, but the arrangement of the capillaries also ensures a uniform distribution of the liquid over the entire sample. These are all factors that increase the accuracy of the measured results. Ciftlik summarizes the advantages of the microfluidic device: "fast and precise!"

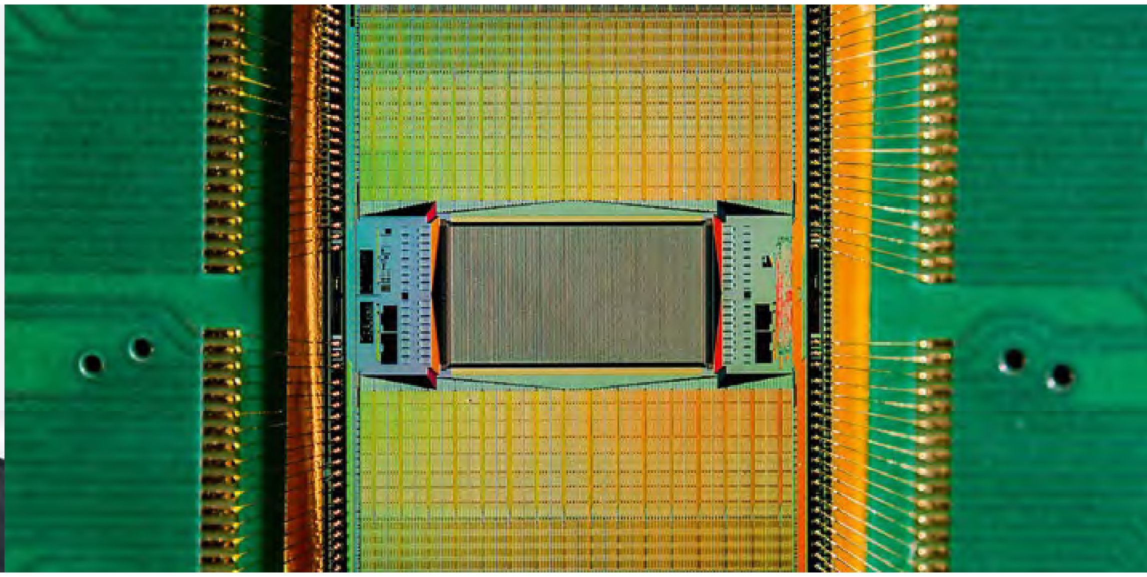
Top-ten finish

Ciftlik and his team envisage that their technology will be mainly used in diagnostic laboratories, where essential information about tissue samples can be passed on to surgeons during time-critical operations to help optimally inform decision-making. "With conventional devices, IHC staining takes several hours. FFeX delivers a result in as little as 12 minutes," emphasizes Ciftlik. Furthermore, the device can also be operated by laboratory personnel without any prior experience with microfluidics – yet another advantage for Lunaphore, which aims to make a name for itself in the diagnosis of breast and lung cancer worldwide. The chances are high that the young entrepreneurs will succeed in their goal. An indication of this is given by the numerous prizes that have been awarded to the company over the past couple of years, not least a top-ten place in the past three years' Top 100 Swiss Startup Awards. In addition, Lunaphore Technologies SA was one of 18 young companies selected to present their business idea to 200 investors and CEOs at the 2017 World Economic Forum's Annual Meeting of the New Champions.

The company is also making progress in its global expansion. Ciftlik and his team have already been able to demonstrate their device at several hospitals and laboratories at home and abroad, where it is being tested by experts. Despite the success, Ciftlik has managed to remain grounded. "Good products need time to grow and constantly develop," he says sagely.

Lunaphore Technologies SA
The power of tissue diagnostics

More information can be found at: **www.lunaphore.ch**

According to Michele Fiscella, the MaxWell technology is an ideal tool for basic research, enabling the long-term monitoring of single-cell activity as well as network dynamics. Photo microchip: Jan Müller et al., Lab Chip, 2015, 15, 2767–2780.

The company MaxWell Biosystems AG was founded in 2016 in Basel. The founding scientists themselves are not the only ones enthusiastic about the enterprise and its business idea. “Last year we received 130,000 Swiss francs from the startup promoter Venture Kick,” says Michele Fiscella with pride. Fiscella is one of the four founders of this startup, which develops microchip platforms. The company currently offers two products, the MaxOne Single-Well and the MaxTwo Multi-Well platforms.

The MaxOne was the first product to be developed, and the main motive behind the establishment of the company. “Two of my business partners, Urs Frey and Jan Müller, developed MaxOne during their PhD studies at ETH Zurich. As part of my SystemsX.ch Interdisciplinary PhD Project (IPhD), I developed methods to make the device compatible with electrophysiological investigations of nerve cells.” At the core of MaxOne is a microchip that measures the functionality of nerve cells. During his IPhD, Michele Fiscella studied the activity of ganglion cells in the mouse retina. “Thanks to the methods I developed, by the end of the project we were able to investigate how different classes of ganglion cells encode a visual stimulus into electrical signals and send them to the brain for further processing,” explains the biotechnologist. With MaxOne, scientists are thus not only able to use the microelectronic platform to measure the function of single neurons, but also for the study of whole neural networks.

Fast and yet exceptionally precise

This is a remarkable achievement in itself, but for Fiscella and his business partners, this was only just the start. Their next step was to apply their technology to the study of human eye disorders. To this end, the team first examined 30 mice which possessed a gene mutation that also occurs in humans. The scientists, however, did not know what effect the specific mutations had on eyesight. They therefore studied the properties of the neurons in the eye tissue of the rodents with MaxOne. They were able to identify a gene mutation that causes comparable vision deficits in mice and humans. “This mouse strain now serves as a model for the investigation of certain eye disorders in humans,” says Fiscella. It took the MaxWell team less than two weeks to determine this. “Using conventional methods, it would have taken several months,” notes the researcher. The MaxWell technology is not only notable for its speed, but also for its high accuracy. This is no wonder, as MaxOne has 26,400 measurement points as compared to its competitors’ 64. “Thanks to its speed and accuracy, MaxOne is the ideal tool for basic research,” says Fiscella.

No time to rest on one’s laurels

But this young startup does not want to stop there. The scientific and pharmaceutical industries are making increasing use of induced pluripotent stem (iPS) cells in their research. These are obtained through the manipulation of human skin or blood cells and are then transformed into different tissues such as neural or heart tissue. These newly manufactured cells can be used in place of animal experiments to test drug safety by measuring the activity of the iPS cells upon exposure to a substance. “This recent development has opened up a completely new market for us,” enthuses Fiscella. In order to stay ahead in this new domain, the MaxWell team developed MaxTwo, a platform which can carry out several electrophysiology measurements in different wells simultaneously. With these innovative products, the team’s interdisciplinary expertise and their pioneering spirit, it seems like we will be hearing even more from MaxWell Biosystems AG in the future.

MaxWell Biosystems AG
High-throughput, high-resolution functional imaging

More information can be found at: **www.mxwbio.com**

Atlant Bieri

Portrait of a former Transition Postdoc Fellow

The biophysicist

Markus Basan looks like your typical student. But the former Transition Postdoc Fellow is already an assistant professor at the renowned Harvard Medical School in Boston.

His office is sparsely furnished. There are no bookcases, and hardly any seating. "I've been waiting for the furniture to arrive for a while now," Basan says with an apologetic smile.

Only two large blackboards adorn the wall behind him. They are crammed with scribbles and graphs. Typical physicist, you think. However, the curves do not describe the decays of exotic particles, but the growth rates of bacterial colonies.

Basan is a systems biologist who uses physics to try to understand living organisms. In a torrent of words, he describes his research interests. "At first I wanted to work in theoretical physics, but I didn't like the fact that it's not very easy to test your theories. You need huge machines like particle accelerators," he says. "Bacteria, on the other hand, are much easier to handle, so I focused instead on the physics of living things."

Steep career path

Basan is just 33 years young. At the age of 25, he had already completed his PhD. From 2013 to 2016, he worked on his SystemsX.ch Transition Postdoc Fellowship (TPdF). "That benefited me a lot," he states. "It gave me as a physicist the opportunity to expand my knowledge and expertise in biology by working directly in a biology department for the first time. And of course it also gave me peace of mind, knowing that I had a secure source of research funding for a couple of years."

After SystemsX.ch came Harvard. For him, it was love at first sight. "After my results were published, I applied for several positions. When I was invited for a job interview here and met the people in the department, I knew immediately where I wanted to go next. Here people understand me and share the interdisciplinary systems biology mindset," says Basan.

Different energy strategies of bacteria

Now he is in charge of a whole team, including a laboratory. Among other things, he is now pursuing the question of why cells use different metabolism strategies to fuel their growth. For example, if you place bacteria in a sugar solution, they break the sugar down, breathing in oxygen and producing the waste substance CO_2. This process is extremely efficient, consuming little sugar to produce energy.

However, there are bacteria that go about producing energy in another way. They leave the oxygen untouched and produce acetic acid instead of CO_2 as waste. This process is known as fermentation, and consumes huge amounts of sugar compared to the other method. Many mammalian cells, including cancer cells, use this strategy.

Basan and his colleagues found out that the energy strategy employed by the bacteria is linked to their growth rate. If they need to grow fast, they prefer fermentation. "Bacteria can drive fermentation with little effort. It's a bit like a coal-fired power station – the process is not very efficient, but it's cheap," says Basan. "Provided there is enough fuel, fermentation is the better choice for rapid growth." Basan would like to find out if the same is true for mammalian cells, particularly in the context of tissue.

The systems biology approach continues to form the cornerstone of Basan's research. "We measure a lot of things," he explains. "We use sensors to track the bacteria's sugar uptake and examine the size of the bacterial cells under the microscope at different growth rates." The team also uses genetic engineering to alter bacterial properties, like the genes that determine whether a bacterium produces CO_2 or acetic acid. "Our goal is to create a mathematical model or simulation that describes the processes occurring in the cells. This will allow us to see whether there are still gaps in our understanding."

Since moving to the US, Markus Basan has bought a house in Brookline, Massachusetts, where he lives with his wife. "It may be the ugliest house in the area, and was in need of renovation," he says. "But it's in a good neighborhood, and I can cycle to work, which only takes 10 minutes. We've even grown to quite like the house," he smiles.

Basan has nevertheless kept his ties to Switzerland. "I am continuing work with the systems biologists at ETH Zurich. My Swiss colleague Hugo Stocker is currently helping us introduce flies as a new model organism," he says. "And of course, the supervisor from my TPdF, Uwe Sauer, remains an important mentor and collaborator."

More information about Markus Basan and his research can be found at:
https://basan.med.harvard.edu

In pictures: 10 years of SystemsX.ch


Dinner, international conference 2011


Social activity, retreat 2013


Poster session, international conference 2014


Panel discussion, All SystemsX.ch Day 2015


Poster prize winners, All SystemsX.ch Day 2016


Scientific talk, All SystemsX.ch Day 2008

You can see more photos at: www.systemsx.ch/photos

A journey through the human body

Last year, SystemsX.ch produced a documentary film which portraits a number of the initiative's research projects. The film, titled "The Human Body: the ultimate frontier of complexity," takes viewers on a journey of discovery into the human body, exploring the frontiers of systems biology research into ageing, memory, personalized medicine and more.

An app accompanies the film, digging deeper into the research being carried out by SystemsX.ch scientists. With the aid of text, videos, images and quizzes, the app educates the user on recent advances in systems biology, and is aimed at anyone interested in learning more about this exciting research field.

Both the film and the app are available for free. You can watch the complete film or individual chapters in English, French, German or Italian on our YouTube channel: www.systemsx.ch/youtube.

The app is currently available in English for tablets only (both iPads and Android devices). It can be found by searching for "SystemsX" on your tablet in the app store.

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SystemsX.ch impact analysis

As part of the evaluation of SystemsX.ch, Leiden University (Netherlands) carried out a bibliometric analysis of the initiative's publication output. SystemsX.ch projects have so far generated more than 1700 peer-reviewed articles. Both the incidence of SystemsX.ch publications in high-impact journals as well as the number of citations are more than twice the world average.

You can find their report on our website: www.systemsx.ch/report-leiden. The full impact analysis will be published this year by the State Secretariat for Education, Research and Innovation.

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The last team outing of the SystemsX.ch MO: (from left) Eavan Dorcey, Daniel Vonder Mühll, Katy Pegg, Vanessa Deppeler, Heide Marie Hess, Christa Smith and Marc Mouci.

Time to say goodbye

This is the 35th and final issue of the X-Letter magazine. Over the past 10 years, countless researchers have collaborated with us to explain their research, grant us interviews, give feedback and share pictures. We would like to thank all of you; it was a pleasure working with such a motivated and passionate community.

Those in the Management Office (MO) would like to take this opportunity to say goodbye. Since 2007, a team of between three and seven people has kept the initiative running by overseeing project finances, organizing training events and conferences, keeping the community and the public up to date on systems biology news, and supporting researchers in a variety of other ways. The MO will now be gradually scaled back until 2019, when the final Financial Report is published and the SystemsX.ch partnership formally disbanded.

Now it only remains to say: It was a great experience participating in this adventure together, and we wish you all the best for the future!

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Irina Abakumova, Sabine Abke, Laurence Abrami, Sebastian Abu, Farca Abud, Martin Ackermann, Izabela Adamczyk, Magdalene Adamczyk, Mojca Adlesic, Ruedi Aebersold, Patrick Aebischer, Sebastien Aeby, Christof Aegerter, Tinri Aegerter-Wilmsen, Markus Affolter, José Aguilar Rodriguez, Auxiliadora Aguilera-Romero, Adriano Aguzzi, Christian Ahrens, Lucila Aimo, Fuat Akal, Izzet Akcay, Nassila Akchiche, Ganime Akin, Serap Aksu, Alessandro Alaia, Cem Albayrak, Edouard Albisser, Ilaria Alborelli, Suslov Aleksei, Davide Alemani, Mahdi AleMohammad, Kevin Alessandri, Helen Alexander, Kiparissides Alexandros, Christian Alliod-Miron, Renato Almeida Gondar, Daniel Alpern, Christian Althaus, Andrea Amantonico, Giovanna Ambrosini, Pierre Amey, Avichai Amrad, Stephanie Anchisi, Mikael Anders Sunnaker, Teemu Andersin, Bill Anderson, Renata Andrade Bitar, Stefano Andreozzi, Daniel Andritschke, Paolo Angelino, Daniel Angst, Martin Angst, Maria Anisimova, Stylianos Antonarakis, Helena Antoniadis, Ron Appel, Lee Applegate, Sophie Aquilar, Guilaine Argoud-Puy, Dominique Arlettaz, Ricardo Alberto Armenta-Calderon, Judith Armitage, Pierre Antoine Arnet, Fabian Arnold, Konstantin Arnold, Phil Arnold, Cécile Arrieumerlou, Marcelle Arrigo, Alina Artcibasova, Panu Artimo, Eirini Arvaniti, Peter Ashcroft, Mariamawit Ashenafi, Nicolas Aspert, Daniel Assmann, Meric Ataman, Suzana Atanasoski, Francesco Atzeni, Ulrich auf dem Keller, Tim Aufdenblatten, Aymeric Auger, Elias August, Johan Auwerx, Ima Avalos, Armen Avetisyan, Omar Awile, Taner Aydinalp, Guillaume Azarias, Nadine Bachmann, Sacha Baginsky, Damien Baigl, Ludovic Baillon, Amos Bairoch, Maciej Bak, Chris Bakal, Miroslav Balaz, Bogos Balazs, Csaba Balazs, Mirjam Balbi, Bengt Balgardt, Christopher Ball, Benedicte Balland, Nathalie Ballanfat, Guillem Ballesteros, Kurt Ballmer, Piotr Balwierz, Amir Banaei-Esfahani, Damiano Banfi, Quoc Tran Bao, Diana Barac, Sophie Baranek, Andrea Barbero, Içvara Barbier, Pierre Barbier de Reuille, Katja Bärenfaller, Mario Baresic, Katja Bargsten, Caterina Barillari, Chris Barnes, Célia Baroux, Yves Barral, Sophie Barret, Manja Barthel, Michaël Baruchet, Aditya Barve, Louise Barys, Markus Basan, Konrad Basler, Pascal Basselet, Frédéric Bastian, Nicolas Battich, Alexander Batyuk, Tuncay Baubec, Angela Bauch, Stephane Baudouin, Antoine Baudrimont, Christophe Bauer, Michael Bauer, Stefan Andreas Bauer, Paul Baumgartner, Roland Baumgartner, Thomas Baumgartner, Damaris Bausch-Fluck, Lucia Bautista, Basil Bayati, Mathias Bayer, David Beauparlant, Mirjam Bebi, Johannes Becker, Attila Becskei, Niko Beerenwinkel, Boris Niklaus Begemann, Jonas Behr, Wolfger Behrens, Christian Beisel, Pascal Belkacem, Gwendoline Bellement, Camilla Bellone, Silvia Bellotto, Mattia Belluco, Sami Ben Saïd, Houchaima Ben-Tekaya, Katrin Benakovitsch, Joseph Benesh, Sara Benmohammed, Nicolas Bennett, Ariel Bensimon, Mohamed Bentires-Alj, Rachel Benzies, Andrea Berardi, Philipp Berger, Karen Bergmann, Sven Bergmann, Ludwig Berland, Brigitte Bernadets, Thomas Bernard, David Bernasconi, Helen Bernhard, Philipp Berninger, Nikolaos Berntenis, Yves Berset, Louis-Félix Bersier, Frederic Bertels, Pierre Berthier, Cathy Berthod, Marina Berti, Elena Bertseva, Marion Betizeau, Marie-Hélène Beuchat, Roel Bevers, David Beyeler, Felix Beyeler, Nissrine Beyrouthy, Tanja Bhuiyan, Kaur Navreet Bhullar, Yatao Bian, Elisa Bianchi, Andrej Bicanski, Sabrina Bichet, Dimi Bieli, Melanie Bieli, Franziska Biellmann, Andrej Bieri, Laurent Bigler, Philippe Bijlenga, Vera Bilan, Aivett Bilbao, Biter Bilen, Adem Bilican, Benjamin Bircher, Mirko Bischofberger, Christin Bissig, Francis Bitsch, Mathieu Blanc, Simon Blanchoud, Diana Blank, Olaf Blanke, Sanja Blaskovic, Dagmar Blatter, Erich Blattmann, Peter Blattmann, Christopher Bleck, Stefan Bleuler, Regula Blösch, Lorenz Blum, Yannick Blum, Clemens Blumer, Tanja Blumer, Marcelo Boareto do Amaral, Marie-Luce Bochaton-Piallat, Thomas Bock, Christina Bocklisch, Bernd 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