



**SystemsX.ch**

The Swiss Initiative in Systems Biology

## **SystemsX.ch Scientific Report 2014-2015**

Submitted according to the administration contract of September 2008 between  
SystemsX.ch  
and  
the Swiss National Science Foundation (SNSF)

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## Executive Summary

The overarching goal of the Swiss Initiative for Systems Biology is to establish and sustain systems biology research in Switzerland at an internationally competitive level. To achieve this ambitious goal SystemsX.ch was formed as a simple partnership that, in turn, advances systems biology in Switzerland by (i) supporting academic research projects, (ii) educating the next generation systems biology scientists, (iii) supporting private-public sector partnerships, and by (iv) participating in international systems biology programs. SystemsX.ch now consists of fifteen partner institutions across Switzerland.

The initiative is now in its 8<sup>th</sup> year. The first phase, the so-called initiation phase, lasted from 2008 to 2012. Most projects approved during this period have been completed, even though some (in particular Interdisciplinary PhD Projects, IPhDs) are still running. The various procedures of SystemsX.ch are well established and became routine. The main activities in the reporting year were the 11<sup>th</sup> and 12<sup>th</sup> calls for proposals, for which a total 109 proposals were submitted. The European Research Area Network (ERA-Net) for Applied Systems Biology entitled “ERASysAPP”, which started in January 2013, launched its first and second joint transnational call for projects and approved 12 projects of international research consortia. SystemsX.ch was mandated by the State Secretariat for Education, Research and Innovation (SERI) and the Swiss National Science Foundation (SNSF) to represent Switzerland as one of 16 European partners from 13 countries within this ERA-Net. SystemsX.ch leads work package 3 “Training and Exchange”, and within that frame co-organizes the biannual “Advanced Lecture Course in Systems Biology” and supports several other workshops and educational events.

In 2015, IBM Zurich Research Laboratory (IBM ZRL) and Zurich University of Applied Sciences (ZHAW) became SystemsX.ch partners. Hence, the simple society counts now 15 institutions. Until August 2015, a total of 248 projects involving 401 research groups from various disciplines and institutions have been approved for funding, after undergoing rigorous international peer reviews, most of them administered by the SNSF and SystemsX.ch. The projects approved in earlier years as well as the newly approved projects contribute to achieve the diverse objectives of SystemsX.ch. During the reporting year, i.e. between September 2014 and August 2015 for 42 new projects (40 SystemsX.ch projects, plus SyBIT, plus two ERASysAPP projects a total amount of CHF 26'665'414 have been approved: nine Medical Research and Development projects (MRD; CHF 18'587'700), two Transfer projects (TF; CHF 600'000), eight Transition Postdoc Fellowships (TPdF; CHF 1'731'587), ten Interdisciplinary PhD projects (IPhD; CHF 1'970'732), SyBIT (1'480'000), ten Special Opportunity Projects (1'738'680) and two ERASysAPP projects (556'716).

A number of measurable indicators suggest that the implemented programs are effective towards the SystemsX.ch goals: (a) about 54% of the scientists participating in the approved projects are not biologists, attesting to the high level of interdisciplinarity that has been achieved; (b) numerous publications reporting SystemsX.ch research appeared in top-ranked international journals (Science, Nature, Cell), indicating the high quality and impact of the work; (c) the PhD students and postdocs supported by IPhD or TPdF projects, but also those working on RTD projects, benefit from retreats, summer schools and other activities. SystemsX.ch PhD students find after completion of their PhD thesis attractive positions at renowned institutions in both, academia and the private sector; (d) the BIP and Special Opportunities projects have forged new interactions between the private and public sector. TF projects solidify these contacts and form the foundation for even more intensive collaborations in the future; and (e) SystemsX.ch is a partner in ERASysAPP and has co-organized and supported a range of international systems biology events for research and educational purposes, indicating that the initiative is becoming well connected and recognized internationally.

## 1 Status report: Activities of SystemsX.ch from September 2014 to August 2015

This reporting period has been the second to fall completely within the second phase of SystemsX.ch. Most of the approved projects of the first phase were already completed, or about to be completed. This is in particular true for RTDs, IPPs and BIPs, as well as some IPhDs.

In this reporting period 26 RTD projects have been active. All RTDs approved in 2009 (BattleX, InfectX, CINA, CellPlasticity, CycliX and MetaNetX) reached their end by the end of 2014. The eleven new RTDs approved after the 6<sup>th</sup> call for proposals started in the first half of 2013, and the nine new RTDs approved in 2013 after the 8<sup>th</sup> call started between January and May 2014. All twenty RTDs approved in 2012 and 2013 have been running during the 2014-2015 reporting period.

In 2014, after reviewing the 10<sup>th</sup> call proposals, nine MRD (Medical Research and Development) projects have been approved, out of which seven reported their activities until July 2015 (since January 2015). One project started in June and one in July 2015.

In order to further stimulate the interaction with the private sector, the new project type Transfer Project (TF) was introduced with the 6<sup>th</sup> call for proposals. Eight TF projects have been active in this reporting period. The first four TF Projects started in 2013 had been completed between December 2014 and April 2015. The two TFs granted after the 8<sup>th</sup> call for proposals started in the Spring of 2014, and the two new TFs granted after the 10<sup>th</sup> call started in April and June 2015.

Three Special Opportunities project have been active in this reporting period (SIB Fellowship, SwissLipids, Ciftlic). The 12<sup>th</sup> call for Special Opportunities projects (May 2015) has generated 51 proposals, after the review procedure nine new Special Opportunities projects were approved by the SEB, five of them with full and four of them with partial funding.

Twenty-two TPdF projects have been active in this reporting period. All three Transition Postdoc Fellows (TPdF) who started in 2012/2013 (5<sup>th</sup> call for proposal) requested a 3<sup>rd</sup> year extension, one of them completed his fellowship in January 2015, two of them are still working until September and December 2015. The 13 TPdF projects approved in 2013 (7<sup>th</sup> call for proposals) are all running, two of the TPdF changed their host laboratory in in the course of this reporting period. Following the 9<sup>th</sup> call for proposals (2014), out of the seven fellowships granted, six have already started, one will start in August 2015. The 11<sup>th</sup> call for proposals (April 2015) has generated 33 TPdF proposals, after the review procedure 8 new TPdF projects were approved by the SEB and SNSF.

44 IPhD projects have been active in this reporting period. All IPhDs granted in 2008 and 2009 terminated before or within this reporting period. Ten of the 13 IPhDs granted in 2010 are running with 4<sup>th</sup> year extensions. All but one of the eleven IPhDs granted in 2012 are running. All nine IPhDs granted in 2013 have been active in 2014/2015. 15 out of the 17 IPhDs granted in 2014 have started already, one will start in November 2015 and for one the IPhD students was not recruited yet. The 11<sup>th</sup> call for proposals (April 2015) has generated 25 IPhD proposals, after the review procedure 10 new IPhD projects were approved by the SEB and SNSF.

The project types Interdisciplinary Pilot Projects (IPP) and Bridge to Industry Projects (BIP), as well as the Industry Sabbaticals in Academia (ISA), were terminated by the SEB. The last projects of these all ended in 2013, therefore they are not included in this Scientific Report.

This first chapter summarizes activities of the SystemsX.ch community and its governing bodies.

## 1.1 Activities of the SystemsX.ch community

The four strategic themes that SystemsX.ch focused on for the first phase 2008-2012 remain and are the basis of the consolidation phase of 2013-2016: (i) Excellent science, (ii) Support of education and training, (iii) Foster ways to promote public-private partnership, and (iv) International outreach, visibility and recognition. Especially the last point is becoming more significant because international networking is contributing towards the sustainability of systems biology in Switzerland. The participation of SystemsX.ch in the ERA-Net ERASysAPP and in multiple internationally renowned systems biology conferences further solidifies this networking. The contributions of the various SystemsX.ch projects towards these goals are detailed in their respective reports appended to this document.

### 1.1.1 Science

#### *Running SystemsX.ch projects*

Overall, out of the 625 submitted proposals a total of 248 projects have been approved by the SNSF and/or the SEB, involving 401 research groups, some participating in two or more projects and every year about 1'000 scientists. The major funding (77%) went to the 34 RTDs (including High-Tech Funds, HTF, in the first phase) plus SyBIT, and to the nine new MRD projects. Eight TF Projects from the 6<sup>th</sup>, 8<sup>th</sup> and 10<sup>th</sup> calls show that the contact with the private sector is proactively encouraged. This is continued with the Special Opportunities projects approved after the 12<sup>th</sup> call, one project here also work with a private partner. With the 5<sup>th</sup>, 7<sup>th</sup>, 9<sup>th</sup> and 11<sup>th</sup> call for proposals 32 TPdF projects were approved, supporting young scientists in acquiring new competencies in the field of systems biology. The 87 IPhD Projects were planned with duration of 3-4 years (with the exception of two projects which were approved for only one year, as an extension of previous funding from different sources). The attractivity of the TPdF and IPhD programs has been illustrated by the great success of the 11<sup>th</sup> call for proposals, in which 33 TPdF and 25 IPhD proposals were submitted.

#### 1.1.1.1 RTD projects

Since March 2008, a total of 34 RTD projects have been approved by the SNSF: eight in 2008, six in 2009, eleven in 2012 and nine in 2013. Details about these RTD projects can be found in Tables A6 to A8 in Appendix A (active RTDs) and in Tables D6 to D10 in Appendix D (all approved RTDs).

The RTDs approved in 2008, 2009 and 2012 underwent a mid-term reviews by the SNSF review panel in October 2010, 2011 and 2014, respectively. The RTDs approved in 2008 were given the opportunity to apply for a one-year extension of funding (for 2012) due to a special mechanism in the procedure of the Federal administration. During the evaluation of these requests, the SNSF review panel decided to reject the continuation of LiverX, whose funding was therefore stopped in 2011. The other seven 2008 RTDs continued for this extra year. The eleven 2012 and nine 2013 RTDs continued their activities in this reporting period. The scientific reports of RTDs can be found in Appendix B.

#### 1.1.1.2 MRD projects

Since the 2<sup>nd</sup> call in 2009, the call text mentioned that medical relevant proposals are of particular interest. However, it turned out that rather few such projects were approved. The BoD decided, therefore, to invite in the 10<sup>th</sup> call for proposals of SystemsX.ch applications for Medical Research and Development (MRD) Projects, with a similar consortium structure to RTDs, but with a medical or clinical orientation and a duration limited to three years (due to the fact that the initiative will come to an end in December 2018). Out of 30 proposals that were received, nine has been approved by the SEB and the SNSF review panel. Eight MRD projects have started since January 2015, and have been active within this reporting period

(before July 2015). The activity/scientific reports of the already active MRDs can be found in Appendix B.

### **1.1.1.3 Special Opportunity projects and High Tech Service Funds**

In 2012, SystemsX.ch introduced the Special Opportunities project type. This funding source is meant to support non-mainstream projects that do not qualify for traditional funding, and which pragmatically contribute to SystemsX.ch and systems biology research in Switzerland. In part, the Special Opportunities projects take over the gap left by the termination of the High Tech Service Funds (HTF) program. Until 2012, SystemsX.ch allocated HTFs, which were funds made available to RTDs after review by the SEB. These funds were meant to cover unforeseeable costs for new, cutting-edge equipment, new/updated technologies or to overcome technology bottlenecks that could not be anticipated during proposal writing. The idea behind this program was to prevent projects from not being able to realize their full potential due to limited access to the latest technologies. An overview of approved HTFs is given in Appendix D, Table D35.

In contrast to HTF, every researcher working in SystemsX.ch partner institutions can apply for Special Opportunity Funds. Six Special Opportunities proposals have been approved by the SEB between October 2011 and December 2014. Three Special Opportunities projects have been active in this reporting period, and following 12<sup>th</sup> call, which was particularly dedicated to Special Opportunities projects, out of the 51 submitted proposals, nine further ones are supported by SystemsX.ch (five with full and four with partial funding). More details about approved Special Opportunities projects can be found in Appendix A, Table A22.

### **1.1.1.4 Transfer Projects (TF)**

These projects specifically promote public-private partnerships between academia and industry in the field of systems biology. Alternatively, TF projects can link academia and (private) hospitals to find systems approaches to clinical questions. The number of principal investigators is at least two (one academic, one private). These projects are awarded for two years, and are extendable – following a successful evaluation – for a third year. With the 6<sup>th</sup> call for proposals, the first four TFs were approved by SEB and SNSF in December 2012 and all four 2012 TFs came to an end within this reporting period. Two TFs were approved after the 8<sup>th</sup> call for proposals in Autumn 2013, and further two after the 10<sup>th</sup> call for proposals in Autumn 2014 (see Appendix A, Table A10-12). The scientific reports of TFs can be found in Appendix B.

### **1.1.1.5 Transition Postdoc Fellowship (TPdF) Projects**

The TPdF project type aims to enable young researchers in systems biology to increase their knowledge and expertise in a scientific field complementary to the domain in which they have worked so far. This funding instrument opens a possibility for graduated PhD students from the first phase of SystemsX.ch to continue their career in the field of systems biology. Furthermore, TPdF enables the entrance of young scientists from Switzerland and abroad into the Swiss systems biology community and therewith into new research groups and additional disciplines.

Since the introduction of these fellowships in 2012, twenty-four fellowships have been granted. The number of submissions has increased from 17 in the 5<sup>th</sup> call to 28 in the 9<sup>th</sup> call, and to 33 in the 11<sup>th</sup> call, proving that the program is attractive and well received. Out of the 33 TPdF proposals that were submitted for the 11<sup>th</sup> call for TPdF projects, eight new TPdF projects were approved by the SEB and SNSF. All approved TPdF projects from 2012 to 2014 are listed in Appendix A, Tables A13 and A16. The scientific reports of TPdFs can be found in Appendix B.

#### **1.1.1.6 IPhD Projects**

The SEB and the SNSF approved a total of 77 IPhD projects between 2008 and 2014. Out of them, 44 were running in this reporting period. Their annual reports can be found in Appendix B. Out of the 25 IPhD proposals that were submitted for the 11<sup>th</sup> call, ten new IPhD projects were approved by the SEB and SNSF in August 2015. The list of all the 87 approved IPhDs from 2008-2015 is shown in Appendix D, Tables D19-D25, and all active IPhD projects are listed in Appendix A, Tables A17-A21.

#### **1.1.1.7 IPP and BIP Projects**

Both IPP (Interdisciplinary Pilot Project) and BIP (Bridge to Industry Project) Project types have come to an end in the 2013-2014 reporting period.

The IPPs were established to facilitate the start in exploring new research directions and ideas. These projects brought together research teams from different disciplines to address "seed" or "high-risk" topics critical for systems biology. The new project type Transition Post-doc Fellowships (TPdF) that was launched in spring 2012 has replaced the IPPs.

The BIPs were established with the aim of fostering academia-industry collaborations, and had a strong focus on developing technologies and/or analytical methods and their applications. The new project type Transfer Project (TF) was launched in November 2011 and has in a certain way replaced the BIPs.

The lists of all 30 approved IPPs from 2008-2012, and all 16 approved BIPs from 2010-2011 are shown in Appendix D, Tables D29-D34.

#### **1.1.1.8 Calls for proposals**

Two SystemsX.ch calls for proposals were published within the reporting phase: the 11<sup>th</sup> call in December 2014 (deadline April 30, 2015) for TPdF and IPhD proposals, and the 12<sup>th</sup> call in March 2015 (deadline May 17, 2015) for Special Opportunities project proposals (see Appendix A, Table A2).

For the 11<sup>th</sup> call, 33 TPdF proposals and 25 IPhD proposals were submitted, out of which 8 TPdF projects and 10 IPhD projects were approved.

In the 12<sup>th</sup> call for proposals, the number of submitted proposals was very high, which confirms the growing importance of cutting-edge systems biology research, as well as the timeliness of providing special funding instruments for interdisciplinary research in this field. Out of the 51 proposals 9 are supported by SystemsX.ch (5 with full and 4 with partial funding).

#### **1.1.1.9 Events and conferences**

Several events have been (co-)organized and/or supported by SystemsX.ch in this reporting period. Clearly, scientists involved in SystemsX.ch attended numerous conferences, congresses, workshops, and seminars. Table A52 in the Appendix A gives an overview of events, which SystemsX.ch organized, co-organized or supported scientifically and/or financially (see also chapter 1.1.5).

#### **1.1.1.10 Awards for SystemsX.ch scientists**

SystemsX.ch scientists have received awards for their work. Although the scientists are recognized for more than just their SystemsX.ch activities, these awards are an indication of the quality of the participating scientists. A summary of the awards received by researchers participating in SystemsX.ch projects is shown in Appendix A, Tables A25 and A26.



### **1.1.2 Education**

Educating the next generation of systems biologists is of central importance to SystemsX.ch. During the reporting year, more than 200 PhD students have worked on SystemsX.ch projects (about 159 on RTD projects and 44 on IPHD projects).

Furthermore, 22 postdocs are being funded through the TPdF program, and eight new projects of the 11<sup>th</sup> call for proposals were approved. Some 175 postdocs have worked on RTDs and TFs.

In order to satisfy the training needs of the growing community of PhD students and postdocs, SystemsX.ch has (co-)offered a number of education events (see details below and in Table A52, Appendix A).

#### **1.1.2.1 Education Advisory Board (EAB)**

The SystemsX.ch Education Board was established in 2008 and was chaired by Michael Hengartner (University of Zurich) until December 2013. Tables with the members of the Education Board and respective meetings can be found in the Appendix A, Tables A46 and A47.

In February 2013 the members of the SEB requested that the necessity for an EAB, as well as its tasks and duties be reevaluated. The EAB discussed this in April 2013, and it was decided that the EAB advises the MO on all questions relevant to SystemsX.ch education (e.g. additional courses, content of education events etc.). The EAB is asked about measures of SystemsX.ch education and their content, and gives recommendations in the case of topics that have to be discussed by the SEB.

#### **1.1.2.2 Swiss Institute of Bioinformatics SIB PhD Fellowship Program**

In 2012, the Swiss Institute of Bioinformatics (SIB) launched a new program to promote young researchers. SystemsX.ch agreed to fund two PhD students within the SIB PhD Fellowship program. Christos Dimitrakopoulos (in Niko Beerenwinkel's research group at D-BSSE of ETH Zurich) and Jannik Vollmer (in Dagmar Iber's research group at D-BSSE of ETH Zurich) are the two supported PhD students.

#### **1.1.2.3 SystemsX.ch Retreat**

The SystemsX.ch Retreat has established a reputation as the main SystemsX.ch event for PhD students but also for postdocs. The aim of the retreat is for young researchers to meet informally, in absence of PhD supervisors, and to exchange information, but also to learn non-scientific skills. The event provides an opportunity to learn about the various student projects supported by SystemsX.ch. This not only allows the students to broaden their understanding of scientific research in systems biology, but is also, hopefully, an opportunity for them to interact in a relaxed and supportive environment where they can freely share information, advice and ideas, which can potentially lead to scientific collaborations.

The format of the SystemsX.ch Retreat in March 2015 held in Rigi Kaltbad was similar to those in the previous year, yet with a different topic: soft skills that are useful in an interdisciplinary field of research were also trained, and networking among the PhD students and postdocs was fostered. The 33 participating young researchers learnt more about how to obtain better results through diversity. This workshop has been very well received, therefore the soft-skills focus of the student retreats will be continued in the next years as well.

#### **1.1.2.4 Postdoc Workshop**

SystemsX.ch organized a Leadership and Management Skills workshop exclusively for postdocs in February 2015 for the first time. 16 participants attended the two-day course, which

took place in Gerzensee, Berner Oberland. The course addressed the human aspects of doing science, by covering the topics: (i) key communication skills, (ii) dealing with conflicts, (iii) organizing work: setting goals, setting priorities, and delegating. The workshop was highly interactive and allowed participants to put theoretical knowledge in practice through multiple exercises. Based on the very positive feedback a one-day follow-up of this workshop is planned for February 2016, as well as the repetition of the same event for new Postdoc participants.

#### **1.1.2.5 Summer/Autumn Schools**

Since 2010, SystemsX.ch has organized or co-organized seven summer schools. In 2015, two joint summer/autumn schools were co-organized: one with the Centre for Genomic Regulation CGR in Barcelona (Spain) and one with the SIB Swiss Institute of Bioinformatics. In both cases it was the third time that SystemsX.ch joined efforts with each partner.

The “5<sup>th</sup> Practical Summer Course: Modeling for Systems Biology” co-organized with the CGR in Barcelona from June 14 to 19, 2015 counted 22 participants (three of them from Swiss research institutions). The course included lectures on basic methods as well as new techniques in systems biology research. The theoretical part was combined with hands-on sessions during which the participants applied and practiced what they had learned.

The SystemsX.ch/SIB joint autumn school “Systems Modeling workshop” is going to take place in Schwarzenberg, from November 08 to 12, 2015. The main organization of this practical modeling course, with introductory theoretical lectures on different topics followed by hands-on modeling sessions has taken place in this reporting period.

#### **1.1.2.6 2<sup>nd</sup> International SystemsX.ch Conference on Systems Biology**

From October 20 to 23, 2014, over 350 scientists in the field of systems biology gathered in Lausanne to participate in the 2<sup>nd</sup> International SystemsX.ch Conference on Systems Biology. The conference, which took place in the new Swiss Tech Convention Center at the EPFL, boasted a full scientific program including talks by world-renowned international as well as Swiss researchers. The focus of this second conference was on systems dynamics in cell- and developmental biology and genetics, which demonstrated a natural development from the omics-focused 1<sup>st</sup> SystemsX.ch Conference in 2011. The program was divided into five sections: “Quantitative Cell Biology”, “Theory and Biophysical Modeling”, “Systems Genetics and Medicine”, “Single Cell Dynamics and Stochastic Phenomena” and “Regulatory Genomics”. In addition to the scientific program, the conference included three poster sessions with over 140 authors presenting their latest research in one of the five focus areas: theory and biophysical modeling, cell- and developmental biology, functional genomics and gene regulation, single-cell biology, and systems genetics and medicine.

#### **1.1.3 Public-private partnership**

Catalyzing interactions between SystemsX.ch and the private sector is important for the program. SystemsX.ch has developed a concept with several new programs to promote private-public partnerships. The idea was to use different ways to reach various stakeholders:

- Seeking collaboration with big pharma companies
- Seeking collaboration with SMEs
- Supporting spin-offs
- Establishing strategic partnerships
- Establishing new project types: in the past Bridge to Industry Projects (BIP) and Industry Sabbaticals in Academia (ISA), currently Transfer Projects (TF).

The current RTDs within SystemsX.ch report numerous collaborations, links and interactions with the private sector (see Table A34 in Appendix A). Several spin-offs were, at least partly, generated out of existing RTDs:

- Biognosys (PhosphoNetX)
- ProteoMedix (PhosphoNetX)
- Microduits GmbH (CINA)
- Genohm SA (CycliX)
- BioDataAnalysis GmbH (TargetInfectX)

Interestingly, one spin-off company (Lunaphore) has spun out from an IPhD project: IPhD student Ata Tuna Ciftlik and his supervisor Martin Gijs, at EPFL, have developed a microfluidic chip that can be used in cancer diagnostics. The device has been patented and will be tested in clinical diagnostics centers in the near future. A side project to further develop and improve the chip is being supported by SystemsX.ch via Special Opportunity Funds.

In 2015, SystemsX.ch welcomed the IBM Zurich Research Laboratory (IBM ZRL) as a new partner organization. The world-renowned private research institution has recently started building up its own systems biology division, and has a strong background in nanotechnology, computational sciences and modeling. Furthermore, the IBM ZRL has already been involved in a SystemsX.ch Transfer Project with pathologists from the University Hospital Zurich.

Further information about various forms of public-private partnerships can be found for each project types in the Appendix B.

#### **1.1.4 International Collaborations and Visibility**

The international visibility of SystemsX.ch, both as a Swiss initiative as on the level of the individual RTD projects, is continuously increasing.

SystemsX.ch and the German Bundesministerium für Bildung und Forschung (BMBF) signed a Memorandum of Understanding (MoU) stating that in case a research group from located in Germany applies in a RTD or MRD consortium and the proposal is funded, The German research group receives its funding from BMBF, since SystemsX.ch cannot send SystemsX.ch Funds abroad.

Other important contributions to this visibility have been among others the following events (for all activities see Table D67 in Appendix D):

- Participation in the ERA-Net ERASysApp (since 2013)
- 2<sup>nd</sup> International SystemsX.ch Conference in Lausanne (October 2014)
- Repetitive support:
  - Bi-annual Advanced Lecture Course on Systems Biology in Innsbruck (2011, 2014)
  - Joint SystemsX.ch/CRG Summer School in Barcelona (2013, 2014 and 2015)
  - BC<sup>2</sup> Computational Biology Conference in Basel (annually since 2008)
  - Systems Biology of Human Diseases (SBHD) in Heidelberg / Boston (2012-2015)
- Support from September 2014 until August 2015:
  - FASEB Mitosis: Spindle Assembly and Function, Big Sky, MT, USA (June 2015)
  - European Conference on Computational Biology in Strasbourg (September, 2014)
  - 9<sup>th</sup> LMB-FMI Graduate Student Symposium in Cambridge (July 2015)
  - EPFL Life Sciences Symposium - LSS 2015 (September 2015)
  - 2<sup>nd</sup> Systems Biology of Infection Symposium (September 2015)

#### **1.1.4.1 ERASysAPP**

The State Secretariat for Education, Research and Innovation (SERI) and the Swiss National Science Foundation (SNSF) mandated SystemsX.ch to represent Switzerland in the ERA-Net (European Research Area Network) for Applied Systems Biology 'ERASysAPP'. This research network was approved by the European Commission in October 2012 and is part of the EU's Seventh Framework Programme for Research FP7. On January 1, 2013 the ERA-SysAPP consortium, composed of 16 partner institutions from 13 countries (Luxembourg, Germany, Switzerland, Spain, Sweden, Iceland, Latvia, The Netherlands, Estonia, Norway, Romania, Cyprus and France), took on its work. The Research Centre Jülich (Germany) is coordinating the activities of this initiative, which are organized in six work packages.

Over a period of three years the partners of ERASysAPP aim to jointly encourage scientist from countries of the ERA-Net to collaborate, exchange knowledge and share existing resources. To set up research networks beyond boundaries, ERASysAPP launches, executes and monitors 2 joint transnational calls for proposals. To reach the aim of setting up transnational research networks it is a requirement that research consortia are composed of minimum three research groups from at least three different ERASysAPP partner countries. The focus of the calls is set on translational research.

In the first joint call, seven out of 32 eligible proposals were approved for funding in June 2014, with a total amount of EUR 9'786'467. Four Swiss research groups were partners in successful research consortia (see Annex D, table D27-28, or Scientific Report 2013-2014).

#### ***2<sup>nd</sup> joint transnational call***

Ten ERASysAPP partner countries were participating in the second joint call for proposal, named 'Further Transfer of Systems Biology Knowledge into Applications' which was launched on October 29, 2014. The earmarked budget for this call added up to EUR 8.4 Mio. Until the submission deadline on January 14, 2015 ten proposals were submitted, involving 48 research groups from 7 different countries. Swiss research groups contributed to four of the submitted proposals. During an intense evaluation process by a group of 15 renowned European experts, six proposals were recommended for funding, three of them were highly recommended. Based on a ranking list elaborated by the evaluation committee and taking available funding from involved countries into account, the participating funding organizations identified five proposals to be funded (EUR 5'771'533) over 36 months. Two Swiss research groups will contribute to two of these projects and will receive a total funding of EUR 463'582 (= CHF 556'716 ) from SystemsX.ch.

#### ***ERASysAPP activities of SystemsX.ch***

As leader of work package 3 (WP3), entitled "Training and Exchange", SystemsX.ch is responsible for the compilation of a catalogue of European graduate study programs as well as the publication of open-access events on the ERASysAPP websites. Another WP3 task is the organization and/or support of systems biology courses. Furthermore, SystemsX.ch is in charge of organizing individually requested know-how transfer for researchers working in projects funded by the ERASysAPP consortium. Listing web-based learning programs, developing an exchange platform to share educational material as well as the design of curricula recommendations are further tasks this work package has to fulfill.

In addition to the duties as work package leader, SystemsX.ch participates in various work packages, especially work package 2 "Funding Activities" and work package 4 "Data Management". SystemsX.ch contributes to the funding activities mainly by determining call topics, supporting the setup of call documents and call procedures, suggesting reviewers and implementation of communication measures. Furthermore, SystemsX.ch was initiating the organization of an ERASysAPP Info and Networking Day, which intended to foster networking and exchange between the researchers funded by the ERASysAPP consortium.

Data management is mainly driven by the service project “FAIRDOM”, which is jointly funded by Germany (BMBF), UK (BBSRC), Switzerland (SystemsX.ch) and the Netherlands (NOW). Through SyBIT, the Swiss partner in the FAIRDOM consortium, SystemsX.ch provides Swiss experience in data and model management internationally. FAIRDOM aims to establish an Europe-wide model for sustainable data and model management services in the life sciences. Initially, FAIRDOM will support research projects funded by the ERASysAPP consortium and will continuously extend its services to the European systems biology community. The total budget granted by the funders is EUR 2.7 Mio for a running time of five years. SystemsX.ch is supporting the FAIRDOM activities with an amount of CHF 660'000 over a period of 2.5 years.

#### **1.1.4.2 Others (international collaboration and visibility)**

In addition, SystemsX.ch carried out the following activities:

- The SystemsX.ch Management Office acts as the secretariat for the International Society for Systems Biology (ISSB).
- Several professors recently recruited by partner institutions testified that SystemsX.ch was an important factor for them to decide to come to a Switzerland.
- The success rate of Swiss applicants to Systems Biology calls of the EU 7th framework program is clearly above average. The RTDs have reported participation in more than 30 EU projects and 7 Marie Curie actions.
- In competing for ERC funding, Switzerland is, together with Israel, the most successful country per capita. Researchers of the SystemsX.ch community have been awarded 40 ERC Advanced Grants, 25 ERC Starting Grants, 3 ERC Consolidator Grant and one ERC Synergy Grant.

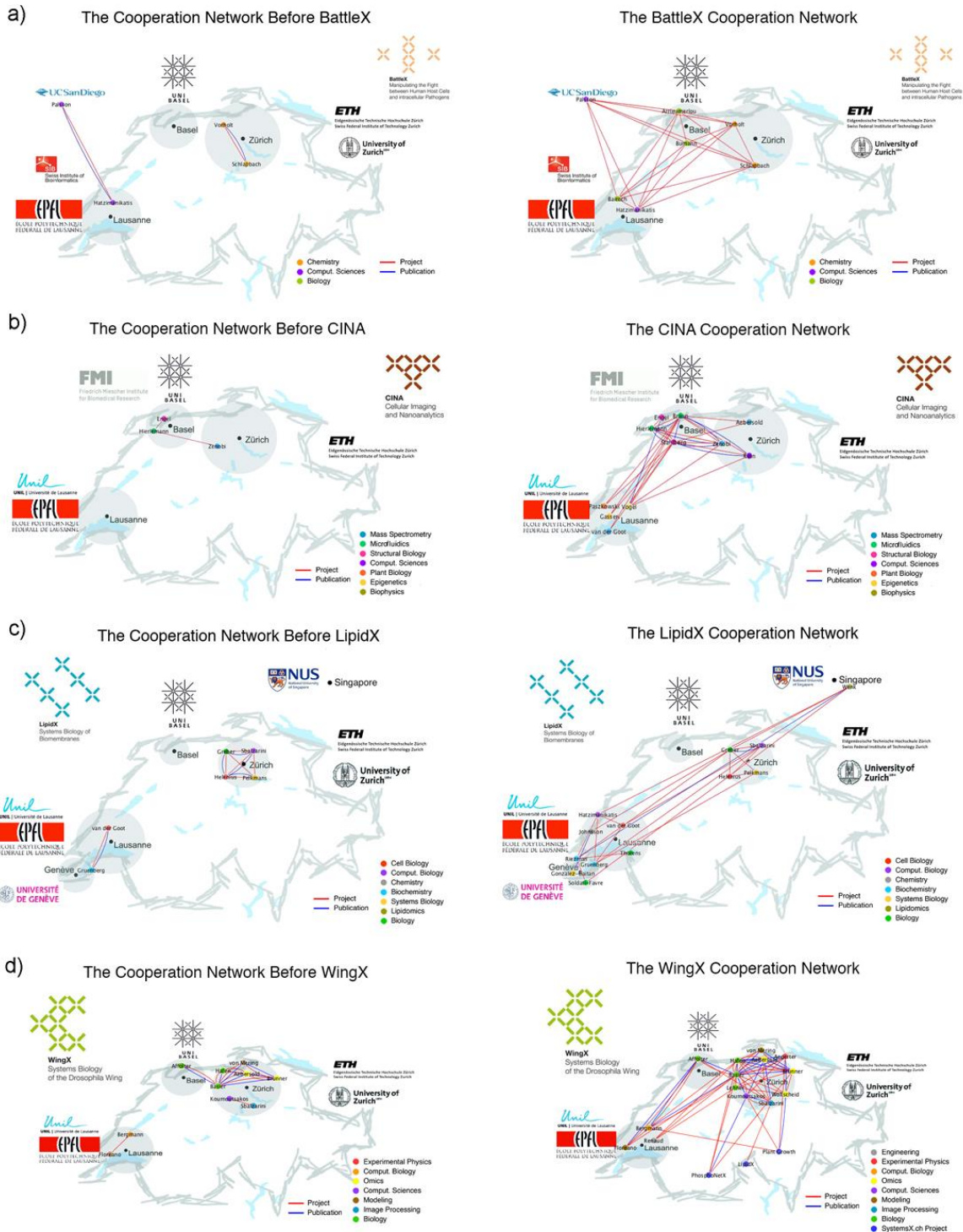
#### **1.1.5 Scientific community**

Community building is a crucial part of this initiative since it is the basis of networking and a measure to overcome barriers between different disciplines, as well as between institutions within Switzerland. The funding activities of SystemsX.ch, namely the calls for RTD and since 2014 MRD proposals are the main driving force to foster networking and to initiate and support cooperation among different Swiss institutions and beyond (see Figure 1a-d).

Many RTD projects reported publications in high-prestige journals during this reporting period. In terms of building a strong Systems Biology community, the most interesting ones are the publications by authors of different groups, institutions or even several RTDs. The interaction networks of some selected publications of RTD projects from 2014-2015 are depicted on Figure 2a-f.

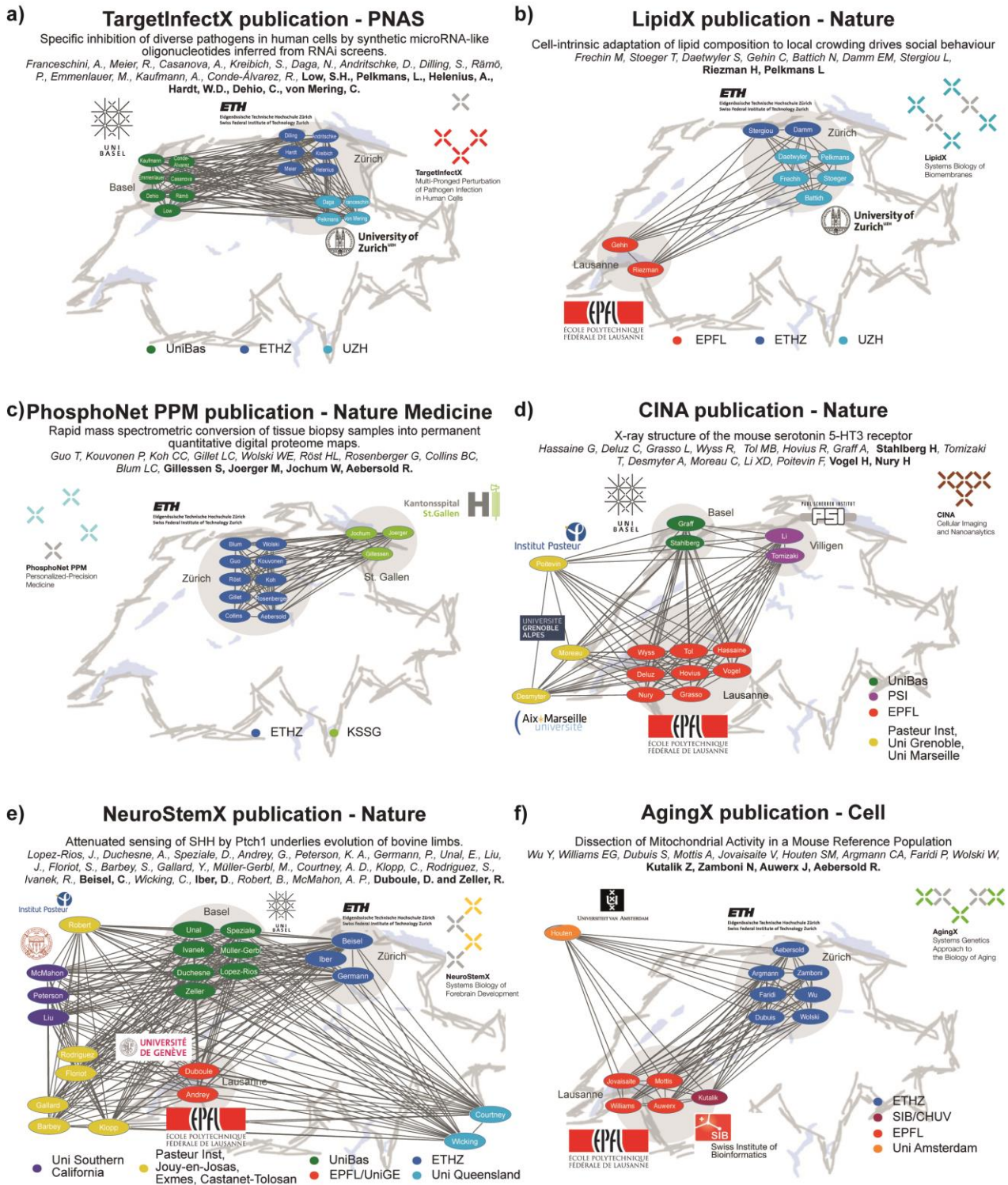
Moreover, an active community in the field of systems biology is an important factor of the sustainability of this initiative and even contributes to the international outreach. To establish such a systems biology community in Switzerland several measures were taken in the past. The most important ones were scientific events such as the five All SystemsX.ch Days and the two International SystemsX.ch conference in Basel in 2011 and in Lausanne in 2014, but also the PI-meetings which are organized twice a year. Other events, organized by the Management Office (MO) or by RTD-related groups contributed to this topic in a similar manner.

In this reporting period, the 2<sup>nd</sup> International SystemsX.ch Conference in October 2014 in Lausanne, the Postdoc Workshop 2015, the SystemsX.ch Retreat 2015 and the joint Summer School with the CRG in Barcelona were the main events in terms of community building. The biannual PI meetings, where all PIs of RTD and TF projects meet to discuss scientific and administrative issues, also enable researchers to network and interact with other SystemsX.ch members (see below).



**Figure 1.** RTD projects generated networks between different Swiss institutions and beyond. Exemplarily different RTDs (BattleX, CINA, LipidX and WingX) are shown, approved in 2009 (a and b) and approved in 2008 (c and d) by the SNSF.

Another indicator of the solidity of interactions established through SystemsX.ch is the development within certain projects of tools that are then used by other projects. An excellent example of such a collaboration is the ISMARA software, developed originally within the Cell Plasticity RTD, and used subsequently also by the NeuroStemX RTD. The close collaborations between the RTDs InfectX and BattleX, or between PhosphoNetPPM and LipidX are further evidence of the community-building effect of SystemsX.ch.



**Figure 2.** The interaction network of selected publications of RTD projects from 2014-2015. Co-authors are the nodes and the edges depict interactions between each co-author. In the author lists the SystemsX.ch PIs are presented in bold.

Additionally, the support of external events and SystemsX.ch internal, sometime bilateral meetings as a measure to increase the make SystemsX.ch to run smoothly and show beneficial effects:

- After approval of new RTDs and MRDs, Daniel Vonder Mühl visited each PI and explained SystemsX.ch as a whole and particular expectations. He was invited to kick-off meetings of the RTDs StoNets RTD (January 2014), TbX RTD (May 2014), Host-PathX (February 2015), SynaptiX (March 2015), MecanX (May 2015) and MetastasiX (June 2015) to presenting the SystemsX.ch initiative to all consortium members of the respective RTD / MRD.
- Eavan Dorcey or Flóra Vajda visited all TPdFs whose fellowships were awarded in 2013 and 2014 in order to inform them about SystemsX.ch activities and specificities.
- SystemsX.ch supported the Annual Retreat of the Systems Biology PhD Program of the Life Science Zurich Graduate School (September 2014), the Systems Biology of Antibiotic Resistance meeting (September 2014), the 4<sup>th</sup> Annual Retreat of the Basel Postdoc Network Retreat (September 2014), the ECCB'14 European computational biology event (September 2014), the LS<sup>2</sup> Annual Meeting (January 2015), the BC2 Computational Biology Conference (June 2015) and the 9th LMB-FMI Graduate Student Symposium (July 2015). Supporting these events increases visibility of the initiative amongst young researchers, making them also aware of funding possibilities within SystemsX.ch.
- SystemsX.ch awarded ten travel grants for young researchers of the initiative attending the Systems Biology of Human Disease 2015 (SBHD) in Heidelberg conference.
- Non-scientific measures to foster community building include diverse communication tools, such as the SystemsX.ch webpage, newsletters, the X-Letter magazine, etc.

### ***PI-meetings***

SystemsX.ch periodically holds PI meetings, ensuring that RTD and TF PIs meet regularly, and not just at larger SystemsX.ch events (e.g. All SystemsX.ch Days, conferences, meetings). In these meetings, besides a small part where organizational and administrative issues are discussed, some four SystemsX.ch projects (typically three RTDs and one TF) are presented and an extended networking break allows for the intense discussions among the PIs. The meeting enables PIs to give their input about strategic issues, to exchange ideas and even to set up collaborations between RTDs. Also, common activities emerge out of such meetings. They are important to create a common sense and corporate identity.

Dates and main topics of the SystemsX.ch PI meetings are shown on Table A48 in Appendix A.



## 1.2 Organization

### 1.2.1 Board of Directors (BoD)

The BoD comprises the rectors and presidents of all SystemsX.ch partner institutions (for BoD members and the meeting dates and topics see Appendix A, Tables A42 and A43). The BoD is the strategic head of the initiative and is responsible for strategy, political issues, and finances. Some decisions can also be voted by circular emails. The SystemsX.ch BoD (with SEB chair Lucas Pelkmans and the Managing Director Daniel Vonder Mühl) met once in the reporting period on November 17, 2014. At this meeting the results of the 9<sup>th</sup> call were presented, the planning of the upcoming 11<sup>th</sup> and 12<sup>th</sup> call and a potential novel bibliometry analysis were discussed, and the SystemsX.ch membership of IBM Zurich Research Lab (IBM ZRL) was approved. Furthermore, as Ralph Eichler retired by end of 2014, the BoD unanimously appointed Detlef Günther as new BoD chairman as of January 1, 2015. It was also proposed and agreed on to only convene at BoD meetings once per year, in November, and replace the earlier June meetings by circular decisions to be communicated per email. The decisions made by circular email since November 2015 include the approval of the University of Applied Sciences Zürich (ZHAW) as a new SystemsX.ch partner, the approval of the Financial Report 2014, and the procedure for extension requests (IPhD, TPdF, TF).

### 1.2.2 Scientific Executive Board (SEB)

The SEB is the executive body of SystemsX.ch. Lucas Pelkmans serves as chairman of the Scientific Executive Board (SEB) since the January 1, 2013.

SEB members were elected for a 2-years term in June 2007, 2009 and 2011. In June 2013, the SEB was (re-)elected by the BoD. The current composition of the SEB representing various disciplines relevant to systems biology is given in Appendix A, Table A44, the meeting dates and topics of the nine meetings are shown in Table A45). The SEB members also represent their home institutions. The board decides on operational tasks and reviews the Special Opportunity Funds proposals for approval or rejection. It also provides the SNSF panel with strategic input for the review of the RTD, MRD, TF, TPdF and IPhD proposals. There are about eight to ten SEB meetings a year.

In this reporting period, Matthias Lutolf, Ruedi Aebersold and Jürg Schifferli have stepped down after having served several years in the SEB board. The BoD had approved on their proposed successors, Bart Deplancke, Uwe Sauer and Alfred Zippelius.

### 1.2.3 Management Office (MO)

The Management Office is affiliated to and located at the ETH Zurich. The amount of personnel has always been kept as low as possible. This is only possible because central entities of ETH Zurich support the MO, in particular the departments Finances and Controlling, Human Resources, and IT services, and because the MO team benefits from external assistances in terms of external contractors (for personnel see Appendix A, Table A51).

Over the years, many tasks of the MO have been optimized. Meetings of the governing bodies (BoD, SEB) are organized and documented, research projects are accompanied and supported, annual reports are coordinated and written, the PhD educational program is coordinated and organized, and workshops, conferences and events are organized.

Another important task of the Management Office is the internal and external communication for SystemsX.ch. A communication concept was elaborated in spring 2008 and corresponding measures have been implemented since: The newsletter X-Letter is widely distributed as hardcopies and electronically, and includes reports about RTD Projects, strategy, events, etc. It is available in English, French and German and is published twice a year. It was decided, that from November 2015 onwards the X-Letter is going to be published in English only. For short and quick announcements, the format X-Flash informs the SystemsX.ch com-

munity about upcoming calls, events or media releases. Since they are distributed by e-mail they are very effective and useful. A new SystemsX.ch brochure was published in October 2014, again in three languages, which presents SystemsX.ch as whole. An extra addendum with an overview containing all SystemsX.ch projects (that can be adapted continuously) complements the brochure. All these items have been matured over time and are made available on the webpage.

### **'Good governance'**

As a public initiative, SystemsX.ch utilizes tax payers' money. It is therefore necessary to apply implicit and explicit attitudes and rules that comply with expectations of the society. An example of such standard is "The Nolan Committee's First Report on Standards in Public Life" (<http://www.archive.official-documents.co.uk/document/parliament/nolan/nolan.htm>) that state "The Seven Principles of Public Life" (Selflessness, Integrity, Objectivity, Accountability, Openness, Honesty, Leadership).

The Boards and the Management Office of SystemsX.ch defined a frame for good governance. In agreement with the SNSF, it was decided that the external auditor who regularly examines the Financial Report of SystemsX.ch. would also analyze and comment on "Good Governance".

SystemsX.ch is a complex organization which has the aim of bringing Switzerland to the international forefront in systems biology research. The program focuses on collaborative research. To reach its goals, the initiative is governed according to best practice, i.e.:

- a) The organization of the governance, administration, internal procedures, roles and duties of the various stakeholders must be transparent, clear, and understood, in order to be implemented and respected. While this does not require that every detail must be regulated (this is in fact neither possible nor useful), this means that for each situation a solution is determined that is acceptable to all stakeholders and that the procedures that lead to the decision are transparent and well communicated.
- b) There are checks and balances in place to minimize potential damage from possible errors. This means that the risk structure within the organization and procedure are known. An internal control system was also set up to ensure a high quality for the procedures. In particular, in high-risk areas, particular measures (e.g. the four-eyes principle, independent, double calculations, etc.) are established systematically. The committees and decision-making bodies of SystemsX.ch have implemented procedures to manage possible conflict of interest situations.
- c) Implementation of written and/or orally stated rules, decision etc. must follow according to checklists in written forms. Two examples may explain that:
  - (1) Members who did not attend a meeting must be able to inform themselves about decisions taken by reading the minutes.
  - (2) Applicants whose proposals were rejected must be informed accordingly and are allowed to receive the original feedback comments of the reviewers.
- d) A large fraction of SystemsX.ch resources goes into personnel. Employees shall be treated with respect, promoted, and supported. Each of the SystemsX.ch partner institutions has a professional Human Resource section in place that takes care of personnel issues.
- e) As far as financial issues are concerned, the annual Financial Report is audited to minimize risk of misuse of SystemsX.ch Funds that are tax-payers' money. The "Letter of Representation" might serve as an example of how SystemsX.ch handles the complexity of financial reporting: Each partner institution collects, examines and consolidates all financial reports of SystemsX.ch projects running at the institution. Each project report is signed by the research group leader and/or the F&C contact person. The Letter of Representation lists all reported projects and declares that all relevant

and required data are complete. This Letter is signed by a member of the institutions directorate.

#### **1.2.4 Swiss National Science Foundation (SNSF)**

The SNSF is the most important Swiss institution promoting and funding basic scientific research. The National Research Council of the SNSF comprises four divisions and three specialised committees. Its task within SystemsX.ch cooperation is mainly the evaluation of research projects and the awarding of grants. Furthermore, the SNSF is eligible to participate as partner in an ERA-Net. Therefore, SystemsX.ch has the mandate from the SNSF to represent Switzerland within this European Network and to manage transnational calls for proposals on the European level.

SNSF division IV is responsible for SystemsX.ch. The SNSF elected the chairman, 5 national and about 12 international members of the SNSF Review Panel Systems Biology, which was in charge of the scientific evaluations for SystemsX.ch as a whole and for the RTD and TF proposals. Chairman Peter Chen stepped down in Spring 2015 and was replaced by Isabelle Mansuy. Since the review of the 11<sup>th</sup> call, a so-called Expert Group was installed and mandated to evaluate the TPdF and IPhD proposals. For the review of the 10<sup>th</sup> call proposals, the SNSF invited two new scientists with expertise in medical research to the Review Panel, following a request from the SEB. Members of the SNSF Review Panel and Expert Group are listed in Appendix A, Table A49 and A50.

#### **1.2.5 Scientific Advisory Board (SAB)**

When SystemsX.ch was set up in 2007, the Scientific Advisory Board (SAB) was responsible for constructive review of the SystemsX.ch research and development plans and their implementation. It also served as a source for reviewing potential members of SystemsX.ch faculty and for advising on general strategic and operational issues. The SAB advised the Board of Directors and the Scientific Executive Board. Members of the SAB met at the 1<sup>st</sup> International SystemsX.ch Conference in October 2011 in Basel.

In the BoD meeting of June 18, 2013, the SAB was dissolved. The SAB was important during the build-up phase. For the second phase, including the ramp down, no particular SAB is needed. If needed, external experts will be invited on request.

The SAB members are listed in the Appendix D, Table D66.

## 2 Activity reports of all research projects

### 2.1 Activity reports of all RTDs approved from 2008 to 2013

The major impact of SystemsX.ch is generated through the RTD projects. In 2008, eight of them (Dynamix, LipidX, LiverX, Neurochoice, PhosphoNetX, PlantGrowth, WingX, YeastX) were approved and started immediately. Most of these RTDs were completed in December 2013 and submitted their final reports, so they are no longer part of the annual scientific reports. Another six RTD projects (BattleX, Cell Plasticity, CINA, CycliX, InfectX, and Meta-NetX) were approved in 2009. These projects were completed in the end of 2014. Eleven RTD Projects (PhosphoNetPPM, TubeX, AntibodyX, NeuroStemX, StoNets, SysGenetiX, MecanX, PlantGrowth2, EpiPhysX, SynaptiX, LipidX) were approved in 2012, and they underwent their mid-term evaluation by the SNSF in October 2014. The nine RTD Projects (MERIC, MorphogenetiX, TargetInfectX, AgingX, TbX, MalarX, SignalX, HostPathX, MicroScapesX) approved in November 2013 have submitted for the first time an activity / scientific report in 2014. The annual scientific reports of all RTDs that were active in this reporting period can be found in Appendix B.

In this chapter selected highlights of all RTDs during the reporting year (July 2014 to June 2015) are presented, in particular within the four focal themes: science, education, public-private partnership, and international outreach.

The SystemsX.ch-initiated IT project SyBIT was approved by the SNSF in October 2008. In the second phase, their budget is approved annually by the SEB and the SNSF.

#### 2.1.1 Science

##### *Publications*

The classical indication of success for research is publication in high-prestige journals, although this, as any other way of quantifying scientific productivity, is the object of recurrent discussion. Most interesting are publications by authors of different groups, institutions or even several RTDs. However, it is worth mentioning that all SystemsX.ch projects are set up to promote the interdisciplinary research, which might cause some problems when it comes to choosing the journal. In the Appendix B of this report, each RTD lists all relevant publications, separated into three different categories:

- a) Publications acknowledging SystemsX.ch explicitly, according to the RTD guidelines
- b) Publications of at least two groups of the RTD and joint-papers of other RTDs
- c) Other publications with minor contributions of the RTD

Some publications of **RTD projects** that have had an especially high outreach during this reporting period have been:

Archetti, M., Ferraro, D., and Christofori, G. **2015**. Heterogeneity for IGF-II production maintained by public goods dynamics in neuroendocrine pancreatic cancer. **PNAS** 112, 1833-1838. **Cell Plasticity**

Tuncay Baubec, Daniele F. Colombo, Christiane Wirbelauer, Juliane Schmidt, Lukas Burger, Arnaud R. Krebs, Altuna Akalin and Dirk Schübeler. **2015**. Genomic profiling of DNA methyltransferases reveals a role for DNMT3B in genic methylation. **Nature**. 520 (7546):243-8. **Cell Plasticity**

Claudi B, Spröte P, Chirkova A, Personnic N, Zankl J, Schürmann N, Schmidt A, Bumann D. **2014** Phenotypic variation of Salmonella in host tissues delays eradication by antibiotic chemotherapy. **Cell** 158:722-33. **BattleX**

- Cornelis G., Vernochet C., Malicorne S., Souquerre S., Tzika A.C., Goodman S.M., Catzefflis F., Robinson T.J., Milinkovitch M.C., Pierron G., Heidmann O., Dupressoir A. & T. Heidmann, **2014**. Retroviral envelope syncytin capture in an ancestrally diverged mammalian clade for placentation in the primitive Afrotherian tenrecs. **PNAS**, 111: E4332-E4341. **EpiPhysX**
- Franceschini, A., Meier, R., Casanova, A., Kreibich, S., Daga, N., Andritschke, D., Dilling, S., Rämö, P., Emmenlauer, M., Kaufmann, A., Conde-Álvarez, R., Low, S.H., Pelkmans, L., Helenius, A., Hardt, W.D., Dehio, C., von Mering, C. **2014**. Specific inhibition of diverse pathogens in human cells by synthetic microRNA-like oligonucleotides inferred from RNAi screens. **PNAS** 111:4548-53. **TargetInfectX**
- Frechin M, Stoeger T, Daetwyler S, Gehin C, Battich N, Damm EM, Stergiou L, Riezman H, Pelkmans L. **2015**. Cell-intrinsic adaptation of lipid composition to local crowding drives social behaviour. **Nature**. Doi: 10.1038/nature14429. [Epub ahead of print] **LipidX**
- Gaidatzis D, Burger L, Florescu M, Stadler MB. **2015**. Analysis of intronic and exonic reads in RNA-seq data characterizes transcriptional and post-transcriptional regulation. **Nature Biotechnology**. doi: 10.1038/nbt.3269. **Cell Plasticity**
- Ganter M, Kaltenbach HM, Stelling J. **2014**. Predicting network functions with nested patterns. **Nature Communications**. 5: 3006. **MetaNetX**
- Ralf Gilsbach, Sebastian Preissl, Björn A. Grüning, Tilman Schnick, Lukas Burger, Vladimir Benes, Andreas Würch, Ulrike Bönisch, Stefan Günther, Rolf Backofen, Bernd K. Fleischmann, Dirk Schübeler and Lutz Hein. **2014**. Dynamic DNA methylation orchestrates cardiomyocyte development, maturation and disease. **Nature Communications**, 5:5288. doi: 10.1038/ncomms6288. **Cell Plasticity**
- Andreas R. Gruber, Georges Martin, Philipp Müller, Alexander Schmidt, Andreas J. Gruber, Rafal Gumienny, Nitish Mittal, Rajesh Jayachandran, Jean Pieters, Walter Keller, Erik van Nimwegen, Mihaela Zavolan **2014**. Global 3' UTR shortening has a limited effect on protein abundance in proliferating T cells **Nature Communications** 5:5465 doi:10.1038/ncomms6465, **Cell Plasticity**
- Guo T, Kouvonen P, Koh CC, Gillet LC, Wolski WE, Röst HL, Rosenberger G, Collins BC, Blum LC, Gillessen S, Joerger M, Jochum W, Aebersold R. **2015**. Rapid mass spectrometric conversion of tissue biopsy samples into permanent quantitative digital proteome maps. **Nature Medicine**. 21(4):407-13. doi: 10.1038/nm.3807. Epub 2015 Mar 2. **PhosphoNet PPM**
- Hassaine, G., et al. **2014**. X-ray structure of the mouse serotonin 5-HT<sub>3</sub> receptor. **Nature** 512(7514), 276-281. **CINA**
- Jean-Philippe P. Theurillat, Namrata D. Udeshi, Wesley J. Errington, Tanya Svinkina, Sylvan C. Baca, Marius Pop, Peter J. Wild, Mirjam Blattner, Anna C. Groner, Mark A. Rubin, Holger Moch, Gilbert G. Privé, Steven A. Carr, Levi A. Garraway, **2014**. Ubiquitylome analysis identifies dysregulation of effector substrates in SPOP-mutant prostate cancer. **Science** 346, 85; DOI: 10.1126/science.1250255. **PhosphoNet PPM**
- Kowal, J., et al., **2014**. Ligand-induced structural changes in the cyclic nucleotide-modulated potassium channel MloK1, **Nature Communications**. 5, Article number: 3106 **CINA**
- Kressmann, S., Campos, C., Castanon, I., Furthauer, M. & Gonzalez-Gaitan, M. **2015**. Directional Notch trafficking in Sara endosomes during asymmetric cell division in the spinal cord. **Nature Cell Biology** 17, 333-339. **EpiPhysX**
- Lopez-Rios, J., Duchesne, A., Speziale, D., Andrey, G., Peterson, K. A., Germann, P., Unal, E., Liu, J., Floriot, S., Barbey, S., Gallard, Y., Müller-Gerbl, M., Courtney, A. D., Klopp, C., Rodriguez, S., Ivanek, R., Beisel, C., Wicking, C., Iber, D., Robert, B., McMahon, A. P., Duboule, D. and Zeller, R. **2014**. Attenuated sensing of SHH by Ptch1 underlies evolution of bovine limbs. **Nature** 511, 46-51. **NeuroStemX**

Mohamed Amin Choukrallah, Shuang Song, Antonius Rolink, Lukas Burger and Patrick Matthias. **2015**. Enhancer repertoires are reshaped independently of early priming and heterochromatin dynamics during B-cell differentiation. **Nature Communications**, in press, **Cell Plasticity**

A. Porro, S. Feuerhahn, J. Delafontaine, H. Riethman, J. Rougemont, J. Lingner. **2014**. Functional characterization of the TERRA transcriptome at damaged telomeres. **Nature Communications** 5, 5379 doi:10.1038/ncomms6379. **SyBIT**

Ranga A, Gobaa S, Okawa Y, Mosiewicz K, Negro A, Lutolf MP. **2014**. 3D niche microarrays for systems-level analyses of cell fate. **Nature Communications**;5:4324. **StoNets**

Ruess J, Parise F, Miliadis-Argeitis A, Khammash M & J Lygeros. **2015**. Iterative experiment design guides the characterization of a light-inducible gene expression circuit. **PNAS** 112:8148-53. **SignalX**

Sevin D, Sauer U. **2014**. Ubiquinone accumulation improves osmotic stress tolerance in E. coli. **Nature Chem. Biol.** 10: 266-272. doi:10.1038/nchembio.1437. **MetaNetX**

Schwan, C., et al., **2014**. Clostridium difficile toxin CDT hijacks microtubule organization and re-routes vesicle traffic to increase pathogen adherence. **PNAS**, 111(6), 2313-2318 (2014). **CINA**

M.S. Bou Sleiman, D. Osman, A. Massouras, A.A. Hoffmann, B. Lemaitre, B. Deplancke. **2015**. Multiple genetic and transcriptional changes mediate high levels of natural variation in gut immunocompetence in Drosophila melanogaster. **Nature Communications**, in press, **AgingX**

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### ***Technology and Development***

SystemsX.ch institutions and RTDs have developed and/or installed a variety of technologies and resources for dynamic network analysis. Some selected examples of Technology and Development are shown in Table A29 in Appendix A. Some of these developments have at least in part lead to patents and licenses (Tables A27 and A28 in Appendix A).

The specific achievements of all projects are detailed in the scientific reports in Appendix B.

### **2.1.2 Education**

As of July 2015, the RTDs counted 159 active PhD-students and 173 active postdocs (Table A38 in Appendix A). We asked for the career tracks of PhD students and postdocs who left or finished working on the RTD projects. The career tracks are summarized in Appendix A (Table A39 and A40).

Among the PhD students and postdocs who left their SystemsX.ch lab until July 2015 and had been reported in the 2014-2015 reporting period:

- 119\* have positions in academia (most of them as postdocs, 7 person received a professorship)
  - 71\* people are working in industry/private sector at different levels.
  - 2\* people started their own company/are self-employed
  - 1\* person is working within public services
  - 2\* others unknown
- (\*out of those who provided information)

### **2.1.3 Cooperation with private sector (public private partnership)**

As described in chapter 1.1.3, the current RTDs within SystemsX.ch have several collaborations, links and interactions with the private sector. This interaction is in some cases the common development of new technologies, methods or tools for analysis, and in some others technology transfer and education (e.g. postdoctoral fellowships). An overview of collaborations, links and interactions with the private sector is listed for each RTD in Appendix A (Table A34). The list of collaborations for each RTD is detailed on each individual report in Appendix B.

### **2.1.4 International outreach**

SystemsX.ch-associated researchers have been successfully involved and integrated in projects supported by the FP7 of the EC. Furthermore, several scientists have had a long-term fellowship from international organizations (e.g. ERC, EMBO, US National Science Foundation, Marie Curie, etc.)

The full list of SystemsX.ch ERC grantees can be found in 3.6 Impact of SystemsX.ch. Between 2007 and 2013, 43 senior SystemsX.ch researchers received Advanced or Consolidator ERC grants and 25 junior SystemsX.ch researchers received Starting ERC grants.

### **2.1.5 Towards sustainability**

SystemsX.ch is conceived as a catalytic program with a finite lifetime, to establish systems biology in Switzerland. Sustainability of systems biology after the conclusion of the program is therefore an important issue. SystemsX.ch will continue until 2018, but in the meantime several early signs already point towards the sustainability of systems biology research in Switzerland:

- SyBIT (IT-platform and Data management),
- participation in SINERGIA projects (e.g. Schübeler, van Niemwegen),
- establishment of the ETH Zurich Department BSSE in Basel (around 13 professorships),
- University of Zurich: University Research Priority Program (URPP) in Functional Genomics and Systems Biology:  
→ Recruitment of four professors in systems biology,
- University of Basel: focus on Systems Biology
- University of Bern and University of Fribourg: Master program in Biomathematics,
- EPF Lausanne, ETH Zurich and University of Zurich: Graduate Schools in systems biology,
- SwissLipids: the SIB will take over the continuous maintenance,

- establishment of IT support centers for life sciences research. In the reporting period such services have been opened at University of Zurich (S<sup>3</sup>IT, Peter Kunszt) and University of Basel (sciCore, Torsten Schwede). These centers add up to the previously existing Vital-IT (University of Lausanne, EPF Lausanne, University of Geneva, University of Bern, University of Fribourg) and Scientific IT Services (ETH Zurich).

## 2.2 Activity reports of all MRD Projects launched in 2014

The 10<sup>th</sup> call for proposals covered Medical Research and Development (MRD) Projects. Seven out of the nine MRD Projects approved in November 2014 (PrionX, AneuX, HIV-X, GutX, VirX, MelanomX, StemSysMed, HDL-X, MetastasiX) have submitted for the first time an activity/scientific report. Several of them just started, therefore most of the requested items were still not applicable to these projects (e.g. publications, patents, etc.). The activity reports of these MRDs that started before June 2015 are part of Appendix B.

## 2.3 Activity reports of all IPhD Projects launched from 2008 to 2014

In the first period (2008-2012) 40 IPhD Projects were approved by the SNSF. In 2012 (5<sup>th</sup> call), further 11 proposals for IPhD were approved, and 9 more after the 7<sup>th</sup> call (2013). After the 9<sup>th</sup> call for proposals (2014), 17 new projects have been approved. Except for two IPhD projects that haven't started yet, all scientific reports of the projects that have been running in this reporting period can be found in Appendix B. An overview of running IPhD projects can be seen also in Appendix A; Tables A17-A21. On average, PhD projects last around four years. As a consequence, most IPhD projects approved in 2008 and 2009 have been completed between 2012 and 2013, and the ones approved in 2010 have been completed between 2014 and 2015.

In details, out of the projects approved in:

- **2008**, 9 started in 2008 and 6 in 2009. Out of the 16 projects, 2 finished before 2012, 7 in 2012, 3 in 2013 and 1 in 2014.
- **2009**, 9 started in 2009 and 3 in 2010. Out of the 12 projects, 3 finished before 2013, 7 in 2013, 1 in 2014 and 1 in 2015.
- **2010**, 4 started in 2010, 7 in 2011 and 2 in 2012. Out of the 13 projects, 2 finished before 2014, 5 in 2014, 5 in 2015 and 1 will come to an end in 2016.
- **2012**, 8 started in 2012 and 3 in 2013. All of these projects are running in their third year, except for one project which was only granted for one year, as an extension of previous funding. The management office expects incoming 4<sup>th</sup> year extension requests potentially for 9 of these projects.
- **2013**, all 9 projects started in 2014 and they are all running in their second year.
- **2014**, 6 started in 2014, 10 started in 2015 and 1 project is still pending.

In five cases IPhD students have prematurely interrupted their project, and have been replaced by other students. For one project this has happened twice (i.e. three different students have worked on the project). In two cases there was a change of co-supervisor. These problems show that the format of IPhD Projects has a certain conflict potential, despite enabling students to achieve a really interdisciplinary training, and also enabling supervisors to closely interact and embark on fruitful collaborations. The difficulties that many PhD students encounter at some point during their doctorate are increased by the possible misunderstandings between co-supervisors, or by the complexity of mastering a project on the interface of two scientific disciplines.

In the following chapters, the annual scientific reports of all IPhD Projects are summarized in terms of Science (2.3.1) and Education (2.3.2). Detailed information of each IPhD Project is attached in Appendix B.



### 2.3.1 Science

#### **Publications**

Especially first authorship is not only desirable but also essential for young scientists and an important factor for their career. The fact the IPhD students are supervised by two mentors of different disciplines is a crucial measure to educate young scientists in this relatively new interdisciplinary field of research. Some IPhD students have been able to publish their results in high impact journals (e.g. *Nature*, *Nature Methods*, *Development*, *PNAS*, *PLoS Genetics*, etc.), thereby also confirming the visibility and importance of systems biology as a discipline.

Out of a total 44 IPhD Projects in the present report, 12 were in their first year, 9 in their second year and 23 projects were in their last year (11 in the 3<sup>rd</sup> and 12 in the 4<sup>th</sup> year). Out of these 23 finishing projects 11 has been completed in this reporting period.

This year the 44 running IPhD projects have generated 32 publications (including papers accepted or under revision). In case 27 of these publications the IPhD authors or co-authors were in their 3<sup>rd</sup> and 4<sup>th</sup> year, and 5 IPhD co-authors were in their 1<sup>st</sup> and 2<sup>nd</sup> year. Overall, 11 first-author papers have been published from currently running IPhD Projects.

IPhD students have furthermore received six awards, and eleven projects report preliminary developments, ideas or insights that might lead to applications, new projects or patents.

Table A26 and Table A27 in Appendix A show awards and patents from different IPhD Projects. Examples of Technology and Development are shown in Table A31 in Appendix A. An overview of collaborations, links and interactions with the private sector is listed IPhD projects in Appendix A (Table A35).

### 2.3.2 Education

The characteristic of the IPhD Projects is that students with a certain scientific background are trained and educated in complementary disciplines. This is achieved though the double mentorship principle, as well as through participation at various workshops, courses and conferences.

Overall IPhD students participated at 55 educational events (e.g. workshops, courses, summer schools, etc.), at these events with 70 attendances. The education events can be classified in the following fields:

- Classical life science (e.g. biology, chemistry, physics): 17 events
- IT, mathematics (e.g. statistics, modeling, informatics): 12 events
- Technologies: 15 events
- Soft skills (e.g. presentation, scientific writing, communication): 8 events
- Management and business related: 3 events.

IPhD students reported 75 visits at 44 different conferences. 19 of these meetings took place in Switzerland, and 25 of them in 12 foreign countries, thereby these attendances partly contributed to the international visibility of SystemsX.ch. The most frequently visited countries were Germany, USA and France.

## 2.4 Activity reports of TPdFs

TPdFs were introduced in 2012, with the aim of enabling young systems biology researchers to acquire competences in a scientific domain complementary to the one they have been active in so far. The postdoc thus undertakes a transition in her or his scientific career. This project type is one of the main tools to accomplish the goal of educating the next generation of systems biologists.

In the 5<sup>th</sup> call, 17 proposals were submitted, out of which four fellowships were granted. One of the fellows then accepted an SNSF Ambizione grant instead. The three fellows started their projects between October 2012 and January 2013. In the 7<sup>th</sup> call, 13 TPdFs were approved out of the 28 proposals submitted. Five of these fellows started their projects in 2013, seven of them in 2014 and one of them in 2015. One of the fellows was also awarded by a Human Frontiers Science Program fellowship and her SystemsX.ch TPdF complements her salary. 28 proposals were submitted during the 9<sup>th</sup> call, out of which seven TPdFs have been approved. Six of these fellows have started their projects between September 2014 and February 2015, and one of them will start in August 2015. By the end of this reporting period, 2 fellows have completed their TPdF projects successfully.

The increase in proposals since the 5<sup>th</sup> call suggests that there is a strong demand for such funding. The fellows have a high scientific profile, and selection criteria are necessarily stringent.

### ***Publications, Technology and Development, Conferences and Education***

The scientific productivity of TPdFs is very high. The 23 projects that were active in this reporting period report yielded 15 accepted publications in peer-reviewed journals and 3 post-docs received various awards (Table A26 in Appendix A). Two patents generated in a TPdF projects are being filed, the idea behind these will probably lead to further applications (Table A27 in Appendix A). Examples of Technology and Development are shown in Table A30 in Appendix A.

The TPd fellows have presented their results at 27 different conferences and meetings (at these events 47 attendances), and have continued their education by attending 17 different courses, workshops and retreats (at these events 21 attendances).

## **2.5 Activity reports of TF Projects**

Transfer Projects were introduced in order to promote public private partnerships between academia and industry in the field of systems biology. Alternatively, TF Projects can link academia and (private) hospitals to find systems approaches to clinical questions. The 6<sup>th</sup> call for projects was the first call where scientists were invited to submit TF proposals. This call was published in 2012: seven applications were received, out of which four TFs were granted funds. In the 8<sup>th</sup> call for projects, in 2013, six groups submitted proposals, and two new TFs were approved. Four TF applications were received within the 10<sup>th</sup> call, in July 2014, and two TFs were approved. The stable number of applications received suggests that this project type is well received by the community.

Out of the four first TFs that were approved in 2012, three have by now been completed. Four projects were running actively in this reporting period and one has started in June 2015. They report a remarkable scientific productivity: six awards (Table A25 in Appendix A), one licence (Table A28 in Appendix A) and ten preliminary developments that could lead to applications or patents (Table A32 in Appendix A).

The annual reports of the seven TFs that were active in this reporting period can be found in Appendix B.

## 2.6 Activity reports of Special Opportunities Projects

The Special Opportunities project type was introduced in 2012 to promote systems biology research in the broader sense, including technology development. This funding source is meant to support non-mainstream projects that do not qualify for traditional funding, and which pragmatically contribute to SystemsX.ch and systems biology research in Switzerland.

Seven Special Opportunities proposals have been approved by the SEB between October 2011 and December 2014. Three Special Opportunities project have been active in this reporting period and one reported a filed patent application (Table A27 in Appendix A).

Following 12<sup>th</sup> call for Special Opportunities projects out of the 51 submitted proposals, further nine were approved by the SEB. The extremely high number of applications received for the 12<sup>th</sup> call suggests that this project type is well received and sought for by the SystemsX.ch community. The annual reports of two Special Opportunities projects that can be summarized in a traditional context can be found in Appendix B. These two projects yielded one publication in peer-reviewed journals, four presentations of results at scientific conferences and two patent/license applications.

### 3 Self evaluation

For Switzerland, SystemsX.ch is an unprecedented program in its scope, size and objectives. Consequently, all organizational items such as governance, procedures, collaboration with the SNSF, funding principles (including matching funds) or reviewing of proposals had to be generated from scratch for the program. Furthermore, the scientific community had to become familiar with and adapt to the requirements of SystemsX.ch. In this chapter we summarize the performance of SystemsX.ch in the past eight years, i.e. the period between the first call for proposals in September 2007 and August 2015.

#### 3.1 Governance

##### 3.1.1 Board of Directors (BoD)

The BoD has worked well together from the start. In cases of disagreement good compromises for decisions were usually reached without the need for additional meetings. The BoD was thus able to carry out its duties well and efficiently. Although the SystemsX.ch agreement states that the President/Rector/Director shall represent the institutions, tendency prevailed that some BoD members sent delegates to the meetings. As an example to show the importance of the BoD, the planning for a national initiative in “Personalized Health” with the aim to start in 2017 can be mentioned. The BoD mandated in its November 2012 meeting a working group to elaborate a concept, and a preliminary report was approved in the June 2013 meeting and have been further discussed in November 2014. Since then, a particular group of the SERI has taken over.

The Managing Director visits each SystemsX.ch partner institution once a year for informal discussion and to receive feedback, input and any individual or collective concerns which might have come up during the year. This provides a good basis for planning BoD-meetings, future events, policies, etc.

→ **Conclusion:** The BoD has operated efficiently from the start of the initiative and has fulfilled its tasks. Since BoD members increasingly delegated deputies, divergence in opinions compared to similarly composed committees (such as the Rectors’ Conference of the Swiss Universities, CRUS) has occasionally occurred. Delegation from rectors to vice-rectors should therefore be minimized. Although this was already remarked in the Scientific Reports 2013 and 2014, and was also pointed out in the BoD meeting of November 2013, no improvement has been seen.

The handing-over of chairman Eichler to the successor Günther was smooth and yielded no problems.

##### 3.1.2 Scientific Executive Board (SEB)

In June 2013, the SEB was (re-)elected by the BoD, but for an the initial overlap phase (the review of the 8<sup>th</sup> call proposals) the newly elected SEB and the previous members were both active. The ‘new’ SEB has been in place since August 2013, and from the 16 members 3 were exchanged during this reporting period. The SEB has worked well and efficiently. The SNSF is of the opinion that the reviews and input from the SEB are an important part of the RTD, TF, TPdF and IPhD reviews and aids the review panel (RTD, TF) and expert group (TPdF, IPhD) on difficult decisions. Potential conflicts of interest have often come up in SEB meetings, as SEB members also represent other interests, namely those of a SystemsX.ch RTD PI, SNF panel member, collaborator etc. Several measures are in place to minimize the effect of conflict of interest on reviews and decisions. Another topic of concern in the past years was the attendance of SEB members at meetings, which has been for certain individual members low. However, in the past two reporting years, attendance has improved slightly.

→ **Conclusion:** The SEB functions well. Attendance and commitment of SEB members improved partially.

### 3.1.3 Management Office (MO)

Both financial and scientific reporting were elaborated efficiently and delivered on time. The external auditor (Ernst&Young) has not found irregularities in any of the seven financial reports already elaborated. After auditing the Financial Report 2014, the collaboration with Ernst&Young was terminated. As of the Financial Report 2015, this task will be taken over by PricewaterhouseCoopers (PwC).

During the past years, the MO has set up certain internal procedure in order to comply with 'good governance'. As an example, one measure aimed at ensuring proper release and administration of payments. Financial reporting for SystemsX.ch is never trivial due to the volume of reports, and the amount of partners and projects involved. In addition, the existence of Own Contributions, and the reporting of 2<sup>nd</sup> and 3<sup>rd</sup> party funds further complicate the process. As before, the MO signed a contract with the Financial Services of ETH Zurich, which allows the MO to profit from know-how in this area from this department for the accounting and preparation of the financial reports for the initiative. This collaboration was very effective. Also, with the gained experience, the initiative is in a good position to deal with all issues related to finances.

→ **Conclusion:** The governance of SystemsX.ch as it was set up works well. Procedures and responsibilities were carefully evaluated and adapted accordingly. Most important is the collaboration with the SNSF to allow unbiased reviews of SystemsX.ch proposals (see 3.1.4). The external audit confirmed that SystemsX.ch fulfills the standards of 'good governance'.

### 3.1.4 Swiss National Science Foundation (SNSF)

Legal documents from the State Secretariat of Education, Research and Innovation (SERI) define that all scientific evaluations as well as the approval of certain project types (RTD, TF, TPdF and IPhD) of SystemsX.ch have to be carried out by the SNSF. All procedures have been installed successfully and in general achieve the agreement of all three cooperating governing bodies (SNSF, SEB and MO).

**Table 1.** Review dates of the two SNSF committees for the 10<sup>th</sup> and 11<sup>th</sup> SystemsX.ch call.

| Committee                            | Call, meeting  |
|--------------------------------------|--|
| SNSF Review Panel<br>Systems Biology | 10 <sup>th</sup> call for MRDs and TFs (January – August 2014?)<br>October 14-15, 2014: review 10 <sup>th</sup> call, midterm review RTDs 2012 |
| SNSF Expert Group<br>Systems Biology | 11 <sup>th</sup> call for TPdFs and IPhDs (December 2014 – April 2015)<br>July 6-7, 2015: review 11 <sup>th</sup> call                         |

→ **Conclusion:** The corporate governance of SNSF, SEB and MO as it was set up works well. The introduction of the Expert Group in 2013 for the review of the TPdF and IPhD proposals aimed to reduce the workload of the Review Panel, and since then has proven to be a success. Despite this adaptation of the composition of the panel, in a few cases the opinions of the SEB and the SNSF Review Panel diverge considerably. In such situations the SEB is always ask to approve the SNSF's suggestion for funding.

### 3.1.5 Declared milestones

The declared milestones, which were originally submitted in June 2007 in the business plan have for the most part been achieved (see Appendix D, Table D1). Milestones for the second period were defined in the respective document of April 2013. The next years milestones are defined in the Scientific Reports.

In the followings, the outlook of the last Scientific Report 2013-2014 is compared with the present situation one year later. A complete overview of all the declared milestones can be found in Table A1 in Appendix A.

#### *10<sup>th</sup> call for proposals: review and start of MRD and TF Projects*

- ✓ Fulfilled: the call for proposals with a deadline on July 31, 2014 generated 30 MRD and 4 TF Project proposals, out of which the SEB and SNSF Review Panels granted 9 MRD and 2 TF Projects, out of which all MRDs and both TF Projects were active by the end of this reporting period (see 1.1.1.2 MRD Projects; 1.1.1.4 TF Projects).

#### *11<sup>th</sup> call for proposal: review and start of IPhD and TPdF Projects*

- ✓ Fulfilled: the call was published in December 2014, and out of 33 TPdF and 25 IPhD applications, 8 TPdF and 10 IPhD projects were granted, respectively (see 1.1.1.8, Calls for proposals). The successful applicants were notified by the SNSF and the SystemsX.ch management office in August 2015.

#### *12<sup>th</sup> call for proposal: review and start of Special Opportunity Projects*

- ✓ Fulfilled: the call was published in February 2014, and out of 51 Special Opportunity Project applications, 9 projects were granted, 5 with full and 4 with partial funding scheme (see 1.1.1.8, Calls for proposals). The successful applicants were notified in July 2015, 2 projects have already started in August 2015.

#### *ERASysAPP*

- ✓ Fulfilled: after the first call for projects 7 projects were granted, including 4 projects with Swiss participants. 10 proposals were received for the second call and 5 were granted, two including Swiss research groups (see 1.1.4.1, ERASysAPP).

#### *2<sup>nd</sup> International SystemsX.ch Conference*

- ✓ Fulfilled: the conference took place in Lausanne from October 20-23, 2014 with over 350 participants and was declared to be a great success (1.1.2.6, 2<sup>nd</sup> International SystemsX.ch Conference).

#### *SystemsX.ch Workshop: Leadership and Management Skills for Postdocs*

- ✓ Fulfilled: the workshop was organized exclusively for Postdocs, in February 9-10, 2015 for the first time. 16 participants attended the two-day course, which took place in Gerzensee, Berner Oberland.

#### *SystemsX.ch Retreat 2015*

- ✓ Fulfilled: the retreat had a focus on soft skill training for how to obtain better results through diversity, counted 33 participants (PhDs and Postdocs), and took place in Rigi Kaltbad from March 9-12, 2015.

#### *Joint SystemsX.ch/SIB Summer/Autumn School 2015*

- Fulfilled partially: the SystemsX.ch/SIB joint autumn school on “Systems Modeling” is going to take place in Schwarzenberg, from November 08-12, 2015. The details of the workshop are being prepared.

### *Systems Medicine 2017-2020*

- ✓ Fulfilled: the working group mandated by the BoD delivered their report. Following the preliminary decision of the SERI in Autumn 2014 concerning the feasibility of a new initiative, the principles of the initiative was discussed on the Workshop «Implementation of a Swiss 'Personalized Health' Network: Initiation of Project Organisation» on August 31, 2015, in Bern.

➔ **Conclusion:** SystemsX.ch has reached most milestones stated in the outlook of the scientific report 2013-2014. The partly fulfilled point is under preparation and will be completed by November 2015.

## **3.2 Science**

By August 2015, 248 SystemsX.ch projects of different types (RTD, MRD, TF, TPdF, IPhD, IPP, BIP, SyBIT, HTF, ERASysAPP) have been approved. This includes two SyBIT project phases and seven ERASysAPP projects as well as HTF projects. In Appendix B, all projects that were active in the period July 2014 to June 2015 present their annual scientific reports. Some projects (RTDs, IPPs, BIPs and IPhDs) were completed already before this reporting period started. Those project reports are enclosed in the previous SystemsX.ch Scientific Reports. This chapter concentrates on an overview complementary to the project reports.

### **3.2.1 Research Projects**

The overarching goal of the Swiss Initiative for Systems Biology is to establish and sustain systems biology research in Switzerland at an internationally competitive level. To achieve this ambitious goal SystemsX.ch was formed as a simple partnership that, in turn, advances systems biology in Switzerland by (i) supporting academic research projects, (ii) educating the next generation systems biology scientists, (iii) supporting private-public sector partnerships, and by (iv) participating in international systems biology programs. SystemsX.ch now consists of fifteen partner institutions across Switzerland.

### **3.2.2 Interdisciplinarity**

One of the major aims of SystemsX.ch is (a) to reduce the boundaries between scientific disciplines, and (b) to reduce boundaries between partner institutions to facilitate the interactions of scientists at Swiss research institutions. An important step to achieve this goal is to attract non-biologists to contribute to and implement the systems research approach.

Previous Scientific Reports of SystemsX.ch showed statistics about disciplines of approved PIs and co-PIs independent of whether or not they already received a SystemsX.ch grant before. The respective numbers are given in **Table 2**. It says that up to now, projects with a total of 696 PIs and co-PIs have been approved, and, as indicated with an asterisk (\*), several research groups received more than one SystemsX.ch grant.

However, the maybe more important and interesting statistics is how many physical research groups in SystemsX.ch participated. Also with respect to disciplines this may be more viable. These statistics are presented in **Table 3** in which for each year only research groups are considered that receive a SystemsX.ch grant for the first time. In total, 401 research groups have had SystemsX.ch projects approved (see also Figure 3).

**Table 2.** Overview of the development of the mixture of disciplines within SystemsX.ch. The PI and co-PIs of each approved project were categorized according to the discipline of their doctoral thesis.

| Year | # Grps* | Bio | Phys | Comp Scien | Chem | Med | Eng | Math | Econ | n.a. |
|------|---------|-----|------|------------|------|-----|-----|------|------|------|
| 2008 | 151     | 52% | 15%  | 10%        | 5%   | 8%  | 5%  | 4%   | 1%   | 0%   |
| 2009 | 246     | 51% | 13%  | 11%        | 11%  | 7%  | 3%  | 4%   | 1%   | 0%   |
| 2010 | 306     | 48% | 12%  | 12%        | 11%  | 7%  | 5%  | 3%   | 1%   | 1%   |
| 2011 | 330     | 49% | 12%  | 12%        | 11%  | 7%  | 5%  | 3%   | 1%   | 0%   |
| 2012 | 354     | 51% | 11%  | 11%        | 11%  | 6%  | 6%  | 3%   | 1%   | 0%   |
| 2013 | 481     | 51% | 11%  | 11%        | 10%  | 7%  | 7%  | 3%   | 0%   | 0%   |
| 2014 | 590     | 51% | 11%  | 12%        | 9%   | 7%  | 7%  | 3%   | 0%   | 0%   |
| 2015 | 696     | 49% | 11%  | 12%        | 9%   | 9%  | 7%  | 3%   | 0%   | 0%   |

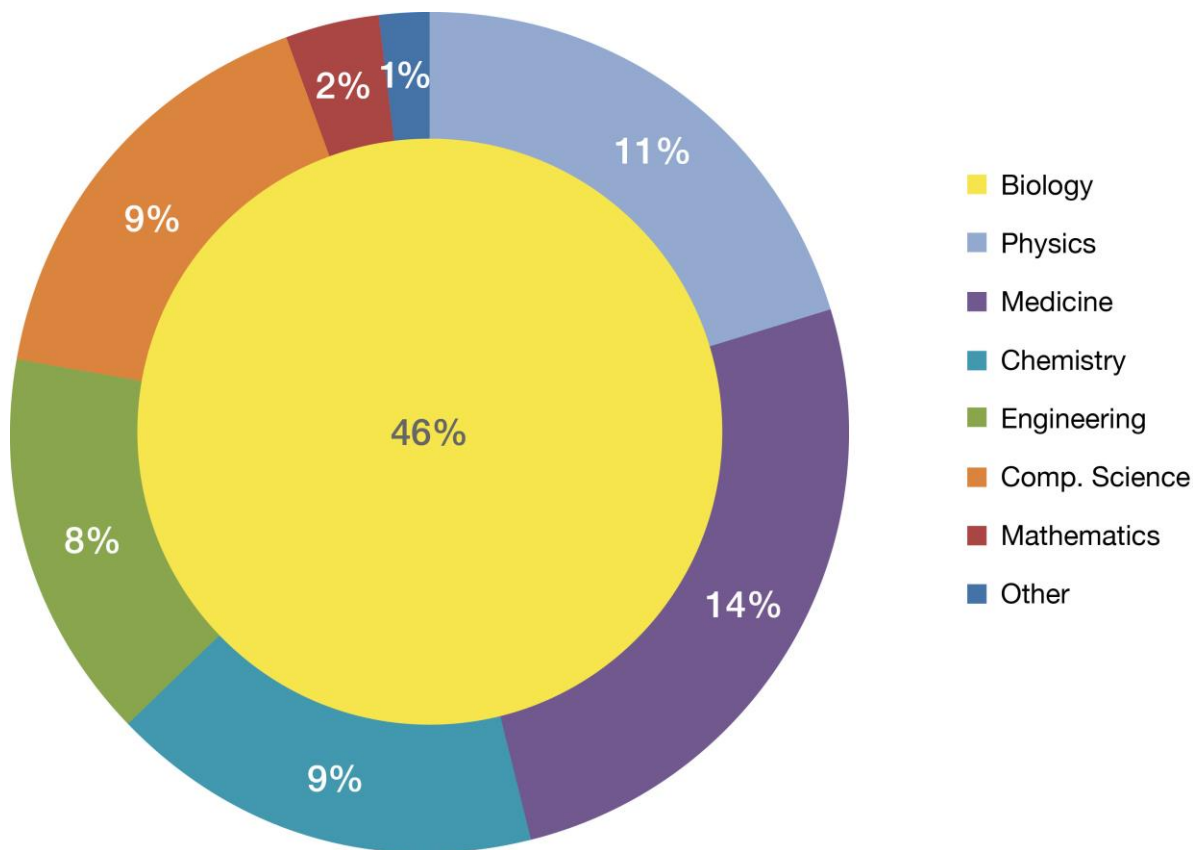
\*several groups are involved in more than one project.

**Table 3.** Overview of the development of the mixture of disciplines of research groups with SystemsX.ch grants. The PI and co-PIs of each approved project were categorized according to the discipline of their doctoral thesis (see also **Figure 3**).

| Year | # Grps | Bio | Phys | Med | Chem | Eng | Comp Sci | Math | Econ | void / others |
|------|--------|-----|------|-----|------|-----|----------|------|------|---------------|
| 2008 | 119    | 55% | 13%  | 10% | 4%   | 4%  | 8%       | 4%   | 2%   | 0%            |
| 2009 | 177    | 53% | 11%  | 10% | 11%  | 3%  | 8%       | 4%   | 1%   | 0%            |
| 2010 | 205    | 49% | 12%  | 10% | 12%  | 6%  | 7%       | 3%   | 1%   | 0%            |
| 2011 | 231    | 52% | 11%  | 9%  | 11%  | 7%  | 6%       | 3%   | 1%   | 0%            |
| 2012 | 277    | 52% | 11%  | 9%  | 10%  | 8%  | 6%       | 3%   | 1%   | 0%            |
| 2013 | 303    | 50% | 11%  | 10% | 10%  | 8%  | 7%       | 3%   | 1%   | 0%            |
| 2014 | 345    | 50% | 11%  | 10% | 9%   | 8%  | 8%       | 3%   | 1%   | 0%            |
| 2015 | 401    | 46% | 11%  | 14% | 9%   | 8%  | 9%       | 2%   | 1%   | 0%            |

In the 248 SystemsX.ch projects approved until August 2015, a total of 401 different research groups are involved. Based on their education, i.e. the topic and discipline of their (first) doctoral thesis, 46% of the PIs/co-PIs are biologists (including biochemists, biophysicists, neurobiologists, etc), 14% MDs, 11% are physicists, 9% chemists, 9% computational scientists (including bioinformaticians), 8% engineers, and 2% mathematicians. **Table 3** and **Figure 3** give an overview of the development of the disciplines with time, as the SystemsX.ch community has grown. These data indicate that Biology is the dominant discipline within the SystemsX.ch community, and that its relative share decreased with time. The remaining parts are more or less similar in size and go MDs, physicists, chemists, computational scientists and engineers with about 10% each. However, the 10<sup>th</sup> call caused a remarkable increase of MDs from 10% to 14%, a textbook example of how incentives and boundary conditions allow to steer research.





**Figure 3.** Out of the 401 PIs and co-PIs of the approved 248 SystemsX.ch projects, 46% did their PhD in biology, 14% in Medicine, 11% in Physics, and 11% in Computational Sciences / Mathematics.

→ Conclusion: A good mixture of disciplines contributes to the scientific output of SystemsX.ch, with biologists constituting slightly less than half of the research groups working on the projects. In 2013, the SNSF pointed out correctly, most RTDs are led by biologists. This was partly compensated by the MRD projects, within which many new medical research groups joined SystemsX.ch.

### 3.2.3 Proposals and success rates

For the scientific review, two main criteria have been applied: (1) scientific quality, and (2) relevance for systems biology and concordance with the scientific goals of SystemsX.ch. In collaboration with the SNSF, these two principles have been implemented successfully. The SNSF and SystemsX.ch carried out the scientific review of the submitted project proposals for RTDs, MRDs, TFs, TPdF and IPhDs jointly. While the SNSF is responsible for assuring the scientific quality of the projects and makes the final decision on RTDs, MRDs, TFs, TPdF and IPhD projects (including the SystemsX.ch-initiated project SyBIT), SystemsX.ch is responsible for the overall strategic guidance of the initiative. All other project types (IPP, BIP, HTF and Special Opportunity Projects) are evaluated just by the SEB (with the support of external reviewers if needed).

**Table 4** shows that out of the 527 (including special projects and ERASysAPP: 625) submitted proposals a total of 216 (248) projects, i.e. 41% (40%) have been approved by the SNSF and/or the SEB, involving 401 research groups and well above 1'000 scientists (see Appendix C). The success rates vary between the project types: For RTDs/MRDs, the success rate is 30%, for TFs 47%, for IPhDs it is as well 47%, whereas TPdFs have a rate of only 29%. Almost every second IPP proposal (47%) was funded. BIP proposals had with over 80% the

highest probability to be funded, and Special Opportunity Projects 26% (for details see Appendix D, Tables D3-4 and Appendix A, Table A4).

The large response of the community to the RTD calls, and even more so to the 1<sup>st</sup> call for MRD Projects, show that SystemsX.ch fulfills a need.

**Table 4.** Overview of proposals that were submitted to SystemsX.ch between 2008 and August 2015 and the respective and success rates. In Tables A3 to A5 in Appendix A and Tables D3 to D5 in Appendix D, a more detailed list is given.

| Project Type<br>Year | Requested<br>Funds [CHF] | # Proposals<br>Submitted | # Proposals<br>Approved | # (Co-)PIs | SysX.ch<br>Funds [CHF] | Success<br>Rate [#] | Success<br>Rate [CHF] |
|----------------------|--------------------------|--------------------------|-------------------------|------------|------------------------|---------------------|-----------------------|
| RTD/MRD              | 648'257'365              | 137                      | 43                      | 306        | 149'274'950            | 30%                 | 27%                   |
| TF                   | 4'677'090                | 17                       | 8                       | 24         | 2'097'716              | 47%                 | 45%                   |
| TPdF                 | 22'802'990               | 106                      | 32                      | 62         | 7'161'969              | 29%                 | 31%                   |
| IPhD                 | 32'717'522               | 184                      | 87                      | 187        | 15'813'609             | 47%                 | 48%                   |
| IPP                  | 7'629'600                | 64                       | 30                      | 69         | 3'509'500              | 47%                 | 46%                   |
| BIP                  | 2'256'175                | 19                       | 16                      | 38         | 1'886'175              | 84%                 | 84%                   |
| <b>Subtotal</b>      | <b>718'340'450</b>       | <b>527</b>               | <b>216</b>              | <b>686</b> | <b>179'743'919</b>     | <b>41%</b>          | <b>25%</b>            |
| SyBIT                | 17'624'000               | 6                        | 2                       | 7          | 15'024'000             | 80%                 | 85%                   |
| HTF                  | 3'193'265                | <b>15</b>                | <b>8</b>                | <b>11</b>  | <b>1'388'521</b>       | <b>53%</b>          | <b>43%</b>            |
| SpecOpp all          | 11'952'219               | 57                       | 15                      | 18         | 2'787'201              | 26%                 | 23%                   |
| ERASysAPP            | 7'644'237                | 18                       | 6                       | 6          | 2'333'836              | 33%                 | 31%                   |
| Fairdom              | 660'000                  | 2                        | 1                       | 2          | 660'000                | 50%                 | 100%                  |
| <b>TOTAL</b>         | <b>759'414'463</b>       | <b>625</b>               | <b>248</b>              | <b>730</b> | <b>201'937'477</b>     | <b>40%</b>          | <b>27%</b>            |

→ Conclusion: These statistics indicate that there is a large interest in systems biology funding and that saturation has not been reached, neither at the level of project concepts and ideas, nor at the level of interested scientists. The deciding committees had the choice to select the most promising proposals for funding. In fact, the SNSF mentioned after several calls that viable and good proposals had to be rejected due to the limited amount of funds.

One interesting remark in the SNSF Review Panel was, that the presented MRD proposals (the first of this kind) were comparable in quality with the RTD proposals in 2008 or 2009. During the course of SystemsX.ch, proposal quality increased considerably as mentioned in the SNSF Panel.

Furthermore, experience showed that some proposals rejected in the first round benefited from additional organizational and planning time as they came back and were evaluated with excellent rankings.

### 3.2.4 Evolution since 2008

It is interesting to consider the evolution of SystemsX.ch RTD Projects from basic towards medically applied science. In 2008 all eight approved could be considered basic research, with three of them aiming to obtain results that could have a medical application. By 2013 three of the nine approved RTDs had a clearly medical focus, and three more had medical aims among their objectives. On the one hand, this increase has been progressive: RTD Projects which aimed to have an application in the medical field were three out of eight in 2008, three out of six in 2009, four out of seven in 2012, and six out of nine in 2013. On the other hand, there has also been a qualitative shift. The RTDs of the first phase focused mainly on fundamental research questions, with some of them considering the possible medical implications of their findings. The 8<sup>th</sup> call in 2013 approved three projects that directly deal with disease treatment and etiology (MERIC, TbX and MalarX), and three more that ap-

proach basic questions but with the aim of obtaining results with impact in medicine (AgingX, TargetInfectX, HostPathX).

Finally, SystemsX.ch called for Medical Research and Development (MRD) projects, where MDs were explicitly encouraged to be more active. As a result, percentage of MDs in the SystemsX.ch community increased from 10 to 14% (out of 401 research groups). It is a textbook example of steering research by providing incentives.

### **3.3 Education**

Education is not under direct control of SystemsX.ch, but the main responsibility and work force is located rather at the partner institutions. This restricts the job of the Education Advisory Board mainly to coordination.

#### **3.3.1 Fellowships**

##### **3.3.1.1 IPhDs**

One of the main educational activities of SystemsX.ch is the support of PhD students through their IPhD Projects. While this program allows students to gain very valuable interdisciplinary experience in at least two scientific domains during their doctoral studies, it also is a format with a certain potential for conflict. This is shown by the fact that in several IPhD Projects the PhD student left prematurely and the PI and co-PI had to find another student who could continue the project. In one case, also the second student left the project. In all cases a student could be found who carried on the project, although sometimes the project was interrupted for several months. The total duration of IPhD Projects is limited to four years, independently of the number of students employed. In another two projects one of the co-supervisors had to be replaced. However, a survey carried out among IPhD supervisors shows that the advantages of the project format largely outweigh its disadvantages.

##### **3.3.1.2 TPdFs**

The Transition Postdoc Fellowship (TPdF) aims to enable young researchers with various scientific background to increase their knowledge and expertise in systems biology, but in a scientific field complementary to the domain in which they have worked so far during their PhDs or early postdocs (referring to the “transition” phrase in the project title). Based on a questionnaire that the first finishing TPdFs and their mentors filled-in, the main advantages of the project type are the chance to become truly interdisciplinary with secured funding that is dedicated for this transition time and without having the feeling that this learning phase is lost time. In the beginning, this project type tend to start slower, as acquiring the new knowledge and skills takes time, however getting to know the new discipline is extremely beneficial towards the end of the project and for the future career steps of the TPdF. With this funding body the TPdF mentors have the opportunity to attract someone with new skills to their labs and benefit from the new line of research.

#### **3.3.2 Events**

In the beginning, the annual PhD student retreats were open for IPhD students but also for students whose PhD position was funded by an RTD-project. Since 2012 the event has been opened also to postdocs. Registration for the Retreat 2012 was low (20 participants), but in 2013 the numbers went up significantly (45 participants), and in 2015 we welcomed 35 participants.

The summer and winter schools (co-)organized by SystemsX.ch and the SIB have all received very good feedback from the participants.

The involvement of SystemsX.ch in ERASysAPP has opened new possibilities in education and networking especially on the European level.

### **3.3.2.1 2<sup>nd</sup> International SystemsX.ch Conference**

From October 20-23, 2014, over 350 people working in the field of systems biology gathered in Lausanne to participate in the 2<sup>nd</sup> International SystemsX.ch Conference on Systems Biology. The PhD students and postdocs involved in SystemsX.ch research projects were represented with high numbers, and among the 140 posters they presented and discussed their research projects in five focus areas: theory and biophysical modeling, cell- and developmental biology, functional genomics and gene regulation, single-cell biology, and systems genetics and medicine.

### **3.3.2.2 SystemsX.ch Retreat 2015**

The student Retreat has established a reputation as the main SystemsX.ch event for PhD students and in 2015 also for postdocs. Following on from the success of the 2012 and 2013 Student Retreat, SystemsX.ch decided to shift the emphasis away from science itself and focus on strengthening soft skills: the collaboration and communication between scientists.

Coaching expert Sašo Kočevár and his team from 'hfp consulting' were invited back for already a third year to lead the workshops. The Retreat in March 2015 was held in Rigi Kaltbad, where the 33 participating young researchers learnt more about how to obtain better results through diversity. Topics covered included techniques for active listening, dealing with group dynamics, managing conflict, stimulating creativity, and presenting work to an audience from a different scientific field. Through focused work in small groups as well as plenary sessions, students were able to practice what they learnt on the spot. The coaches used a diverse set of approaches ranging from group discussions to improvisation sessions in order to convey the subject matter. The retreat also gave participants plenty of time to interact with other young scientists working in the field of systems biology. This workshop has been very well received, therefore the soft-skills focus of the student retreats will be continued in the next years as well.

### **3.3.2.3 Postdoc Leadership Workshop**

For the first time, this year SystemsX.ch organized a Leadership and Management Skills workshop exclusively for Post-docs in February 2015. 16 participants attended the two-day course, which took place in Gerzensee, Berner Oberland. The highly interactive workshop was designed and conducted in a way that considerably influence and support both the present scientific work and future careers of participating postdocs. The workshop was very well received, and based on the very positive feedback a one-day follow-up of this workshop for this event is planned for February 16, 2016, as well as the repetition of the same event for new Postdoc participants from February 17-18, 2016 at the same location: at the Gerzensee

### **3.3.2.4 Joint CRG/SystemsX.ch Summer School 2015**

This international course was organized together with the Centre for Genomic Regulation (CRG) in Barcelona, Spain. Focusing on the dynamical modeling of networks, the course aimed to provide a broad introduction to systems biology. It was directed at PhD students and postdocs with backgrounds in biology or bioinformatics. In addition to introducing researchers to new techniques and know-how, this course aimed to foster interactions between students and established figures in the field of systems biology. After an optional introductory

session on elementary calculus and algebra (ordinary differential equations, linear algebra) and an introduction to Matlab, the course consisted of theoretical lectures which covered the following topics: dynamical systems theory, stochastic systems, frameworks and methods for modeling biological networks, multivariate and multidimensional data analysis, techniques for parameter inference, reverse engineering, biophysical and cellular models. All theoretical concepts covered in the course were accompanied by a series of hands-on exercises.

➔ **Conclusion:** In total, well above 200 PhD students have been educated so far within SystemsX.ch projects. Almost 90 IPhD students have been mentored by two supervisors from different disciplines, carrying out projects at the interface of disciplines. Education is on track. Most IPhD projects need a fourth year to accomplish the planned milestones because of individual reasons. The reduced interest of the students in the Retreat and the Autumn School in 2012 might have been caused by the excessive offer of such education events on a national and international level. The MO took this issue into consideration and decided to 1) focus on co-organizing already well-established events, and 2) open retreats also to post-docs. The increased number of registrations and participants since Autumn 2013, as well as the very positive feedback for the four events organized since then, suggest that this strategy has been successful.

### 3.4 Public-Private Partnership

SystemsX.ch has tried numerous and different approaches to create close ties to the private sector: A so-called Industry Day was organized in October 2008, a SystemsX.ch workshop for SMEs was held in October 2009 at ETH Zurich, visits of industry companies, investigating how a SystemsX.ch Industry Club could be set up, or presentations and attendance of biotechnology fairs. Two representatives from big pharma were invited permanent guests in the boards in the first six years of the initiative (2007 – 2013).

By setting up particular project types (BIP and ISA), the involvement of the private sector was fostered in the past. New type of projects (TF and Special Opportunity) currently continue these efforts. The private sector was involved already during the preparation and proposal phase, and scientists from the private sector are present as co-PIs in RTD and TF Projects of the second phase. After the 6<sup>th</sup> and 9<sup>th</sup> call for proposals, six TF projects have been approved. So far, 77 (121 incl FMI) private groups were included in submitted proposals, and 24 (38 incl FMI) have been participating in approved projects. Four more TF proposals with six private co-applicants were submitted to the 10<sup>th</sup> call. A total of 11 private groups are co-applicants on MRD proposals for the 10<sup>th</sup> call. The 12<sup>th</sup> and final call for SystemsX.ch Special Opportunities proposals attracted 51 applications, out of which 7 involved the participation of private groups.

An important step towards promoting interactions of Academia with industry was the launching of the pilot project “Entrepreneur in Residence (EiR) / Innovation Scout Service (ISS)”. Even though the goal and the set milestones were difficult to reach, it was considered to have been an interesting experience.

➔ **Conclusion:** The success of the BIP proposals was the first step in the right direction for fostering and advancing industrial collaborations. The follow-up projects, namely TF Projects, which started in January 2013, will have to demonstrate effectiveness in the future. The involvement of private groups in Special Opportunities projects is also relatively high. The EiR/ISS pilot project was a valuable learning experience, even if it did not deliver the expected results.

### 3.5 International outreach

On an international level, SystemsX.ch is obtaining increasing recognition. Besides the participation in ERASysAPP, it is the various contacts, collaborations and activities, be it from members of the MO or individual SystemsX.ch scientists to foreign stakeholders that contribute towards this end (see chapter 1.1.4). The participation of Swiss groups (all of them also involved in SystemsX.ch projects) in six of the twelve projects funded by ERASysAPP shows that Switzerland is a key actor in systems biology research at the European level.

The second International SystemsX.ch Conference on Systems Biology at the new Swiss Tech Convention Center at EPF Lausanne continued to mark an important step forward in increasing the international visibility of SystemsX.ch. The conference took place from October 20-23, 2014.

An important step in terms of international outreach of SystemsX.ch was the Consortial Agreement between BMBF and SystemsX.ch. Since the beginning of the initiative SystemsX.ch has had a regular informal exchange with the German Ministry for Education and Research (BMBF). In 2013, a Consortial Agreement was signed to foster the BMBF-SystemsX.ch collaboration in scientific systems biology and in particular medicine research. SystemsX.ch researchers collaborate with German research groups with the goal of combining their expertise and gain the largest possible benefit for their projects. German research groups involved in SystemsX.ch RTD Projects receive their funds from BMBF (see **Table 5**).

**Table 5.** These RTDs and German research groups currently benefit from within the Consortial Agreement between BMBF and SystemsX.ch.

| RTD project    | PI                                    | German research group                |
|----------------|---------------------------------------|--------------------------------------|
| PhosphoNet_PPM | Ruedi Aebersold, ETH Zurich           | Andreas Beyer, University of Cologne |
| PlantGrowth2   | Chris Kuhlemeier, University of Bern  | Richard Smith, MPI Cologne           |
| HostPathX      | Thierry Soldati, University of Geneva | Heinz Koepl, TU Darmstadt            |
| MorphoGenetiX  | Damian Brunner, University of Zurich  | Richard Smith, MPI Cologne           |

Moreover, foreign groups are increasingly often co-applicants on proposals for SystemsX.ch projects (three foreign research groups are in applying MRD consortia. The participation of students from abroad in the educational activities organized by SystemsX.ch also confirms the international visibility of the initiative.

Mid October 2013, the Norwegian Science Foundations organized a panel meeting with an International Advisory Board (IAB) composed of nine experts. Two of them (René Imhof and Daniel Vonder Mühl) were recruited because SystemsX.ch was considered a good role model for the strategic initiative called “Digital Life – Convergence for Innovation”. In March 2015, four (including Daniel Vonder Mühl) out of the nine IAB members were invited to advise with the concrete implementation of “Digital Life Norway”.

➔ **Conclusion:** The longer SystemsX.ch is active, the more its visibility increases within the international community.

### 3.6 Impact of SystemsX.ch

Based on the mid-term reviews by the SNSF and various individual feedbacks (e.g. international conferences, ERASysAPP, etc), it is visible that SystemsX.ch has a high impact on the Swiss but also on the international systems biology community. Most expectations stated when the initiative was launched have been met.

The SEB initiated a PhD project (“impact study”) to investigate this issue: Alban Frei, a historian in the group of David Gugerli (Science History ETH Zurich), started his project in March 2012. As a side product, Alban Frei published an article on SystemsX.ch in a book to the 200 year anniversary of Swiss Academy of Sciences (SAS, scnat).

In August 2013 and in July 2015, SystemsX.ch sent out a questionnaire for PIs of IPhD projects that have been completed. An online-survey will gather regularly information also in the future about the impact and benefit for students and applicants of these funding types.

A major impact of SystemsX.ch is that several hundred research groups elaborated and submitted interdisciplinary research proposals, almost 250 projects were approved and funded within a SystemsX.ch. Almost half of them are involved in an inter-institutional RTD Project. In fact, numerous feedbacks show that a great increase in collaborations has been triggered across disciplines but also across institutions.

Progress in the area of education has been made, not only due to the organization of SystemsX.ch educational events (retreats, workshops, summer schools). SystemsX.ch also makes an effort to support educational activities even if it is not the initiator. One example for this is the support of multiple different events organized by PhD students and postdocs: the Basel Postdoc Network Retreat is being supported by SystemsX.ch for the fifth time, the Retreat of the Systems Biology PhD Program of the Life Science Zurich Graduate School for the third time, and the 8<sup>th</sup> Conference of the International PhD Program in Basic and Applied Life Sciences of the University of Geneva is also being supported for the second time.

SystemsX.ch also provides financial support for courses and meetings organized by members of the community. Examples of such events that have been supported within this reporting period include the Joint SystemsX.ch/CRG Summer School in Barcelona (June-July 2014 and 2015), the European Conference on Computational Biology in Strasbourg (September, 2014), the 12<sup>th</sup> BC<sup>2</sup> Computational Biology Conference in Basel (June 2015), the FASEB Mitosis: Spindle Assembly and Function meeting in Big Sky, MT, USA (June 2015), the Systems Biology of Human Diseases (SBHD) meeting 2015 in Heidelberg (July 2015) and the EPFL Life Sciences Symposium - LSS 2015 (September 2015). The numerous requests for support received by the MO show that the initiative is well-known and appreciated (see Appendix A Table A52).

Another evidence of the impact of SystemsX.ch are the efforts that several partner institutions have undertaken to integrate systems biology into PhD or Masters curricula. Although SystemsX.ch cannot expect that all partner institutions offer systems biology courses or programs, the discussion around educational activities in systems biology have promoted new programs at some of the partner institutions. The RTDs have been particularly important in promoting such initiatives. As an example, both Plant Growth and Neurochoice now offer Systems Biology courses at the University of Bern. In addition, RTDs often use wiki platforms and other tools to encourage interactions among students and other researchers.

Furthermore, the establishment of IT research support entities at the Universities of Zurich and Basel bear witness to the impact of SystemsX.ch:

- S<sup>3</sup>IT (Service and Support for Science IT), led by Peter Kunszt, operates at University of Zurich since January 2014.
- SIS (Scientific IT Services), led by Bernd Rinn, was re-organized at ETH Zurich in 2013.
- University of Basel opened sciCore, led by Torsten Schwede, in 2013.

In addition, SystemsX.ch has had an impact that goes beyond the strictly scientific realm:

- First, it has established a new governance and organizational model for large interdisciplinary and inter-institutional programs in Switzerland. This model has already been adopted for another large program, NanoTera.ch.
- Second, it has catalyzed the emergence of a cross-disciplinary research culture and recruited a significant number of non-life-science researchers to the life sciences.

- Third, it has created a philosophy of sharing limited resources between participating institutions, resulting in the establishment of unique high tech capabilities at specific institutions that are accessible to the whole SystemsX.ch community. There are several examples for this:
  - the cryo-EM at the RTD project CINA
  - the screening facilities at ETH Zurich and EPF Lausanne
  - jointly acquired and shared reagent libraries
  - the single-cell mass spectrometric approach called mass cytometry (CyTOFTM) at Bernd Bodenmiller's lab.
- Fourth, the allocation of matching funds by the partner institutions has opened up new opportunities and led for instance to the recruitment or reorientation of numerous professors to partner institutions.
- Fifth, the dual mentoring of IPhD students to educate them in a truly interdisciplinary manner resulted in very positive feedbacks from both the students and the supervisors.
- Sixth, the efforts to involve the private sector in joint research programs has led to the reorientation of the initially naïve plans towards realistic, bottom-up initiatives that aim at long-term and sustainable interactions.
- Seventh, several PhD students graduating from SystemsX.ch projects continue their training in the best systems biology programs worldwide.

The success of the initiative can also be measured by scientific excellence. Certainly the impressive list of publications, and the awards received by scientists involved in SystemsX.ch projects are such measures. SystemsX.ch scientists are also internationally competitive by any measure. Other indicators of the scientific excellence of the SystemsX.ch community are for example:

- the number of SystemsX.ch members who received **SNSF Professorships**. Between 2007 and 2015 the following 23 current and former SystemsX.ch scientists received SNSF professorships:

| Last Name   | First Name     | Affiliation            |
|-------------|----------------|------------------------|
| Baubec      | Tuncay         | UZH                    |
| Bellone     | Camilla        | Université de Lausanne |
| Bodenmiller | Bernd          | Universität Zürich     |
| Cabernard   | Clemens        | Universität Basel      |
| Fellay      | Jacques        | EPFL                   |
| Gagneux     | Sébastien      | Universität Basel      |
| Gatfield    | David          | Université de Lausanne |
| Hamaratoglu | Fisun          | Université de Lausanne |
| Hangartner  | Lars           | Universität Zürich     |
| Heinis      | Christian      | EPF Lausanne           |
| Koepl       | Heinz Wolfgang | ETH Zürich             |
| Liberali    | Prisca         | FMI/BS                 |
| Murr        | Rabih          | Université de Genève   |
| Müller      | Martin         | Universität Zürich     |



| Last Name | First Name | Affiliation            |
|-----------|------------|------------------------|
| Pelet     | Serge      | LA                     |
| Pertz     | Olivier    | Universität Basel      |
| Pfister   | Pascal     | Universität Zürich     |
| Picotti   | Paola      | ETHZ                   |
| Sprecher  | Simon      | Universität Bern       |
| Suter     | David      | EPF Lausanne           |
| Tussiwand | Roxane     | Universität Basel      |
| Zehn      | Dietmar    | Université de Lausanne |
| Zippelius | Alfred     | Universität Basel      |

- the number of SystemsX.ch members who received **ERC Grants**.

Between 2007 and 2013, 43 senior SystemsX.ch researchers received Advanced or Consolidator ERC grants and 25 junior SystemsX.ch researchers received Starting ERC grants.

- Senior SystemsX.ch scientists who have been awarded **ERC Advanced or Consolidator Grants**:
  - ERC Advanced Grants (2013): Pascale Cossart, Pierre Gönczy, Jeffrey Alan Hubbell, Christoph Georg Fritz Dehio, Petros Koumoutsakos, Marcos Antonio Gonzalez Gaitan, Francoise Gisou Van Der Goot
  - ERC Consolidator Grants (2013): Christoph Handschin, Robbie Joseph Loewith, Sylvie Roke
  - ERC Advanced Grants (2012): Douglas Hanahan, Melody Ann Swartz, Martinus Adela Maria Gijs, Christian Lüscher, Dani Or
  - ERC Advanced Grants (2011): Ernst Fehr, Carl Christian Holger Petersen
  - ERC Advanced Grants (2010): Bradley James Nelson, Michael Unser, Bernard Marie Thorens, Didier Trono, Wulfram Gerstner, Andreas Reinhold Hierlemann  
Andreas Georg Plückthun, Lukas Sebastian Bonhoeffer, Matthias Peter
  - ERC Advanced Grants (2009): Yves Barral, Sotirios Pratsinis, Stylianos Antonarakis, Antonio Lanzavecchia, Ulrich Grossniklaus, Demetrios Christodoulou, Adriano Aguzzi, Laurent Keller, Ulrich Schibler
  - ERC Advanced Grants (2008): Pierre Gönczy, Konrad Basler, Viola Vogel, Jeffrey Hubbell, Rudolf Aebersold, Marcos Antonio Gonzalez Gaitan, Johan Auwerx, Denis Duboule, Ari Helenius
- SystemsX.ch scientists who have been awarded **ERC Synergy Grant**:
  - ERC Synergy Grant (2013): “Mechanisms of Evasive Resistance in Cancer” (MERiC). Michael Hall, Gerhard Christofori, Markus Heim, and Niko Beerwinkel.
- Junior SystemsX.ch scientists who have been awarded **ERC Starting Grants**:
  - ERC Starting Grants (2013): Tanja Stadler, Dietmar Zehn, Paola Picotti, Bernd Bodenmiller, Savas Tay
  - ERC Starting Grants (2012): Govindkrishna Govind Kaigala, Sebastien Gagneux, Aurelien Raymond Roux, Simon Sprecher, Rainer Andreas Krause, Matthias Lutolf, Mihaela Luxita Zavolan
  - ERC Starting Grants (2011): Kathleen Mccoy

- ERC Starting Grants (2010): Botond Roska, Felix Naef, Roland Karl Oliver Sigel, Emmanouil Dermizakis, Aleksandra Radenovic
- ERC Starting Grants (2009): Mohamed Bentires-Alj, Christian Von Mering
- ERC Starting Grants (2007): Christian Wolfrum, Melody A. Swartz, Dirk Schübeler, Petra Stephanie Dittrich, Robbie Joseph Loewith

➔ **Conclusion:** In the second phase 2013-2016 of SystemsX.ch it is crucial to continue the successfully launched paradigm shift. The participation in ERASysAPP, in which SystemsX.ch leads the Work Package 3 (Training and Exchange), will continue to push these efforts forward. Therewith, new international projects can be supported, which will improve the international network and visibility of SystemsX.ch.

## 4 Outlook 2015 and 2016

### All SystemsX.ch Day 2015

The sixth All SystemsX.ch Day, on September 15, 2015, at the Stufenbau in Bern, will offer participants an excellent chance to network with SystemsX.ch researchers and the wider systems biology community in Switzerland. Throughout the day there will be talks by SystemsX.ch scientists on their cutting-edge work, as well as a panel discussion on the challenges of interdisciplinary research. The highlight will be a keynote lecture by Steven Altshuler from the University of California San Francisco. 82 poster abstracts have been received for the conference, and up to 200 participants are expected.

### Invitation to apply for one year extension for IPhD, TPdF and TF projects

SystemsX.ch has to allocate all funds (except for events and Management Office) by December 2015. It will not be possible to approve projects or their extensions after this date. The issue of an extra year concerns potentially around 60 current projects. If all of these projects requested an additional year on the same funding level, it would require CHF 5.6 million in total. The amount put aside for these extension years amounts to CHF 4.6 million. However, firstly not all projects will need an extension, and secondly, it is not guaranteed that they will be granted one if they apply. In Autumn 2015, the concerned PIs will be invited to submit a request for an extra year. In the case that not all requests for extensions can be funded, based on the following order of priority:

- i) IPhD projects will be favoured over TPdFs, followed by Transfer Projects, and
- ii) a project that is close to its end will have a better chance of getting an extension than a project that started only recently.

### ERASysAPP

During the second half of 2015, the following task will predominate the activities of SystemsX.ch as partner of the ERA-Net ERASysAPP:

- Conduct measures to fulfill Task 3.4 'Exchange of individually-requested knowhow'
- Organizational and financial support of 2<sup>nd</sup> ERASysAPP Exchange Day beginning of December 2015
- Continually update Graduate Study Program Website and add content of ISBE Education report
- Communication measures to further disseminate elaborated tools for Training & Exchange as well as the curricula recommendations
- Sustainability: Handing over tools elaborated by ERASysAPP WP 3 to ISBE WP 10 Education and Training
- Final Financial and Scientific Reporting to the European Commission
- Supervision and support of activities of FAIRDOM.

### SystemsX.ch Course Leadership and Management Skills for Postdocs

In response to a wish expressed and feedback by several postdocs, SystemsX.ch will organize for the second time in February 17-19, 2016, a two-day workshop in lab management skills for postdocs. The workshop will once again be led by Sašo Kočevar and his team from hfp consulting. Postdocs will improve their communication and collaboration skills, will develop awareness of "leading with or without being in charge", and will learn and practice useful tools for their career in science. Moreover, they will be encouraged to establish and maintain a peer support group. hfp has developed and established such workshops for postdocs for

example at EMBO and the PRBB in Barcelona, and these programs are among Europe's most successful leadership training programs for scientists.

Additionally, a follow-up session of the Postdoc Workshop 2015 is planned for February 16, 2016, where the participants from the previous event could reflect on their leadership and management development during the year.

### **SystemsX.ch Retreat 2016**

The 7<sup>th</sup> SystemsX.ch Retreat will take place in May 24-27, 2016. The Retreat in 2016 runs under the title: Career Development for Young Scientists, and it is targeted at PhD students and postdocs. It offers an ideal platform for exchanging experiences and expert knowledge but this year also an opportunity to educate young scientists about their career development options. Scientific excellence plays an important role in predicting successful career progression, so does active networking, the ability to write grants and publications well, as well as the flexibility to move wherever a suitable position is on offer. Sašo Kočevár, an international coaching expert and his colleagues will provide concepts and skills that are immediately applicable to the career planning of the participants.

### **Joint Autumn School of SystemsX.ch and SIB**

SystemsX.ch and the Swiss Institute of Bioinformatics (SIB) are jointly organizing an Autumn School to educate PhD students on cutting-edge methodologies relevant to systems biology and bioinformatics. The objective is to teach how these two approaches can be integrated when modelling and simulating metabolic networks, gene regulatory networks and population genomics models. The four day Autumn School will take place from November 08-12, 2015 in the Hotel & Bildungszentrum Matt in Schwarzenberg (Luzern), and it aims to offer a small and selected group of PhD students (from SystemsX.ch and the SIB Training Network) an eminently practical modeling course, with introductory theoretical lectures on different topics followed by hands-on modeling sessions.

### **6<sup>th</sup> Advanced Lecture Course on Systems Biology 2016**

The 6<sup>th</sup> edition of the biannual "Advanced Lecture Course on Systems Biology" is going to be organized from February 28 - March 5, 2016 in Innsbruck (Austria). This course aims to train young scientists in modern concepts and techniques in systems biology. This includes lectures on experimental and theoretical techniques and advances, as well as black board teaching on concepts and computer practical on software, including data management. SystemsX.ch has been a long-standing sponsor of this training course and has become the lead supporting organization for the event. This course will be organized by a German-, Swiss- and Austrian committee (Ursula Kummer, Edda Klipp, Uwe Sauer and Karl Kuchler). This international course will be supported and co-organized by SystemsX.ch and the German BMBF.

### **Personalized Health 2017-2020**

A working group mandated by the BoD elaborated a detailed report for a national initiative which integrates experiences gained through SystemsX.ch and the strength of life science research in Switzerland. This research initiative would aim to foster the systems approach in the medical and clinical domains in order to support the Swiss health system. The success of the 10<sup>th</sup> call for proposals of SystemsX.ch, inviting Medical Research and Development Projects to apply systems biology approaches to medical and clinical questions, highlights the timeliness of such an initiative. Following the Workshop "Implementation of a Swiss 'Personalized Health' Network: Initiation of Project Organization" organized on August 31, 2015 in Bern, the final decision by the State Secretariat for Education, Research and Innovation whether or not this initiative will happen is expected in November 2015.

## 5 Financial overview

SystemsX.ch officially started in 2008 with a 4-year period as defined by the financial period of the Education Research and Innovation (ERI) 2008-2011, followed by a one-year ERI message for 2012, which SystemsX.ch used to extend the first phase of the initiative. Based on the contract between SNSF and SystemsX.ch, a Financial Report, that was audited by Ernst and Young and approved by the BoD, was submitted every year to the SNSF and the SERI in due time (i.e. before June 30 of the year following the reporting period). The Financial Reports show all financial details of the initiative and each of the projects. Tables are structured in a way that the actual annual amount are complemented by a table showing the cumulative amount since 2008 (or the respective project start).

Financial reporting of SystemsX.ch covers four funding categories:

- Federal money for SystemsX.ch,
- “Own Contributions” provided by SystemsX.ch partners as required by law,
- 2<sup>nd</sup> Party Funds from competitive research foundations, and
- 3<sup>rd</sup> Party Funds from private contributors (e.g. industry, SME, etc).

While the annual reporting period of the scientific report is from July to June, finances are reported by calendar year (January to December).

**Table 6.** Overview of financing of SystemsX.ch based on the business plan January 2007, updated in May 2011 (see also Financial Reports).

| in million CHF                  | Total<br>'08-'12 | Year *      |             |             |             | Total<br>'13-'16 | Total<br>'08-'16 |
|---------------------------------|------------------|-------------|-------------|-------------|-------------|------------------|------------------|
|                                 |                  | 2013        | 2014        | 2015        | 2016        |                  |                  |
| Federal ERI <sup>1)</sup>       | 119.7            | 24.5        | 24.5        | 25.3        | 24.5        | 98.8             | 218.5            |
| Own Contributions <sup>2)</sup> | 121.0            | 25.0        | 28.0        | 31.0        | 35.0        | 119.0            | 240.0            |
| Third Party <sup>3)</sup>       | 17.3             | 5.0         | 5.3         | 5.5         | 4.5         | 20.3             | 37.5             |
| <b>Subtotal</b>                 | <b>258.0</b>     | <b>54.5</b> | <b>57.8</b> | <b>61.8</b> | <b>64.0</b> | <b>238.0</b>     | <b>496.0</b>     |
| Second Party <sup>4)</sup>      | 38.7             | 17.0        | 18.0        | 19.0        | 20.0        | 74.0             | 112.7            |
| <b>Total contributions</b>      | <b>296.7</b>     | <b>71.5</b> | <b>75.8</b> | <b>80.8</b> | <b>84.0</b> | <b>312.0</b>     | <b>608.7</b>     |

| in million CHF                  | 2008        | Year *      |             |             |              | Total<br>'08-'11 | Year *<br>2012 | Total<br>'08-'12 |
|---------------------------------|-------------|-------------|-------------|-------------|--------------|------------------|----------------|------------------|
|                                 |             | 2009        | 2010        | 2011        |              |                  |                |                  |
| Federal ERI <sup>1)</sup>       | 13.0        | 27.0        | 28.5        | 30.5        | 99.0         | 20.7             | 119.7          |                  |
| Own Contributions <sup>2)</sup> | 13.0        | 27.0        | 29.0        | 31.0        | 100.0        | 21.0             | 121.0          |                  |
| Third Party <sup>3)</sup>       | 0.2         | 0.8         | 4.5         | 7.0         | 12.5         | 4.8              | 17.3           |                  |
| <b>Subtotal</b>                 | <b>26.2</b> | <b>54.8</b> | <b>62.0</b> | <b>68.5</b> | <b>211.5</b> | <b>46.5</b>      | <b>258.0</b>   |                  |
| Second Party <sup>4)</sup>      | 1.0         | 2.7         | 8.0         | 12.0        | 23.7         | 15.0             | 38.7           |                  |
| <b>Total contributions</b>      | <b>27.2</b> | <b>57.5</b> | <b>70.0</b> | <b>80.5</b> | <b>235.2</b> | <b>61.5</b>      | <b>296.7</b>   |                  |

<sup>1)</sup> Contribution SUC/ETH Board (cut 2011: SUC 3,758%, ETH Board 2,5%)

<sup>2)</sup> The SystemsX.ch BoD decided on July 6, 2007 to treat contributions "in kind" and "in cash" equally

<sup>3)</sup> 3rd Party Funds from private sector (industry, SMEs, private foundations, etc)

<sup>4)</sup> 2nd Party Funds from competitive research foundations

\*) 2008-2010 Actual, 2011 cut Actual, 2012 Debit

## 5.1 Financial plan 2008-2016

The SystemsX.ch initiative was granted about CHF 220 Mio for the period 2008-2016. Every year, SystemsX.ch received a certain allocation of Federal funds in order to fund projects and the administrative cost of the initiative. SystemsX.ch is financed through the two channels, the ETH-Domain and SUC by 50% each. The annual tranches are sent via the SNSF to SystemsX.ch. The initial financial planning for the period 2008-2011 was revised, adapted (e.g. Federal payment 2011 was cut by 2,5%), extended for 2012 and renewed for a second (and last) phase 2013-2016.

**Table 6** shows the adapted overall finances, budgeted for 2008-2011, for 2012, and for 2013-2016. Please note that the activities are in fact running from 2008 to 2018 with funds that are paid from 2008 to 2016. Although this was anticipated during the planning, it makes the display of the respective numbers difficult.

## 5.2 Financial report 2008-2014

### SystemsX.ch Funding Income

**Table 7** shows all the federal payments made to and from the SystemsX.ch open accounts in 2014 and summarized over the calendar years 2008 to 2014, including interest. The payments to SystemsX.ch were made by the SUC and ETH-Board via SNSF. As of December 2014, the SystemsX.ch open accounts show a cumulated surplus in the amount of CHF 28.5 million.

**Table 7.** Overview of the income (from SNSF originally from ETH Rat and SUK), payments (to SystemsX.ch partner institutions) and interest on the open accounts.

| Year 2014             | SystemsX.ch |                | 01.01.2008 -<br>31.12.2014 | SystemsX.ch  |               |
|-----------------------|-------------|----------------|----------------------------|--------------|---------------|
|                       | Payments    | yearly balance |                            | Payments     | Total balance |
| Total Open accounts   |             |                |                            |              |               |
| SNSF payments SUK     | 12'000'000  | 12'000'000     | SNSF payments SUK          | 83'786'300   | 83'786'300    |
| SNSF payments ETH-Rat | 12'500'000  | 24'500'000     | SNSF payments ETH-Rat      | 84'937'500   | 168'723'800   |
| Open account interest | 54'130      | 24'554'130     | Open account interest      | 486'258      | 169'210'058   |
| Total payments        | -22'737'793 | 1'816'337      | Total payments             | -140'754'601 | 28'455'457    |
| Total                 |             | 1'816'337      | Total                      | 28'455'457   | 28'455'457    |

### Approved project funds, payments

SNSF decisions, allocations by the MO and payments for 2014 and summarized over the calendar year 2008-2014 are given in Table X4. In 2014, a total of CHF 22.7 million was paid from SystemsX.ch to the partner institutions (including MO and SNSF). Up to December 2014, the SNSF decided on a total amount of CHF 187.8 million, which adds up to CHF 198.3 million, including decisions made by the SEB (2008-2014). Please note that (a) IPhDs are approved for three years with the option for a fourth year (decision by SystemsX.ch), (b) TPdFs are approved for two years with the option for a third year (decision by SystemsX.ch) and (c) High-Tech Funds for RTDs were approved similarly by the SEB. These three categories are not reflected in **Table 8**.

**Table 8.** SNSF-decisions and allocations per project type

| Year 2014    | SystemsX.ch       |                   | 01.01.2008 -<br>31.12.2014 | SystemsX.ch        |                    |
|--------------|-------------------|-------------------|----------------------------|--------------------|--------------------|
|              | SNSF decisions    | Payments          |                            | SNSF decisions     | Payments           |
| Management   |                   | 84'271            | Management                 | -                  | 2'943'271          |
| Events (all) |                   | 288'798           | Events (all)               | -                  | 1'177'705          |
| SNSF fee     |                   | 200'000           | SNSF fee                   | -                  | 1'396'400          |
| RTD          | 2'239'175         | 15'024'245        | RTD                        | 132'426'309        | 98'387'377         |
| RTD-HT       | -                 | -                 | RTD-HT                     | -                  | 1'440'087          |
| SIP          | 1'480'000         | 1'565'000         | SIP                        | 15'024'000         | 13'269'500         |
| IPhD         | 3'277'549         | 2'274'178         | IPhD                       | 13'911'126         | 11'364'099         |
| IPP          | -                 | -27'817           | IPP                        | -                  | 3'455'728          |
| BIP          | -                 | -                 | BIP                        | -                  | 1'865'904          |
| TPdF         | 1'549'916         | 1'845'342         | TPdF                       | 5'134'400          | 2'847'873          |
| SpecOp       | -                 | 625'000           | SpecOp                     | -                  | 1'338'655          |
| TF           | 600'000           | 671'146           | TF                         | 2'097'716          | 1'080'373          |
| IntAct       | 659'322           | 187'629           | IntAct                     | 659'322            | 187'629            |
| MRD          | 18'587'697        | -                 | MRD                        | 18'587'697         | -                  |
| <i>Total</i> | <i>28'393'659</i> | <i>22'737'793</i> | <i>Total</i>               | <i>187'840'570</i> | <i>140'754'601</i> |

All the budgeted and expended funds for 2014 are given in **Table 9** according to project type, including the MO and the SNSF service fee each as a separate item. The amounts budgeted and reported in 2014 (see in the tables column “Budget” “Reported” and “Delta %”) differ by an under expenditure of -7%. Overall, the initiative has a significant surplus of 13%. The Own Contributions are highest for the RTD Projects since the partners are required to make them available. OCs of the MO are in the form of annual fees from the partner institutions.

In 2014, SystemsX.ch released a total of CHF 22.2 million for the project types RTD, SIP, IPhD, TPdF, SpecOpp, TF and IntAct and CHF 573'069 for the Management Office (MO), the Swiss National Science Foundation and Events. The total released amount was CHF 22.7 million. On the other hand, the overall amount of reported SystemsX.ch Funds was CHF 21.4 million. At the end of 2014 there was a balance of CHF 38.1 million.

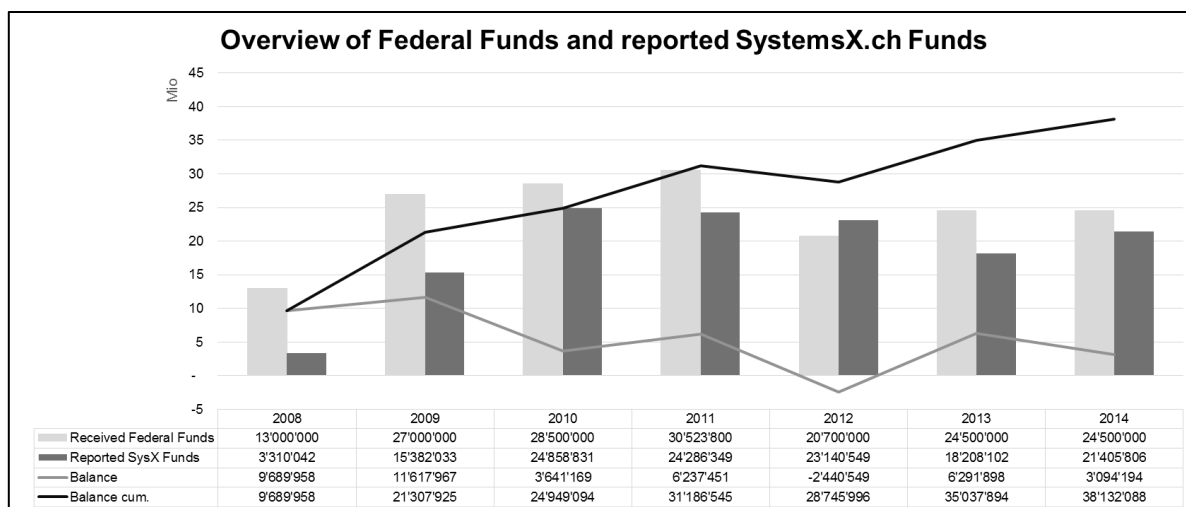
### Report of used resources

Comparing the cash flow (annual balance) of the Federal Funds to the reported use of funds from projects (all expenditures), one notices that as of yet, 2012 was the only year in which more spending was reported than SystemsX.ch received from the SNSF (see **Figure 4**). From 2008-2014 SystemsX.ch received a total of CHF 168.7 million in Federal Funds, whereas within the same time frame, a total amount of CHF 130.6 million SystemsX.ch Funds were used and reported.

**Table 9.** Funding categories per project type (incl. Management, Events, SNSF)

| Year 2014    | SystemsX.ch       |                   | Own Contribution  | Third P          | Total             |
|--------------|-------------------|-------------------|-------------------|------------------|-------------------|
|              | Budget            | Reported          | Reported          | Reported         | Reported          |
| Management   | 650'000           | 539'118           | 389'033           | -                | 928'151           |
| Events (all) | 107'052           | 105'618           | 41'278            | 91'772           | 238'668           |
| SNSF fee     | 200'000           | 200'000           | -                 | -                | 200'000           |
| RTD          | 13'349'288        | 13'828'700        | 18'534'132        | 801'516          | 33'164'348        |
| RTD-HT       | -                 | 58'620            | -                 | -                | 58'620            |
| SIP          | 1'805'000         | 1'387'084         | 792'158           | -                | 2'179'242         |
| IPhD         | 2'722'732         | 1'979'738         | 2'058'326         | -                | 4'038'064         |
| IPP          | -                 | 178'142           | 87'890            | -                | 266'032           |
| BIP          | -                 | -                 | -                 | -                | -                 |
| TF           | 697'039           | 710'155           | 360'516           | 746'805          | 1'817'476         |
| TPdF         | 2'227'335         | 1'590'685         | 1'068'656         | -                | 2'659'341         |
| SpecOpp      | 240'000           | 750'447           | 560'910           | -                | 1'311'357         |
| IntAct       | 938'099           | 77'499            | 89'700            | -                | 167'199           |
| <b>Total</b> | <b>22'936'544</b> | <b>21'405'806</b> | <b>23'982'599</b> | <b>1'640'093</b> | <b>47'028'498</b> |

| 01.01.2008 -<br>31.12.2014 | SystemsX.ch        |                    | Own Contribution   | Third P           | Total              |
|----------------------------|--------------------|--------------------|--------------------|-------------------|--------------------|
|                            | Budget             | Reported           | Reported           | Reported          | Reported           |
| Management                 | 5'036'000          | 3'287'207          | 2'275'209          | -                 | 5'562'416          |
| Events (all)               | 1'157'503          | 956'437            | 41'278             | 159'286           | 1'157'001          |
| SNSF fee                   | 1'401'000          | 1'396'400          | -                  | -                 | 1'396'400          |
| RTD                        | 99'284'615         | 90'719'498         | 138'086'927        | 10'028'266        | 238'834'691        |
| RTD-HT                     | 6'000'000          | 1'352'187          | 420'431            | -                 | 1'772'618          |
| SIP                        | 13'304'000         | 13'495'666         | 4'456'843          | 60'615            | 18'013'124         |
| IPhD                       | 11'128'208         | 9'970'559          | 10'330'576         | -                 | 20'301'135         |
| IPP                        | 3'499'178          | 3'571'404          | 2'323'848          | 38'500            | 5'933'752          |
| BIP                        | 1'961'242          | 1'847'928          | 1'373'752          | 1'119'355         | 4'341'035          |
| TF                         | 1'281'762          | 908'513            | 484'106            | 892'943           | 2'285'562          |
| TPdF                       | 4'322'140          | 2'076'195          | 1'374'330          | -                 | 3'450'525          |
| SpecOpp                    | 1'412'800          | 932'221            | 584'871            | -                 | 1'517'092          |
| IntAct                     | 938'099            | 77'499             | 89'700             | -                 | 167'199            |
| <b>Total</b>               | <b>150'726'546</b> | <b>130'591'712</b> | <b>161'841'871</b> | <b>12'298'965</b> | <b>304'732'548</b> |



**Figure 4.** Overview of Federal Funds and reported SystemsX.ch Funds in CHF.



Over the seven years from 2008-2014, about CHF 92.0 million in SystemsX.ch Funds was used and reported by the 34 RTD Projects, CHF 13.5 million by SyBIT, and CHF 10.0 million by 77 IPhD Projects. For the Management Office, including Events, CHF 2.3 million was used. All other project types reported CHF 9.4 million (see **Table 10**).

All Own Contributions amount to CHF 161.8 million. The SystemsX.ch community reported the acquisition of more than CHF 16.4 million in 3<sup>rd</sup> Party Funds, and CHF 30.0 million in competitive research grants with a synergy and/or collateral benefit (2<sup>nd</sup> Party Funds) for SystemsX.ch.

**Table 10.** Reported use of SystemsX.ch Funds and Own Contributions in CHF for 2008-2014 (a) per project type, and (b) per cost type.

a)

| <i>Project Type</i>       | <i>Reported SystemsX.ch Funds</i> | <i>Reported Own Contributions</i> |
|---------------------------|-----------------------------------|-----------------------------------|
| MO                        | 3'287'207                         | 2'275'209                         |
| Events                    | 956'437                           | 41'278                            |
| SNSF review & admin costs | 1'396'400                         | -                                 |
| RTD                       | 90'719'498                        | 138'086'927                       |
| RTD-HT                    | 1'352'187                         | 420'431                           |
| SIP                       | 13'495'666                        | 4'456'843                         |
| IPhD                      | 9'970'559                         | 10'330'576                        |
| IPP                       | 3'571'404                         | 2'323'848                         |
| BIP                       | 1'847'928                         | 1'373'752                         |
| TF                        | 908'513                           | 484'106                           |
| TPdF                      | 2'076'195                         | 1'374'330                         |
| SpecOpp                   | 932'221                           | 584'871                           |
| IntAct                    | 77'499                            | 89'700                            |
| <b>Total</b>              | <b>130'591'712</b>                | <b>161'841'871</b>                |

b)

| <i>Cost Type</i> | <i>Reported SystemsX.ch Funds</i> | <i>Reported Own Contributions</i> |
|------------------|-----------------------------------|-----------------------------------|
| Personnel        | 94'386'725                        | 117'174'801                       |
| Consumables      | 19'455'192                        | 9'843'050                         |
| Miscellaneous    | 6'689'024                         | 4'116'653                         |
| Equipment        | 9'529'125                         | 19'122'797                        |
| Infrastructure   | -                                 | 11'488'449                        |
| Various          | 531'647                           | 96'121                            |
| <b>Total</b>     | <b>130'591'712</b>                | <b>161'841'871</b>                |

The SystemsX.ch Funds allocated and released to each partner institution are shown in **Table 11**. Please note that selection criteria for SystemsX.ch proposals are “scientific quality” and “added value to Systems Biology”. **Table 11** shows how the CHF 140.8 million paid out are distributed to the SystemsX.ch partner institutions. By December 31, 2014, CHF 130.6 million of SystemsX.ch Funds and CHF 161.8 million of Own Contributions were used and reported.

**Table 11.** allocations and payments of SystemsX.ch Funds and reported Own Contributions per SystemsX.ch partner 2008-2014.

| 01.01.2008 -<br>31.12.2014 | SystemsX.ch        |                    | 01.01.2008 -<br>31.12.2014 | Own Contribution   |                    |
|----------------------------|--------------------|--------------------|----------------------------|--------------------|--------------------|
|                            | MO act. allocation | Payments           |                            | Allocation         | Total Actual       |
| Management                 | 2'944'000          | 2'943'271          | Management                 | 1'870'000          | 2'275'209          |
| Events (all)               | 533'088            | 963'463            | Events (all)               | -                  | 41'278             |
| SNSF fee                   | -                  | 1'396'400          | SNSF free                  | -                  | -                  |
| EPFL                       | 27'596'550         | 20'541'273         | EPFL                       | 22'693'160         | 20'131'237         |
| ETHZ                       | 61'910'368         | 44'021'123         | ETHZ                       | 52'850'799         | 44'449'205         |
| FMI                        | 3'706'657          | 3'094'388          | FMI                        | 4'176'370          | 4'133'713          |
| PSI                        | 791'925            | 512'503            | PSI                        | 833'000            | 581'343            |
| SIB                        | 7'026'766          | 6'359'033          | SIB                        | 3'812'700          | 4'845'264          |
| UniBE                      | 8'818'215          | 5'823'699          | UniBE                      | 10'304'995         | 6'033'283          |
| UniBS                      | 26'556'870         | 18'634'386         | UniBS                      | 29'251'898         | 28'276'697         |
| UniFR                      | 2'512'761          | 1'712'098          | UniFR                      | 2'692'729          | 2'357'175          |
| UniGE                      | 16'090'681         | 9'414'555          | UniGE                      | 19'820'727         | 13'960'185         |
| UniL                       | 11'208'038         | 7'219'415          | UniL                       | 11'672'584         | 9'083'025          |
| UniNE                      | 158'905            | 172'767            | UniNE                      | 100'000            | 301'876            |
| USI                        | 595'447            | 65'507             | USI                        | -                  | 47'842             |
| UZH                        | 26'891'995         | 17'796'387         | UZH                        | 29'225'036         | 25'285'039         |
| ZHAW                       | 531'703            | -                  | ZHAW                       | 517'000            | -                  |
| others                     | 425'800            | 84'333             | others                     | 464'450            | 39'500             |
| RTD-HT undefined           | -                  | -                  | RTD-HT undefined           | -                  | -                  |
| <b>Total</b>               | <b>198'299'769</b> | <b>140'754'601</b> | <b>Total</b>               | <b>190'285'448</b> | <b>161'841'871</b> |

The setting up of a complex organization like SystemsX.ch is challenging. Since 2010, the initiative has been audited, also to assess its "Good Governance". In general, this means to apply best practices, e.g. that procedures and roles are transparent, that checks and balances are established, and that areas of potential high risk are known and managed adequately.

## Abbreviations

|         |  |
|---------|--|
| BIP     | Bridge to Industry Project   |
| BMBF    | German Ministry for Education and Research (Bundesministerium für Bildung und Forschung)           |
| BoD     | Board of Directors (all Presidents and Rectors of SystemsX.ch partner institutions)                |
| DKFZ    | Deutsches Krebsforschungszentrum (German Cancer Research Center)                                   |
| E(A)B   | SystemsX.ch Education (Advisory) Board   |
| EiR     | Entrepreneur in Residence  |
| ESF     | European Science Foundation  |
| EU      | European Union   |
| FEBS    | Federation of European Biochemical Societies   |
| HTF     | High Technology Service Funds  |
| IPhD    | Interdisciplinary PhD Project  |
| IPP     | Interdisciplinary (high risk and seed) Pilot Project   |
| ISA     | Industrial Sabbatical in Academia  |
| KNIME   | Konstanz Information Miner   |
| MO      | SystemsX.ch Management Office  |
| MRD     | Medical Research and Development Project   |
| PI      | Principal Investigator   |
| RTD     | Research, Technology and Development Project   |
| SBFI    | Staatssekretariat für Bildung, Forschung und Innovation  |
| SEB     | Scientific Executive Board (Scientists of different Systems Biology fields & partner institutions) |
| SERI    | State Secretariat on Education, Research and Innovation (german: SBFI)                             |
| SNSF    | Swiss National Science Foundation  |
| SpecOpp | Special Opportunity Funds  |
| SUC     | Swiss University Conference  |
| SyBIT   | SystemsX.ch Initiated Project: IT-support for RTDs   |
| TF      | Transfer Project   |
| TPdF    | Transition Postdoc Fellowship  |