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Interdisciplinary research

The recipe for innovative systems biology projects

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"Interdisciplinary research requires curiosity, openness, and the willingness to learn from other disciplines."

Photo: © David Schweizer

In fields such as climatology or the engineering sciences, the collaboration between classically separate disciplines has been standard for some time now. But in the life sciences, interdisciplinary research has only started to gain significance over the past 20 years thanks to technological progress. With modern technologies such as next-generation sequencing, systems biology research now generates huge amounts of data, which of course need to be analyzed. With the help of such data, mathematical models can be developed that allow predictions to be made about the processes and behavior of biological systems. In order to accomplish this, however, biologists must work closely with mathematicians, informaticians and specialists from other disciplines.

Interdisciplinary research such as this is the focus of this X-Letter. Biologists, chemists, physicists, mathematicians, engineers, IT specialists and others work together on the projects described here, in order to shed light on the complex relationships underlying biological systems. In this way, the EpiPhysiX project recently uncovered the well-guarded secret as to how chameleons change their color. The collaboration of scientists from a range of fields also has great potential for the future of medicine, where the application of results and methods from systems biology promises to revolutionize healthcare. For this reason, an increasing number of medical doctors are involved in SystemsX.ch research, for example in the PhosphoNet PPM project.

A particularly attractive example of interdisciplinary work is that of Martin Oeggerli, who shows us just how beautiful the marriage of biology and art can be, as seen on the cover of this X-Letter. Through the painstaking coloration of his electron micrographs, the biologist-turned-artist produces beautiful works of art out of the purely scientific.

The challenges as well as the opportunities that interdisciplinary research brings were recently under discussion at the All SystemsX.ch Day. One of the points discussed was that the interdisciplinarity of systems biology research is trickling down to the undergraduate level and that this sort of research will help shape the education of the next generation of systems biologists.

SystemsX.ch actively supports young scientists through its Interdisciplinary PhD Projects and Transition Postdoc Fellowships. Two such fellows, Joao Guimaraes and Julien Limenitakis, talked to us about the ups and downs of interdisciplinary research and are of the opinion that although this type of research is more demanding, it is also much more interesting and effective. Postdoc Severine Urdy would probably wholeheartedly agree; her career shows us the essential ingredients for a successful interdisciplinary research project: curiosity, openness, and the willingness to learn from other disciplines.

We would like to wish you the greatest successes in your own interdisciplinary research, and we hope that you find this newsletter an interesting read.

Daniel Vonder Mühll
Managing Director SystemsX.ch

The physics of epithelia (EpiPhysX)

“If it were easy, it wouldn’t be fun”

The scientists working on the EpiPhysX project seek to find out how skin forms and changes and also how feathers, scales, spines and hairs develop. Their discoveries have even captured the imaginations of fashion designers.

Every child knows that chameleons change color. These animals use this feature as camouflage against predators, to recruit a mate or to intimidate their rivals. But until now, nobody knew how this color change worked. In March this year, researchers from the EpiPhysX project published the solution to this puzzle: the different colors of the chameleon come about not only due to a yellow pigment and cells which can make the overall color seem lighter or darker, but predominantly due to a regular lattice of intracellular nanoscopic crystals within specialized skin cells. “These cells reflect different wavelengths of light depending on the distance between their nanocrystals. Chameleons are able to tune this distance, generating any color in the whole visible spectrum”, explains Michel Milinkovitch, professor in the Department of Genetics and Evolution at the University of Geneva and principal investigator on the EpiPhysX project. Additionally, a second layer of more chaotically-arranged nanocrystals situated underneath the first protects the chameleon from excessive heating.

Michel Milinkovitch investigates how chameleons change their color.

Chameleons, snakes and crocodiles

The chameleon’s ability to change color is just one phenomenon that the researchers are trying to shed light on. They also investigate the formation of skin and its appendages such as hair, spines, feathers and scales. For example, Milinkovitch’s team was able to establish that the scales on a crocodile’s jaws are not like those of a snake, which are genetically determined. In contrast, physical forces cause the formation of cracks on the stiff skin of the crocodile, similar to those in parched earth. Other matters which the researchers strive to elucidate include why the skin of some lizards is hyperhydrophobic, alterations in a snake’s color pattern, or differences in the formation of spines on hedgehogs and tenrecs – spiny mammals which resemble hedgehogs, but are genetically much more closely related to elephants.

“The complexity and diversity of the living world becomes apparent when comparing the different species”, explains the evolutionary biophysicist Milinkovitch, whose group works not with the more common model organisms such as fruit flies or mice, but with rather unorthodox creatures like crocodiles and chameleons. However, working with such animals complicates the research process, as the scientists must first establish the necessary basic information on the breeding and development of these species, which have much longer generation times than common model organisms.

In collaboration with Marcos Gonzáles-Gaitán, Milinkovitch is trying to apply some of the state-of-the-art imaging and biochemistry tools available for the fruit fly and zebrafish to his non-model species. It doesn’t bother Milinkovitch that everything is a bit more complicated with his exotic research subjects. On the contrary. “If it were easy, it wouldn’t be fun”, beams the full-blooded scientist.

Spanning several dimensions

The scientists from EpiPhysX research how epithelia fold and how mechanical forces influence their growth on both a macro- and microscopic scale. While some investigate the formation of crocodile scales or the forces contributing to the development of zebrafish fins, others, including Aurélien Roux, look into what happens when growing tissue is confined inside a small capsule or when dividing cells are physically pulled apart.

In order to collect quantitative data to address these questions, the project members must often think up new methods or develop novel equipment. A prime example is the robot R²OBBIE-3D. "R²OBBIE is able to scan objects up to 1.5 meters long using its moveable arm, which has an integrated digital camera", enthuses Milinkovitch. "On the resulting 3D model, it's possible to discern structures as small as 15 micrometers across, over the whole body of a fully-grown snake or lizard, down to the smallest details such as the shape and color of individual skin cells." This is no mean feat, as imaging methods typically either cover a large area at low resolution or a very small area at high resolution. In collaboration with Bastien Chopard and Andreas Wagner, Milinkovitch uses these 3D images to build cell-based computer models that simulate the development of epithelia.

Extreme interdisciplinarity

Researchers from disparate disciplines work closely together on this project. To explain the chameleon's color change abilities, the involved biologists, physicists, engineers and modelers combined multifarious techniques such as tissue probes, electron microscopy, spectroscopy and computational modeling of photon behavior in soft matter.

"Only with the support from SystemsX.ch were we able to realize an interdisciplinary project on this scale", says Milinkovitch. In his opinion, the research initiative has contributed significantly to a general increase in interdisciplinary research, which he welcomes.

Basic research with practical potential

"We carry out basic research", emphasizes Milinkovitch. However, it turns out that some of the project's findings and developments have great potential for a variety of practical applications. Pathologists and forensic scientists have expressed interest in R²OBBIE the robot for examining their samples.

Even the capsules in which the scientists lock multiplying cells have stirred interest; the EpiPhysX team is growing neurons in capsules that could be smuggled into the brain to produce deficient substances in patients with neurodegenerative diseases such as Alzheimer's or Parkinson's.

"Superhydrophobic skin, like a lizard's, could be used to cover stents which are placed in bodily vessels to keep them open, in order to prevent deposits and blockages from forming", Milinkovitch adds.

Even the world of fashion is keenly interested. "Since we published our chameleon paper, I've received several requests from the textile industry", says Milinkovitch. "Fashion designers are fascinated by the idea of producing clothes that can change color."

EpiPhysX at a glance

Principle investigator: Prof. Michel Milinkovitch

Research groups:

- Prof. Michel Milinkovitch, Laboratory of Artificial & Natural Evolution, Department of Genetics & Evolution, University of Geneva and SIB Swiss Institute of Bioinformatics – Evolution, development and biophysics of non-model organisms
- Prof. Bastien Chopard, Scientific and Parallel Computing Group, CUI, Department of Computer Science, University of Geneva – Numerical modeling
- Prof. Marcos González-Gaitán, Department of Biochemistry, University of Geneva – Development and biophysics of epithelia in *Drosophila* and zebrafish
- Prof. Aurélien Roux, Department of Biochemistry, University of Geneva – Cell and tissue biophysics
- Prof. Andreas Wagner, Institute of Evolutionary Biology and Environmental Sciences, University of Zurich – Robustness analysis of numerical models

Total budget (2013–2017): CHF 7.0 million, including CHF 2.9 million from SystemsX.ch

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

EpiPhysX
The Physics of Epithelia

The tissue thin sections that Peter Wild uses in his work are robotically stained in the lab.

Personalized Precision Medicine (PhosphoNet PPM)

Unnecessary prostate operations could be avoided

Prostate operations can have unpleasant consequences, including incontinence and impotence. Researchers are working on new methods which should allow doctors to distinguish more precisely between insignificant and aggressive prostate tumors, meaning that in future, unnecessary operations will be minimized and fewer patients will have to expose themselves to the associated risks.

Most men over a certain age fall victim to prostate cancer. “At the age of 80, there is a roughly 80 percent chance of contracting the disease”, says Peter Wild, head of the Systems Pathology & Clinical High-Throughput Genomics Laboratory at the University Hospital Zurich. “But fortunately not every tumor is aggressive nor must it be removed.”

As with any other operation, removal of the prostate involves a likelihood of internal bleeding, infection and also particularly unpleasant side effects such as incontinence or impotence. “It’s therefore very important to be able to clearly differentiate between the insignificant and aggressive cases”, explains Wild, who leads one of the research groups involved in RTD Project PhosphoNet PPM. Diagnosis is based on a tissue sample, or biopsy, taken from the patient. A pathologist then examines the tissue under a microscope and assesses how severely it differs from healthy tissue. If the malignant tumor appears aggressive, it is surgically removed or irradiated. If clearly insignificant, it stays, and patients are actively monitored.

“The problem lies in those cases which are not so clear-cut, where the carcinoma appears neither unequivocally aggressive nor insignificant”, explains pathologist Wild. Even nowadays there is no set of reliable criteria to aid the decision as to whether or not to operate. This means that in case of doubt, doctors as well as patients would rather decide in favor of an operation to be on the safe side. Wild is convinced that many prostate operations would be avoided if we could more accurately judge how aggressive a tumor is.

“In future every patient should be able to profit from a tailor-made therapy thanks to a personalized diagnosis.”

This is exactly what the researchers involved in PhosphoNet PPM wish to address. The acronym PPM stands for Personalized Precision Medicine, the project’s overarching goal. It is hoped that in future, patients will receive much more precise diagnoses and tailor-made treatments as a result of more individualized analyses on the level of proteins or genes. At this stage, the PhosphoNet PPM

team is looking for characteristic features of the cancer that may aid evaluation in ambiguous cases. Based on these findings, they want to develop a test that allows the rapid and precise verification of a tumor's nature, so that patients must only undergo operation if the tumor is aggressive.

Large collection of prostate carcinomas

For their work, the researchers require a supply of cancerous tissues. "I've been collecting prostate tumors for years", says Wild. As part of the large-scale ProCOC study, the pathologist collected tissue and blood plasma samples, as well as the medical histories of around 450 consenting patients.

"The PhosphoNet PPM project could act as a template for further projects focusing on different types of cancer."

Every single prostate from this study will be dissected into various parts after removal. One such part will be rapidly "snap-frozen" and thus preserved for later examination. A large part will then be preserved in formalin and subsequently poured into paraffin blocks to enable it to be sliced. These wafer-thin slices will then be mounted onto microscope slides and stained.

"These thin sections contain a wealth of information", emphasizes Wild. "For example, we can see how much of the prostate tissue is affected, how much the tissue has changed and how heterogeneous the tumor is." Using certain staining methods or antibodies with colored markers, the researchers are able to identify particular proteins that the cancer produces. In a similar way, they are able to single-out individual genes and discern whether they are altered in different parts of the tumorous tissue. One such gene in which the researchers are particularly interested is *PTEN,* responsible for inhibiting tumor growth. Wherever this gene is lacking, the cancer is allowed to spread unchecked.

In order to analyze peculiarities in the tumor's genome and protein composition, the team uses tiny samples taken from either freshly extracted or conserved prostate tissue, subjecting these to cutting-edge high-throughput methods. One example of these is so-called next-generation sequencing, which is able to quickly deduce a sample's DNA and RNA sequences. Another example is a mass spectrometry-based technology developed by Ruedi Aebersold's group, which can identify a sample's entire protein profile.

Clever computing

The goal is to be able to use this new abundance of data, coupled with medical histories, in order to predict the further course of the disease in each individual patient. In time, pathologists will be supported in their work by a computer model. "We're developing a classifier in collaboration with IBM Research – Zurich", says Wild. "The model is currently learning how to differentiate between aggressive and insignificant tumors." It has the difficult task of sifting through countless variables for relevant information, identifying crucial patterns and indicators, known collectively as markers, in order to reveal the possible future progress of the tumor.

The first data sets from the ProCOC cohort have already been integrated into the model. These include parameters such as gene and protein composition, as well as information from medical histories like details of administered drugs or survival rates. Using cognitive computing technology, the model will continue learning using the remaining ProCOC data until it can reliably differentiate between aggressive and insignificant tumors. "We will then use data from a second cohort, where we already know the disease's outcome, in order to validate the model," explains Wild. "This will show us just how precisely our model predicts a cancer's development."

Understanding the cancer's tricks

Beside the classification of prostate carcinomas, the researchers involved in the PhosphoNet PPM project are also working on another unsolved problem, that of castration-resistant prostate cancers. "Sometimes the cancer has spread too far to be cured by surgery or radiation, and particularly aggressive prostate tumors that have been removed can still reoccur", clarifies Wild, "mostly in the form of bone metastases." These cases call for even more drastic measures. Since the tumor is driven by testosterone, this hormone's production must be halted with drugs or surgically hindered by the removal of the testes. This can lead to side effects like reduced libido, impotence, hot flushes, growth of breast tissue or weight gain in the affected men, but the hormone therapy is usually enough to cause the tumor to stop or even recede.

Unfortunately, this does not always work. After a while, castration-resistant tumors manage to circumvent even these proce-

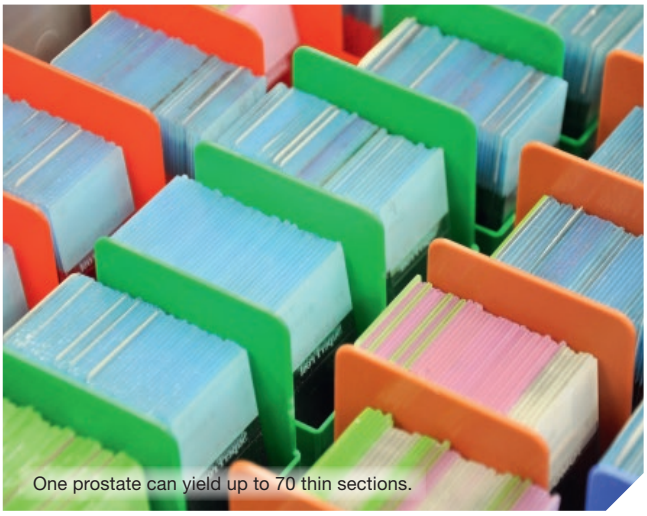
Pathologist Wild marks the place where the tissue has been altered by cancer.

dures. They can, for example, form more androgen receptors in order to exploit even the smallest concentrations of testosterone left in the body. Or they can start stimulating production themselves, or simply switch to a different hormone to use as fuel.

The PhosphoNet PPM team wants to explore the mechanisms behind the tumor's ability to survive the withdrawal of testosterone. This knowledge will also have an impact on the choice of appropriate medication. Especially since we know that new, otherwise effective medicines can paradoxically stimulate a tumor's growth in some patients. "The more we know about the behavior of the tumor, the better we can predict which medication will be most effective in each case", explains Wild. "With this new-found knowledge, we might even identify novel drug targets."

Towards a more personalized medicine

The research work is in full swing and will continue even after PhosphoNet PPM finishes. "This project could act as a template for further projects focusing on different types of cancer", says Wild. The archiving of data and samples is something the pathologist is very passionate about. His goal is to digitize the thin sections and archive them, along with the gene and protein profiles, in a central, digital biobank. In future, researchers will be able to access and use this resource to extract relevant information, which will of course be anonymized.



One prostate can yield up to 70 thin sections.

Without doubt the most important facet for Wild is that the results coming out of projects like this are actually applied in hospitals. "The patients always come first. In future every patient should be able to profit from a tailor-made therapy thanks to a personalized diagnosis." The findings of the PhosphoNet PPM project will be an important step in this direction.

PhosphoNet PPM at a glance

Principal investigator: Prof. Ruedi Aebersold

Research groups:

- Prof. Ruedi Aebersold, Institute of Molecular Systems Biology, ETH Zurich – Proteomics
- Prof. Andreas Beyer, CECAD, University of Cologne – Systems and computational biology
- Prof. Bernd Bodenmiller, Institute of Molecular Life Sciences, University of Zurich – Imaging mass spectrometry and network analysis
- Prof. Manfred Claassen, Institute of Molecular Systems Biology, ETH Zurich – Computational biology
- Prof. Dr. med. Silke Gillessen, Department of Medical Oncology, Kantonsspital St. Gallen – Oncology
- Prof. Lucas Pelkmans, Institute of Molecular Life Sciences, University of Zurich – Image based transcriptomics
- Prof. Dr. med. Peter Wild, Institute of Surgical Pathology, University Hospital Zurich – Systems Pathology & Clinical High-Throughput Genomics Laboratory
- Prof. Christian von Mering, Institute of Molecular Life Sciences, University of Zurich – Bioinformatics

Total budget (2013–2016): CHF 7.1 million, including CHF 3.0 million from SystemsX.ch

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

PhosphoNet PPM
Personalized-Precision Medicine

Maja Schaffner Christa Smith

All SystemsX.ch Day 2015

Interdisciplinary research in all its diversity

This year's All SystemsX.ch Day underlined just how interdisciplinary the research in systems biology has become. The panel discussion addressed some of the challenges associated with this type of research.

The SystemsX.ch community gathered at the Stufenbau in Bern on September 15, 2015. Around 200 researchers from all over Switzerland took part in the fully booked event to present and discuss their projects, and get to know the work of others.

The talks, which featured young, upcoming researchers as well as experienced scientists, showcased the breadth of SystemsX.ch research and offered insight into a number of diverse projects. For example, Paola Picotti from the ETH Zurich described her research on the function of genes that protect the brain from protein aggregation and associated diseases such as Alzheimer's. John McKinney from the EPF Lausanne talked about the development of new microscopy techniques involving the combination of optical and atomic force microscopy, making it possible to observe individual living bacterial cells for a whole week.

The diversity of topics was also evident in the 82 posters presented at the event. The three best posters in each of two categories were awarded prizes. The winner in the PhD student category was Denis Samuylov from the ETH Zurich, and in the postdoc category Hartland Jackson from the University of Zurich took first prize.

The keynote speaker, Steven Altschuler from the University of California San Francisco, presented a beautiful example of interdisciplinary systems biology research. In his talk, Altschuler explained how he and his team, using a combination of imaging techniques and computer modeling, investigated how the many optical nerves of the fly's compound eye manage to wire themselves efficiently to the brain – so as to result in a single image.

The panel discussion on the challenges of interdisciplinary research focused largely on the education of the next generation of systems biologists. One of the principle issues discussed was whether systems biology benefits more from scientists who are very specialized in their fields, or from generalists who are familiar with a range of disciplines. The panelists, along with some members of the audience, were of the opinion that students should be armed with principles, concepts and methods that they can use in many different areas, instead of being required to learn material by heart, as used to be the case in traditional biology studies. They were also united in their viewpoint that the key to successful interdisciplinary research lies in the ability of each team member to understand the language used by their fellow scientists, no matter what field they come from.

Last but not least, the end of day barbecue dinner in the garden provided the opportunity for participants and speakers to relax and get to know each other better in an informal and atmospheric setting.

Researchers at the All SystemsX.ch Day discuss the challenges of interdisciplinary research: (from left) Verdon Taylor (UniBas), Nouria Hernandez (UniL), Dieter Imboden (moderator), Thierry Soldati (UniGE), Lucas Pelkmans (UZH), Niko Beerenwinkel (ETHZ).

Two young researchers talk about their Transition Postdoc Fellowships (TPdF)

Diving into a new scientific field

The SystemsX.ch Transition Postdoc Fellowships enable young researchers to immerse themselves in a new, systems biology-relevant field. Joao Guimaraes from the University of Basel, and Julien Limenitakis from the University of Bern have seized this opportunity and now work on their own interdisciplinary projects supported by SystemsX.ch.

Julien Limenitakis (left) and Joao Guimaraes have very different scientific backgrounds, and both are currently working as computational biologists on their own interdisciplinary projects.

Why did you decide to apply for a Transition Postdoc Fellowship (TPdF)?

Joao: One of my goals was to develop my own project and to become more independent in my research. An advantage of the TPdF is that besides the salary, further support is available for your own experiments. My second goal was to shift my focus away from synthetic biology and start using systems biology approaches to study more complex, natural systems. The TPdF enables me to do both these things.

Julien: During my PhD and first postdoc position, I had been increasingly confronted with more and more complex data and large data sets. The TPdF offered me the chance to complement my biology background with new skills in data analysis and modeling, so that I could begin to evaluate the data myself.

Potential postdocs must find a host group for their TPdF. How did you choose yours?

Julien: I had already begun further training in data analysis and modeling when I heard about the call for proposals. It was clear to me that I wanted to continue to focus on microbiota, communities of microorganisms that colonize the human body. For this reason, I thought about what kinds of questions I would like to address in my project, and looked for a suitable lab. At that time, the researchers in my current group were not carrying out any computational analysis but were planning to start. It was perfect timing.

Joao: I had already started working in my current host group when I found out about the call for proposals for Transition Postdoc Fellowships. My host group offered me the perfect conditions for setting up my own interdisciplinary project.

Was it difficult to write your own project proposal?

Joao: I did in fact find it very challenging. First, I had to become familiar with a whole new field of research in a very short time. Then, I had to identify an ambitious and provocative research question based not only on existing publications but also on my own preliminary results. In addition, the proposal had to be extremely detailed. But the most difficult part of all was defining a research plan that was feasible within the time given. Scientists tend to be rather overly optimistic in this context. (laughs)

Maja Schaffner Christa Smith

What sort of transition have you undergone as part of your TPdF?

Julien: The focus of my first postdoc project was on molecular biology-based methods. In contrast, in my TPdF project I am now responsible for data analysis and modeling. The research area has remained similar; my interests still revolve around microbes. But through my current work as a computational biologist, I have gained a new perspective, which helps me approach research questions from different angles.

Joao: For me it was the other way around. I was already working as a computational biologist and have shifted to a different research area for my Transition Postdoc Fellowship, from synthetic to systems biology. Instead of investigating bacterial genomes, as I did during my PhD, I wanted to learn how more complex systems, such as mammals, regulate gene expression.

The collaboration between computational biologists and experimentalists in my current lab is also a new experience for me. Here, I have been heavily involved in the experimental side for the first time. This means that I take part in the planning of experiments and also help with the troubleshooting if something goes wrong.

Which initial challenges did you face?

Joao: Everything was new to me. I first had to familiarize myself with the literature in my new field. I also had to become acquainted with several next-generation sequencing methods, what sort of data they generate and what kind of questions they can be used to address. It was also essential for me to learn how the other people in my research group thought.

Julien: The greatest challenge was and still is the fact that I am the sole computational biologist in our group. I managed to learn a lot before the start of my TPdF through courses and private study. In addition, I picked up a great deal of know-how from my external mentor at the Swiss Institute of Bioinformatics, who helps and advises me still.

However, knowing what I know now, if I had found a lab with an integrated computational group working on microbiota, I would probably have chosen to go there. I think I would have been able to learn more, and faster.

What is the most exciting part of interdisciplinary research for you?

Joao: As a scientist, you're always curious and eager to know more: what's going to happen next, and how can I explain what I see? When you approach your research problem from multiple perspectives using methods from other scientific disciplines, it's easier to see and understand the bigger picture.

Julien: I find interdisciplinary projects extremely stimulating. In this kind of research, scientists from all sorts of different disciplines constantly learn from one another. Through this, innovative ideas spring up, contributing to the development of biology as a whole and systems biology in particular.

Do you think your TPdF will help you in your future careers?

Julien: Definitely! It allows us to carry out research independently and make our own decisions. This builds self-confidence and prepares us for the next step in our careers. For example, I am now thinking about applying for further funding beyond my TPdF.

Joao: Yes, I'm sure it will. By gaining insight into a new research field, we have been given the chance to learn a great deal and to expand our scientific horizons. I'm also convinced that the fellowship helps us develop competencies that we'll be able to draw on as future group leaders: we already have experience in formulating research questions and writing our own project proposals, as well as outlining research timelines and budgets. I also think that being part of the close network of the SystemsX.ch community is definitely a great advantage. These are the optimal conditions for the next step on the way to an academic career.

Julien Limenitakis's SystemsX.ch project at a glance

Project title: Systems modeling of the metabolic network of a gut microbial community

Fellow: Dr. Julien Limenitakis, University of Bern

Host research group: Prof. Dr. med. Andrew Macpherson, Inselspital, University of Bern

Project duration: 2013–2015

Joao Guimaraes's SystemsX.ch project at a glance

Project title: Mediation of specificity in mRNA translation by heterogeneous ribosomes

Fellow: Dr. Joao Guimaraes, University of Basel

Host research group: Prof. Mihaela Zavolan, Biozentrum, University of Basel

Project duration: 2014–2016

With his art, Oeggerli wants to showcase the beauty of science to a wider audience.

The perfect union of two contrasting disciplines

Biology meets art

Martin Oeggerli is the Micronaut. With an electron microscope, the microbiologist-turned-artist dives into the microcosm to explore its hidden treasures. He makes the invisible visible and shows us beauty where we would least suspect it.

The delicate mouthparts of mosquito larvae, a dividing cancer cell or intestinal bacteria colored like jolly sweets, the science photographer Martin Oeggerli leads us into an unknown world with his captivating pictures. The microbiologist from Basel first came into contact with this new world during his diploma thesis on bat hairs. “Under the scanning electron microscope, the bat hairs looked like nested ice cream cones. I was immediately fascinated by their aesthetic”, explains Oeggerli.

Since then, the artist has been exploring the microcosm, discovering details and structures that no one had ever seen before. The pictures from his expeditions into the unchartered world of the microscopic have received numerous international science and photography awards, and have appeared in journals such as Cell and Nature. In February this year, Oeggerli’s work was featured for the fifth time in National Geographic; the renowned science magazine published an entire series of his pictures, titled “Mighty Mites”.

Making the invisible visible

The starting point for a Micronaut picture is usually an animal or plant specimen, which Oeggerli receives from scientists all over the world. For the artist, the selection of a sample is an important step in the process of creating the perfect image, because in nature, not all specimens are equal. “I want to show Nature in all her perfection, which is why I look for pristine specimens with every bristle intact”, says the scientist with a grin.

“This is the most exciting part of my work. I never know what’s awaiting me down there.”

However, it’s still a long journey until the finished work of art. Micronaut painstakingly completes each individual step of the process himself. First, he fixes and dries out his treasured samples so that the shape and surface structure remain perfectly preserved. Next, the samples are coated with an ultrathin layer of gold so that they become electrically conductive and can be scanned with the electron microscope.

The heart of the scanning electron microscope (SEM) is a beam of electrons. The beam excites the atoms in the sample, causing

Christa Smith

further electrons to be emitted. These are then captured by a detector, which converts the signal into a grey value for each individual pixel. The electron beam scans the surface of the sample line by line, resulting in a sharp, two-dimensional monochrome image.

The SEM is able to magnify the tiny samples up to 500,000 times. Structures can be visualized even down to the level of viruses. “This is the most exciting part of my work”, says Oeggerli. “I never know what’s awaiting me down there.”

Bringing pictures to life

Thanks to the SEM’s large depth of field, the images show a wealth of detail – almost too much for the human eye. This is why Oeggerli starts by tidying up once he has found a scientifically interesting and aesthetic detail. He selects similar structures and shapes, and colors them uniformly. “Only then can I begin to comprehend everything that I see in the picture”, emphasizes the microbiologist. He colors the images layer upon layer on his laptop, slowly breathing life into them.

“I try to use color to shine a spotlight on interesting details in each picture.”

As a scientist, Oeggerli does not simply reach blindly into the paint pot, but carefully selects colors that lend his works a photo-realistic quality. For him, even the smallest details are important. He carries out extensive research on the subject of his images, for example on color variability amongst individuals, in order to represent reality as accurately as possible.

He takes certain features or structures that he finds particularly interesting from a scientific point of view, and colors them in such a way that the eye is naturally drawn to these details. His use of color helps to pull certain details “into the spotlight”, as he himself describes, and creates a work of art out of something purely scientific.

Gateway to the microcosm

Micronaut spends up to 100 hours honing a single image, not least due to the size of his works. Oeggerli’s original works are 1 by 1.5 meters in size, inviting the viewer to discover an abundance of detail.

With his pictures, Oeggerli opens the gateway to a new world. Miniscule pollen grains become beautiful structures, big as balloons, with grooves, nodules, barbs and delicate filigree. Tiny mites grow into terrifying monsters. Surfaces, which to the naked eye appear flat, are revealed as the turbulent, complex landscapes they really are. As an observer, one feels suddenly dwarfed, a tiny speck in the midst of the microcosm.

In his latest series of pictures, Oeggerli transforms the lowly mite into a star. This specimen belongs to the genus *Speleorchestes*. The mouthparts of many mites are equipped with more tools than a Swiss army knife. They include short pincer-like appendages and tiny limbs for handling food. Picture: *Speleorchestes sp.*, Magnification 2,500:1, © Martin Oeggerli, supported by School of Life Sciences FHNW.

Micronaut calendar 2016

The new tabletop calendar from Micronaut is now available. Find out more about Martin Oeggerli and his work at: **www.micronaut.ch,** or take a look at his fine art editions at: **www.oeggerli.com.**

How to become a highly multidisciplinary scientist

Sometimes all it takes is a change of perspective

Severine Urdy has been interested in the living world since she was a child. Today she is a highly interdisciplinary systems biologist. The young researcher has repeatedly switched research fields to address a fundamental biological question from a multitude of perspectives.

On her path to becoming an interdisciplinary researcher, Severine Urdy studied the growth of the mollusk shell.

"I just don't understand how some people manage to be interested in only one thing", jokes Severine Urdy, Transition Postdoc Fellow at the University of Zurich, when asked why she has changed research fields so often. But this statement summarizes her approach to science in a nutshell: conventional specialization is not Severine Urdy's style.

Early fascination for the living world

Her interest in all facets of the living world manifested itself early in Severine Urdy's life. In her family's garden in the countryside near Lyon in France, she spent much of her time observing small creatures like earthworms, insects and snails. "Once I received a children's microscope as a present", she remembers. "From then on I collected and observed almost everything with it."

But books also fascinated Severine. "I especially loved a 12-volume encyclopedia, which allowed me to learn something new on every page", recalls Urdy. She also owned a series of anatomy books and a book full of pictures of Siamese twins, double-headed and deformed babies. "I think these books influenced me a lot, since all of my scientific interests revolve around anatomy and how anatomical structures change through development and evolution", says Urdy.

Starting on the interdisciplinary track

After high school and a short stint at an engineering school, Urdy realized that she was motivated mostly by fundamental biological questions. A book sharpened her interest."'Developmental Biology' by Scott Gilbert was love at first sight. I read it from cover to cover over the summer", Urdy remembers. She then decided to study biology at the University of Lyon, starting with the most general option, which included anatomy and embryology. Disappointed by the lack of evolutionary emphasis, she switched to geology for her master's studies. "At that time in France, the theory of evolution and the history of life on Earth was almost exclusively taught to the master's students in the geology section", she explains.

To strengthen her mathematical background, Urdy subsequently changed her specialization yet again to complete her master's degree in analysis and simulation of biological systems, a

kind of precursor of systems biology. At this time she also wrote her first models in Matlab. “I loved my undergraduate years and decided that I definitely wanted to spend the rest of my life working as a researcher.”

The evolutionist’s viewpoint

Urdy started out on her path to a scientific career with a PhD at the Paleontological Institute in Zurich. The aim of her project was to draw links between the development and evolution of mollusks and to find out more about the relationship between their growth and form. “I raised marine snails in aquariums to study the growth and shape of their shells”, she recounts. She monitored the growth of the shells of these living gastropods and established mathematical simulations of their morphogenesis. “These models are general to mollusks and can therefore also be applied to extinct ammonites, which we cannot study in the same way as living organisms.”

Gaining a computational biologist’s perspective

After finishing her PhD and a subsequent postdoc position in the same lab, Urdy continued pursuing the question of why tissues grow, stop growing and have the shape they do. At the Center for Mathematics and Informatics in Amsterdam in the Biomodeling and Biosystems Analysis Group, she learned how to write developmental cell-based models and began to apply them to a wider range of topics, including the development and organization of epithelial tissues. “Theoretical modeling and simulations help us understand biological systems”, the scientist is convinced. “With their help, we can more easily predict what will happen when factors like the rate of cell proliferation change.”

Stepping into a cell biologist’s shoes

“In Amsterdam I realized that to test my models, I had to work closely with experimentalists”, says Urdy. She found the ideal conditions for doing so during her postdoc position at the University of California San Francisco. Under the supervision of two medical doctors, she worked both in the Department of Bioengineering and Therapeutic Sciences and in the Department of Cell Biology and Anatomy concurrently. “Participating in experimental design was enlightening for me”, Urdy admits. “Only then do you realize how many constraints there are and how many compromises are necessary.”

She developed a cell-based model of growth regulation in dog kidney cysts and was able to compare it directly to the experimental data acquired in the lab. “Although the study on cysts was not related to evolution, I kept an evolutionary eye on it”, Urdy remembers. She used multivariate statistics methods such as analysis of variance. “Such methods may appear novel to cell biologists, but they are standard in ecology and evolutionary studies.” In Urdy’s opinion, the study of variation is crucial in disciplines such as evolutionary biology, where there is little control over the different sources of variation. But it also plays a role in *in vitro* systems, where variation appears to be under control. “Quite often, it is actually variation itself that guides us towards elucidating the mechanisms underlying a particular phenomenon”, Urdy adds.

Learning to think like a physicist

Currently, Urdy is working in the Disordered and Biological Soft Matter Group, led by Christof Aegerter, at the Physics Institute of the University of Zurich as part of her Transition Postdoc Fellowship (TPdF). “This is by far the most multidisciplinary lab I’ve worked in yet. Everybody comes from a different background”, says Urdy. The group’s scientific work covers topics ranging from the development of new imaging techniques to the investigation of the behavior of foams and the effects mechanical forces have on the developing wing discs of *Drosophila melanogaster*. Once more Urdy is modeling; this time to study the principles driving growth arrest and fold formation in *Drosophila* wing discs.

“My TPdF is a great opportunity to complement my background by learning how to approach the relationship between growth and shape from a physicist’s point of view.” Urdy’s recipe for successful interdisciplinary cooperation is simple: one has to be interested in others’ research topics and learn from each other. Urdy herself likes “absolutely everything” about interdisciplinary research. The best part: “If you get bored or stuck, you can look at a problem from a different perspective and find an unexpected solution.”

Severine Urdy’s SystemsX.ch project at a glance

Project title: Morphogenesis of monolayer epithelia: models and experiments

Fellow: Dr. Severine Urdy, University of Zurich

Host research group: Prof. Christof Aegerter, Physics Institute, University of Zurich

Project duration: 2014–2016

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

Bart Deplancke examines the genes of hundreds of fruit flies in order to unravel the mystery of cellular aging.

Systems biology of aging (AgingX)

Our fate lies in our genes

Getting old is easy, but doing so healthily is not. This is why researchers at the EPF Lausanne are investigating the genetic basis of the body's decline in old age. Their findings could help us live healthier for longer.

It seems that the members of some families live much longer than others, with some, for example, living to a ripe old age of over 90 despite smoking heavily their whole lives. Researchers now know that our genes are largely responsible for such long lifespans, although exactly which genes play a role is as yet unknown.

Bart Deplancke, bioengineer and head of the Laboratory for Systems Biology and Genetics at the EPF Lausanne, wants to change this. He is the project leader of the AgingX project, which takes a closer look at the hereditary causes of aging.

The project focuses largely on establishing the genetic factors contributing to a long healthspan; that is, the part of our lives in which we are relatively fit and healthy. Sadly, many people simply become sicker as they grow older. "We want to find out in what ways some people are genetically predisposed to healthy old age and how their genetic make-up slows the aging process", explains Deplancke.

Eliminating environmental factors

These questions are extremely difficult to answer. There are around 25,000 genes in the human genome. Researchers have already managed to link a few hundred of these to the aging process, although exactly which combinations help us grow old in good health is still unknown. To make things even more complicated, environmental factors such as diet, exercise or smoking habits can influence whether or not our genes can exploit their full potential.

With AgingX, Deplancke and his collaborators want to remove such environmental factors from the equation to gain an unclouded view of the complex interplay of genes. To tackle this, four research groups work together to combine their expertise. They work with mice and fruit flies, all of which live in a standardized environment. Every animal receives the same food and lives under the same light and temperature conditions.

Inbreeding sheds light on aging process

Even the animals' genomes need to be standardized. This is why Deplancke's colleague at EPFL, Johan Auwerx, works with 60 inbred mouse strains. Each mouse from any one of these strains can be traced back to one female and one male mouse, which also came from inbred strains.

Normal mice possess two sets of genes, one from the mother and one from the father. This is like an insurance policy. If one gene is missing or faulty, its partner can take over the job. These conditions are however not very practical for statistical analysis, as it is impossible to tell which of the two genes is active in any one mouse. With an inbred mouse strain, this is no longer a problem, since both sets of genes are identical.

The researchers are now observing the life cycles of these mice. They are particularly interested in their fitness and time of death. The initial results are striking. Despite the fact that these 60 mice strains all belong to the same "family", the lifespan varies hugely from mouse to mouse.

"Mice typically live for about two or three years", explains the project leader, "but the Auwerx Lab has identified some mice strains which have already passed the three-year mark and are still going strong." Other strains, in contrast, died of old age after just a year and a half.

This means that the oldest mouse lived at least twice as long as the mouse that died youngest due to its particular combination of genes. "This shows us that even just the distribution of maternal and paternal genes has a huge impact on the lifespan", concludes Deplancke. The analysis of the results will later tell us which combinations of genes contribute to a long, healthy life.

In the next step, the researchers aim to investigate the healthspan of the mice in the same way. "This, however, is more difficult to measure", says Deplancke. To analyze this, the mice are for example put in an exercise wheel at regular intervals, where they undergo a sort of fitness test.

The cell's powerhouse

Another important topic for AgingX is mitochondria. These are tiny powerhouses that supply our cells with energy. They are the only organelles within cells that possess their own DNA. Deplancke suspects that even here, there could be genes or combinations thereof, which influence our health- and lifespans. "The mitochondrial genome has often been neglected in research until now. That's why we're taking a closer look", says Deplancke.

Mitochondria convert sugars and fats into chemical energy, which drives every process in a living organism, from muscle contraction to the transmission of nerve impulses in the brain. We know that the cell's energy supply becomes less reliable with age, leading to ailments such as obesity, diabetes, cardiovascular disease and fatty liver.

To find out which mitochondrial genes contribute to particularly rapid aging, Deplancke and his team work with 140 strains of fruit flies. These flies must also undergo regular fitness tests. The flies are placed in a glass tube with a beam of light in the center. The fitter the fly, the more often it crosses this light barrier. A computer registers each occurrence, establishing how active each fly is. The fruit flies' genes being known, it is possible to then link them to the fitness data.

The statistical analyses from both experiments are currently underway. Ideally, Deplancke and his colleagues will be left with a list of genes and gene combinations known to contribute to a long, healthy life. "We will then compare these results with the human genome", says Deplancke. Flies share around 60 percent of their genes with humans, and mice 80 percent, meaning that many of these results will be relevant for us, too.

Living healthier, longer

This knowledge will one day help us to stay fit as long as we can. "In the future it will be completely normal to have a genetic test done at the age of 20 or so, to find out one's life expectancy", predicts Deplancke. But that's not all. A genetic test may also be able to show which bodily systems will be the first to degenerate. "If we had this information, we would be able to take preventative measures in our youth", enthuses Deplancke. For example, if the test shows that muscular atrophy is due to set in at the age of 60, the affected person could start attending regular muscle-building training at the age of 50, or taking medication which hinders progress of the disease. "We will live longer, healthier and happier lives", says Deplancke.

AgingX at a glance

Principal investigator: Prof. Bart Deplancke

Research groups:

- Prof. Bart Deplancke, Institute of Bioengineering, EPF Lausanne – Systems genetics
- Prof. Johan Auwerx, Institute of Bioengineering, EPF Lausanne – Systems physiology and genetics
- Dr. Zoltan Kutalik, Department of Medical Genetics, University of Lausanne – Medical genetics and statistics
- Prof. Marc Robinson-Rechavi, Department of Ecology and Evolution, University of Lausanne – Evolutionary and computational biology

Total budget (2013–2016): CHF 6.0 million, including CHF 3.0 million from SystemsX.ch

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

AgingX
Systems Genetics Approach to the Biology of Aging

Self-organization of plant root growth

Communication on the growth front

Plant stem cells are master architects, able to grow complex structures such as root systems. Researchers at the University of Lausanne want to understand this process with the help of computational models.

Alice Breda tries to understand the communication between cells in the root tips of plants.

"We carry out fundamental research, but our results could be exploited for practical applications."

"Plants are very complex life forms", says Alice Breda, biologist at the Department of Plant Molecular Biology at the University of Lausanne. One of the greatest puzzles in the field of botany concerns the root tips of flowering plants. The root tip contains stem cells, which are able to grow roots, but just how they form all of a root's different tissues, is still a mystery.

It is thought that at least in part, this is possible thanks to intensive communication between the cells. Breda's research, as part of her SystemsX.ch Interdisciplinary PhD Project (IPhD), aims to understand the mechanisms behind this.

Two-way system

Roots help plants retrieve water and nutrients from the soil. The transportation of these substances requires an internal system of tubes, called xylem, commonly known as wood. This network transports nutrients and water to the leaves, where photosynthesis takes place. A second, more complex system of tubes is the phloem, which distributes the sugars produced in leaves during photosynthesis throughout the plant body. Sugars are directed to the growing sink organs, including the root tips, where they are used as fuel and building material for root growth.

But the phloem has another important function. "The sap flowing through the phloem also transports hormones and other substances, similar to what blood does in animals", explains Breda. By this means, individual tissues or cells can communicate with each other and coordinate growth.

Coordination without a coordinator

The first step in the growth process is the division of stem cells in the meristem at the root tip to produce daughter cells. Initially, they

remain similar to the meristem stem cells, but later start to differentiate into other types of cells. It is not yet clear how they do this. The command to differentiate may come from surrounding cells or from a process within the daughter cells themselves.

Depending on the external and internal signals the daughter cells receive, they start turning particular genes on or off, giving rise to a specific pattern of active and inactive genes in each cell. The active genes control the production of proteins that determine how the cell will develop. For example, the cell can either continue to divide, or become specialized for a particular function. The impressive feat here is that all the cells manage to coordinate their development so as to turn into cells of the xylem, phloem and other root tissues, in a clearly defined pattern. But how does this complex coordination work exactly? What sort of information do neighboring cells pass on? There are still many unanswered questions.

Genetic defects hinder root growth

Breda and her colleagues already know that two genes essential to healthy root growth are OCTOPUS (OPS) and BREVIS RADIX (BRX). A defect in one of these two genes leads to shortened roots due to deformation of the phloem tissue, which disrupts the delivery of growth regulators and sugars to the meristem.

"I am trying to find out what relationship these genes share with one another", says Breda. To do this, she works with thale cress *(Arabidopsis thaliana)* as a model organism. She compares the root growth of normal plants to that of plants with mutations in the OPS or BRX genes. Using genetic engineering, she modifies for example the OPS gene, so that the resulting protein exhibits alterations at different locations. "In this way, I can see which parts of the protein play an important role in its function and interaction with other proteins", explains Breda.

Proteins act as information carriers

Before she can begin her investigations, Breda has to incorporate the modified OPS and BRX genes into the genome of the thale cress. This process itself is not time-consuming, but the recovery of the plants is. "Typically, it takes up to half a year until the genetically modified thale cress is ready for further tests", says Breda. Once this step is over, the scientists can analyze the behavior of the genes and proteins that are produced in the root tissue of the modified plants.

Proteins are an extremely important component in a plant's root growth. They tell a cell whether it should grow, divide, specialize or die off. Some proteins communicate with each other by connecting and triggering the production of a new protein, which in turn moves on, connecting to another partner protein, and so on.

In order to understand this language, Breda localizes and follows the proteins inside living roots with special microscopes, or extracts the proteins from the genetically modified plants to analyze them in a mass spectrometer. This device determines the exact protein composition of the sample and can also help find out whether two distinct proteins react with each other.

Between biology and mathematics

The ultimate goal of the project is to simulate this complex information network using a computer model. This will help the scientists see through the complexity of the system in an attempt to understand the process thoroughly, but it may also provide some missing links. For example, if according to the model, two proteins are involved in a particular process, the simulation can check whether this in fact works with just two proteins or whether another is required. If the latter is the case, the researchers can go back to the lab in search of the missing protein.

In order to program the model, Breda is working in partnership with a bioinformatician. The researchers start with a static model, a sort of map showing the basic functions of the genes and proteins. From here, a dynamical model is developed, which can simulate phloem formation dependent on molecular events.

"We carry out fundamental research, but our results could be exploited for practical applications, for example biotechnological uses in crops", reflects Breda. If the model works and is able to realistically reproduce root growth, researchers will be able to better understand self-organization in plant tissues and learn how to manipulate it. For example, they will be able to investigate how root growth responds to drought or high soil salinity at the molecular level. These results may some day be used to benefit agriculture, and improve the food supply in countries with a harsh climate or adverse soil conditions. And since roots are at the very beginning of the human food chain, those who understand their secrets hold the key to the future of the world's food supply.

The project at a glance

Project title: An extended computational morphodynamics approach to understand self-organization in plant growth control

PhD student: Alice Sarah Breda, University of Lausanne

Supervisors: Prof. Christian Hardtke, University of Lausanne; Prof. Richard Smith, Max Planck Institute for Plant Breeding Research, Köln

Project duration: 2013–2016

Project type: Interdisciplinary PhD Project (IPhD) – PhD students work at the interface between two systems biology-relevant fields. During their interdisciplinary doctorate, they are supervised by one mentor from each of these two distinct subject areas.

Results 11th and 12th calls for proposals

The last SystemsX.ch projects get underway

The SystemsX.ch Scientific Executive Board and the Swiss National Science Foundation (SNSF) have approved a total of 27 new projects from the last two SystemsX.ch calls for proposals. The projects will be funded with over CHF 5 million.

The focus of the 11th call lay on the promotion of young scientists. In the Transition Postdoc Fellowship (TPdF) category, 8 out of 33 project proposals were approved and will receive funding for two years (see table 1). In the Interdisciplinary PhD Project (IPhD) category, 10 out of 25 proposals were approved and will be funded for three years (see table 2). Neither the approved IPhD Projects nor TPdFs can be extended beyond their standard duration due to the fact that SystemsX.ch will come to an end in 2018.

The 12th call invited proposals for Special Opportunities Projects. 9 projects out of 51 submitted proposals will be funded for a maximum duration of two years (see table 3). Besides possessing a "high risk, high gain" factor and innovative character, an important criteria for these projects was that they are not eligible for other sources of funding, such as SNSF or European grants.

Table 1: The TPdFs approved in 2015

Title	Principle investigator	Host research group
Exploring the silent fitness landscape	Victor Garcia (ZHAW)	Maria Anisimova
A systems biology approach to the regulation of compartmentalization through liquid phase transitions	Reinoud de Groot (UZH)	Lucas Pelkmans
Targeting bottlenecks in the evolution of metastatic potential – modeling metastatic signaling networks with imaging mass cytometry	Hartland Jackson (UZH)	Bernd Bodenmiller
Targeted intron retention as a novel mechanism for neuronal plasticity	Oriane Mauger (UniBas)	Peter Scheiffele
Reconstituting ESCRT-III-mediated membrane fission in vitro	Joachim Moser von Filseck (UniGE)	Aurélien Roux
Single cell analysis of the onset of circadian oscillations in differentiating ES cells	Eric Paquet (EPFL)	Felix Naef
Molecular signalling fingerprinting of human hematopoietic stem cell fate	Weijia Wang (ETHZ)	Timm Schroeder
Modeling mechano-biology of the artery to drive the design of novel bioresorbable stents	Gautham Sivachander Yepuri Ramesh (ZHAW)	Sven Hirsch

SystemsX.ch is supporting 27 new research projects.

Table 2: The IPhD Projects approved in 2015

Title	Supervisors
Nuclear organization of expanded trinucleotide repeats	Vincent Dion (UniL); Ioannis Xenarios (SIB, UniL)
A systems immunology-guided strategy for immunogen engineering	Bruno Emanuel Ferreira De Sousa Correia (EPFL); Sai Reddy (ETHZ)
Molecular mechanisms of stochastic chromatin effector interaction dynamics	Beat Fierz (EPFL); Vassily Hatzimanikatis (EPFL)
Decision-making: A multi-stage approach	Michael Herzog (EPFL); Wulfram Gerstner (EPFL)
Baysian learning of quantal parameters at single synapse resolution	Martin Müller (UZH); Jean-Pascal Pfister (UZH, ETHZ)
Deciphering a prototypical MAP kinase signaling network at the single cell level using a genetically-encodable opto-genetic circuit	Olivier Pertz (UniBas); Mustafa Khammash (ETHZ)
A systems biology approach to understanding the mode of action of new antibiotics against Gram-negative bacteria	John A. Robinson (UZH); Leo Erbel (UZH)
Modeling the neural circuit for sensorimotor transformations in *Drosophila*	Simon Sprecher (UniFR); Walter Senn (UniBE); Christian Mazza (UniFR)
Systems analysis of the bistable transfer competence pathway of a prokaryotic integrative and conjugative element	Jan Roelof van der Meer (UniL); Christian Mazza (UniFR)
Evolutionary systems biology: Robustness, cryptic genetic variation and innovation in transcription factor binding	Andreas Wagner (UZH); Yolanda Schärli Renggli (UZH); Joshua Payne (UZH)

Table 3: The Special Opportunities Projects approved in 2015

Title	Principle investigators
SynucleiX: A platform for systems biology of Parkinson's disease	Adriano Aguzzi (USZ/UZH); Simone Hornemann (USZ/UZH)
Bidirectional, tunable and spatio-temporally controlled multigene regulation using CRISPR-sgRNA-arrays	Konrad Basler (UZH)
Protein-LEGO: A high-throughput approach to dissect protein-genome interactions by quantifying the contribution of individual protein domains	Tuncay Baubec (UZH/FMI)
An integrative microfluidic platform for rapid and parallel gene expression and chromatin landscape profiling in few (<100) to single cells	Bart Deplancke (EPFL)
High-throughput single yeast cell secretion analysis in nL-droplets	Petra S. Dittrich (ETHZ); Lars Blank (RWTH Aachen)
Development of a high-throughput platform for systems immunology and protein engineering	Sebastian Maerkl (EPFL)
A new technology for affinity proteomics in systems biology	Andreas Plückthun (UZH)
In vivo group II intron folding and self-splicing on the single molecule level	Roland Sigel (UZH)
Associating HDL synapse nano-organisation with clinical HDL particle signaling capacity	Bernd Wollscheid (ETHZ); Manfred Claassen (ETHZ)

Heide Hess

Transnational promotion of systems biology research

The ERASysAPP research network is nearing its conclusion

Since the beginning of the ERASysAPP research network three years ago, SystemsX.ch, in partnership with 15 further partners, has promoted systems biology across Europe. This cooperation will come to a conclusion in December this year. What remains are not just the 12 transnational research projects, but also a close-knit, European systems biology community.

The ERA-Net for applied systems biology, ERASysAPP, was set up with a lifespan of three years at the beginning of 2013. Since then, ERASysAPP has been facilitating interaction between scientists from different countries through a variety of measures, so that existing resources can be optimally exploited, synergies put to better use and innovation promoted.

Switzerland joined the consortium in order to pave the way for Swiss groups to take part in collaborative research projects on a European scale. “With our involvement in ERASysAPP, we’re not only supporting the further networking of our scientists in Europe, but also contributing know-how and experience from our own projects to the international systems biology community”, explains Daniel Vonder Mühll, Managing Director of SystemsX.ch.

16 million Euros for applied systems biology research

The ERA-Net published a transnational call for proposals both in 2013 and in 2014. To be eligible for funding, proposed projects were required to include research groups from at least three different partner countries. A total of 12 research projects were approved, receiving funding of almost 16 million Euros. Swiss researchers are working on six of these projects, with Manfred Claassen from the ETH Zurich acting as project coordinator for the Rootbook project. SystemsX.ch provides the Swiss groups with funding totaling CHF 2.34 million.

Sustainable investment through data management

In spring 2014, ERASysAPP launched the data management project FAIRDOM in partnership with the European network ISBE. This project promotes the Europe-wide exchange and long-term use of systems biology data and models. With the help of a central platform for the management, exchange and archiving of data, results and data will be available for further use in research even after a project’s conclusion. SystemsX.ch supports FAIRDOM with CHF 660,000, as well as contributing expertise from the Swiss bioinformatics and IT project SyBIT. “Conversely, Switzerland profits from its participation in the development of new tools, processes and standards for the management of data across international borders”, explains Vonder Mühll.

Training and education

ERASysAPP has also contributed to the training and education of the next generation of systems biologists. For example, it supported the training of over 400 postdocs, master’s and PhD students through an extensive range of available courses in systems biology-relevant topics such as data integration and management. The ERASysAPP website also offers an overview of the best training and education opportunities in systems biology across Europe.

Europe-wide network of scientists

In order to further stimulate knowledge transfer and networking between systems biologists in Europe, ERASysAPP has organized a number of events, for example the networking events in Berlin in 2014 and Luxembourg this year, where representatives from universities and industry exchanged ideas on how to enhance cooperation. Another workshop addressed the optimal conditions for connecting systems biology research centers in Europe.

Through events such as this and the other sustainable measures described, systems biology will continue to be supported and encouraged in Europe beyond the lifespan of ERASysAPP.

ERASys *APP*
ERA-Net for Applied Systems Biology

More information is available at:
www.erasysapp.eu

Reader survey with prize draw

We value your opinion. Picture: © VRD – Fotolia.com

Do you read the X-Letter cover to cover? Or are you only interested in a couple of articles? Which articles do you find particularly interesting, and what would you like to see in the next issue? We'd like to ask our readers all of these questions, in order to help us create an even more engaging publication.

Our survey can be completed via the online questionnaire. Your answers will help us make the X-Letter even more appealing for the SystemsX.ch community. Participants will be entered into a prize draw to win an original piece of artwork by Martin Oeggerli (as featured on cover) or one of 10 Micronaut tabletop calendars (see article, page 12).

csl

Online questionnaire:
www.surveymonkey.com/r/X-Letter

X-Letter now only in English

Most of our readers probably haven't noticed this change. But a few may have observed that they are now reading the X-Letter in English, and not in German or French as they are used to.

The SystemsX.ch newsletter has been available in German and French in addition to English since 2008. Most of our readers have always received the X-Letter in English. Due to a decline in demand for the other two versions, the X-Letter will once again only be available in English, the common language of science that binds and connects the SystemsX.ch community.

vdm

Thank you, Peter Kunszt!

Peter Kunszt has led the bioinformatics and IT project SyBIT, which supports researchers in data management, since 2009. Trained as a theoretical physicist, he has acquired a wealth of IT knowledge over the years. Early in his career, Peter Kunszt developed his skills to become a competent IT specialist, particularly concerning the challenges associated with big data. For example, working at the Johns Hopkins University in Baltimore (USA), he developed one of the first large-scale astronomy databases, and later at CERN worked on grid computing and evaluating huge amounts of data.

As part of SystemsX.ch, he and his team of around 40 embedded bioinformaticians provided support to scientists in the analysis, management and publication of their data. In September this year, Peter Kunszt took a new job in a private IT company in Zurich, handing over the management of SyBIT to Bernd Rinn from the ETH Zurich.

We would like to wish Peter all the best in his new position and to thank him for his commitment and competent support of SystemsX.ch researchers over the past seven years.

vdm

Peter Kunszt led SyBIT until September this year.

Upcoming Events

February 15–16, 2016
Life Sciences Switzerland (LS²) Annual Meeting
Lausanne, Switzerland

February 17–18, 2016
SystemsX.ch Postdoc Workshop: Leadership and Management Skills for Postdocs
Gerzensee, Switzerland

February 28–March 5, 2016
Advanced Lecture Course on Systems Biology
Innsbruck, Austria

May 24–27, 2016
SystemsX.ch Retreat: Career Development for Young Scientists
Münchenwiler, Switzerland

June 14–16, 2016
International Conference on Systems Biology of Human Disease (SBHD)
Boston, USA

September 16–20, 2016
International Conference on Systems Biology (ICSB)
Barcelona, Spain

Cover: A delicate pollen grain starts to germinate, attached to the pistil of a flower.
Picture: Magnification 3,000:1, © Martin Oeggerli