X-Letter 30

Big data in systems biology

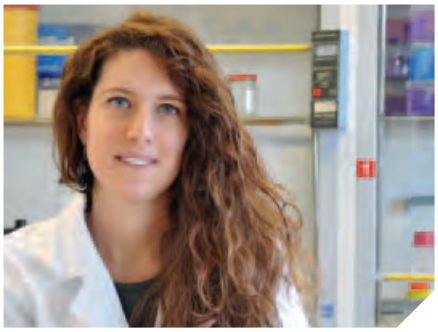
Challenges and opportunities

Contents

4

7

16



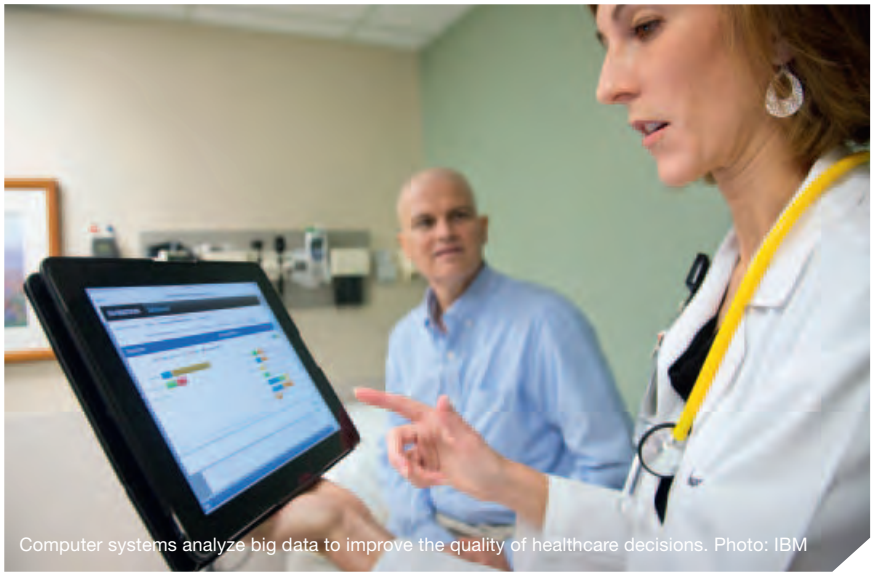
SystemsX.ch
The Swiss Initiative in Systems Biology

Imprint

Publisher: SystemsX.ch, Clausiusstr. 45, CLP D 2, CH-8092 Zurich — Contact: admin@systemsx.ch, phone +41 44 632 42 77, www.systemsx.ch — Editors: Maja Schaffner (mas), Christa Smith Lopez (csl) — Collaboration: Daniel Vonder Mühll (vdm), Heide Hess (hh) — Translation: scitrans.ch — Graphic design and Print: Mattenbach AG, Winterthur
Newsletter subscription: communications@systemsx.ch

Cover: A dividing cell. Illustration: Daniel Zwimpfer, Lucerne

"Big data is set to become one of the most valuable resources of the 21st century."



Computer systems analyze big data to improve the quality of healthcare decisions. Photo: IBM

When you look back over the last 70+ years of the computing revolution and see how far we've come in such a relatively short time, you have to be amazed. The first electronic, programmable computers built in the 1940s were essentially high-speed calculators. Then came the mainframe, the PC, the Internet and social networking. Today, we're entering the era of cognitive computing, in which machines help us think and make better decisions.

IBM's Watson marks a turning point in this revolution. The former Jeopardy! TV quiz show champion is now reading millions of pages of medical texts in preparation to assist healthcare staff. However, while Watson can understand all manner of things, and learns from its interactions with data and humans, it is just the first step into this new era.

Imagine a world of tomorrow, where computer systems help people accelerate their productivity by a factor of 10 or 100 to be able to solve complex problems that involve overwhelming amounts of what is known as big data. This concept of human-computer interaction would have been inconceivable ten years ago, but is entirely imaginable in this new era of computing. However, taking this from concept to reality requires extensive investment in R&D and in collaborations such as those supported by SystemsX.ch.

All this is a good thing, particularly for systems biology, which is a quintessential big data challenge. Thankfully, researchers have come up with some really clever ideas for how to tame this big data beast, including a trick we call data uncertainty quantification. I would liken this to reading a 25-word summary of a 300-page mystery novel, where you still find out who committed the crime, why and how, without ever reading the book.

If you translate this to systems biology and healthcare, it means fast, near-100% accuracy in diagnosing patients, without having to analyze all of the data. We can do this by extracting the patterns in the data best describing the molecular phenotypes at hand, which in the case of a cancer patient enables us to detect and decipher the underlying cancer heterogeneity. Additionally, we are developing statistical models that identify the populations of cancerous cells which have the most relevant characteristics for targeting with treatment. As a result, we can do more extensive analysis and therefore provide optimized treatment recommendations for patients on an individual basis.

Through applications such as this and many more, big data is set to become one of the most valuable resources of the 21st century.

Dr. Alessandro Curioni
Vice President and Director
IBM Research – Zurich

Peter Kunszt is familiar with the challenges that accompany research involving big data.

Peter Kunszt manages SyBIT, the SystemsX.ch bioinformatics and IT project

"SyBIT gets scientists in shape for big data"

In systems biology as elsewhere, big data has long been recognized as an invaluable source of information. Yet important insights into biological systems are only conceivable if it is possible to extract the relevant information from the enormous volume of available data. Peter Kunszt and his team support researchers in automating such processes. Through the IT support project SyBIT, they help Swiss scientists keep pace with the world leaders in the long term.

Where does the data flood in systems biology come from?

Research in the field of systems biology only became possible after significant advances had been made in the technologies required to monitor biological systems. Considerable developments have been achieved, for example in DNA sequencing equipment. The progress in mass spectrometry and, most recently, microscopy techniques is also impressive. All these devices produce increasingly large amounts of data. This situation can be compared to progressively more powerful digital cameras; new models offering more megapixels are released each year. These call for new storage devices with more storage capacity. The same is true for research, but with much bigger dimensions, which is why we call it big data.

What does the concept of big data encompass for you?

Particularly in systems biology, big data is not only characterized by huge volumes of information but also by its complexity. Often, we have to deal with different types of values and must first determine how they are linked. Such data is not easy to interpret. Another aspect is speed. Large volumes of data are increasingly difficult to analyze within a reasonable period of time. Data uncertainty, i.e. the quality and reliability of the information, is an additional factor, as values can be inaccurate due to measuring errors.

Which one of these aspects poses the greatest challenge?

Volume, complexity and speed always go hand in hand. It is our job to rapidly find the best solutions to scientific problems together with the investigators, using the technology available today while taking these three factors into account.

How exactly does SyBIT support SystemsX.ch scientists?

Every project is different. Depending on the needs of the investigators, we help them assemble the required hardware and software or we arrange for access to mainframe computers. But we also help the scientists analyze, interpret, manage and store their data.

Through the SyBIT project, we place the whole know-how related to data management at the disposal of the researchers, and help them automate their processes and make them efficient. In a manner of speaking, we get the scientists in shape for big data so they can fully exploit the potential of new technologies.

Christa Smith

Has the need for IT support increased?

Yes, definitely. As the volume and complexity of the data increases, it becomes more and more difficult and time-consuming for the investigators to manage their data. You might think this is easy to do, but the recording of the data alone is complex when dealing with volumes such as those generated by mass spectrometry, for example. The data stemming from different experiments must be correctly annotated and filed in a structured manner. This is essential so that the information can later be assigned to the correct projects and, if necessary, be reproduced. The analysis and the assessment of the huge data volumes call for algorithms that automatically pinpoint characteristics and patterns of interest.

Can you mention a specific example?

We are currently supporting MorphogenetiX. In this project, the scientists are studying cell specialization using 3-D microscopy. Thanks to this new technology, the samples no longer need to be formalin-fixed, but can be filmed live. The 3-D microscope takes up to 700 pictures per second, allowing the researchers to witness cell division and ultimately demonstrate how a cell such as a specialized brain cell comes into being.

The data volume generated by this procedure is enormous. SyBIT is helping the MorphogenetiX project team with the computer-assisted processing of the data. One of my collaborators is on site for several months; he is testing the developed algorithms alongside the project's specialists in order to automate the processing of the vast amount of data.

The sheer amount of data calls for high storage capacity. What is stored and what is rejected?

We need to understand the data extremely well to be able to decide what is relevant. This is why, in today's data-heavy research, it is of utmost importance to first grasp the meaning of the data and to detect patterns and correlations. At the beginning of a project, especially in basic research, the meaning behind the data is often not understood, which is why scientists usually want to hold on to it all. Often it only becomes clear towards the end of a project which data are relevant and which data can be deleted, due to the fact that they can be easily and even more precisely reproduced at a later time.

And how do you make sure the data is still accessible in the future?

Unfortunately, long-term data storage is still a largely unsolved problem. In the fields of genomics and proteomics, international central databases have already been established, but long-term financing is not yet guaranteed. No solution is yet available for the archiving of data generated by imaging technology. Once SyBIT comes to an end, no institution will take over the management of this data.

Who, in your opinion, needs to take on responsibility for this matter?

In my view, data archiving is the libraries' job. Scientists should not have to pay for the storage of their data. The government must find solutions. Luckily, the problem has been identified, and several options are currently being tested and discussed at the political level.

SyBIT and SystemsX.ch will both come to an end in 2018. Who will guarantee IT support thereafter?

Local support groups. The idea for these originated in the Lake Geneva region. The Vital-IT group was founded there as early as in 2004. This organization offers computing power, memory and support in the area of bioinformatics. We were able to establish local SyBIT partners at the Universities of Zurich and Basel, as well as at the ETH Zurich based on this model. By doing so, support for the scientists is guaranteed beyond the duration of SyBIT and SystemsX.ch.

And how can this know-how be anchored within the community?

Fortunately, we are already seeing SystemsX.ch investigators applying their newly acquired skills to new projects. The SyBIT specialists do not exclusively support SystemsX.ch projects, so the acquired competences are introduced into other research groups as well.

Are Swiss universities now prepared for data-intensive research after SyBIT?

Yes, in principle. The local support groups offering bioinformatics services are firmly established in the universities and the SIB Swiss Institute of Bioinformatics will handle their coordination after SyBIT expires. Over the past few years, we have also helped the SystemsX.ch partner institutions develop the required IT infrastructure. The task now is to establish connections between these local IT resources, so that the universities can take advantage of all the available services and specialized infrastructure. This will help Swiss scientists remain among the global leaders in systems biology research in the long term.

Christine Durinx, SIB

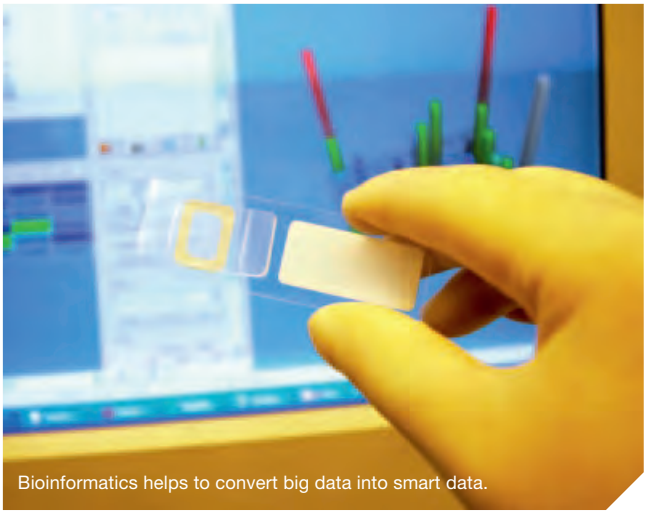
SIB Swiss Institute of Bioinformatics

Converting big data into knowledge

Data management in the field of life sciences is the business of the SIB Swiss Institute of Bioinformatics. This SystemsX.ch partner institution supports researchers in analyzing, modeling and storing their data, and is involved in numerous SystemsX.ch projects.

In recent years, it has become difficult to imagine a life science project without bioinformatics. Among the eleven projects approved for funding in the 10th SystemsX.ch call, for example, seven groups from the SIB Swiss Institute of Bioinformatics are involved.

Bioinformatics involves the application of computer technology to the understanding and effective use of biological data. In other terms, it helps to convert big data into smart data or knowledge, from understanding the 3-D structure of macromolecules to designing drugs and mapping molecular pathways.



Bioinformatics helps to convert big data into smart data.

Applied research in medicine

Big data has the potential to help improving diagnosis and therapy in medicine. For several years now, the SIB has been involved in applied research directly linked to the medical field. For example, SIB's high-performance computing (HPC) center, Vital-IT, has developed the algorithm for a non-invasive prenatal test which is able to detect the most frequent trisomies and chromosomal rearrangements from a pregnant woman's blood sample. The test has already been commercialized. Another SIB group developed a model which predicts the evolution of an aneurysm, and is intended to support clinicians in deciding upon the best treatment for a patient. A third group offered its support during last year's outbreak of the Ebola virus in West Africa by estimating the infection's dynamics, which is of crucial importance for controlling an epidemic.

These are just three of the many projects developed by the SIB in the field of human health – not to mention those that are involved in the diagnosis and treatment of different kinds of cancer.

Coordinating bioinformatics in Switzerland

The SIB Swiss Institute of Bioinformatics is an academic, non-profit foundation recognized as a public utility. It coordinates bioinformatics activities throughout Switzerland. The SIB provides world-class core bioinformatics resources for the life science community, including

- Biocuration and bioinformatics expertise, enabling life scientists to create accurate and comprehensive representations of biological knowledge and take full advantage of bioinformatics technologies
- Databases and knowledge bases, giving life scientists access to curated biological data and information
- Software for analyzing, visualizing, interpreting and comparing biological data and for modeling biological systems
- Computing and storage infrastructure for storing, analyzing and processing biological data, including big data

From software tools to computing power

The SIB develops, supplies and maintains more than 150 high-quality databases, software tools and platforms for the global life science research community. Most SIB resources are available through open-access on ExPASy, the SIB bioinformatics resource portal. The SIB resources cover different areas of life sciences, including genomics, proteomics and evolution.

Through eight core facilities and HPC centers, as well as embedded bioinformaticians, SIB groups provide expert data analysis services and computing power to life scientists from academia and industry, enabling them to perform world-class biomedical research.

The services provided include the analysis of high-throughput data, scientific support of (bio)medical projects, development of algorithms, biostatistics training, as well as access to computational space, helpdesk and support.

More information is available at:
www.isb-sib.ch

Atlant Bieri

Big data – an opportunity for medicine

Smarter than cancer

Big data has the potential to revolutionize human medicine. On this, Swiss scientists are agreed, for within the flood of genetic data, the key to the cure for cancer and other serious diseases may lie hidden.

Mr. Miller is having trouble breathing. His general practitioner diagnoses cancer. Rather than sending his patient to a specialist, the physician takes a tissue sample and inserts it into a device, as small and easy to use as a laptop. The machine immediately begins to decipher the cancer cells' genetic code. In just a few minutes it provides all the therapy-relevant data and even a prescription for the most effective drug combination.

Gene library

Thanks to big data, this scenario has become conceivable. "We can already sequence the genome of a tumor within a week", says Niko Beerenwinkel, professor of computational biology in the Department of Biosystems Science and Engineering at the ETH Zurich. Medicine has not yet come as far as Mr. Miller's visit to his general practitioner, "but with the help of big data, we can gain a precise overview of this disease at the molecular level for the first time in the history of medicine", explains Beerenwinkel.

Scientists are sequencing the genes of various types of cancer from thousands of patients, and are comparing this information with the disease's pathological process. Which combination of gene mutations led to this cancer? Somewhere in the flood of data lies the answer, and whoever finds it will be a big step closer to a successful therapy. Beerenwinkel is convinced that "with this knowledge, we can selectively search for new drugs".

New drugs

Big data is leading the search for novel therapies away from indiscriminately acting chemotherapies. The new approach consists in switching off genes that are essential for the survival of the tumor. This could be a drug that acts like a sort of copy protection by covering the relevant gene. The problem lies in the fact that the key genes can be located in a different place in every type of cancer and in every person. Big data is the perfect tool to find them all.

Large patient information databases are indispensable for this kind of research, although currently they also present a weak point. "Universities such as the ETH Zurich can easily handle large amounts of data, but they must improve security", warns Beerenwinkel. Who is allowed to access the data and with whom can it be shared? The universities must clarify these questions. Beerenwinkel has already taken action. "In our institute, access to different parts of the database is clearly regulated", he says.

The situation is reversed in the hospitals, the potential end-users of the data. Their data security is well organized, but they can barely deal with the huge volume of data. "We must unite these two worlds", muses Beerenwinkel.

Bigger than big

Scientists' ambitions are not dampened by such problems. Thanks to big data, they now know how smart cancer really is. Contrary to previous assumptions, a tumor is not a homogenous cell mass but a complex system of differentiated cells. This means that in each cell, different genes can carry a mutation, and individual cells are capable of becoming resistant to one or several drugs. A single-drug treatment may therefore not be enough to combat the disease.

"In an ideal situation, we would sequence the genes in every cell", comments Beerenwinkel. This could amount to billions of cells multiplied by ten billion genes per cell. This is a large figure, even by big data standards. Beerenwinkel therefore refers to it as an even higher level: "This is 'huge data'." Only when the scientific community has mastered this level, will we have reached the situation experienced by Mr. Miller in his physician's office. Personalized cancer treatment will have become a reality.

Big data determines the perfect drug combination for every patient.

RTD Project MicroScapesX

Focussing on microorganisms

Microorganisms are usually invisible to the naked eye, yet they are omnipresent. Scientists involved in the MicroScapesX project are studying how the complex communities in which they live function. Their results could contribute to the improvement of treatments without the use of antibiotics for patients with burns.

Jan van der Meer checks the proliferation of the bacteria in the shake flask.

Microorganisms are found in soil and water, in the air, in other living organisms and on all surfaces. Whether they are useful or harmful primarily depends on which species live together. “They usually build useful communities”, says Jan van der Meer, a microbiology professor at the University of Lausanne, and the project leader of the RTD Project MicroScapesX. Yet for many reasons, it would be of interest to be able to selectively influence the microorganism mix, for instance in the human intestine. “Until now, this has been done by trial and error”, explains van der Meer, mentioning by way of example readily available probiotics, used to enrich the intestinal flora.

At the present time, the basic knowledge required for targeted interventions in the composition of such populations is missing. Little is known about which microorganisms occur together, how they colonize new habitats, and how their communities change in time and space. “Within the scope of MicroScapesX, we hope particularly to figure out what happens when additional species are introduced into an established ecosystem”, explains the project leader.

Considering microbial communities as a whole

Microorganism associations are often highly complex. “In the soil, for example, thousands of different species live together”, says van der Meer. The MicroScapesX scientists chose a systems biology approach to investigate the interactions between these tiny organisms more closely. The interdisciplinary team, consisting of microbiologists, modeling specialists and physicians, considers microbial communities as a whole and examines this system from different angles. Their approach is experimental but also involves computer models developed in-house. In this manner, they are able to accumulate many new insights regarding the coexistence of microorganisms. The models developed by scientists working under Dani Or at the ETH Zurich and Vassily Hatzimanikatis at the EPF Lausanne should in future make it possible to precisely predict the behavior and development of microbial communities.

Using microorganisms to clean soils

However, models can only be developed if they are supplied with data and tested. Van der Meer and his group are therefore investigating a soil system and its resident bacteria. Microorganisms have already been experimentally introduced into soil, in order to eliminate chemical contaminants such as oil. “Yet what the microorganisms actually do in the soil is not completely understood”, says van der Meer. Through their experiments, the researchers hope to determine what happens when they introduce new species into the system to eliminate pollutants. For example, they hope to learn how the preexisting microbes react, and whether they adapt once the composition of the community changes. The scientists are also interested in finding which particular species have a positive effect. In the long run, the plan is to introduce complete communities into contaminated soils to act as cleaning crews under controlled conditions, and to steer them in a targeted manner.

Colonization and coexistence

Before the scientists can implement such ambitious goals, they must identify the factors that promote the thriving of these beneficial communities. These could include the existence of nutrients, the availability of oxygen, or the way in which different species get along with each other.

Maja Schaffner

The experiments performed in the groups of Dani Or and David Johnson at the ETH Zurich should elucidate this last point and provide data for the development of models. The researchers are currently studying the interactions of different bacteria in artificial communities (see illustration). They are observing whether the microbes cooperate or compete with each other, and how these relationships influence their spatial distribution.

Fighting infections in burn wounds

Not only the interactions between various microorganisms, but also the microbes' colonization of new habitats is a subject of great interest to the scientists. Instead of restricting themselves to lab experiments, Yok-Ai Que and his team at the Lausanne University Hospital will also investigate this process by studying patients' burn wounds.

"Immediately after a burn has occurred, the destroyed areas of skin are nearly aseptic, but are then rapidly colonized by pathogenic microorganisms", explains van der Meer. These infections are dangerous and, in serious cases, lead to septic shock and even death. In addition, an invasion by harmful microbes is difficult to stop with antibiotics, as the pathogens very rapidly become resistant to the drugs during treatment.

The physicians at the Lausanne University Hospital are therefore investigating how the colonization of such a wound happens. They are particularly interested in determining which bacteria appear at which moment and whether they were already present on the skin prior to the burn. They also hope to find out if and how it is possible to stop the pathogen invasion without antibiotics. Nowadays, burnt areas of skin are, where possible, covered with skin from the patient's own body, washed regularly and treated with antibiotics to counter infection. "It might be possible to improve treatment by colonizing the wound with harmless microbes. These would occupy the territory and thus prevent the pathogens from spreading", explains van der Meer.

The scientists stain different bacteria with different colors in order to reveal their growth patterns within the community.
Illustration: Felix Goldschmidt, Eawag

Fruitful interdisciplinary collaboration

Van der Meer is obviously excited to be able to study life at the microscopic level, from a number of very different angles in such an interdisciplinary team. The partners meet regularly to discuss their progress. According to the project leader, it is very helpful that all the participants are knowledgeable in microbiology, even though they come from very diverse fields.

The project is still in the start-up phase and the scientists are not yet able to fully answer their numerous questions, however van der Meer already finds the collaboration between the five partners highly inspiring. "We learn so much from each other, for instance new techniques and approaches, or we exchange bacterial strains", the project leader happily reports. "In this way, we also come up with new ideas and starting points that bring us closer to our objective, which is to gain extensive knowledge of microbial communities."

MicroScapesX at a glance

Principle investigator: Prof. Jan Roelof van der Meer

Research groups:

- Prof. Jan Roelof van der Meer, Department of Fundamental Microbiology, University of Lausanne – Soil microbes and diversity analysis
- Dr. David Johnson, Institute of Biogeochemistry and Pollutant Dynamics, Department of Environmental Systems Science, ETH Zurich – Synthetic communities
- Prof. Dani Or, Institute of Terrestrial Ecosystems, Department of Environmental Systems Science, ETH Zurich – Agent-based spatial modeling of microbial communities
- Dr. med. Yok-Ai Que, Service of Intensive Care Medicine, Department of Adult Critical Care Medicine, Lausanne University Hospital – Burn wound treatments
- Prof. Vassily Hatzimanikatis, Laboratory of Computational Systems Biotechnology, Department of Chemistry and Chemical Engineering, EPF Lausanne and SIB Swiss Institute of Bioinformatics – Modeling of metabolic interactions

Total budget (2014–2018): CHF 5.215 million, including CHF 2.531 million from SystemsX.ch

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

MicroScapesX
Design and Systems Biology of Functional Microbial Landscapes

Sébastien Gagneux in the biosafety laboratory airlock at the Swiss Tropical and Public Health Institute.

Systems biology of drug-resistant tuberculosis

The stealthy superbug

Tuberculosis is transmitted via tiny, coughed-up droplets. In Switzerland, this disease was almost forgotten, but is now back again. Over the last sixty years, multi-drug-resistant strains have developed in Central Asia and Eastern Europe and are now spreading. The scientists working on the TbX project intend to forestall this development.

Each year, tuberculosis, caused by the *Mycobacterium tuberculosis* bacterium, leads to the death of 1.5 million people worldwide. Nine million new cases are registered each year. However, the main problem lies elsewhere. Three percent of all new infections are triggered by bacterial strains which have developed multi-drug resistance, meaning they can no longer be eliminated by a number of antibiotics. “Cases caused by such strains are very difficult to treat”, explains Sébastien Gagneux, head of the tuberculosis research unit at the Swiss Tropical and Public Health Institute in Basel.

Around the world, approximately half a million patients develop multi-drug-resistant tuberculosis each year. This is a matter of serious concern to global health authorities as well as Gagneux, which is why he and his TbX RTD Project team are attempting to identify the biological processes underlying resistance development.

Prisons – breeding grounds for superbugs

To this end, they are collaborating with the Georgian Health Ministry. In Georgia, multi-drug-resistant tuberculosis is relatively common and represents 20 to 30 percent of all cases. The reasons for this are in part historical, says Gagneux. “Georgia was part of the USSR. During this time, the prisons were full and sanitary and medical conditions were poor.” Not only could tuberculosis easily spread in these surroundings, but it was also able to develop resistance against standard antibiotics.

For treatment to be effective, a patient must be treated with four different types of antibiotic over six months. Only then can one be sure that all bacteria have been killed. In Georgian prisons, antibiotics were often in short supply and the treatment duration was insufficient. Under these conditions, weak strains were killed whereas more robust ones survived and were thereafter immune to the drug. “These are the so-called superbugs”, Gagneux warns.

After the collapse of the Soviet Union, many prisoners were released, and this led to the spread of the resistant tuberculosis strains among the population at large. Poor healthcare after the fall of the USSR then promoted their proliferation.

Arms race in a flask

Gagneux has the Georgian strains sent to his lab in Basel where he examines their genetic differences. “We compare the strains to determine which ones are more successful and which ones less so.”

In practice, this means bringing two strains together so they can compete against each other. To this end, he adds them to a growth medium in a flask and observes which one has the upper hand after one month. In a second step, he compares them on the molecular level, using tandem mass spectrometry and a high-performance computer to analyze the protein composition of the bacteria. This procedure was developed by the Aebersold group at the ETH Zurich.

Using this data, the scientists can draw conclusions regarding the mode of action of various genes, as these directly affect protein production. “By doing so, we can establish a model that takes into account a bacterium’s genes as well as its molecular phenotype”, explains Gagneux. This could lead to novel therapeutic options in the future, such as the switching off of specific genes of a tuberculosis strain, thereby cancelling its resistance to an antibiotic. Gagneux is collaborating with an industrial partner, BioVersys AG in Basel, to realize this goal (see article, page 12).

Sluggish evolution

From an evolutionary point of view, tuberculosis is somewhat lazy. Cell division in tuberculosis-causing bacteria occurs only once every 24 hours, whereas other bacteria divide every hour. Besides being slow, *M. tuberculosis* has a further disadvantage. The bacterium lacks so-called plasmids, circular DNA molecules which allow the bacteria to exchange genetic information between themselves. Plasmids notably code for resistance to antibiotics.

When plasmids are not available, each bacterial strain is forced to develop the resistance on its own through numerous divisions and random mutations. Due to these unfavorable preconditions, the tuberculosis bacteria need more time to develop resistance. Even so, hundreds of multi-resistant tuberculosis strains now exist. “These are the strains of interest to us, as they raise many important questions”, ponders Gagneux.

One of them concerns fitness costs. A bacterial strain must pay for resistance development, not in cash but in terms of its own fitness, which decreases. “Resistant strains are usually less infectious in an initial phase”, concedes Gagneux. The bacterium pays for immunity against an antibiotic by becoming less virulent. However, its evolution does not stand still. Many strains offset this disadvantage after a few generations as a result of further mutations in their genetic material. Gagneux points out that “the strains are subsequently just as virulent as before”.

Models help design appropriate therapy

In order to better understand the mechanisms behind these processes, the data collected during mass spectrometry is fed into a metabolic model. Gagneux summarizes the aims of his team: “We hope to be able to predict whether or not a given strain of *M. tuberculosis* can proliferate.” Depending on the result, a patient may or may not have to be isolated. This has a significant impact on the quality of life of the patient and also has an influence on medical costs. “This allows us to design individual treatment strategies”, explains Gagneux. The data and models might also prove useful in the development of novel antibiotics.

The scientists have also developed a model for the geographic distribution of tuberculosis. “We will use this model to predict where a given strain will appear next”, says Gagneux. This is also relevant for Switzerland, where approximately 500 new cases are registered each year. Three quarters of these patients are immigrants. The others are long-time residents, for instance grandparents who contracted the disease 50 years ago. According to Gagneux, “the bacteria can remain inactive in the body for decades”. If, at some point, the immune system is weakened, an outbreak can occur.

To date, few cases of multi-resistant tuberculosis have been registered in Switzerland. “But with the eastward expansion of the EU and the accompanied free movement of its citizens, it will be all the easier for these germs to be introduced here too. It is therefore only a matter of time until further cases appear in Switzerland as well.”

TbX at a glance

Principal investigator: Prof. Sébastien Gagneux

Research groups:

- Prof. Sébastien Gagneux, Swiss Tropical and Public Health Institute, University of Basel – Infection and evolutionary biology, molecular epidemiology
- Dr. Xueli Guan, Swiss Tropical and Public Health Institute – Lipidomics
- Prof. Ruedi Aebersold, Institute of Molecular Systems Biology, ETH Zurich – Proteomics
- Prof. Uwe Sauer, Institute of Molecular Systems Biology, ETH Zurich – Metabolomics
- Dr. Christian Beisel, Department of Biosystems Science and Engineering (D-BSSE), ETH Zurich – Genomics
- Prof. Tanja Stadler, Department of Biosystems Science and Engineering (D-BSSE), ETH Zurich – Phylodynamic modeling
- Jörg Stelling, Department of Biosystems Science and Engineering (D-BSSE), ETH Zurich – Metabolic modeling

Industrial partner: BioVersys AG, Basel

Total budget (2014–2018): CHF 6.068 million, including CHF 2.999 million from SystemsX.ch

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

TbX
Systems Biology of Drug-resistant Tuberculosis in the Field

Maja Schaffner © Martin Heimann

BioVersys

A start-up takes on antibiotic resistance

An increasing number of pathogens are becoming resistant to antibiotics and are threatening the health of millions of people worldwide. Perhaps not for much longer. The start-up BioVersys is developing active substances which, in future, may be able to shut off resistance.

Resistance is, in a manner of speaking, life insurance for pathogens. When resistant bacteria are confronted with antibiotics, they activate a protective mechanism and in so doing secure their survival. But this may soon be a thing of the past: BioVersys, a start-up also involved in the SystemsX.ch TbX project, is currently developing active substances aimed at switching off the dreaded resistance genes. "The patients would have to take this substance at the same time as the appropriate antibiotic", explains Marc Gitzinger, a biotechnologist and CEO at BioVersys. The substance would prevent the reading of the pathogen's resistance gene and the activation of the protective mechanism. This strategy could even put ineffective antibiotics back on track – bad luck for the resistant bacteria.

Marcel Tigges (left) and Marc Gitzinger came up with the idea for their start-up during their PhD studies.

Efficient battle against tuberculosis

"So far, we have made most progress in the development of a substance against resistant tuberculosis pathogens", says Gitzinger. His team has already produced several promising candidates that were able to cancel the resistances in animal experiments. "We will continue to develop the best substance and later perform clinical studies", adds Gitzinger.

A key question for the scientists is whether the tuberculosis pathogen will manage to develop a further resistance to the new substance, rendering it ineffective. As a partner in the SystemsX.ch TbX project (see page 10), BioVersys has access to a whole collection of tuberculosis bacteria from around the world. "We will use these bacterial strains to test if resistance to our substance develops, and if so how quickly", explains Gitzinger. According to him, this is a unique opportunity to determine whether the substances remain effective in the long run, and whether they might one day help save millions of lives.

A start-up on the road to success

BioVersys was founded in 2008 in the Department of Biosystems Science and Engineering of the ETH Zurich, located in Basel, where the two biotechnologists Marc Gitzinger and Marcel Tigges were working on their PhD theses. The company has since won several awards such as *Venture Kick 2008* and the *Swiss Technology Award 2011.* In 2013, the Handelszeitung and the Institut für Jungunternehmen awarded BioVersys the title of second-best start-up in Switzerland.

The two young entrepreneurs have already concluded a second financing round with external investors and are working with pharmaceutical companies such as GlaxoSmithKline. When asked what is required to launch a successful start-up, Gitzinger explains that "one requirement is definitely faith in the project." It is also important to ask for help from institutions such as the Commission for Technology and Innovation CTI or venturelab, which support people wanting to found a company. Gitzinger also recommends performing a reality check by asking such questions as "How far are we from a therapeutic application?".

Gitzinger is convinced that the support from competent advisors accounts for the success of his company. "Another important factor", adds the entrepreneur, "is our strong team, which has been pushing the development of these substances".

More information is available at:
www.bioversys.com

Daniel Vonder Mühll

10th call for proposals

Eleven new projects with a medical focus

Nine Medical Research and Development (MRD) Projects will begin this year. They were approved by the Swiss National Science Foundation at the end of 2014 and will run for three years with a total of CHF 18.5 million funding from SystemsX.ch. In these large-scale projects, systems biology approaches will be specifically applied to medically or clinically relevant subjects. The research themes range from aneurysms to breast cancer and HIV (see table 1). Nearly all principal investigators are physicians employed by one of the five Swiss university hospitals. A total of 53 research groups working in different disciplines and institutions are involved.

Two new research collaborations with industry, also focused on medical themes, have been launched in the Transfer Projects (TF) category (see table 2). These Transfer Projects will run for two years and will be funded by SystemsX.ch with CHF 600,000 in total. In this category, SystemsX.ch not only supports applied research in systems biology but also the collaboration between research groups working in the academic and private sectors.

Table 1: SystemsX.ch will support these nine MRD Projects until the end of the initiative in 2018.

Project title	Principal investigator	Involved institutions
PrionX: Systems biology of prion diseases	Adriano Aguzzi	UZH/USZ, UZH, UniL, SIB, University of Cambridge
AneuX: Modeling shape as a biomarker for instability of intracranial aneurysms	Philippe Bijlenga	UniGE/HUG, ZHAW, UZH, ETHZ, UniGE, UZH/USZ
HIV-X: The interplay of host and viral factors in the hurdle to cure HIV-1	Huldrych Günthard	UZH/USZ, ETHZ, EPFL, UZH, UniBas, SIB
GutX: Systems biology of intestinal microbial metabolism in inflammatory bowel disease	Andrew Macpherson	UniBE/Inselspital, ETHZ, SIB
VirX: A systems approach to the HDAC6/Ub/aggresome pathway and Ubiquitin proteasome system in viral disease	Patrick Matthias	FMI, UZH, UniGE/HUG, ETHZ, SIB, UniL/CHUV
MelanomX: Single cell level systems biology of tumor/micro-environment cross-talks in adaptive resistance to melanoma therapy	Olivier Michielin	UniL/CHUV, SIB, UniL, EPFL
StemSysMed: A systems medicine approach to hematopoietic stem cell diseases	Radek Skoda	UniBas, UZH/USZ, ETHZ, UniBas/USB
HDL-X: A systems biology approach to anti-atherogenicity and anti-diabetogenicity of high density lipoproteins (HDL)	Arnold von Eckardstein	UZH/USZ, ETHZ
Breast cancer MetastasiX: Mathematical modeling of tumor heterogeneity during progression to metastases and clinical validation	Walter Paul Weber	UniBas/USB, UniBas, UZH, FMI, SIB, IBM

Table 2: Two new research collaborations have been launched this year.

Project title	Applicants	Cooperation between
MoDeLoMX – MacrOphage DiffErenciation LOgical Modeling	Ioannis Xenarios	SIB, Roche
Harnessing the immunome's potential to fight cancer: evaluating synergistic antibody drug conjugate – immunotherapy treatments for cancer by comprehensive systems biology analysis	Alfred Zippelius	UniBas/USB, ETHZ, NBE-Therapeutics

Peter Blattmann analyzes the protein composition of cells using a mass spectrometer.

Transition Postdoc Fellowship (TPdF)

Genes make cholesterol deadly

A lack of physical activity, rich meals and being overweight are ingredients for a heart attack. Over the last few years, an additional component has become the center of attention: one's genetic makeup. The way our genes work evidently determines how our cells deal with cholesterol. Scientists at the ETH Zurich now want to find out how this works.

Cardiovascular diseases are the leading cause of death in developed countries. For a long time, scientists thought this was mostly due to an excessive intake of cholesterol on the account of rich foods and the ensuing arteriosclerosis. But in recent years, the focus has increasingly shifted towards a genetic explanation. "Some people are at higher risk of arteriosclerosis than others because of their genes", says Peter Blattmann, a biochemist at the Institute for Molecular Systems Biology at the ETH Zurich. With his SystemsX.ch Transition Postdoc Fellowship, he hopes to find out how the interplay between genetic makeup and cell chemistry determines whether arteriosclerosis develops or not.

The problem is very complex: as is true for cancer or diabetes, innumerable genes play a role in blood cholesterol levels. In the past few years, genome-wide association studies have revealed the regions of the genome in which these genes are located. Thousands of DNA positions, extracted from the blood samples of test subjects, were analyzed. The results were then compared to the cholesterol levels measured in these people's blood. It was discovered that well in excess of one hundred genes are in fact linked to cholesterol.

Cells filter cholesterol

Cholesterol is a double-edged sword. On the one hand it can be deadly; on the other hand it is irreplaceable. We cannot survive without it because it acts as a kind of cement that imparts stability to our cell membrane. Most cells in the body are able to produce their own cholesterol, although it would be preferable if they would instead filter the cholesterol provided by the diet out of the blood. Cells would then have the building material they need at their disposal, and the danger of arteriosclerosis would be averted.

It is not known exactly how genes influence the cholesterol metabolism in our cells, and this is the starting point of Blattmann's project. In order to establish a clinical picture, he hopes to decode the function of every single gene linked to cholesterol and determine how these genes affect each other. For this purpose, he works with human cell lines cultivated in Petri dishes. Some of these are liver cells. The liver is a key element in cholesterol regulation, as it removes cholesterol from the blood and, by way of bile, sends it to the intestine from where it leaves the body. Some people's liver cells do this very well; others' cells, however, are not so efficient due to their genes.

Atlant Bieri

Understanding proteins

In order to understand this variability, Blattmann selectively turns off genes in his cell lines. To do so, he interferes with the cell's internal chain of command. Genes first convert their orders into RNA, a construction plan of sorts. The cells then use this RNA to produce proteins, the workhorses of the cells, which ultimately decide how a cell handles cholesterol.

Blattmann interrupts the chain of command by introducing siRNA into the cell. These are short fragments of RNA that bind to specific sections of RNA, so disrupting their function. This can be likened to a blind spot in the construction plan. As a consequence, the cell becomes incapable of producing certain proteins. Blattmann hopes to find out how the protein composition in the cells is modified on account of these blind spots.

To do so, he must measure their concentration, something that has only recently become possible. Just a few years ago, the Aebersold group at the Institute of Molecular Systems Biology at the ETH Zurich developed an analysis method capable of dealing with large amounts of data. It involves, among other things, two serially connected mass spectrometers, called a tandem mass spectrometer, which can measure the concentrations of up to three thousand different proteins.

Computer sorts fragments

To start with, Blattmann must disaggregate the cells into their individual components by pouring urea over them. The cells then disintegrate into a slurry of proteins which are still too large for the mass spectrometer. They are then further fragmented by means of enzymes and reduced to peptides, their basic components. Using chromatography, these peptides are sorted according to their chemical properties and then slowly injected into the mass spectrometer.

The tandem mass spectrometer determines the exact amount of each peptide present. Subsequently, a high-performance computer assigns each peptide to the correct protein. One might compare this to determining the nature of a completed Lego model simply by looking at a box of disassembled blocks without a construction plan. Mass spectrometers and computers are very good at this. They can recognize more than 15,000 peptides simultaneously and will provide information regarding the composition of the most frequent proteins present in a cell within two to three hours.

Blattmann feeds this data into a model resembling a circuit diagram that illustrates the interactions between the proteins. "This provides an exclusive glimpse into the cell", says Blattmann. He can now follow the entire chain of command between the proteins, for instance identifying the effect of changes in the chain on the capacity to remove cholesterol from the bloodstream.

Developing improved drugs

The results of this work might one day help explain why cholesterol-reducing drugs are more effective in some patients than in others. One such group of drugs is statins. These curb the cell's own cholesterol production and simultaneously stimulate the uptake of cholesterol from the bloodstream.

Many people with high cholesterol levels take this sort of medication. "They work very well for most people", says Blattmann. Yet in some patients they are not so effective, presumably due to an unfavorable combination of genes.

In order to investigate the interplay between statins and the genome, Blattmann adds different concentrations of a statin to his cell lines. At the same time, he blocks one gene after another and observes the influence this has on cholesterol uptake. "We still know very little about our cells. However, once we have models, we can grasp what happens in a cell exposed to a given drug", explains Blattmann. In future, this could contribute to the development of more effective drugs.

The project at a glance

Project title: Understanding the genotype to phenotype transformation for cholesterol regulation using a network-based approach

Fellow: Dr. Peter Blattmann, Institute for Molecular Systems Biology, ETH Zurich

Host research group: Prof. Ruedi Aebersold, Institute for Molecular Systems Biology, ETH Zurich

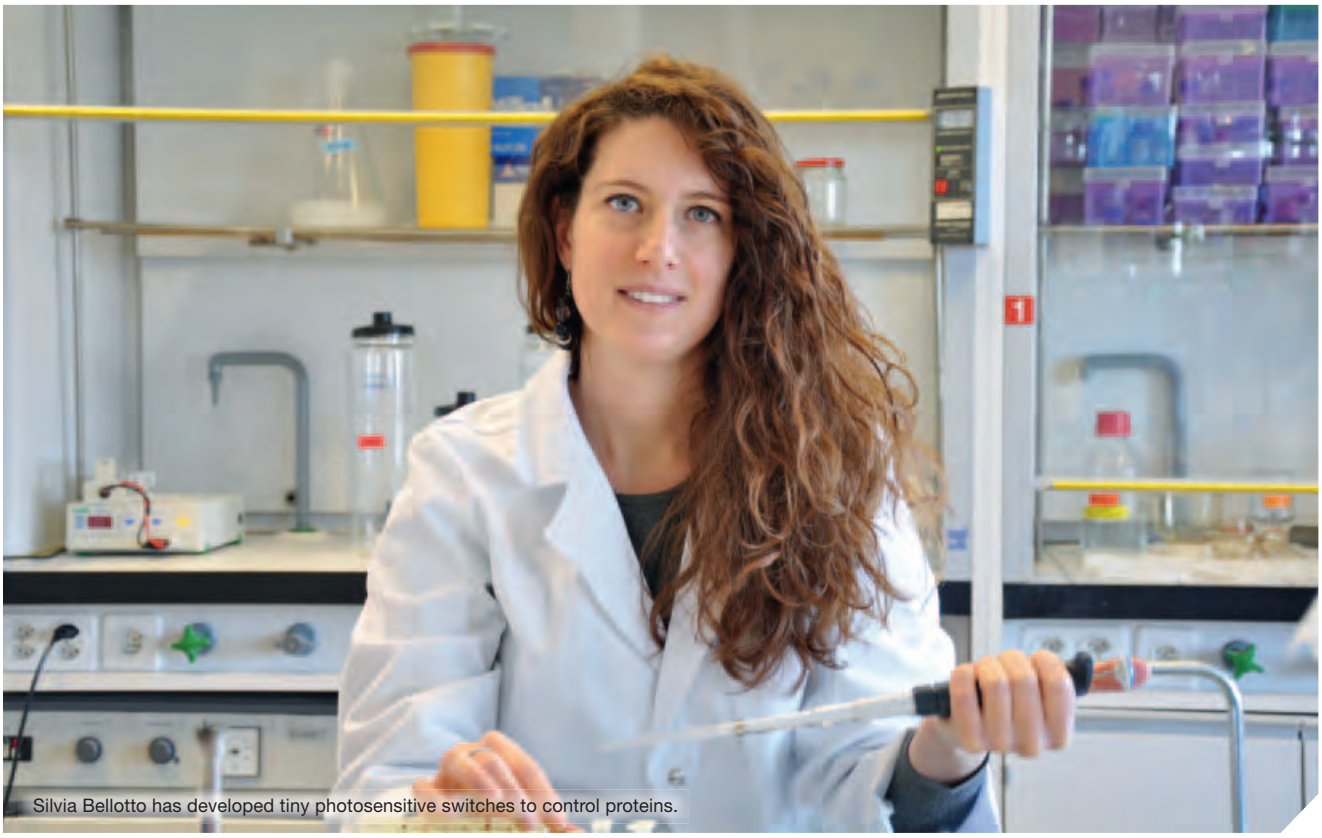
Project duration: 2013–2015

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

Interdisciplinary PhD Project (IPhD)

Steering proteins with light

Biotechnologists are dreaming of being able to modulate the activity of proteins very precisely within a cell or organism. Molecules that help them do so, and which can be switched on and off highly selectively at a specific region or point in time, would be of enormous value as tools in fundamental research. Silvia Bellotto's IPhD Project is a step in the right direction for turning this vision into reality.



Silvia Bellotto has developed tiny photosensitive switches to control proteins.

In the cells of living organisms, proteins are important players in nearly every process. Amongst other things, they are involved in transporting, building and breaking down substances. Researchers investigate the role of proteins, for example in cell metabolism, cell-to-cell communication, cell motility or cancer development. But as proteins are so numerous and often have more than one task to fulfill, it is difficult to ascertain just what a particular one of them does. In order to investigate this, researchers use molecules that recognize and bind to specific proteins, inactivating them. This way, the function of the affected proteins can be examined.

There is a catch, however. Typically, these molecules are added at a specific point in time to a cell or whole organism, but cannot be rapidly removed or switched off. In addition, most of them cannot be added locally to a distinct region of the cell or organism. In order to modulate proteins at a particular temporal and spatial resolution, it would therefore be ideal if there were such molecules available which could be switched on or off at desired times and in isolated regions.

In her PhD thesis, the biotechnologist Silvia Bellotto shows how this could work by use of molecules which spread throughout the whole cell or organism, but which are only activated by light, where and when desired. To this end, the scientist has developed so-called photoswitchable ligands. These are molecules which, under the influence of light, change their shape and only then bind to a specific protein, inhibiting it. "A molecule which functions according to this principle can be steered by light, and therefore it is possible to precisely determine when and in which part of the cell or organism it should act", explains Bellotto.

Tiny light-sensitive switches

The photoswitchable ligands developed by Silvia Bellotto feature two components: they consist of an azobenzene, which bends when subjected to light, and a peptide which binds to the target protein. The two elements are connected to each other at each end (see illustration page 17).

The ligand can be pictured as a kind of mini switch: "When light falls on the ligand, the light-sensitive azobenzene bends, causing the peptide to do the same", explains Bellotto. The bent peptide is then able to bind to the target protein and block it. This process is reversible. "When darkness is maintained for long enough, the

wavelength of radiation changed or the temperature raised, the ligand stretches out once more and separates from the protein. Thus the protein returns to its functional state", explains the scientist.

Experimenting in the chemistry lab

"Photoswitchable ligands such as these, which are capable of inhibiting proteins by changing their shape under the influence of light, already exist", concedes Bellotto. But they are not yet technically perfect: most of them bind to target proteins in the unilluminated state as well, albeit less strongly. "Ideally, the illuminated form would bind very well and the unilluminated form not at all", clarifies the scientist.

In order to reach this objective, Bellotto worked assiduously on the development of appropriate light-sensitive azobenzenes during the first stage of her IPhD project. She is not yet completely satisfied with the results. "There are still too many ligands binding in both conformations, bent and unbent", says the young scientist. "Further research and development are still necessary."

Evolution in a test-tube

However, Bellotto is very happy with her solution to a further problem: at this point in time, photoswitchable ligands are only available for a small number of proteins. "Until now, the production of such ligands was very complex", explains Bellotto. The scientist has therefore developed a method by which light-sensitive ligands can be produced comparatively quickly for any given protein.

She chose streptavidin as a model protein. Instead of selectively producing and testing individual peptides for their suitability, the scientist's method relied on chance. Using microorganisms called bacteriophages, she produced billions of randomly assembled peptides, to which she then added light-sensitive azobenzenes to produce photoswitchable ligands.

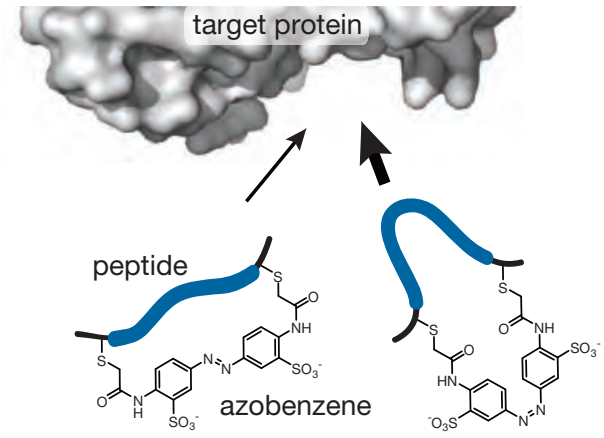
In order to determine which of these billions of potential mini switches are able to bind to the model protein, Bellotto exposed all of them to light and combined them with the target protein in a test tube. "This is similar to playing the lottery", says the biotechnologist. "The more tickets you purchase, the better your odds of winning are."

As a matter of fact, several ligands bound to the model protein. In the course of the following test cycles, the scientist always selected the most efficiently binding ligands. Thanks to this selection method, a sort of small-scale evolution, she was able to identify suitable ligands within only two cycles. Using a human protein, a protease which plays an important role in tumor growth and metastasis formation, Bellotto then demonstrated that this method also works for other proteins.

Temporal and spatial modulation of proteins

Now is the time to apply photoswitchable ligands to research and the study of complex biological systems. "Such ligands could, for instance, be used to block an enzyme essential to the metabolism of cancer cells", illustrates Bellotto. The ligands could be triggered by UV light and switched on precisely when and where needed in the tumor cells. Scientists could then find out which role the blocked enzyme actually plays and which other enzymes it interacts with. "As this blocking is reversible, the system could be restored and then another protein or enzyme targeted", explains the scientist. Based on these investigations and the resulting data, researchers would be able to build mathematical models that help understand the complex biological system of a tumor cell.

The work on this project is now over for Silvia Bellotto. She completed her PhD thesis in January 2015, and is particularly enthusiastic about the interdisciplinary aspect of her IPhD: "I had two project advisors specialized in different disciplines, and therefore had the opportunity to work in two different research groups. Thanks to this situation, I discovered many things I would not otherwise have been able to see". She found the change of perspective this gave her particularly valuable. Next, Silvia Bellotto is going to work for a biopharma company. "I am really looking forward to starting there and applying all the knowledge gained from my PhD and ultimately contributing to the development of therapeutic proteins."



The photoswitchable ligand on the right has been exposed to light. Having changed its shape, it binds much more efficiently to the target protein than the unexposed ligand. Illustration: Reprinted with permission from J. Am. Chem. Soc. 2014, 136, 5880–5883. Copyright 2014 American Chemical Society

The project at a glance

Project title: Quantifying the activity contribution of individual matrix metalloproteinases (MMPs) to the overall MPP activity in the extracellular space using highly specific and photoswitchable inhibitors

PhD student: Silvia Bellotto, EPF Lausanne and Justus Liebig University Giessen

Supervisors: Prof. Christian Heinis, Laboratory of Therapeutic Proteins and Peptides, EPF Lausanne; Prof. Hermann A. Wegner, Institute for Organic Chemistry, Justus Liebig University Giessen

Project duration: 2010–2015

Project type: Interdisciplinary PhD Project (IPhD)

Heide Hess

FAIRDOM

Data management at the European level

The FAIRDOM project was launched in the spring of 2014. This joint initiative of the international ERASysAPP and ISBE networks encourages the exchange and long-term use of scientific data and models generated in systems biology projects throughout Europe. SystemsX.ch has contributed 750,000 Swiss francs to FAIRDOM, as well as the know-how from its own SyBIT data management project.

The FAIRDOM project aims to facilitate collaborations between systems biologists in Europe: research data and models from systems biology projects are to be made available for further research thanks to "fair" data management (see box).

The heart of the FAIRDOM project is the organization of a central platform for the management, exchange and archiving of scientific data and models. Switzerland, Great Britain, Germany and the Netherlands are involved in the project. Wolfgang Müller, the German representative in the FAIRDOM consortium, is convinced that a central infrastructure is extremely important for the future of systems biology research in Europe. "FAIRDOM facilitates collaboration in systems biology projects and guarantees that the research results can be used on a long-term basis", says the German data management expert.

Re-using research results

Until now, systems biology research results were often not accessible for further scientific research after a project was completed. The central FAIRDOM platform should change this, not least because "research investments only become sustainable once the data can be reused for follow-up research projects", emphasizes Wolfgang Müller.

FAIRDOM has defined two measures to ensure that the published research data remains available and usable beyond the end of a project. The participants have access to the published data and results of all involved research groups, and they can count on support regarding the standardized and central storage of their data, which can be archived for at least ten years.

IT tools and services

Not only can research groups exchange information and data thanks to the central FAIRDOM platform, but the so-called FAIRDOMHub also helps scientists with project management and resource planning. The data management platforms openBIS and SEEK provide the technical basis for this. Additionally, a toolbox provides a wide range of IT modules and tools, for example for the modeling of biological processes. Researchers can select tools for their projects based on their individual needs.

"FAIRDOM services go far beyond providing a central infrastructure", explains Müller. "For instance, in preparation for a project, FAIRDOM helps scientists write their proposal and provides valuable support through webinars and checklists for data management." After a project has been launched, an international network of experts offers advice and active support with respect to the implementation of project-wide data management. The services range from data exchange templates to software adaptation and discussions regarding data flow within the project. In order to establish know-how at the local level, thereby guaranteeing long-term standardized data management, FAIRDOM also organizes events such as courses and user meetings.

Active participation

SystemsX.ch has decided to support the FAIRDOM project, contributing the data management platform openBIS, which has been in development since 2007 at ETH Zurich and is used in many SystemsX.ch projects. The groups of Peter Kunszt (University of Zurich) and Bernd Rinn (ETH Zurich) are actively participating in FAIRDOM, using their extensive experience from SyBIT. Through its contribution to FAIRDOM, Switzerland as a center for systems biology research will be able to firmly anchor itself in the European research sector.

The FAIRDOM project

Findable, **A**ccessible, **I**nteroperable and **R**eusable (**FAIR**) **D**ata, **O**perating procedures and **M**odels (**DOM**)

These countries and institutions support the project:

Germany	The Federal Ministry of Education and Research (BMBF), Dr. Wolfgang Müller, HITS, Heidelberg
Great Britain	Biotechnology and Biological Sciences Research Council (BBSRC), Prof. Carole Goble, University of Manchester (Coordinator)
The Netherlands	The Netherlands Organization for Scientific Research (NWO), Dr. Katy Wolstencroft, Leiden University
Switzerland	SystemsX.ch, Dr. Peter Kunszt, University of Zurich and SIB Swiss Institute of Bioinformatics; Dr. Bernd Rinn, ETH Zurich and SIB Swiss Institute of Bioinformatics

For more information, visit **www.fair-dom.org**

Welcome to the team, Maja!

Maja Schaffner joined the SystemsX.ch communications team in the summer of 2014, first standing in for a colleague on maternity leave, and since the beginning of this year working 60 percent as a permanent member of the team. Being both a biologist and a scientific journalist, she mainly writes scientific articles but also takes care of the initiative's website and newsletter.

Maja studied biology at the ETH Zurich, then successfully completed a degree in journalism and finally discovered her dream job as a scientific journalist. Before she joined SystemsX.ch, she was a freelance journalist, writing for "ETH News", "Tierwelt" and the scientific spread in "20 Minuten", among others. Maja loves to write about research themes and is especially looking forward to portraying different SystemsX.ch projects.

We would like to thank Maja for her great work so far and look forward to a continuing fruitful collaboration.

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IBM and ZHAW are new SystemsX.ch partners

SystemsX.ch is pleased to welcome two new partners. In January 2015, the IBM Zurich Research Laboratory joined the Swiss Initiative in Systems Biology. The renowned private research institution is already involved in several SystemsX.ch projects and is currently establishing its own systems biology department.

In March 2015, the Zurich University of Applied Sciences (ZHAW) also became a SystemsX.ch partner institution. Several ZHAW research groups use systems biology approaches in their work. One of these teams is involved in the AneuX Medical Research and Development Project.

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First SystemsX.ch Postdoc Workshop

Titled "Leadership and Management Skills for Postdocs", the first SystemsX.ch workshop for postdoctoral fellows took place in Gerzensee in February 2015. The aim of the two-day course was to support postdoctoral researchers in their current work as well as their future careers. Led by hfp consulting, the 16 participants were engaged in subjects such as conflict management, work organization and leadership. The format met with high approval. Julien Limenitakis from the University of Bern said: "I recommend this workshop to all postdocs, no matter what plans they have for their career." Another edition of the successful event is planned for 2016.

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Thank you and goodbye, Matthias!

Matthias Scholer took on responsibility for SystemsX.ch communications in 2010. Thanks to his concise writing style and creativity, the veterinarian and science journalist has significantly contributed to the professional establishment and development of the initiative's communications management. He was in charge of the design of the new website, contributed to the new layout of the X-Letter and wrote about numerous research projects.

He produced the first film describing a SystemsX.ch research project, as movies were always close to his heart: "The Tef Improvement Project" shows a scientist at the University of Bern who hopes to significantly improve the nutritional situation in Ethiopia with the help of systems biology methods.

Since January 2015, Matthias and his wife have been traveling across Europe with their photo equipment, a voice recorder and an idea for a book. We would like to thank Matthias for his tireless commitment to SystemsX.ch, and wish him all the best for his professional and personal future.

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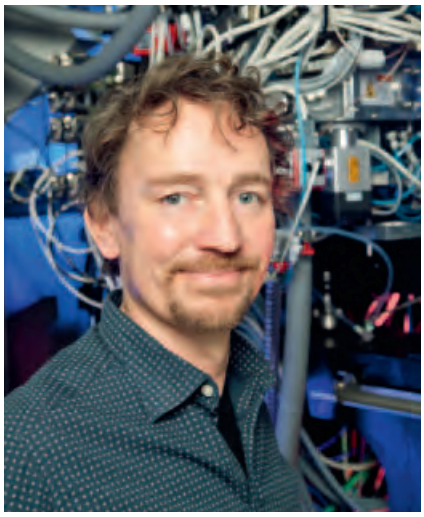

All SystemsX.ch Day 2015

September 15, 2015, Stufenbau, Ittigen, Bern

Swiss-wide systems biology networking and information exchange event

Presentations in 3 sessions:

- Young researchers (PhD students and postdocs)
- Fundamental systems biology research
- Challenges of interdisciplinary research

Plus poster sessions and barbecue

Contact: katy.pegg@systemsx.ch, www.systemsx.ch

SystemsX.ch
The Swiss Initiative in Systems Biology