



**SystemsX.ch**

The Swiss Initiative in Systems Biology

## **SystemsX.ch Scientific Report 2016-2017**

Submitted according to the administration contract of December 2013 between  
SystemsX.ch  
and  
the Swiss National Science Foundation (SNSF)

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15 September 2017, Zurich



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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 advances systems biology in Switzerland by (i) supporting academic research projects, (ii) educating the next generation of systems biology scientists, (iii) supporting private-public sector partnerships, and through (iv) international outreach: participating in international systems biology programs and becoming a worldwide acknowledged gravity center in systems biology research. SystemsX.ch now consists of fifteen partner institutions across Switzerland.

The initiative is now in its 10<sup>th</sup> year. The first phase, the so-called initiation phase, lasted from 2008 to 2012. All projects approved during this period have been completed. The various procedures of SystemsX.ch are well established. The last calls for proposals were published in 2015: after the decisions on these calls were issued, the initiative entered its ramping-down phase. The main activities in the reporting year were the self-evaluation of the impact analysis of the initiative, mandated by the State Secretariat of Education, Research and Innovation (SERI); the production of a documentary film about the initiative; the organization of the 3<sup>rd</sup> and final International SystemsX.ch Conference on Systems Biology; the mid-term review of MRD Projects by the Review Panel of the SNSF; the support of running projects, and the (co-)organization of several training activities.

Until August 2017, a total of 249 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. All SystemsX.ch funds for research projects were allocated per end of 2015, with only minor adjustments (due to changes in salaries or social charges, or to possible budget cuts) foreseen for 2018.

The self-evaluation carried out by SystemsX.ch in the frame of the impact analysis mandated by the SERI has clearly illustrated the impact that the initiative has had in the life sciences research landscape in Switzerland. Moreover, this analysis has allowed the quantification of a number of indicators that show that the programs implemented since 2007 by SystemsX.ch are effective towards reaching the original goals:

- a) about 54% of the principal and co-principal investigators (PIs and co-PIs) leading SystemsX.ch-approved projects are not biologists, attesting to the high level of interdisciplinarity that has been achieved;
- b) a bibliometric analysis of the more than 1'400 papers published within the frame of the initiative was performed as part of the self-evaluation of SystemsX.ch: this analysis revealed the very high impact of SystemsX.ch publications, also in an international comparison;
- c) the PhD students and postdocs supported by IPhD or TPdF projects, but also those working on RTD or MRD Projects, benefit from retreats, workshops, courses and other activities. SystemsX.ch PhD students generally find, after completion of their PhD thesis, attractive positions at renowned institutions in both academia and the private sector;
- d) the Special Opportunities projects and previously the BIP projects have forged new interactions between the private and public sector. TF projects solidified these contacts and formed the foundation for even more intensive collaborations in the future;
- e) more than 100 new interactions have appeared between research groups that did not collaborate prior to SystemsX.ch;
- f) the partner institutions have undertaken measures to ensure the sustainability of the initiative after 2018;

- g) almost 30 assistant professors and postdocs from RTDs, as well as TPdFs, have attained professorships at renowned institutions;
- h) SystemsX.ch was a partner in ERASysAPP and has co-organized and supported a wide range of international systems biology events for research and educational purposes, indicating that the initiative became well connected and recognized internationally; and
- i) the continued support of certain international conferences attests to the international visibility of the initiative.

Last but not least, SystemsX.ch has produced a film and an interactive touchbook aimed at the general public. These communication measures help bringing research in life sciences closer to the public, with a particular emphasis on explaining what systems biology is, how quantitative research has brought about a paradigm shift in biology, and how SystemsX.ch has contributed to the establishment of these new research approaches. The film and touchbook, which were launched in September 2017, also provide transparency about the use of federal funds for life sciences research.

## **1 Status report: Activities of SystemsX.ch from September 2016 to August 2017**

This reporting period has been the fourth to fall completely within the second phase of SystemsX.ch. The last project from the first phase, an IPhD Project, was completed in June 2016, so this was the first reporting period during which only projects from the second phase were active.

In this reporting period 20 RTD Projects (plus SyBIT) have been active. The 11 RTDs approved after the 6<sup>th</sup> call for proposals started in the first half of 2013, and the nine RTDs approved in 2013 after the 8<sup>th</sup> call started between January and May 2014.

All nine MRD (Medical Research and Development) projects that were approved in 2014, following the 10<sup>th</sup> call for proposals, have been active in the 2016-2017 reporting period. In January 2017 the SNSF Review Panel convened for the mid-term review of the MRD Projects.

Three Transfer Projects (TFs) have been active in this reporting period, two of them reaching completion. This project type was introduced with the 6<sup>th</sup> call for proposals, in 2012, in order to further stimulate the interaction with the private sector.

All nine Special Opportunities projects that were approved after the 12<sup>th</sup> call for proposals have been active in this reporting period. The SEB approved these projects out of the 51 proposals submitted to the 12<sup>th</sup> call in May 2015, five of them with full and four of them with partial funding.

In this reporting period, 25 TPdF projects have been active. All but one of the postdocs who were granted their fellowships in 2013 (7<sup>th</sup> Call for Proposals) completed their 3<sup>rd</sup> year during this reporting period, as did two of the TPdFs awarded in 2014 (9<sup>th</sup> call for proposals). Seven of the eight TPdF projects approved by the SEB and the SNSF after the 11<sup>th</sup> call for proposals (April 2015) were active during the current reporting period, the remaining postdoc will start his fellowship in January 2018 and will only receive one year of funding.

41 IPhD projects have been active in this reporting period. All IPhDs granted in 2008, 2009 and 2010 were completed before this reporting period. The seven projects granted in 2012 that were still running were completed before July 2016, as was one of the nine projects granted in 2013. 16 out of the 17 IPhDs granted in 2014 were active in 2016/2017. Ten IPhD projects were approved by the SEB and SNSF out of the 25 proposals submitted to the 11<sup>th</sup> call for proposals (April 2015). All of them were active during the current reporting period.

Beyond research projects, SystemsX.ch accomplished several different activities between September 2016 and August 2017: the organization of the 7<sup>th</sup> and final All SystemsX.ch Day in Bern in 2016, the production of a film and an interactive app about systems biology research, the elaboration of a self-evaluation report mandated by the SERI within the frame of the impact analysis of the initiative, and the organization of the 3<sup>rd</sup> International SystemsX.ch Conference on Systems Biology, conceived as the closing event of the initiative. Moreover, the SEB and the PIs of SystemsX.ch projects agreed to create the Swiss Society of Systems Biology, which will offer the community that has been established through the initiative the possibility to maintain its strong bonds.

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 focuses on are: (i) Excellent science, (ii) Support of education and training, (iii) Fostering ways to promote public-private partnership, and (iv) International outreach, visibility and recognition. This last point has gained significance towards the end of the initiative because international networking contributes 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 629 submitted proposals a total of 249 projects have been approved by the SNSF and/or the SEB, involving 401 research groups, some participating in two or more projects, and engaging every year about 1'000 scientists. The largest proportion of funding (77%) went to the 34 RTDs (including High-Tech Funds, HTF, in the first phase) plus SyBIT, and to the nine MRD Projects. The contact with the private sector has been proactively encouraged, and the eight TF Projects from the 6<sup>th</sup>, 8<sup>th</sup> and 10<sup>th</sup> calls show that these interactions have indeed been strengthened. This encouragement continues through the Special Opportunities Projects approved after the 12<sup>th</sup> call, one of which includes a private partner. Through 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 to 4 years (with the exception of two projects which were approved for only one year, as an extension of previous funding from different sources).

#### **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, 2012 and 2013 underwent mid-term reviews by the SNSF review panel in October 2010, 2011, 2014 and November 2015, respectively. The eleven 2012 and nine 2013 RTDs continued their activities in this reporting period, five of them reaching completion. The scientific reports of RTDs can be found in Appendix B.

#### **1.1.1.2 MRD Projects**

In the 10<sup>th</sup> call for proposals, SystemsX.ch invited 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. Out of the 30 proposals that were received, nine were approved by the SEB and the SNSF review panel. All nine MRD Projects started between January and July 2015, and have been active within this reporting period. They all underwent a mid-term review by the Review Panel of the SNSF in January 2017. Details about these projects can be found in Table A8 in Appendix A. Their scientific reports can be found in Appendix B.

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

In March 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.

Seven Special Opportunities proposals were approved by the SEB between October 2011 and December 2014. The proposals could be submitted at any time, and underwent a thorough but fast review period by the SEB and optionally also external reviewers.

The SEB decided to publish a final 12<sup>th</sup> call for proposals for Special Opportunities in 2015. The main reasons were to increase the visibility of this project type, and to ensure the availability of funds not used up by TF Projects, as the number of TF proposals received were always relatively low. The call aimed to promote relatively short (one- to two-year duration) and especially innovative, high-risk, high-gain projects, including the establishment of novel technologies, prototypes or software. Participation of private partners was encouraged. Out of the 51 submitted proposals, nine projects were approved (five with full and four with partial funding), and all of them started between September 2015 and January 2016. More details about approved Special Opportunities projects can be found in Appendix A, Table A18. The scientific reports of Special Opportunities projects can be found in Appendix B.

#### **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 PIs is at least two (one academic, one private). These projects are awarded for two years. With the 6<sup>th</sup> call for proposals, the first four TFs were approved by SEB and SNSF in December 2012. All of them, plus two TFs approved in 2013, came to an end before this reporting period. The remaining TF approved in 2013 as well as the two TFs granted in 2014 after the 10<sup>th</sup> call for proposals were completed between October 2016 and May 2017 (see Appendix A, Table A9 and A10). Therefore, all TFs funded by SystemsX.ch have now been completed. The scientific reports of the three final TFs can be found in Appendix B.

#### **1.1.1.5 Transition Postdoc Fellowships (TPdF)**

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 opened 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, 31 fellowships were granted. The number of submissions increased from 17 in the 5<sup>th</sup> call 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 to 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 A11-A13. The scientific reports of TPdFs can be found in Appendix B.

25 TPdF projects were active during this reporting period. The last remaining postdoc received also another competitive fellowship, and decided to postpone the start of his TPdF until January 2018. This project will therefore only receive funding for one year.

All SystemsX.ch funds for research projects had to be allocated by December 2015. Therefore, running TPdF projects were invited to submit applications for a 3<sup>rd</sup> year extension in October 2015. 13 applications were received, and 12 were granted.

#### **1.1.1.6 IPhD Projects**

The SEB and the SNSF approved a total of 87 IPhD Projects between 2008 and 2015. Out of them, 41 were running in this reporting period (one of them was completed in September 2016 and had submitted its final report in 2016. The IPhD students defended his thesis successfully in Autumn 2016). The annual reports of IPhD Projects can be found in Appendix B. The list of 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 A14-A17.

41 IPhD projects have been active in this reporting period. All IPhDs granted in 2008, 2009 and 2010 were completed before this reporting period. The seven projects granted in 2012 that were still running were completed before July 2016, as was one of the nine projects granted in 2013. 16 out of the 17 IPhDs granted in 2014 were active in 2016/2017. Ten IPhD projects were approved by the SEB and SNSF out of the 25 proposals submitted to the 11<sup>th</sup> call for proposals (April 2015). All of them were active during the current reporting period.

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

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

The IPPs were established to facilitate the start for scientists 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 Postdoc Fellowships (TPdF) that was launched in spring 2012 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 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**

All calls for proposals within the SystemsX.ch initiative were closed before this reporting period. In the 12<sup>th</sup> and final 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.

In October 2015, PIs of TPdF and IPhD Projects were invited to submit requests for a 3<sup>rd</sup> or 4<sup>th</sup> year extension. 37 of the 38 received requests were granted.

After the resolutions of the 11<sup>th</sup> and 12<sup>th</sup> calls, and the decisions on TPdF and IPhD Project extensions, all SystemsX.ch funds for research projects were allocated by the end of 2015. Until the end of 2018, only minor adjustments may be made, due to budget cuts, changes in salaries or social charges, or similar circumstances.

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

Several events have been (co-)organized and/or supported by SystemsX.ch in this reporting period. Furthermore, SystemsX.ch awarded travel grants for young scientists to certain conferences, enabling PhD students and postdocs from the SystemsX.ch community to attend those events. Table A48 in 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).

## **1.1.2 Education**

Educating the next generation of systems biologists is of central importance to SystemsX.ch. During the reporting year, 225 PhD students have worked on SystemsX.ch projects (about 184 on RTDs, MRDs, TFs and Special Opportunities projects and 41 on IPhD projects).

Furthermore, 25 postdocs funded through the TPdF program, and 190 postdocs funded through RTDs, MRDs, TFs and Special Opportunities worked on SystemsX.ch projects during this reporting period.

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 A48, 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. In 2010 it was renamed as Education Advisory Board, as most executive tasks were undertaken by the SEB or the Management Office (MO). 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. Since 2014, Uwe Sauer is the chair of the EAB. Tables with the members of the Education Board and respective meetings can be found in the Appendix A, Tables A42 and A43.

### **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. Both PhD projects were completed during this reporting period.

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

The annual SystemsX.ch Retreat is organized yearly since 2009, and 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 improve their transferable skills and become aware of the skills they already have. The event further provides an opportunity to become familiar with the diverse PhD projects supported by SystemsX.ch. This not only allows the students to broaden their understanding of scientific research in systems biology, but is also an opportunity for them to network: they can 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 held in May 2017 in Kandersteg was similar to those of the previous years, yet with a different topic: presentation skills for scientists. 18 PhD students and 4 postdocs attended this retreat. The aim of the retreat was to give participants tools to improve the preparation and delivery of their scientific presentations, while proactively addressing individual difficulties. It remains to be decided whether it will be the last SystemsX.ch retreat, or whether there will be another one in 2018.

#### **1.1.2.4 Postdoc Workshop**

SystemsX.ch organized a Leadership and Management Skills workshop exclusively for postdocs in November 2016 for the third time. 15 participants attended the two-day course, which took place in Muri bei Bern. The course addressed the human aspects of doing science and having a leader role, 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. As with the first edition of the workshop, a one-day follow-up course of the workshop organized in February 2016 was carried out in November 2016. The two first editions of the postdoc workshop, including their follow-ups, have received very positive feedback from the participants.

#### **1.1.2.5 SystemsX.ch/SIB Machine Learning course**

Since 2010, SystemsX.ch has co-organized several training activities with the SIB Swiss Institute of Bioinformatics. In the current reporting period, both organizations joined forces with the Next-Generation Sequencing Discussion Group of the University of Zurich, a group of PhD students and postdocs, to organize a one-week course in Machine Learning for Bioinformatics and Computational Biology. From November 21-25, 2016, 36 young scientists got together in Zurich to follow an introductory course with a large hands-on component. The course started with two days of general introduction to machine learning concepts and approaches, including practical exercises. The three final days were each dedicated to a single topic, illustrating different applications of machine learning in diverse domains. The course generated a remarkable interest: it was booked out very fast, and had a long waiting list. Based on the clear demand, SystemsX.ch and the SIB are currently organizing an Autumn School on Machine Learning applied to Systems Biology, which will take place in November 2017.

#### **1.1.2.6 7<sup>th</sup> All SystemsX.ch Day**

On September 1, 2016, the SystemsX.ch community gathered at the Zentrum Paul Klee in Bern for the 7<sup>th</sup> All SystemsX.ch Day. Around 200 researchers from all over Switzerland took part to present and discuss their projects, and get to know the work of others. The event focused on interdisciplinary research, including talks from young, upcoming researchers as well as experienced scientists. The talks showcased the breadth of SystemsX.ch research, and offered insight into a number of diverse projects. The diversity of topics was also evident in the nearly 90 posters presented at the event. For the first time at a SystemsX.ch event, lightning poster talks were also offered. Here, young researchers were given the chance to present their projects on stage. They each had only 90 seconds and a single slide with which to convince the audience to visit their posters. The aim was to explain the main points of their project simply, clearly and understandably in this short time; a great challenge, given the complexity of the projects.

The keynote speaker, Jan Ellenberg from the EMBL Heidelberg, presented a beautiful example of interdisciplinary systems biology research. In his talk, Ellenberg highlighted recent technological advances in the systems biology analysis of cell division. This process, along with all of the involved proteins, can now be observed and recorded with the help of new technologies in light microscopy.

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

### 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 and MRDs within SystemsX.ch report numerous collaborations, links and interactions with the private sector (see Table A28 and A29 in Appendix A). Several spin-offs were, at least partly, generated out of existing RTD and IPhD Projects:

- Biognosys (PhosphoNetX)
- ProteoMedix (PhosphoNetX)
- Microduits GmbH (CINA)
- Genohm SA (CycliX)
- BioDataAnalysis GmbH (TargetInfectX) (former TargetInfectX postdoc Mario Emmenlauer founded the company, which offers a software, screeningBee, as well as services for Automated High Content Screening data analysis)
- MaxWell Biosystems (IPhD Michele Fiscella, D-BSSE ETHZ and FMI)
- Lunaphore (IPhD Ata Tuna Ciftlik, EPFL). A side project to further develop and improve the chip was supported by SystemsX.ch via Special Opportunity Funds between April 2014 and March 2015.

Further information about various forms of public-private partnerships can be found for each project types in the Appendix B. The interactions with private partners are summarized in Tables A28-A31 in Appendix A.

### 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.

Within this reporting period, SystemsX.ch organized its 3<sup>rd</sup> International SystemsX.ch Conference on Systems Biology from September 4-7, 2017 in Zurich. Approximately 240 participants attended the event, including many scientists from outside Switzerland, and almost 150 posters were presented. The conference was meant as a closing event for the initiative, and was inaugurated by the Chairman of the Board of Directors (BoD), Detlef Günther, ETHZ Vicepresident for Research and Corporate Relations, who gave an overview of the achievements of the initiative since 2007. Among an exceptional line-up of international speakers, the highlights were the keynote lectures by James Ferrell (Stanford University) and Chris Sander (Dana-Farber Cancer Institute and Harvard Medical School).

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

Other important contributions to this visibility have been the participation in the ERA-Net ERASysApp (since 2013), or the support of international events and conferences. The following events have been repetitively supported:

- Bi-annual Advanced Lecture Course on Systems Biology in Innsbruck (2011, 2014, 2016)

- Joint SystemsX.ch/CRG Summer School in Barcelona (2013, 2014 and 2015)
- BC<sup>2</sup> Computational Biology Conference in Basel (biennially since 2008)
- Systems Biology of Human Diseases (SBHD) in Heidelberg / Boston (2012-2017)
- International Conference on Systems Biology in Barcelona (2016)

For most of these events, SystemsX.ch has been actively involved in the organization, besides sponsoring the conferences or courses and offering travel grants for young scientists of the SystemsX.ch network.

For all events and activities that have cemented SystemsX.ch's international visibility, please see Table D68 in Appendix D.

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

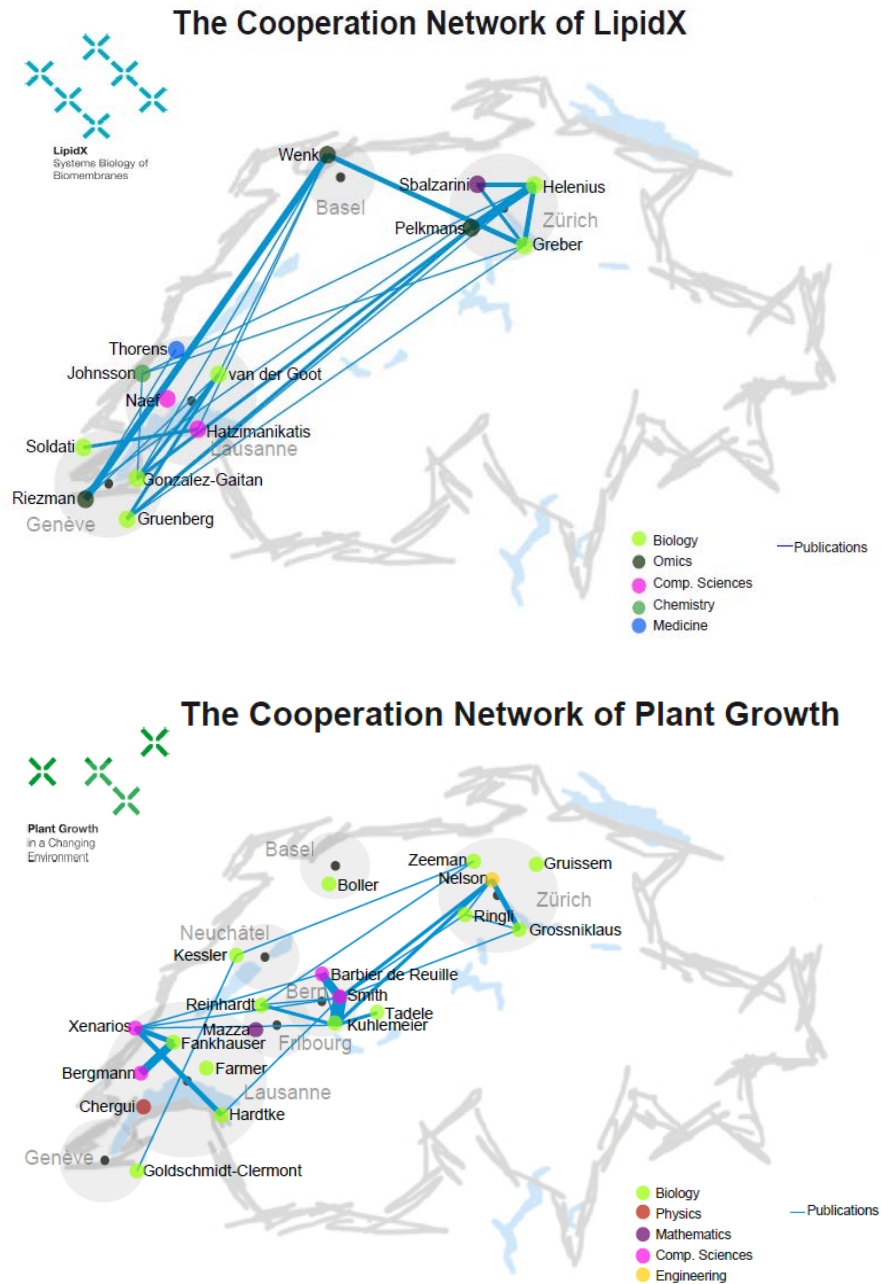
- The SystemsX.ch Management Office acts as the secretariat for the International Society for Systems Biology (ISSB).
- Several professors recently recruited by partner institutions testified that SystemsX.ch was an important factor for them to decide to come to a Switzerland.
- The success rate of Swiss 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 45 ERC Advanced Grants, 25 ERC Starting Grants, three ERC Consolidator Grant and one ERC Synergy Grant. Within this reporting period, the following SystemsX.ch researchers have received ERC grants:
  - ERC Advanced Grants: Susan Gasser (FMI), Laurent Keller (UniL), Mustafa Khammash (ETHZ), Cris Kuhlemeier (UniBE), Andrew Macpherson (UniBE), Ralph Müller (ETHZ), Bradley Nelson (ETHZ), Andreas Wagner (UZH), Renato Zenobi (ETHZ).
  - ERC Consolidator Grant: Michael Bronstein (USI), Beat Fierz (EPFL), Sebastian Maerkl (EPFL).
  - ERC Starter Grant: Prisca Liberali (FMI), Matthias Erb (UniBE), Mahmut Selman Sakar (EPFL), Bruno Correia (EPFL). It's particularly encouraging to note that the first three were originally postdocs within SystemsX.ch projects, which highlights the impact that the initiative has had in promoting the career of talented young scientists.

A full list of all SystemsX.ch researchers who have been awarded ERC grants since 2007 can be found in Appendix D, Table D39.

### 1.1.5 Scientific community

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

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 seven All SystemsX.ch Days and



**Figure 1.** RTD Projects generated networks between different Swiss institutions and beyond. Exemplarily different RTDs (LipidX and PlantGrowth) are shown, approved in 2009 by the SNSF. The figure shows the joint publications of different members of the consortia between 2008 and 2017.

the three International SystemsX.ch conferences (in Basel in 2011, in Lausanne in 2014, and in Zurich in 2017), but also the PI meetings which have been organized once a year. Other events, organized by the MO or by RTD-related groups contributed to this topic in a similar manner.

In this reporting period, the 3<sup>rd</sup> International SystemsX.ch Conference on Systems Biology, the 7<sup>th</sup> All SystemsX.ch Day in September 2016 in Bern, the Postdoc Workshop in November 2016, the SystemsX.ch Retreat 2017 and the joint Machine Learning course with the SIB in Schwarzenberg were the main events in terms of community building. The final annual PI meeting took place in Bern on May 29, 2017, enabling PIs of RTD, MRD and TF projects to meet and discuss scientific and administrative issues, as well as to network and interact with other SystemsX.ch members (see below).

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 MorphoGraphiX software, whose development was started under the first phase RTD Plant Growth, was further developed as a collaborative effort between PlantGrowth2, WingX, MorphogenetiX and SyBIT.

There are several examples of RTDs that collaborate closely: a textbook example is the collaboration between HostPathX, MetaNetX, TbX and SwissLipids sharing data and coordinating efforts on metabolism representation and modeling. Other collaborations between RTDs include:

- NeuroStemX, StoNets and MetastasiX: active cooperation on a single-cell genomics platform
- InfectX with BattleX
- PhosphoNetPPM with MetastasiX
- HostPathX with SignalX: following the establishment of a contact at a SystemsX.ch PI meeting, HostPathX invited two members of SignalX to their RTD meeting for an exchange of technical know-how
- SynaptiX with SysGenetiX: close collaboration regarding the technical aspects of low-input RNAseq protocols
- TbX consults with Marco Pagni (MetaNetX) regarding database management, particularly to align to the needs of genome scale metabolic modelling
- AntibodyX and TF 2014/280 “Harnessing the Immunome’s potential to fight cancer” (Alfred Zippelius, NBE Therapeutics)
- The RTDs TargetInfectX, TbX and BattleX organized together the 2<sup>nd</sup> edition of the Systems Biology of Infection symposium in Ascona in September 2015.

Furthermore, several IPhD students and TPdFs have collaborated on other SystemsX.ch projects. These interactions enable the young scientists to intensify their exposure to different scientific domains, as well as to expand their network, while the RTDs profit from the young researchers’ interdisciplinary training. Some examples of such collaborations are TPdFs Julien Limenitakis with GutX, Hartland Jackson with MetastasiX, Joachim Moser with EpiPhysiX, and IPhD students Sunil Kumar with MetastasiX or Tiziano Dallavilla with LipidX.

The EPFL spin-off company Lunaphore was started from the IPhD Project of Ata Tuna Ciftlik, with the aim of building tissue processing platforms to be used in breast cancer diagnostics. The company went on to collaborate with the uFluidiX TF (PI: Alex Soltermann, USZ, in collaboration with IBM Zurich Research Lab), in order to develop a microfluidic tissue processor for non-small cell lung carcinoma. This collaboration has further led to Soltermann becoming an member of the advisory board of Lunaphore. BioData Analysis GmbH, another spin-off company which stemmed from the InfectX RTD, continues to interact closely with the Target-InfectX RTD.

Additionally, the support of external events and SystemsX.ch internal, sometimes bilateral meetings, is a measure that increases the sense of community among SystemsX.ch researchers, besides enabling the initiative to run smoothly:

- After approval of new RTDs and MRDs, Daniel Vonder Mühl visited each PI and explained SystemsX.ch as a whole and the particular expectations for RTD and MRD projects. He was invited to kick-off meetings of the RTDs StoNets RTD (January 2014), TbX RTD (May 2014), HostPathX (February 2015), SynaptiX (March 2015), MecanX (May 2015) and MetastasiX (June 2015), in order to present the SystemsX.ch initiative to all consortium members of the respective RTDs/MRDs.
- Eavan Dorsey has visited all TPdFs whose fellowships were awarded since 2013 in order to inform them about SystemsX.ch activities and specificities.



- During this reporting period, SystemsX.ch supported the following events:
  - 4<sup>th</sup> Annual ETH Life Sciences Postdoc Day 2016, Sep 9, 2016 (Zurich)
  - International Conference on Systems Biology, September 16-20, 2016 (Barcelona)
  - Annual retreat of the Systems Biology PhD Program of the Life Science Zürich Graduate School, September 28-30, 2016 (Leissingen)
  - EPD 30<sup>th</sup> Anniversary Symposium, September 29-30, 2016 (Lausanne)
  - Physics of Biology 2, November 23-25, 2016 (Geneva)
  - SystemsX.ch/SIB Machine Learning Course, November 21-25, 2016 (Zurich)
  - Annual Retreat of the International PhD Program in Basic and Applied Molecular Life Sciences at UniGE, January 18-20, 2017 (Montreux)
  - LS2 Annual Meeting 2017, February 2-3, 2017 (Zurich)
  - 2<sup>nd</sup> Annual Swiss Proteomics Society Meeting, April 20-21, 2017 (Thun)
  - 1<sup>st</sup> HUPO-HIPP Workshop, May 4-5, 2017 (Zurich)
  - Systlms, May 14-17, 2017 (Ascona)
  - FMI-IGC joint grad student retreat, May 27-31, 2017 (Lisbon)
  - Basel Postdoc Network Retreat, June 21-23, 2017 (Zermatt)
  - SWATH Targeted Proteomics Course, June 26-30, 2017 (Zurich)
  - Systems Biology of Human Diseases, July 5-7, 2017 (Heidelberg)
  - Systems Biology of the Brain workshop, September 11-12, 2017 (Fribourg)
  - Shaping the Future of Bioengineering summer school, September 10-16 (Davos)
  - BC<sup>2</sup> 2017, September 12-15, 2017 (Basel)
  - Life Sciences Postdoc Day 2017, September 15, 2017 (Zurich)
  - Cell Dynamics in Plant Development and Evolution symposium, November 30-December 1, 2017 (Zurich)

Supporting these events increases visibility of the initiative amongst young researchers, making them also aware of funding possibilities within SystemsX.ch.

- SystemsX.ch has awarded four travel grants for young researchers of the initiative to attend the Systems Biology of Human Disease (SBHD) 2017 conference in Heidelberg.
- Several non-scientific measures have been implemented since 2008, among others in order to foster community building. These include diverse communication tools, such as the SystemsX.ch webpage, newsletters, the X-Letter magazine, and since August 2016 a SystemsX.ch Twitter account. Most importantly, In 2017 SystemsX.ch has produced a documentary film and an interactive touchbook about systems biology, which portray several projects funded by SystemsX.ch and illustrates the systems approach to biological research through these projects and interviews with Ruedi Aebersold and Lucas Pelkmans (former and current chairmen of the SEB) and Ralph Eichler (former chairman of the BoD). The film and touchbook were launched at the 3<sup>rd</sup> International Conference.

As the SystemsX.ch initiative is gradually coming to an end, the question arose of how to maintain the systems biology community bonds after 2018. To this end, SystemsX.ch has agreed on a collaboration with Life Sciences Switzerland (LS2): from 2018, the LS2 Annual Meetings will include a symposium on systems biology, sponsored by SystemsX.ch. Chairs of the symposium are Lucas Pelkmans (UZH) and Bart Deplancke (EPFL), both members of the SystemsX.ch SEB. These symposia will be organized by the newly created Swiss Society of Systems Biology, a section of LS2, which will be active from November 2017. SystemsX.ch scientists will be encouraged to join the society and use these symposia as a meeting point for the community. Several communication measures from both organizations will increase the awareness of the community towards this possible future meeting point.

### ***PI meetings***

SystemsX.ch periodically holds PI meetings, ensuring that RTD, MRD and TF PIs meet regularly, and not just at larger SystemsX.ch events (see above). In these meetings, besides a small part where organizational and administrative issues are discussed, three to four SystemsX.ch projects (typically three RTDs or MRDs 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. As stated by the PIs themselves these meetings are important to strengthen the ties within the community. The last PI meeting was held in May 2017. The PIs agreed to create the Swiss Society of Systems Biology. Two MRDs (HIV-X and MetastasiX), an RTD (MicroScapesX) and a TF Project (Friends or Foes) were presented.

Dates and main topics of the SystemsX.ch PI meetings are shown on Table A44 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 meeting dates and topics see Appendix A, Tables A37 and A38). 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 22, 2016. At this meeting the impact analysis mandated by the SERI was discussed, and the project for a documentary film as well as the phasing out of SystemsX.ch were presented. An update on the financial status (allocations, accounting and budget for 2017) was given, as well as an overview of the upcoming Swiss Personalized Health Network (SPHN) initiative. As convened in November 2014, the earlier June meetings were replaced by circular decisions to be communicated per email. No circular decisions were necessary in June 2017.

Besides the BoD meetings, contacts with the BoD members are maintained through the yearly informal visits that Daniel Vonder Mühl undertakes at all partner institutions. In these visits, BoD members plus other relevant people at the institution are given a detailed overview of the current status of the initiative, the financial situation of the initiative as a whole and of the institution, and the outlook for the next year.

The members of the BoD and the dates and topics of the BoD meetings in 2016 are listed in Appendix A, Tables A38 and A39.

### 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-year term in June 2007, 2009, 2011 and 2013. In June 2015, 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 was responsible for reviewing the Special Opportunity Funds proposals for approval or rejection. It also provided the SNSF panel with strategic input for the review of the RTD, MRD, TF, TPdF and IPhD proposals, and decided on the 3<sup>rd</sup> or 4<sup>th</sup> year extensions of TPdF and IPhD Projects. Since 2007 there have been about eight to ten SEB meetings a year. As the amount of operational tasks has diminished since the last call for proposals was closed, in 2016 the number of SEB meetings was reduced accordingly. Only one live SEB meeting was organized in 2017, on March 7. The meeting scheduled for August 17, 2017 was replaced by a circular email.

The members of the SEB and the dates and topics of the SEB meetings in 2015-2016 are listed in Appendix A, Tables A40 and A41.

### 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 A47).

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 and postdoc educational

program is coordinated and organized, and workshops, conferences and events are organized.

Another important task of the MO 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 different SystemsX.ch research projects, strategy, events, etc. It is available in English and is published twice a year. A survey among readers of the X-Letter carried out in Autumn 2015 showed that readers appreciate the format and contents of the magazine. Certain suggestions gathered in the survey have since been implemented. For short and quick announcements, the format X-Flash informs the SystemsX.ch community about upcoming calls, events or media releases. Since they are distributed by e-mail they are very effective and useful. A SystemsX.ch Twitter account was created in August 2016, and has proved a very useful tool to disseminate research results and papers published by SystemsX.ch researchers, as well as to communicate more generally with the systems biology community, both in Switzerland and abroad. The SystemsX.ch Twitter channel is used actively by the members of the community, and the number of followers of SystemsX.ch has grown steadily since September 2016.

During the current reporting period a documentary film about SystemsX.ch has been produced. The aim of the film is to inform the general public about the initiative and its achievements, as well as to educate in what systems biology is and how it has impacted research in the life sciences. It is a modular film, whose modules, portraying individual projects, can be shown independently by the groups or institutions involved. The film is currently in the post-production phase. The German version of the film was pre-launched at the Scientifica outreach event of UZH and ETHZ, and the English version was premiered at the 3<sup>rd</sup> International SystemsX.ch Conference. Several screenings are being organized in the next few months at different institutions throughout Switzerland. Besides the film, a touchbook has been launched: this interactive app for tablets explains the projects and the initiative in further depth and presents several other projects that could not be included in the film due to time limitations. The touchbook is being distributed together with the film, and it will be marketed especially among secondary school teachers, as an educational tool to illustrate the importance of interdisciplinary approaches in life science research.

As of July 1, 2017, Eavan Dorsey (previously Scientific Coordinator and Deputy Managing Director) took over the Managing Direction of SystemsX.ch. Daniel Vonder Mühl has moved on to direct the ETH Domain Strategic Focus Area Personalized Health and Related Technologies, and remains Deputy Managing Director at SystemsX.ch with a reduced workload of 20%.

### ***'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"

([https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/336919/1stInquiryReport.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/336919/1stInquiryReport.pdf)) that state "The Seven Principles of Public Life" (Selflessness, Integrity, Objectivity, Accountability, Openness, Honesty, Leadership).

The Boards and the MO 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 or-

der 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 in 2014, 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 A45 and A46.

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

When SystemsX.ch was set up in 2007, the Scientific Advisory Board (SAB) was responsible for the 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 D67.

## 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 underwent their mid-term evaluation by the SNSF in November 2015. 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 2016 to June 2017) are presented, focusing in particular on the four main 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, its 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 joint publications from 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 and MRD Projects that have had an especially high impact during this reporting period have been:

Chevrier S, Levine JH, Zanutelli VRT, Silina K, Schulz D, Bacac M, Ries CH, Ailles L, Jewett MAS, Moch H, van den Broek M, Beisel C, Stadler MB, Gedye C, Reis B, Pe'er D, Bodenmiller B. (2017): An Immune Atlas of Clear Cell Renal Cell Carcinoma. *Cell* 169(4):736-749.e18. **PhosphoNetPPM , NeuroStemX, MetastasiX**

Liu Y, Beyer A, Aebersold R.: On the dependency of cellular protein levels on mRNA abundance. *Cell* 165(3):535-50. **PhosphoNetPPM**

Groner AC, Cato L, de Tribolet-Hardy J, Bernasocchi T, Janouskova H, Melchers D, Houtman R, Cato AC, Tschopp P, Gu L, Corsinotti A, Zhong Q, Fankhauser C, Fritz C, Poyet C, Wagner U, Guo T, Aebersold R, Garraway LA, Wild PJ, Theurillat JP, Brown M. (2016): TRIM24 Is an Oncogenic Transcriptional Activator in Prostate Cancer. *Cancer Cell* 13;29(6):846-58. **PhosphoNetPPM**

Rusert P, Kouyos RD, Kadelka C, Ebner H, Schanz M, Huber M, Braun DL, Hoze N, Scherrer A, Magnus C, Weber J, Uhr T, Cippa V, Thorball CW, Kuster H, Cavassini M, Bernasconi E, Hoffmann M, Calmy A, Battegay M, Rauch A, Yerly S, Aubert V, Klimkait T, Boni J, Fellay J, Regoes RR, Gunthard HF, Trkola A, Swiss HIVCS (2016) Determinants of HIV-1 broadly neutralizing antibody induction. *Nat Med* 22: 1260-1267 **AntibodyX, HIV-X**

Giachino, C., Boulay, J-L., Ivanek, R., Alvarado, A., Tostado, C., Lugert, S., Tchorz, J., Coban, M., Mariani, L., Bettler, B., Lathia, J., Frank, S., Pfister, S., Kool, M., and Taylor, V. (2015). A tumor suppressor function for Notch signaling in forebrain tumor subtypes. *Cancer Cell*. 28, 730-742. **NeuroStemX**

Rolando C., Erni A., Grison A., Beattie R., Engler A., Gokhale P.J., Milo M., Wegleiter T., Jessberger S., and Taylor V. (2016). Multipotency of Adult Hippocampal NSCs In Vivo Is Restricted by Drosha/NFIB. *Cell Stem Cell* 19: 653-662. **NeuroStemX**

Manukyan L., Montandon S.A., Fofonjka A., Smirnov S., M.C. Milinkovitch (2017) A Living Mesoscopic Cellular Automaton Made of Skin Scales *Nature* 544, 7649: 173–179 **EpiPhysiX**

Aylett, C.H., E. Sauer, S. Imseng, D. Boehringer, M.N. Hall, N. Ban, and T. Maier. 2016. Architecture of human mTOR complex 1. *Science* 351, 48-52. **MERIC**

Pasakarnis L., Frei E., Caussin E., Affolter M. & Brunner D. (2016) Tissue-specific, acute MyosinII activity depletion dismisses current models of tissue force orchestration in dorsal closure. *Nature Cell Biology*, 18, 1161–1172 **MorphoGenetiX**

D. Ryu, L. Mouchiroud, P.A. Andreux, E. Katsyuba, N. Moullan, A.A. Nicolet-Dit-Félix, E.G. Williams, P. Jha, G. Lo Sasso, D. Huzard, P. Aebischer, C. Sandi, C. Rinsch, J. Auwerx. (2016) Urolithin A induces mitophagy and prolongs lifespan in *C. elegans* and increases muscle function in rodents. *Nature Medicine*. **AgingX**

H. Zhang, D. Ryu, Y. Wu, K. Gariani, X. Wang, P. Luan, D. D'Amico, E.R. Ropelle, M.P. Lultolf, R. Aebersold, K. Schoonjans, K.J. Menzies, J. Auwerx. (2016). NAD<sup>+</sup> repletion improves mitochondrial and stem cell function and enhances life span in mice. *Science* **AgingX**

E.G. Williams\*, Y. Wu\*, P. Jha, S. Dubuis, P. Blattmann, C.A. Argmann, S.M. Houten, T. Amariuta, W. Wolski, N. Zamboni, R. Aebersold#, J. Auwerx#. (\*, first author; #, corresponding author) (2016) Systems proteomics of liver mitochondria function. *Science*. **AgingX**

C. Merkwirth\*, V. Jovaisaite\*, J. Durieux, O. Matilainen, S.D. Jordan, P.M. Quiros, K.K. Steffen, E.G. Williams, L. Mouchiroud, S.U. Tronnes, V. Murillo, S.C. Wolff, R.J. Shaw, J. Auwerx#, A. Dillin#. (\*, first author; #, corresponding author) (2016) Two Conserved Histone Demethylases Regulate Mitochondrial Stress-Induced Longevity. *Cell*. **AgingX**

Marbach D, Lamparter D, Quon G, Kellis M, Kutalik Z, Bergmann S.(2016) Tissue-specific regulatory circuits reveal variable modular perturbations across complex diseases. *Nat. Methods* **AgingX**

Stucki D, Brites D, Jeljeli L, Coscolla M, Liu Q, Trauner A, Fenner L, Rutaihua L, Borrell S, Luo T, Gao Q, Kato-Maeda M, Ballif M, Egger M, Macedo R, Mardassi H, Moreno M, Tundo Vilanova G, Fyfe J, Globan M, Thomas J, Jamieson F, Guthrie JL, Asante-Poku A, Yeboah-Manu D, Wampande E, Ssengooba W, Joloba M, Boom WH, Basu I, Bower J, Saraiva M, Vaconcellos S, Suffys P, Koch A, Wilkinson R, Gail-Bekker L, Malla B, Ley S, Beck HP, de Jong BC, Toit K, Sanchez-Padilla E, Bonnet M, Gil-Brusola A, Frank M, Penlap Beng V, Eisenach K, Alani I, Wangui Ndung'u P, Revathi G, Gehre F, Akter S, Ntoumi F, Stewart-



Isherwood L, Ntinginya N, Rachow A, Hoelscher M, Cirillo DM, Skenders G, Hoffner S, Bakonyte D, Stakenas P, Diel R, Crudu V, Moldovan O, Al-Hajoj S, Otero L, Barletta F, Carter J, Diero L, Supply P, Comas I, Niemann S, Gagneux S. *Mycobacterium tuberculosis* Lineage 4 is comprised of globally distributed and geographically restricted sublineages. *Nat Genet* 2016, 48: 1535–43. **TbX**

Blondiaux N, Moune M, Desroses M, Frita R, Flipo M, Mathys V, Soetaert K, Kiass M, De-lorme V, Djaout K, Trebosc V, Kemmer C, Wintjens R, Wohlkönig A, Antoine R, Huot L, Hot D, Coscolla M, Feldmann J, Gagneux S, Locht C, Brodin P, Gitzinger M, Déprez B, Willand N, Baulard A. Reversion of antibiotic resistance in *Mycobacterium tuberculosis* by spiroisoxazoline SMART-420. *Science* 2017, 355: 1206-11. **TbX**

Wacker R, Eickel N, Schmuckli-Maurer J, Annoura T, Niklaus L, Khan SM, Guan JL, and Heussler VT. (2017). LC3-association with the parasitophorous vacuolar membrane of *Plasmodium berghei* liver stages follows a non-canonical autophagy pathway. *Cell Microbiol.* doi: 10.1111/cmi.12754. **MalarX**

Oliveira AP, Ludwig C, Zampieri M, Weisser H, Aebersold R & U Sauer. 2015. Dynamic P-proteomics reveals TORC1-dependent regulation of yeast nucleotide and amino acid biosynthesis. *Science Signaling* 8(374):rs4. **SignalX** and **YeastX**.

Prouteau M, Desfosses A, Sieben C, Bourgoignie C, Mozaffari NL, Demurtas D, Mitra AK, Guichard P, Manley S and Loewith R. 2017. TORC1 Organised in Inhibited Domains (TOROIDs) regulate TORC1 activity. *Nature*. In press. **SignalX**

Leiba J., Sabra A., Bodinier R., Marchetti A., Lima W.C., Burdet B., Pagni M., Soldati T., Pan M., Jin T., Lelong E., Cosson, P. (2017) Vps13F links bacterial recognition and intracellular killing in *Dictyostelium*. *Cell Microbiol.* Jul;19(7). **HostPathX**

### **Technology and Development**

SystemsX.ch institutions and RTDs have developed and/or implemented a variety of technologies and resources for dynamic network analysis. Some selected examples of Technology and Development are shown in Table A27 in Appendix A. Some of these developments have at least in part lead to patents and licenses (Tables A25 and A26 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 2017, the RTDs and MRDs counted 168 active PhD students and 175 active postdocs (Tables A38 and A39 in Appendix A). The MO has asked for the career tracks of PhD students and postdocs who have left or finished working on the RTD and MRD 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 2016 and had been reported in the 2015-2016 reporting period:

- 132\* have positions in academia (most of them as postdocs, 13 people became group leaders or professors)
- 62\* people are working in industry/private sector at different levels.
- 1\* person started his own company
- 25\* people are working within public services (including staff at hospitals)
- for several people, either no information was provided, or their next career steps are 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 and MRDs 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 or MRD in Appendix A (Table A28 and A29). The list of collaborations for each RTD or MRD 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 and H2020 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, Human Frontiers Science Program, etc.).

The full list of SystemsX.ch ERC grantees can be found in Table D39 in Appendix D. Between 2007 and 2017, 60 senior SystemsX.ch researchers received ERC Advanced or Consolidator grants and 29 junior SystemsX.ch researchers received ERC Starting grants.

Besides being invited speakers at numerous international conferences, PIs and co-PIs of RTD Projects have also been involved in the organization of several conferences, which has contributed to the visibility of RTDs beyond Switzerland.

### **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.

In order to compile the self-evaluation report mandated by the SERI for its impact analysis, SystemsX.ch distributed representatives of the partner institutions. Their answers illustrate the extent of the structural impact of SystemsX.ch, in terms of creation of departments, faculty positions, acquisition of equipment and other investments. The structural impact on partner institutions shows that the sustainability of the initiative is secured: 12 out of 15 institutions established new departments (4), units (4), facilities or competence centers (10) with a focus on systems biology. Examples are the Department of Computational Biology at the University of Lausanne or the new Proteomics and Imaging Facility at the University of Basel.

More than 60 new research groups in the field of systems biology were created at the partner institutions. About half of the group leaders were educated as non biologists (i.e. in computational biology, bioinformatics/modeling, scientific computing, bioengineering, mathematics/statistics, physics or analytics).

SystemsX.ch institutions reported investing more than CHF 75 million in equipment and devices enabling systems biology research. More than 80% of the invested infrastructure and equipment is made accessible to other research groups within the home institution, and more than half is offered to researchers outwith. Those numbers impressively reflect the spirit of sharing limited resources between the partners.

Some concrete examples of measures that highlight the sustainability of SystemsX.ch are:

- SyBIT (IT-platform and data management)
- participation in SINERGIA projects (e.g. Schübeler, van Nimwegen)

- establishment of the ETH Zurich department D-BSSE in Basel (currently 17 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 of the database, funded initially through Special Opportunity funds
- establishment of IT support centers for life sciences research. In the reporting period a science IT unit was created at the University of Bern (Science IT Support, SciTS, Sigve Haug), enlarging the list of similar centers created in the past few years at University of Zurich (S<sup>3</sup>IT, Marcel Riedi) and University of Basel (sciCore, Torsten Schwede). These newer 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).
- University of Lausanne: establishment of the new Department of Computational Biology, created on January 1, 2016, which encompasses the former Department of Medical Genetics and is currently recruiting two professors (a tenure-track assistant professor and an associate professor).

## 2.2 Activity reports of all MRD Projects launched in 2015

The 10<sup>th</sup> call for proposals covered Medical Research and Development (MRD) Projects. All nine MRD Projects approved in November 2014 (PrionX, AneuX, HIV-X, GutX, VirX, MelanomX, StemSysMed, HDL-X, MetastasiX) were started between January and July 2015, and they all have submitted for the second time a scientific report. An overview of running MRDs can be found in Appendix A, Table A8. The scientific reports of these MRDs are part of Appendix B.

### 2.2.1 Science

Most MRD Projects are beginning their third year of activity. First results have now been obtained and published, and all MRDs underwent successfully a mid-term review by the SNSF Review Panel in January 2017. The panel issued, in several cases, recommendations for the PIs and co-PIs, with the aim of fine-tuning certain aspects of the projects to improve their potential outcomes. In some cases these recommendations have been specifically addressed by the PIs and co-PIs in their annual scientific reports (see App B).

In terms of publications, MRD Projects reported 56 published papers in this reporting period, several of them in collaboration with SystemsX.ch RTDs. Among the publications with a high impact are the following:

Küffer, Alexander; Lakkaraju, Asvin K. K; Mogha, Amit; Petersen, Sarah C; Airich, Kristina; Doucerain, Cédric; Marpakwar, Rajlakshmi; Bakirci, Pamela; Senatore, Assunta; Monnard, Arnaud; Schiavi, Carmen; Nuvolone, Mario; Grosshans, Bianka; Hornemann, Simone; Bassilana, Frederic; Monk, Kelly R; Aguzzi, Adriano (2016). The prion protein is an agonistic ligand of the G protein-coupled receptor Adgrg6. *Nature*, 536(7617):464-468. **PrionX**

Rusert P, Kouyos RD, Kadelka C, Ebner H, Schanz M, Huber M, Braun DL, Hoze N, Scherrer A, Magnus C, Weber J, Uhr T, Cippa V, Thorball CW, Kuster H, Cavassini M, Bernasconi E, Hoffmann M, Calmy A, Battegay M, Rauch A, Yerly S, Aubert V, Klimkait T, Boni J, Fellay

J, Regoes RR, Gunthard HF, Trkola A, Swiss HIVCS (2016) Determinants of HIV-1 broadly neutralizing antibody induction. *Nat Med* 22: 1260-1267 **HIV-X and AntibodyX**

Gomez de Agüero M, Ganal-Vonarburg SC, Fuhrer T, Rupp S, Uchimura Y, Li H, Steinert A, Heikenwalder M, Hapfelmeier S, Sauer U, McCoy KD, Macpherson AJ. 2016. The maternal microbiota drives early postnatal innate immune development. *Science* 351: 1296-302. **GutX**

Brugiroux S, Beutler M, Pfann C, Garzetti D, Ruscheweyh HJ, Ring D, Diehl M, Herp S, Lotscher Y, Hussain S, Bunk B, Pukall R, Huson DH, Munch PC, McHardy AC, McCoy KD, Macpherson AJ, Loy A, Clavel T, Berry D, Stecher B. 2016. Genome-guided design of a defined mouse microbiota that confers colonization resistance against *Salmonella enterica* serovar Typhimurium. *Nat Microbiol* 2: 16215. **GutX**

Miyake Y, Keusch JJ, Wang L, Saito M, Wang X, Melancon BJ, Helquist P, Hess D, Gut H & Matthias P (2016) Structural insights into HDAC6 tubulin deacetylation and its selective inhibition. *Nature Chemical Biology*, 12, 748–754 (2016) doi:10.1038/nchembio.2140 (Matthias and Gut) **VirX**

Buggenthin, F., Buettner, F., Hoppe, P.S., Endeke, M., Kroiss, M., Strasser, M., Schwarzfischer, M., Loeffler, D., Kokkaliaris, K.D., Hilsenbeck, O., et al. (2017). Prospective identification of hematopoietic lineage choice by deep learning. *Nat. Methods* 14, 403–406. **StemSysMed**

Filipczyk, A., Marr, C., Hastreiter, S., Feigelman, J., Schwarzfischer, M., Hoppe, P.S., Loeffler, D., Kokkaliaris, K.D., Endeke, M., Schaubberger, B., Hilsenbeck, O., Skylaki, S., Hasenauer, J., Anastasiadis, K., Theis, F.J., and Schroeder, T. (2015). Network plasticity of pluripotency transcription factors in embryonic stem cells. *Nature cell biology* 17, 1235-1246. **StemSysMed**

Hilsenbeck, O., Schwarzfischer, M., Skylaki, S., Schaubberger, B., Hoppe, P.S., Loeffler, D., Kokkaliaris, K.D., Hastreiter, S., Skylaki, E., Filipczyk, A., Strasser, M., Buggenthin, F., Feigelman, J.S., Krumsiek, J., van den Berg, A.J., Endeke, M., Etzrodt, M., Marr, C., Theis, F.J., and Schroeder, T. (2016). Software tools for single-cell tracking and quantification of cellular and molecular properties. *Nature Biotechnology* 34, 703-706. **StemSysMed**

Hoppe, P.S., Schwarzfischer, M., Loeffler, D., Kokkaliaris, K.D., Hilsenbeck, O., Moritz, N., Endeke, M., Filipczyk, A., Gambardella, A., Ahmed, N., Etzrodt, M., Coutu, D.L., Rieger, M.A., Marr, C., Strasser, M.K., Schaubberger, B., Burtscher, I., Ermakova, O., Burger, A., Lickert, H., Nerlov, C., Theis, F.J., and Schroeder, T. (2016). Early myeloid lineage choice is not initiated by random PU.1 to GATA1 protein ratios. *Nature* 535, 299-302. **StemSysMed**

An Immune Atlas of Clear Cell Renal Cell Carcinoma. Chevrier S, Levine JH, Zanotelli VRT, Silina K, Schulz D, Bacac M, Ries CH, Ailles L, Jewett MAS, Moch H, van den Broek M, Beisel C, Stadler MB, Gedye C, Reis B, Pe'er D, Bodenmiller B. *Cell*. 2017 May 4;169(4):736-749.e18. **MetastasiX, PhosphoNetPPM and NeuroStemX**

Gene bivalency at Polycomb domains regulates cranial neural crest positional identity. Minoux M, Holwerda S, Vitobello A, Kitazawa T, Kohler H, Stadler MB\*, Rijli FM\*. *Science*. 2017 Mar 31;355(6332). pii: eaal2913. **MetastasiX**

The Hippo kinases LATS1 and 2 control human breast cell fate via crosstalk with ER $\alpha$ . Britschgi A, Duss S, Kim S, Couto JP, Brinkhaus H, Koren S, De Silva D, Mertz KD, Kaup D, Varga Z, Voshol H, Vissieres A, Leroy C, Roloff T, Stadler MB, Scheel CH, Miraglia LJ, Orth

AP, Bonamy GM, Reddy VA, Bentires-Alj M. Nature. 2017 Jan 26;541(7638):541-545. **MetastasiX**

Tackling Resistance to PI3K Inhibition by Targeting the Epigenome. Koren S, Bentires-Alj M. Cancer Cell. 31(5):616-618 (2017) **MetastasiX**

### 2.2.2 Education

As is the case with RTDs, MRDs play an important role towards enabling the training of young systems biologists. PhD students and postdocs working on MRD Projects are exposed to a highly interdisciplinary way of doing research in the medically oriented life sciences, and MRD meetings and retreats provide them with good opportunities to exchange knowledge and build their network. X PhD students and X postdocs have worked in MRD Projects during the current reporting period.

### 2.2.3 Cooperation with private sector (public-private partnership)

MRDs reported 10 different collaborations with private companies, ranging from punctual collaborations on subprojects of interest to financial support by the industrial partner of a new project spun off the MRD. In the case of HIV-X, IBM Research is one of the partners of the projects.

### 2.2.4 International outreach

The international visibility of MRD Projects increased in this third year of activity. This international outreach stems mainly from collaboration networks of the MRD co-PIs, as well as from their participation in international conferences mainly as invited speakers. 20 international collaborations were reported by the MRDs. Moreover, GutX PI Andrew Macpherson was awarded an ERC Advanced Grant in 2017, further confirming to the international visibility of MRD researchers.

## 2.3 Activity reports of all IPhD Projects launched from 2008 to 2015

In the first phase of SystemsX.ch (2008-2012), 40 IPhD Projects were approved by the SNSF. In 2012 (5<sup>th</sup> call), further 11 proposals for IPhD were approved, nine more after the 7<sup>th</sup> call (2013), and 17 more after the 9<sup>th</sup> call (2014). After the 11<sup>th</sup> call in 2015, 10 new projects were approved. Except for one IPhD Project which was completed in October 2016, all scientific reports of the projects that have been active 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 were completed between 2012 and 2013, and the ones approved in 2010 were completed between 2014 and 2015.

In detail, out of the projects approved in:

- **2008**, nine started in 2008 and six in 2009. Out of the 15 projects, two finished before 2012, seven in 2012, three in 2013 and one in 2014.
- **2009**, nine started in 2009 and three in 2010. Out of the 12 projects, three finished before 2013, seven in 2013, one in 2014 and one in 2015.
- **2010**, four started in 2010, seven in 2011 and two in 2012. Out of the 13 projects, two finished in 2013, four in 2014, six in 2015 (one of them within this reporting period) and one came to an end in June 2016.
- **2012**, eight started in 2012 and three in 2013. One of these projects was completed in 2013, three in 2015, and one was only granted for one year, as an extension of previous funding. All others are running in their fourth year. Eight of these projects requested a and obtained a fourth year extension.

- **2013**, all nine projects started in 2013 or 2014. One of them was completed in 2015, and the rest are all running in their third year. Seven of these projects requested a and obtained a fourth year extension.
- **2014**, six projects started in 2014 and 11 in 2015. Ten of these projects requested and obtained a fourth year extension.
- **2015**, one project started in October 2015, eight between January and March 2016, and the last one in May 2016. These projects were not eligible for an extension request, and are limited to a maximum of three years (or less, if they started after January 1, 2016).

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**

Out of a total 41 IPhD Projects in the present report, one was in her first year, 11 in their second year, 22 in their third year and seven projects were in their fourth year. Out of these seven finishing projects, six have been completed in this reporting period.

Publications, especially as first author, are essential for young scientists' careers. Some IPhD students have been able to publish their results in multidisciplinary and high impact journals (e.g. *Nature*, *Science*, *Nature Methods*, *Nature Biotechnology*, *Nature Microbiology*, *Cell Systems*, *Nucleic Acids Research*, *Blood*, *PLoS ONE*, *PLoS Genetics*, *Cell Reports*, *Bioinformatics*, *Molecular Systems Biology*, etc.), thereby also confirming the visibility and importance of systems biology as a discipline.

During this reporting period the 41 running IPhD projects have generated 43 publications, including two reviews. Overall, 25 first-author papers have been published from currently running IPhD Projects.

Seven projects report preliminary developments, ideas or insights that might lead to applications, new projects or patents.

Table A25 in Appendix A shows patents generated from IPhD Projects. Examples of Technology and Development are shown in Table A29 in Appendix A. An overview of collaborations, links and interactions of IPhD Projects with the private sector is listed in Appendix A (Table A34).

### 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 mainly through the double supervision principle, as well as through participation in workshops, courses and conferences.

Overall IPhD students participated at 74 different educational events (e.g. workshops, courses, summer schools, etc.), many of which were attended by more than one IPhD student. Several of the events took place outside Switzerland. The education events can be classified in the following fields:

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

Moreover, IPhD students reported teaching at six different courses or workshops.

Overall, IPhD students attended a total of 117 different conferences, most of them attended by several IPhD students. 64 of these meetings took place in Switzerland, and 53 of them abroad, thereby partly contributing to the international visibility of SystemsX.ch. The most frequently visited countries were USA, Germany, the UK 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 their scientific career. These transitions allow the Transition Postdoc fellows to become real interdisciplinary scientists, mastering at least two disciplines of high relevance for systems biology research. Furthermore, a transition can greatly contribute to the maturity of the researcher. Francis Collins, leader of the Human Genome Project and currently director of the US National Institutes of Health, is a renowned example of a transitioner: halfway through his PhD in theoretical chemistry he decided to start medical school in order to study biological and medical problems. Collins recently said that transitions in a career are „when you grow the fastest; they're when you're really alive“. This project type is one of the main tools to accomplish the goal of educating the next generation of systems biologists.

In detail:

- in 2012, 17 proposals were submitted to the 5<sup>th</sup> call, 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 2013, 13 TPdFs were approved out of the 28 proposals submitted to the 7<sup>th</sup> call. 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.
- in 2014, 28 proposals were submitted to the 9<sup>th</sup> call, out of which seven TPdFs were approved. All of them started their projects between September 2014 and August 2015.
- in 2015, 33 proposals were submitted to the 11<sup>th</sup> call, out of which eight projects were approved. Four of them started between September 2015 and January 2016, the remaining four will start during the next reporting period.
- By the end of the current reporting period, four 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 this type of funding. The fellows have a high scientific profile, and selection criteria are necessarily stringent.

In October 2015, 13 TPdFs submitted requests for a 3<sup>rd</sup> year extension of their fellowship. 12 of the requests were granted, one was rejected based on the unsatisfactory progress of the project compared to the milestones set in the original proposal.

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

The scientific productivity of TPdFs is very high. The 25 projects that were active in this reporting period report yielded 68 accepted publications in peer-reviewed journals (up from 40 in the previous reporting period). One patent generated in a TPdF

Project is being filed, the ideas behind this patent will probably lead to further applications (Table A25 in Appendix A). 10 preliminary developments were reported. Examples of Technology and Development are shown in Table A28 in Appendix A.

The TPd Fellows have presented their results at 76 different conferences and meetings, in many cases as invited speakers. Several of these events were attended by more than one TPd Fellow. Moreover, the fellows have continued their education by attending 29 different courses, workshops and summer schools (many of these attended by several transition postdocs).

## **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 evolution of the number of proposals and approved projects over time is as follows:

- in 2012, the 6<sup>th</sup> call for proposals was the first call where scientists were invited to submit TF proposals. Seven applications were received, out of which four TFs were granted funds. Two of them were completed before January 2015, and the other two within the current reporting period (both in December 2015)
- in 2013, six groups submitted proposals to the 8<sup>th</sup> call, and two new TFs were approved. One of these projects was completed within the current reporting period.
- in 2014, four TF applications were received within the 10<sup>th</sup> call, and two TFs were approved. Both projects were completed within the current reporting period.

The relatively stable number of applications received suggests that this project type is well received by the community. However, the interest that TFs have attracted has been clearly the most limited of all SystemsX.ch project types.

TFs report three publications in peer-reviewed journals, ten collaborations (two of them with private partners) and one development that could lead to industrial applications.

The annual reports of the three 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.

Originally, Special Opportunities proposals were submitted at any time, and were approved by the SEB (with the possibility of requesting external reviews). Six Special Opportunities projects were approved in this manner between October 2011 and December 2014:

- 2011: Impact study
- 2012: SIB Fellowship Program, Micronaut CINA, SwissLipids,



- 2013: Entrepreneur in Residence, Development of a microfluidic immunofluorescence tissue processor

In 2015 the SEB decided to publish a call for Special Opportunities, with the main aim of increasing their visibility. The 12<sup>th</sup> call (the final SystemsX.ch call for proposals) was a great success, as shown by the very high number of applications received (51), which suggests that this project type is well received and sought for by the systems biology community in Switzerland. Nine proposals were approved by the SEB. All nine projects started between August 2015 and January 2016, and all but one have submitted their scientific report. Two Special Opportunities projects approved before the 12<sup>th</sup> call (the support of the database SwissLipids, and the participation in the SIB PhD fellowship program) have also been active in this reporting period, but do not submit reports.

Special Opportunities Projects granted after the 12<sup>th</sup> call reported 17 peer-reviewed publications, two filed patent applications (Table A21 in Appendix A) and seven preliminary developments that can lead to new projects or patent applications (Table A27 in Appendix A).

The scientific reports of the nine Special Opportunities approved within the 12<sup>th</sup> call can be found in Appendix B.

### 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 ten years, i.e. the period between the first call for proposals in September 2007 and August 2017.

#### 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 was finalized in June 2014. Since then, a particular group mandated by the SERI has taken over. The initiative has been launched in 2017.

During this reporting period, one change in the composition of the BoD (the representative of the EPFL) has taken place. The full list of BoD members can be found in Appendix A, table A38, and the list of meetings and topics discussed in Appendix A, table A39.

The Managing Director visited each SystemsX.ch partner institution once a year until 2016, for informal discussions and to receive feedback, input and any individual or collective concerns which might have come up during the year. This regular contact provided 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 their tasks to deputies, divergence in opinions compared to other committees of a similar composition (such as the Rectors’ Conference of the Swiss Universities, CRUS) has occurred occasionally. Delegation from rectors to vice-rectors should therefore be minimized. Although this was already remarked in the Scientific Reports 2013, 2014 and 2015, and was also pointed out in the BoD meeting of November 2013, no improvement has been seen.

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

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

In June 2015, the SEB was re-elected by the BoD. 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 aid the review panel (RTD, MRD, 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, SNSF panel member, collaborator etc. Several measures were put 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. With the initiative coming to an end in 2018, and as there are no more calls for proposals and therefore no more reviewing processes, less operational tasks are needed. This has also had an impact on attendance, and has led to reducing the number of meetings. Between January and August 2016, two meetings were held. In the second one it was discussed whether to change the format of the contents, and it was decided to maintain the current format, but reduce the frequency to approximately three meetings per year, at least one of them live. In this reporting period, two live meetings have taken place, on October 14, 2016 and on March 7, 2017. A further meeting scheduled for August 17, 2017 was replaced by a circular email.

The list of SEB members can be found in Appendix A, table A40, and the list of meetings and topics discussed in Appendix A, table A41.

→ **Conclusion:** The SEB functions well. Due to the decreased amount of work that the SEB has to face, the number of SEB meetings has been reduced to three per year, at least one of them live.

### 3.1.3 Management Office (MO)

Both financial and scientific reporting were elaborated efficiently and delivered on time. In 2016 the Financial Report was audited externally for the second time by PricewaterhouseCoopers (PwC). No irregularities were found. Neither PwC in 2016, nor the previous external auditor (Ernst&Young) had found irregularities in any of the eight financial reports that had already been previously elaborated.

During the past years, the MO has set up certain internal procedures in order to comply with 'good governance'. For instance, different measures ensure the 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 procedure. A new contract between ETHZ Rechnungswesen and SystemsX.ch was signed in June 2015: this collaboration with the Financial Services of ETH Zurich allows the MO to profit from their know-how in this area for the accounting and preparation of the financial reports for the initiative. This collaboration has proved 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 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 were installed successfully and in general achieved the agreement of all three cooperating governing bodies (SNSF, SEB and MO). The members of the Expert Group and Review Panel can be found in Appendix A, tables A45 and A46.

**Table 1.** Meeting dates of the SNSF Review Panel in 2017

Committee	Call, meeting
SNSF Review Panel Systems Biology	Mid-term review of MRDs approved in 2013 (January 19-20, 2017)

→ **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 proved to be a success. Despite the 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 requested to approve the SNSF's suggestion for funding.

### 3.1.5 Declared milestones

Milestones for the second phase of SystemsX.ch were defined in the respective document of April 2013. The following years' milestones are defined in the Scientific Reports.

In the following pages, the outlook of the last Scientific Report 2015-2016 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.

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

- ✓ In response to the very positive feedback received for the first two editions, SystemsX.ch organized for the third time in November 17-18, 2016, a two-day workshop in lab management and leadership skills for postdocs. The workshop was led by Sašo Kočevár and his team from hfp consulting. Postdocs improved their communication and collaboration skills, developed awareness of "leading with or without being in charge", and learnt and practiced useful tools for their career in science. Moreover, they were 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. Fifteen participants attended the workshop: the attendance was slightly reduced compared to the first two editions, possibly due to the fact that the previous workshop had been organized just 9 months before. However, the feedback from the participants was very positive. A follow-up session of the Postdoc Workshop of February 2016 was also organized on November 16, 2016: the five participants from the previous event reflected on their leadership and management development since attending the workshop.

#### Machine Learning Course (SystemsX.ch, SIB and NGS Discussion Group)

- ✓ Fulfilled: The Next-Generation Sequencing Discussion Group of the University of Zurich, SystemsX.ch and the Swiss Institute of Bioinformatics (SIB) jointly organized an introductory course which provided a hands-on introduction to machine learning, and included sessions led by biologists that use machine learning techniques in their research. The course took place from November 21-25, 2016 at the Irchel Campus of the University of Zurich. The 30 places that the course offered were booked out, and the feedback from the participants was very positive.

#### SystemsX.ch Retreat 2017

- ✓ Fulfilled: The 7<sup>th</sup> SystemsX.ch Retreat took place in May 2017. The Retreat focused on presentation skills, and it is targeted at PhD students and postdocs. It offered an ideal platform to improve the content and delivery of scientific presentations, as well as to exchange experiences and knowledge. The coaches from hfp consulting, all of them scientists, provided concepts and skills that are immediately applicable to the career of the participants. Networking among the young scientists of the SystemsX.ch network was also fostered through social activities and group exercises.

## Impact Analysis

- ✓ Fulfilled: The SERI is carrying out an Impact Analysis of SystemsX.ch. According to the concept elaborated by the SERI, within this analysis SystemsX.ch was mandated to elaborate a self-evaluation. This evaluation included quantitative and qualitative assessments of the achievements of the initiative, with a focus on the objectives set out in 2007. The evaluation looked into a) the structural impact on the SystemsX.ch partner institutions (structural changes); b) the impact on interdisciplinary and inter-institutional collaborations (networking and partnerships); c) the educational impact (promoting young talents); and d) the scientific impact (excellence in science) The internal impact analysis was delivered in March 2017, and an expert panel assessed the report and interviewed the main actors of the initiative in June 2017. The conclusions of the impact analysis by the SERI are expected in November 2017.

## ERASysAPP

- ✓ Fulfilled: By the end of 2016, the handing over of tools elaborated by ERASysAPP WP 3 to ISBE WP 10 Education and Training was finalized, concluding the involvement of SystemsX.ch in the ERANet. The Swiss partners in six transnational research projects funded through ERASysAPP will complete their participation in the projects during 2018.

## Personalized Health 2017-2020

- ✓ Fulfilled: The involvement of SystemsX.ch in the recently launched Swiss Personalized Health Initiative was concluded in 2016, but Daniel Vonder Mühll has continued to provide additional help and consulting punctually, when needed.

➔ **Conclusion:** SystemsX.ch has reached all milestones stated in the outlook of the scientific report 2015-2016. The partly fulfilled points are either ongoing or under preparation and will be completed by the end of 2016.

## 3.2 Science

By August 2016, 249 SystemsX.ch projects of different types (RTD, MRD, TF, TPdF, IPhD, Special Opportunities, IPP, BIP, SyBIT, HTF, ERASysAPP) have been approved. This includes two SyBIT project phases, six ERASysAPP projects and FAIRDOM, as well as seven HTF projects. In Appendix B, all projects that were active in the period July 2016 to June 2017 present their annual scientific reports. Some projects (RTDs, IPPs, BIPs, TFs, TPdFs 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 summarizing overview complementary to the project reports.

### 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. Table 2 lists the cumulative number of research groups involved in SystemsX.ch projects throughout the years, and the proportion of groups from each scientific discipline. Several of the listed groups participated in more than one project.

However, the possibly more important and interesting statistics is how many actual research groups participated in SystemsX.ch (i.e., counting each group only once, independently of the number of projects it was involved in). These statistics are presented in Table 3, which lists the number of groups that have received SystemsX.ch funds (independently of the number of SystemsX.ch projects they have participated in), as well as the scientific disciplines they work on. In total, 401 research groups have had SystemsX.ch projects approved (see also Figure 2).

**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%

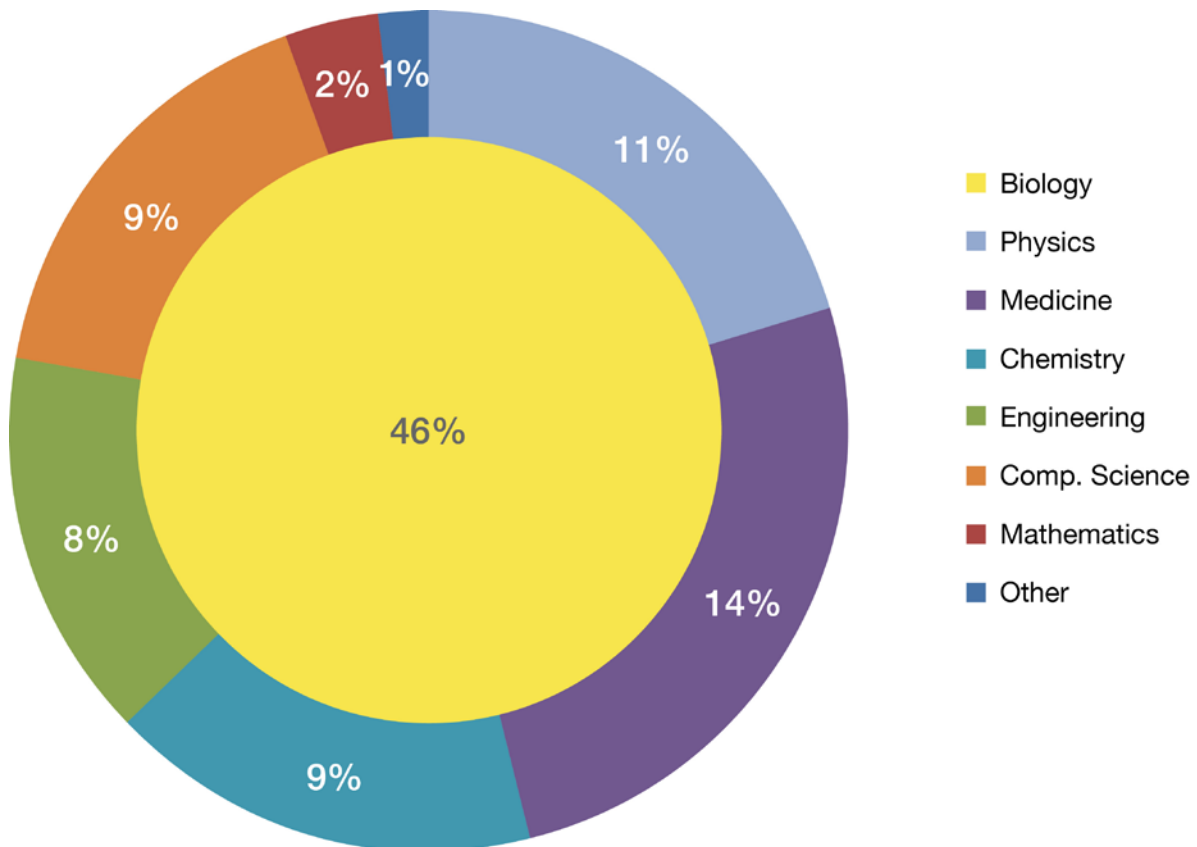
\*several groups are involved in more than one project.

**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 2).

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 249 projects that have been approved by SystemsX.ch, a total of 401 different research groups have been 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% medical doctors (MDs), 11% physicists, 9% chemists, 9% computational scientists (including bioinformaticians), 8% engineers, and 2% mathematicians. Table 3 and Figure 2 give an overview of the development of the distribution of disciplines with time, as the SystemsX.ch community has grown. These data indicate that biology is the dominant discipline within the SystemsX.ch community, but that its relative share has decreased with time. The remaining parts are more or less similar in size, with MDs, physicists, chemists, computational scientists and engineers representing about 10% each. However, the 10<sup>th</sup> call caused a remarkable increase in the proportion of MDs, from 10% to 14%, a textbook example of how incentives and boundary conditions allow to steer research.



**Figure 2.** Out of the 401 PIs and co-PIs of the approved 248 SystemsX.ch projects, 46% did their doctoral thesis in biology, 14% in Medicine, 11% in Physics, and 9% in Computational Sciences / Mathematics.

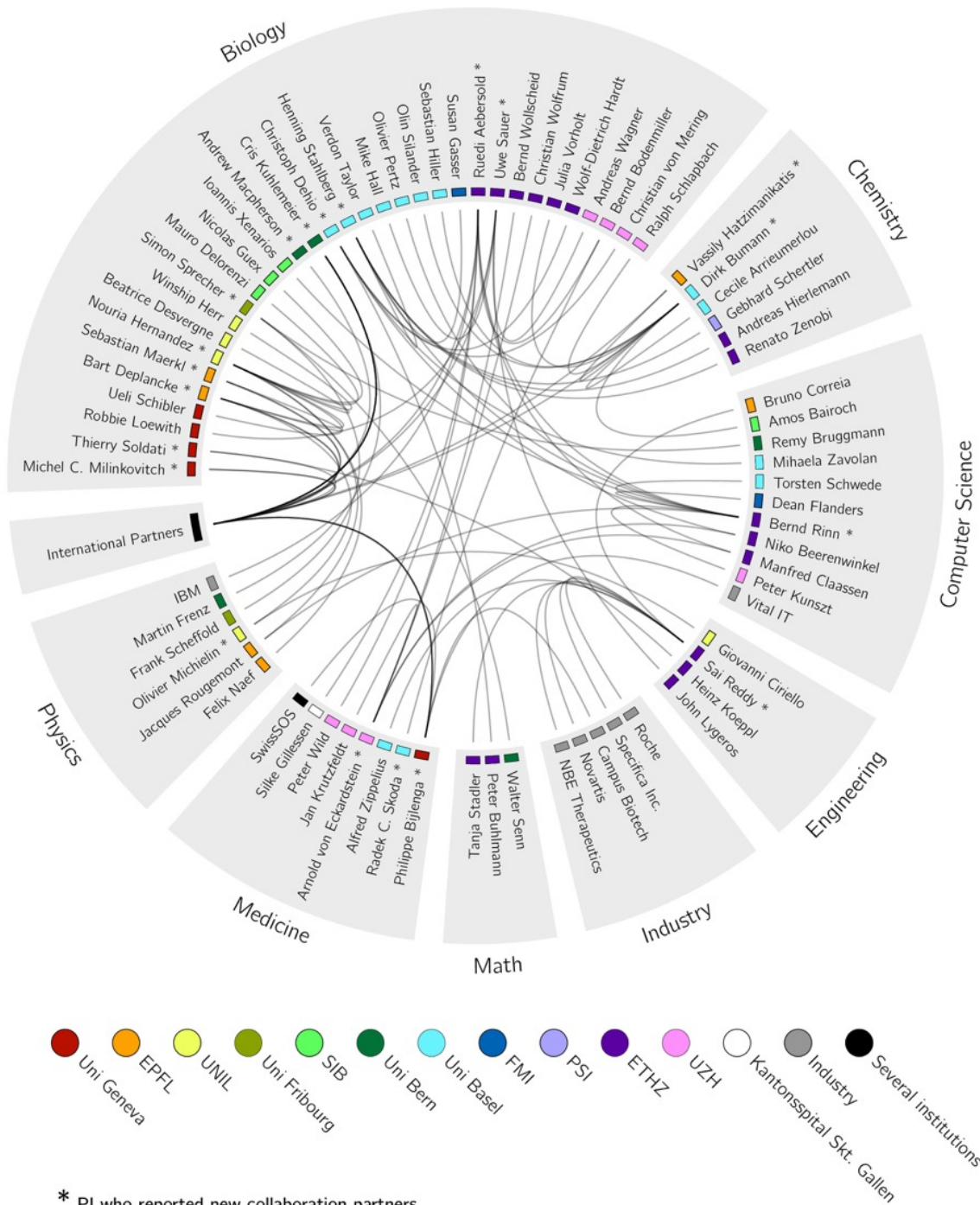
→ **Conclusion:** A good mixture of disciplines contributes to the scientific output of SystemsX.ch, with biologists constituting slightly less than half of the research groups working on the projects. In 2013, as the SNSF pointed out correctly, a large majority of RTDs were led by biologists. This was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

The interdisciplinarity of the systems biology community in Switzerland is also a result of collaborations between scientists from different fields. Since 2008, collaborations between systems biology researchers have increased significantly, thanks to the implemented funding measures: 80% of the interviewed PIs and co-PIs of RTD and MRD projects answered that they gained new research partners they had never worked with before through their RTD or MRD project. On average, three new cooperation partners were given. A questionnaire completed by PIs of RTD and MRD Projects within the frame of the self-evaluation of the initiative provided information about novel research partners with whom the PIs started to collaborate through SystemsX.ch projects. that arose through SystemsX.ch projects. These numerous new partnerships illustrate a highly interdisciplinary and inter-institutional landscape.

According to the survey up to 74% of these newly established networks resulted in subsequent publications, new joint project proposals, the exchange of personnel or sharing of technologies. Further outcomes of the newly encouraged collaborations were jointly organized symposia, training courses or even the joint purchase of equipment.



### New Collaborations Arising from RTD and MRD Projects

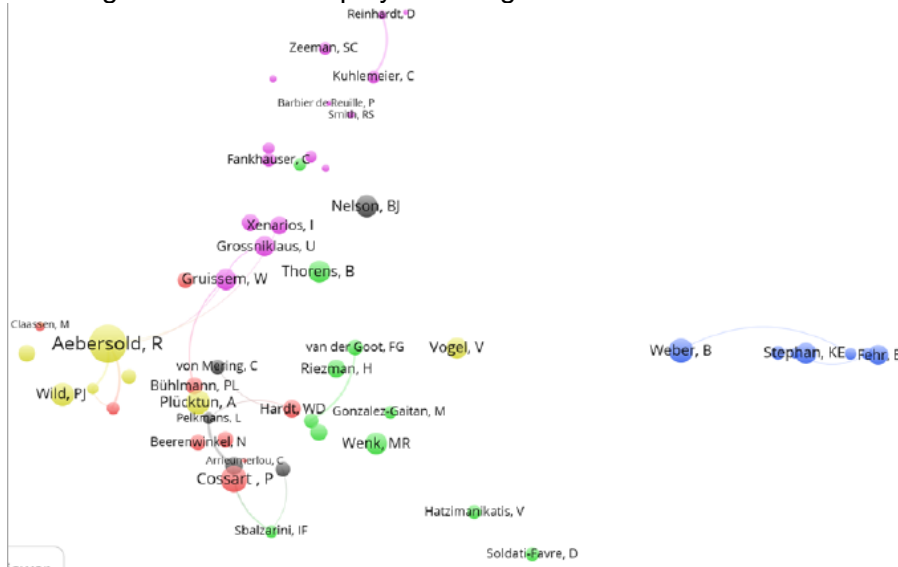


**Figure 3.** Novel interdisciplinary, inter-institutional collaborations of SystemsX.ch research groups as reported in the SystemsX.ch questionnaire for PIs. Disciplines have been determined based on the topics the PIs' doctoral thesis.

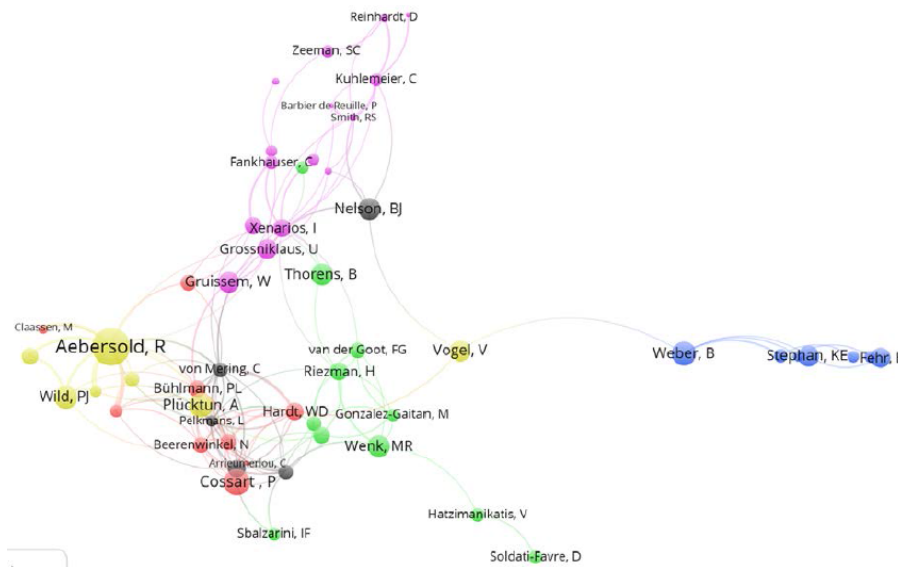
To verify the above statements, the Center for Science and Technology Studies (CWTS) at University Leiden carried out a co-authorship analysis of selected RTDs. Since an evaluation of the whole of SystemsX.ch was considered too work-intensive, a subset of publications from selected RTDs (LipidX1&2, PlantGrowth1&2, InfectX/TargetInfectX, PhosphoNetX/

PhosphoNetPPM, Neurochoice) was chosen to investigate the collaboration patterns between PIs/co-PIs.

For 59 PIs and co-PIs involved in those projects, publications were collected for the period under study. In order to investigate the effect of SystemsX.ch funding on the collaboration network, the period 2008-2015 was compared to the situation in the period 2000-2007. The resulting networks are displayed on Figures 4 and 5.



**Figure 4:** Collaboration map for a subset of SystemsX.ch researchers based on a co-authorship analysis over the period 2000-2007. Each (co-)PI is characterized with a colour to indicate the project he/she belongs to (green: LipidX 1&2; yellow: PhosphoNetX/PhosphoNetPPM; pink: Plant Growth 1&2; blue: Neurochoice; red: InfectX/TargetInfectX). Those who are active in more than one project are coloured in grey. The closer two labels appear, the closer the collaboration. The bigger the circle, the more publications and the broader the connections, the more joint publications.



**Figure 5:** Collaboration map for a subset of SystemsX.ch researchers based on a co-authorship analysis over the period 2008-2015.

Comparing the two resulting networks, a clear acceleration of connections can be seen since 2008: up until 2007, only 17 connections between PIs/co-PIs can be identified, while in the period since 2008 the connections amount to 144. This number includes all co-authorships, regardless of whether the analyzed publications were funded by SystemsX.ch or not. If only SystemsX.ch publications are considered, 116 out of those 144 connections remain, which

demonstrates the influence of targeted SystemsX.ch funding on the development of national collaboration networks.

The fact that interdisciplinarity has been adopted in SystemsX.ch projects also becomes obvious through the bibliometric analysis carried out on SystemsX.ch publications within the frame of the self-evaluation of the initiative (see Appendix E). The research profile of SystemsX.ch publications shows that the category with the highest number of publications (162) is “Multidisciplinary Sciences” with an average MNCS of 2.98 (i.e. three times more cited than the world average), and more than 60 of them are among the top 10% cited publications. This indicates that most papers are published in journals of multidisciplinary character, such as Nature, Science, PLoS or PNAS.

### 3.2.3 Proposals and success rates

For the scientific review of project proposals, two main criteria were 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 were 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 was responsible for assuring the scientific quality of the projects and made the final decision on RTDs, MRDs, TFs, TPdF and IPhD projects (including the SystemsX.ch-initiated project SyBIT), SystemsX.ch was and remains responsible for the overall strategic guidance of the initiative. All other project types (IPP, BIP, HTF and Special Opportunity Projects) were evaluated just by the SEB (with the support of external reviewers if needed).

Table 4 shows that out of the 527 submitted proposals (629 including special projects and ERASysAPP), a total of 216 projects (249), i.e. 41% (40%) were 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, the success rate is 32%, for MRDs 30%, for TFs 47%, for IPhDs it is as well 47%, whereas TPdFs have a rate of only 30%. Almost every second IPP proposal (47%) was funded. BIP proposals had with 84% the highest probability to be funded, and Special Opportunity Projects 27% (for details see Appendix D, Tables D3-4 and Appendix A, Table A3).

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 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 Year	Requested Funds [CHF]	# Proposals Submitted	# Proposals Approved	# (Co-)PIs	SysX.ch Funds [CHF]	Success Rate [#]	Success Rate [CHF]
RTD	580'593'090	107	34	253	130'687'250	32%	23%
MRD	67'664'275	30	9	53	18'587'695	30%	27%
TF	4'677'090	17	8	24	2'097'716	47%	45%
TPdF	22'802'990	106	32	62	7'161'969	30%	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>718'340'742</b>	<b>527</b>	<b>216</b>	<b>686</b>	<b>179'743'914</b>	<b>41%</b>	<b>25%</b>
SyBIT	20'472'000	7	2	7	17'824'000	29%	87%
HTF	3'193'265	15	8	11	1'440'586	53%	45%
SpecOpp	11'952'219	60	16	19	3'027'201	27%	25%

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>762'262'463</b>	<b>629</b>	<b>249</b>	<b>731</b>	<b>205'029'537</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 made by the SNSF Review Panel during their 2014 meeting was that the presented MRD proposals (the first of this kind) were comparable in quality with the RTD proposals submitted in 2008 or 2009. The panel considered that this showed clearly how the quality of proposals had increased over the course of SystemsX.ch, with RTD Projects granted at later calls being more integrated and coherent.

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 approach basic questions but with the aim of obtaining results with a potential impact on 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, the main responsibility and competences being located at the partner institutions. This restricts the job of the Education Advisory Board mainly to coordination.

In Switzerland, systems biology education became an inherent part of academic education over the last nine years, be it through new Master- and PhD programs specialized in systems biology or the integration of systems biology aspects in existing curricula. Although these programs were not directly launched by SystemsX.ch, the majority of universities stated that SystemsX.ch had a catalytic effect on the development or expansion of their systems biology curricula and “kick-started” the process. This effect was mainly achieved by funding systems biology research projects and PhD fellowships, which led to an increase in public recognition of systems biology and its potential. Furthermore, it revealed deficiencies in existing tradition-

al curricula in the education of scientists in a truly interdisciplinary manner, which prompted universities to create new educational programs or refine existing ones.

To date, the academic partners have reported nine PhD and nine Masters programs with a focus on systems biology (a new one will be offered by the ZHAW as of 2017) and a total of 8 lectures, courses and practicals in systems biology which are embedded in Bachelor curricula. A variety of additional lectures, courses, summer schools and symposia for Masters and PhD students as well as postdocs complement the undergraduate and graduate study programs.

## **Fellowships**

### **3.3.1.1 IPhDs**

One of the main educational activities of SystemsX.ch is the support of PhD students through 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.

Surveys carried out among IPhD supervisors and students within the frame of the SystemsX.ch self-evaluation show that the advantages of the project format (mainly the interdisciplinary training, plus the broader perspective and promotion of creativity) largely outweigh its disadvantages (projects requiring more effort and time to be completed, the risk of gaining less proficiency in a given field than students focusing on that field alone, and the challenges related to bridging the gap between two different labs). The students consistently remarked the advantages of belonging to a tight-knit community, and of the numerous training opportunities provided by the SystemsX.ch initiative. Furthermore, many supervisors declared that these projects had allowed them and their labs (and not only the IPhD student) to learn much more from the other field, and in several cases the IPhD Projects paved the way for future collaborations with the co-PI's lab, thus being an important tool in the establishment of networks within the systems biology community.

### **3.3.1.2 TPdFs**

The TPd Fellowship aims to enable young researchers with diverse scientific backgrounds 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 (referred to as "transition" in the project name). Based on the questionnaires that transition postdocs and their supervisors completed for the SystemsX.ch self-evaluation, 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. Furthermore, and as in the case of IPhDs, the sense of belonging to a community and having chances to network and interact was mentioned as a great advantage. The host lab PIs remarked that transition postdocs impacted the way the whole lab did research in many cases (e.g. quantitative approaches in labs that were thus far more biologycentered, or development of software or techniques that the whole lab uses). PIs also stressed the advantage of interdisciplinarity being embedded in the lab vs. being achieved through collaborations with other labs. Of all PIs that answered the questionnaire, none stated any disadvantages of this program.

In the beginning, projects of this type tend to start slower, as acquiring the new knowledge and skills takes time. However, gaining expertise in the new discipline is extremely beneficial towards the end of the project and for the future career steps of the TPdF. With this funding vehicle the TPdF supervisors also benefit, as they have the opportunity to attract someone with new skills to their labs and can benefit from the new line of research.

### **3.3.2 Events**

Originally, 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). After a pause in 2014, when no retreat was organized, 2015 SystemsX.ch welcomed 35 participants in 2015, 41 in 2016, and in 2017 22 students and postdocs attended the retreat.

The summer, autumn and winter schools (co-)organized by SystemsX.ch and the SIB have all received very good feedback from the participants. The upcoming autumn school in machine learning, the last that will be jointly organized, was booked out within a few days of being announced.

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

#### **3.3.2.1 All SystemsX.ch Day**

On September 1, 2016, almost 200 people working in the field of systems biology gathered in Bern to participate in the 7<sup>th</sup> All SystemsX.ch Day. The PhD students and postdocs involved in SystemsX.ch research projects were represented in high numbers, and almost 90 of them presented posters to share and discuss their research projects. Some of the posters were selected for flash talks, in which the scientist had 90 seconds and one slide to summarize the poster.

#### **3.3.2.2 SystemsX.ch Retreat 2017**

The retreat has established a reputation as the main SystemsX.ch event for PhD students and postdocs. Since 2012, SystemsX.ch decided to shift the emphasis away from science itself and focus on strengthening soft skills. Building on the success of the 2012, 2013, 2015 and 2016 retreats, where topics such as collaboration and communication between scientists, addressing diversity in research or career development for young scientists were addressed, the 2017 retreat focused on presentation skills.

Coaching expert Sašo Kočevar and his team from hfp consulting were invited to lead the workshops for the fifth time. The Retreat in May 2017 was held in Kandersteg, where the 22 participating young researchers learnt more about how to prepare and deliver a presentation, connect with their audience, or confront individual challenges, such as stage fright or impostor syndrome. The retreat also gave participants plenty of time to interact with other young scientists working in the field of systems biology. This workshop was very well received, although the number of registrations was clearly reduced compared to previous years. This probably reflects two issues: the fact that there are gradually fewer active PhD students in SystemsX.ch projects, as well as, probably, a certain saturation among the PhD student community, with most students attending several retreats every year (department, institute, funding network).

#### **3.3.2.3 Workshop in Leadership and Management Skills for Postdocs**

For the third time, SystemsX.ch organized a Leadership and Management Skills workshop exclusively for postdocs in November 2016. 15 participants attended the two-day course,

which took place in Muri bei Bern. The highly interactive workshop was designed and conducted in a way that will considerably influence and support both the present scientific work and future careers of participating postdocs. The workshop was very well received. Based on the very positive feedback of the first two editions, a one-day follow-up of the February 2016 event was organized the day before the workshop. This follow-up, however, was very poorly attended. There are currently no plans to organize a final edition of the workshop in 2018.

#### **3.3.2.4 Joint SIB/SystemsX.ch Machine Learning Course 2016**

Following the initiative of the Next Generation Sequencing Discussion Group of the UZH, SystemsX.ch and the SIB co-organized a course in Machine Learning for Bioinformatics and Computational Biology in November 2016. The course gave an introduction to machine learning techniques and approaches, and dedicated three days to hands-on exercises on different topics. 36 young researchers from Switzerland and abroad took part in the intensive course from November 21-25, 2016 at the Irchel Campus in Zurich and took home new concepts and machine learning knowledge that they will be able to apply in their own scientific research. The very positive feedback received for this course guided the decision to organize an autumn school in November 2017 on a similar topic (machine learning applied to systems biology).

➔ **Conclusion:** In this reporting year, 225 PhD students have been educated within SystemsX.ch projects (RTDs, MRDs, TFs, Special Opportunities and IPhD Projects). 41 IPhD students have been supervised by at least two supervisors from different disciplines, carrying out projects at the interface of different scientific domains. Most IPhD projects need a fourth year to accomplish the planned milestones because of individual reasons. The educational events organized during this reporting period have been a great success, as seen through the number of participants and the feedback they have given.

### **3.4 Public-Private Partnership**

Partnerships with industry were originally one of the priorities of the initiative. In both SystemsX.ch committees, BoD and SEB, two representatives from industry were invited as guests to ensure that public-private-partnerships were efficiently implemented. In addition, the FMI, which is core-funded by the Novartis Foundation and academically affiliated with the University of Basel, became one of the earliest SystemsX.ch partners in 2007. All of the FMI projects had collaborative links to Novartis.

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).

In order to foster collaboration between academic and private research groups, SystemsX.ch organized several events (e.g. Industry Day, SME Workshop), participated actively at biotech fairs (MipTec), connected to the Swiss Biotech Association (SBA) and visited numerous companies right from the beginning. For example, the SME-SystemsX.ch workshops were held jointly with the SBA and local university tech-transfer offices to present both sides with their needs and requests. Similar events with industry were organized but did not take place due to the low number of registrations. In 2012, an “Entrepreneur in Residence” (Michael Dillhoyon) visited various SystemsX.ch research groups as an innovation scout to find appropriate private partners. As the interest of the private sector was vague, the decision was made to concentrate on supporting spin-off companies.

By setting up particular project types (BIP, ISA, TF and Special Opportunities), the involvement of the private sector has been fostered by SystemsX.ch. 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. Following the 6<sup>th</sup>, 9<sup>th</sup> and 10<sup>th</sup> call for proposals, eight TF projects were approved. In total, 77 private groups (121 including groups from the Friedrich Miescher Institute, FMI) were included in submitted proposals, and 24 (38 including the FMI) have participated in approved projects. A total of 13 private groups (including 9 groups from the FMI and 3 from IBM Research Lab Zurich) are co-PIs on RTD and MRD Projects. The collaborations with industrial partners of all active SystemsX.ch projects are listed in Tables A28-A31, Appendix A.

In total, 29 private co-PIs contributed to SystemsX.ch projects (for a complete list see Appendix D, Table D46). Almost 50% (13 out of 30 PI) of all large projects (RTDs, MRDs) reported that at least one co-PI of the consortium was a private partner (i.e. receiving no SystemsX.ch money but providing expenses via the company). Their main motivation was the access to advanced methods and technology, as well as access to relevant data. Half of the PIs are of the opinion that the industry partner definitely benefitted from the collaboration and that the expectations were met (public -> private), while 40% stated that their own research group benefitted from the collaboration (private -> public). Only in one case did the research group cease collaboration with the respective private partner.

Despite a variety of measures aimed at initiating public-private partnerships, there is a large discrepancy between the planned and realized 3<sup>rd</sup> Party Funding. Nevertheless, a considerable number of collaborations kicked-off by SystemsX.ch turned out to be sustainable: no fewer than 77% of the collaborations continued after SystemsX.ch funding ended.

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 16 BIP projects in three years 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 demonstrate a limited effectiveness: only eight projects (out of 17 submitted proposals) were funded over three years, suggesting that the interest in public-private collaborations in the field of systems biology had decreased. Co-PIs from both the academic and the private partners acknowledge that the collaboration is challenging, but also enriching and valuable. Researchers from the private sector participate in several RTD, MRD, Special Opportunities and IPhD Projects, showing that the private sector is interested in systems biology and in nurturing the relationship with academia. SystemsX.ch welcomed IBM Research Lab Zurich as a partner institution in 2015, further proving the importance of the discipline for the industry.

### 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 except for Igor Pivkin 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.



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.** RTDs and German research groups currently benefiting from the Consortial Agreement between the 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 Koeppl, TU Darmstadt
MorphoGenetiX	Damian Brunner, University of Zurich	Richard Smith, MPI Cologne

Moreover, throughout the initiative there has been a steady presence of foreign research groups who have acted as co-applicants on proposals for SystemsX.ch projects (from four co-applicants in the 31 proposals submitted to the 1<sup>st</sup> Call for Proposals in 2007, to five in the 25 proposals submitted to the 8<sup>th</sup> Call in 2013 (the last call for RTD proposals) and four in 31 MRD proposals submitted to the 10<sup>th</sup> Call in 2014). The participation of students from abroad in the educational activities organized by SystemsX.ch also confirms the international visibility of the initiative.

SystemsX.ch supported, within the PhosphoNetX RTD of the first phase, the development of the SWATH mass spectrometry technology. This technology is at the core of the ProCan center which was opened in 2016 in Australia, dedicated to analyzing proteomics in cancer. ProCan became in 2016 an integral part of the Cancer Moonshot program launched by Vicepresident Joe Biden in the frame of President Barack Obama's personalized health initiative. Tiannan Guo, a former postdoc on the PhosphoNetPPM RTD, has become the scientific director of ProCan, which further highlights the central role played by the scientific developments of PhosphoNetX and PhosphoNetPPM in the establishment of the center.

In this reporting period, SystemsX.ch has supported several international conferences and events, which have further contributed to the international visibility of the initiative:

- International Conference on Systems Biology, September 16-20, 2016 (Barcelona)
- EPD 30<sup>th</sup> Anniversary Symposium, September 29-30, 2016 (Lausanne)
- Physics of Biology 2, November 23-25, 2016 (Geneva)
- LS2 Annual Meeting 2017, February 2-3, 2017 (Zurich)
- 1<sup>st</sup> HUPO-HIPP Workshop, May 4-5, 2017 (Zurich)
- Systlms, May 14-17, 2017 (Ascona)
- FMI-IGC joint grad student retreat, May 27-31, 2017 (Lisbon)
- SWATH Targeted Proteomics Course, June 26-30, 2017 (Zurich)
- Systems Biology of Human Diseases, July 5-7, 2017 (Heidelberg)
- Systems Biology of the Brain workshop, September 11-12, 2017 (Fribourg)
- Shaping the Future of Bioengineering summer school, September 10-16 (Davos)
- BC<sup>2</sup> 2017, September 12-15, 2017 (Basel)
- Cell Dynamics in Plant Development and Evolution symposium, November 30-December 1, 2017 (Zurich)

Last but not least, funding of high-impact research projects itself added to continued international recognition of Swiss systems biology research and led to international collaborations: 45% of the PIs and co-PIs of SystemsX.ch projects, who stated that their participation in Sys-

temsX.ch opened up new opportunities, referred to international collaborations, be it new foreign research partners, EU funding of follow-up projects or increased international visibility.

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

### 3.6 Impact of SystemsX.ch

SystemsX.ch has had a clear and lasting impact on the life sciences research landscape in Switzerland over the past 10 years. This impact, while in many cases indirect, has been both on the structural and on the scientific level.

#### Structural impact

On a structural level, 12 out of 15 institutions established new departments (4), units (4), facilities or competence centers (10) with a focus on systems biology. Examples are the Department of Computational Biology at UniL or the new Proteomics and Imaging Facility at UniBas. More than 60 new research groups in the field of systems biology were created at the partner institutions, led by 24 full professors, 11 associate professors, 15 assistant professors, 8 SNF professors and 9 group leaders. About half of them were educated as nonbiologists (i.e. in computational biology, bioinformatics/ modeling, scientific computing, bioengineering, mathematics/statistics, physics or analytics). Christian von Mering and Lucas Pelkmans are two cases in point who, after their non-tenure track assistant professorships, both got faculty positions within the University Research Priority Program for Systems Biology of UZH.

SystemsX.ch institutions reported investing more than CHF 75 million in equipment and devices enabling systems biology research. More than 80% of the invested infrastructure and equipment is made accessible to other research groups within the home institution, and more than half is offered to researchers outwith.

#### Scientific impact

In scientific terms, SystemsX.ch successfully promoted the shift towards a quantitative research approach in life sciences by means of targeted research funding. Within the SystemsX.ch funded projects, novel insights into a variety of complex biological networks were gained that are of high scientific and societal impact, for example concerning the growth of plants or the pathogenesis of prostate cancer.

Each year, approximately 1000 researchers contributed to SystemsX.ch projects. In total more than 2'100 people were involved in SystemsX.ch funded projects: 234 professors, 213 senior researchers, 575 postdocs, 237 technicians, 557 PhD students, 69 research assistants, 128 administrators and 42 other personnel. The information on the function of 59 people was not available.

Output performance as measured by bibliometric studies of SystemsX.ch-acknowledged publications (see Appendix E) show an increase over the years with a peak in 2012. SystemsX.ch researchers published in high impact journals more than twice as often as the world average. This can, for example, be compared to the UK's score, which is only 27% above the world average. This shows that SystemsX.ch publications are of high impact and that SystemsX.ch researchers are internationally competitive. More than 1400 publications have acknowledged SystemsX.ch as their funding source, more than 120 of them in high-ranked journals such as Cell, Nature or Science.

#### Community building

A major impact of SystemsX.ch is that several hundred research groups elaborated and submitted interdisciplinary research proposals, leading to almost 250 projects being approved and funded within the initiative. Almost half of the groups that participate in SystemsX.ch projects are involved in a large inter-institutional RTD or MRD Project. In fact, most

PIs reported, through the surveys completed for the self-evaluation of SystemsX.ch, that they had acquired new collaboration partners through their participation in projects of the initiative. Progress in the area of education has been made not only due to the organization of SystemsX.ch educational events (retreats, workshops, summer schools).

The active, well-connected systems biology community which has established itself over the past 10 years will live on after the completion of the initiative, and will be an important success factor for future systems biology research. In fact, the establishment of a Swiss-wide systems biology research network is seen as the most important legacy of SystemsX.ch, as many of the statements from researchers and partners indicate. The creation of the Swiss Society of Systems Biology as a section of LS2 is a further step in this direction.

### **Support of events and educational activities**

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, the Retreat of the Systems Biology PhD Program of the Life Science Zurich Graduate School, and the yearly Conference of the International PhD Program in Basic and Applied Life Sciences of the University of Geneva have all been supported by SystemsX.ch several times.

Moreover, SystemsX.ch 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 Systems Biology of the Brain workshop (Fribourg, September 2017), the 1<sup>st</sup> HUPO-HIPP Workshop (Zurich, May 2017) and the 2<sup>nd</sup> Physics of Biology meeting (Geneva, November 2016). The numerous requests for support received by the MO show that the initiative is well-known and appreciated (see Appendix A Table A48).

### **Integration of systems biology into academic curricula**

Another evidence of the impact of SystemsX.ch are the efforts that several partner institutions have undertaken to integrate systems biology into graduate 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 has promoted new programs at some of the partner institutions. 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.

### **Establishment of IT research support units**

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

- S<sup>3</sup>IT (Service and Support for Science IT), led originally by Peter Kunszt and since January 2016 by Marcel Riedi, 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.
- University of Bern created Science IT Support (SciITS), led by Sigve Haug, in 2016.

### **Publication record of SystemsX.ch projects**

Although often discussed controversially, publication records in high-impact journals are one of the main indicators for measuring research performance. To be able to quantify the performance of SystemsX.ch researchers, the publications resulting from projects funded by the initiative were analyzed in detail by CWTS Leiden (see Appendix B). Out of the 248 SystemsX.ch funded projects, an excellent publication record of 1419 publications resulted.

This number includes all publications that have been reported up to July 2016 and only includes publications that acknowledge SystemsX.ch explicitly and joint publications authored

by at least two groups involved in SystemsX.ch projects.

The SystemsX.ch Scientific Executive Board put together a short list of highly regarded publications of SystemsX.ch projects. These publications are regarded as having the deepest conceptual impact among the SystemsX.ch publication, independent of the impact factor of their journals:

1. Wu Y, Williams EG, Dubuis S, Mottis A, Jovaisaite V, Houten SM, Argmann CA, Faridi P, Wolski W, Kutalik Z, Zamboni N, Auwerx J, Aebersold R. (2014), *Multilayered genetic and omics dissection of mitochondrial activity in a mouse reference population*. **Cell** **158** (6), 1415-1430, 10.1016/j.cell.2014.07.039, **AgingX**
2. Battich N, Stoeger T, Pelkmans L. (2015), *Control of Transcript Variability in Single Mammalian Cells*. **Cell**. **163** (7), 1569-610, 10.1016/j.cell.2015.11.018, **PhosphoNetX**, **PhosphoNetPPM**, **InfectX**, **LipidX**, **PrionX**, **MorphogenetiX**
3. Kierzkowski D, Nakayama N, Routier-Kierzkowska AL, Weber A, Bayer E, Schorderet M, Reinhardt D, Kuhlemeier C, Smith RS. (2012) *Elastic domains regulate growth and organogenesis in the plant shoot apical meristem*. **Science** **335** (6072), 1096-1099, **PlantGrowth**
4. Picotti P, Clément-Ziza M, Lam H, Campbell DS, Schmidt A, Deutsch EW, Röst H, Sun Z, Rinner O, Reiter L, Shen Q, Michaelson JJ, Frei A, Alberti S, Kusebauch U, Wollscheid B, Moritz RL, Beyer A, Aebersold R. (2013), *A complete mass-spectrometric map of the yeast proteome applied to quantitative tranalysis*. **Nature**, **494**(7436), 266-270, **PhosphoNetPPM**
5. Stadler MB, Murr R, Burger L, Ivanek R, Lienert F, Schöler A, van Nimwegen E, Wirbelauer C, Oakeley EJ, Gaidatzis D, Tiwari VK, Schübeler D. (2011), *DNA-binding factors shape the mouse methylome at distal regulatory regions*. **Nature** **480** (7378), 490-495, 10.1038/nature10716, **MetastasiX**, **Cell Plasticity**

To measure not only the output but also the impact of research funded by SystemsX.ch, the CWTS in Leiden was mandated to conduct a bibliometric performance analysis of all publications captured in Web of Science (WoS) that explicitly acknowledge SysteemsX.ch funding. In total, 1245 acknowledged publications were identified in Web of Science, from which 1145 qualified for analysis.

From 2009 onwards, a continuous increase in publications was observed, with the highest number of 210 publications in 2012. This peak reflects the publications generated by the RTDs of the first phase. In the following years the totals dropped slightly. Over the next few years, a new peak is to be expected as the running RTD and MRD projects publish their results.

As the mean normalized journal score (MNJS) shows, SystemsX.ch researchers have their results published in high impact journals. The MNJS for the whole sample is 2.14 – more than two times the world average, and in the case of PhosphoNetX/PhosphoNetPPM even four times the world average. Furthermore, 75% of SystemsX.ch publications involve collaboration between at least two institutions, and 55% involve international collaboration. Also, the impact is high, as a mean field normalized citation score (MNCS) of 2.35 indicates: For the whole sample, the impact is more than two times the world average, and for two of the projects it is even four to five times world average. The PPTop10 indicator, which is less sensitive to outliers, confirms the high impact: 32% of SystemsX.ch publications (i.e. 366 publications) rank in the top 10% of highly cited publications, which is more than three times the expected 10%. Furthermore, an international comparison shows that that the impact of SystemsX.ch publications is more than two times world average (MNCS of 2.48), compared to 20% above world average in Germany or 38% in UK.

In addition, SystemsX.ch has had an impact 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 (CyTOF™) 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, many PhD students graduating from SystemsX.ch projects continue their training in the best systems biology programs worldwide.
- Sixth, the dual supervision of IPhD students to educate them in a truly interdisciplinary manner resulted in very positive feedbacks from both the students and the supervisors.
- Seventh, the unique availability of funds to train postdocs in new and complementary disciplines, through TPdFs, has received excellent feedback both from postdocs and supervisors. Importantly, it has been remarked that the actual format of IPhD Projects and TPdFs has been a major and successful innovation of SystemsX.ch. To our knowledge, there had been no comparable funding instruments for promoting the interdisciplinary training of young scientists in Switzerland prior to SystemsX.ch. Several different members of the community have reported plans to create similar fellowships within different programs (national research initiatives, e.g. PHRT; institutional programs, e.g. at EPFL).
- Eighth, several TPdFs and postdocs from RTD Projects have become group leaders or professors at prestigious institutions:
  - Marcus Basan (assistant professor, Harvard Medical School)
  - Christoph Zechner (group leader, Max Planck Institute, Dresden)
  - Prisca Liberali (group leader, FMI)
  - Serge Pelet (SNF professor, UniL)
  - Manfred Claassen (assistant professor, ETHZ)
  - Matthias Erb (assistant professor, UniBE)
  - Alex Ebhardt (group leader, University College Dublin)
  - Selman Sakar Mahmut (assistant professor, EPFL)
  - Agata Burian (group leader, University of Katowice)
  - Ewa Szczurek (assistant professor, University of Warsaw)
  - Arnault Graindorge (Maître de conference, University of Montpellier)
  - Hannes Link (group leader, MPI Marburg)
  - Alberto Busetto (assistant professor, University of California, Santa Barbara)
  - Markus Geuking (assistant professor, University of Calgary)
  - Abdullah Karaman (professor, Koc University, Istanbul)
  - Mireia Coscolla (group leader, University of Valencia)
  - Anne Lise Routier (assistant professor, University of Montreal)
  - Keir Menzies (assistant professor, University of Ottawa)

- Ninth, 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.
- Tenth, young assistant and SNF professors involved in SystemsX.ch projects have been tenured or moved on to associate or full professorships at different institutions:
  - Bernd Bodenmiller (UZH)
  - David Gatfield (UniL)
  - Vincent Zoete (UniL)
  - Clemens Cabernard (University of Washington, Seattle)
  - Lars Hangartner (The Scripps Research Institute, La Jolla, California)
  - Olivier Pertz (UniBE)
  - Savas Tay (University of Chicago)
  - Kathleen McCoy (full professor, University of Calgary)
  - Robbie Loewith (full professor, ETHZ)
  - Jörg Stelling (full professor, ETHZ)

The success of the initiative can also be measured by scientific excellence. Certainly the impressive list of publications by scientists involved in SystemsX.ch projects is one such measure. 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 scientists who received **SNSF Professorships**. In 2017, IPhD co-PI Josh Payne became SNSF Professor at ETHZ. Between 2007 and 2015, 24 current and former SystemsX.ch scientists received SNSF professorships. The full list can be found in Appendix D, table D40.
- the number of SystemsX.ch scientists who received **ERC Grants**. In 2016-2017, the following SystemsX.ch researchers were awarded ERC grants:
  - ERC Advanced Grants: Susan Gasser, Laurent Keller, Mustafa Khammash, Cris Kuhlemeier, Andrew Macpherson, Ralph Müller, Bradley Nelson, Andreas Wagner, Renato Zenobi.
  - ERC Consolidator Grant: Michael Bronstein, Beat Fierz, Sebastian Maerkl.
  - ERC Starter Grant: Prisca Liberali, Matthias Erb, Mahmut Selman Sakar, Bruno Correia. It's particularly encouraging to note that the first three were originally postdocs within SystemsX.ch projects, which highlights the impact that the initiative has had in promoting the career of talented young scientists.

Between 2007 and 2015, senior SystemsX.ch researchers received 60 Advanced or Consolidator ERC grants and junior SystemsX.ch researchers received 29 Starting ERC grants. The full list of SystemsX.ch scientists who were awarded ERC grants between 2007 and 2015 is shown in Appendix D, Table D39. Please note that in 2014, researchers based in Switzerland were not eligible for ERC grants.

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 published to mark the 200 year anniversary of Swiss Academy of Sciences (SAS, scnat). (Alban Frei: Biografie eines Netzwerks. SystemsX und naturwissenschaftliches Forschen im 21. Jahrhundert. In: Patrick Kupper, Bernhard C. Schär (Hg.): Die Naturforschenden. Auf der Suche nach Wissen über die Schweiz und die Welt, 1800–2015. Baden: hier + jetzt 2015, p. 257 – 271.)

In September 2017, SystemsX.ch launched a documentary film and an interactive touchbook which aim to bring systems biology closer to the general public. Both communication tools should educate the general population, with a special focus on secondary school students, on the paradigm shift in life sciences research, as well as on the importance of interdisciplinary research. Moreover, they will contribute towards the transparency about the use of public money for funding research.

➔ **Conclusion:** A very large number of indicators attest to the impact that SystemsX.ch has had on the life sciences research landscape in Switzerland since 2007. In the phasing out of the initiative it is crucial to continue the successfully launched paradigm shift and to further solidify the international network and visibility of SystemsX.ch.

## 4 Outlook 2017 and 2018

### **Autumn School in Machine Learning Applied to Systems Biology (SystemsX.ch and SIB)**

SystemsX.ch and the SIB are jointly organizing an introductory course which will provide a hands-on introduction to machine learning, and include sessions led by biologists that use machine learning techniques in their research. The course will take place from November 19-24, 2017 in Schwarzenbach. The course is designed for up to 30 PhD students and postdocs from SystemsX.ch and the SIB Training Network, with some places available for scientists from outside Switzerland.

### **Impact Analysis**

The SERI is carrying out an Impact Analysis of SystemsX.ch. According to the concept elaborated by the SERI, within this analysis SystemsX.ch elaborated a self-evaluation, which included quantitative and qualitative assessments of the achievements of the initiative, with a focus on the objectives set out in 2007. The results of the impact analysis carried out by the SERI will be published during 2018.

### **Documentary film and touchbook**

The distribution and marketing of the documentary film and touchbook about SystemsX.ch will continue. Film screening events open to the public are being organized at several partner institutions, and several contacts have been undertaken with the media to try and increase the exposure of the film or of the projects therein. Secondary school teacher associations will also be contacted to inform them about the documentary and the touchbook, as they could be useful educational tools for Gymnasium students.

### **Swiss Society of Systems Biology**

The SEB and the SystemsX.ch PIs agreed to create the Swiss Society of Systems Biology, structured as a section of LS2. This will allow the organization of a yearly symposium within the frame of the LS2 Annual Meetings. The first symposium will be celebrated in February 2018 in Lausanne, the preparations are ongoing. Different communication measures will aim to encourage the SystemsX.ch community to become members of the society.

## 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 externally (until 2014 by Ernst and Young, since 2015 by PricewaterhouseCoopers) 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	Year *				Total	Total
	'08-'12	2013	2014	2015	2016	'13-'16	'08-'16
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	Year *				Total	Year *	Total
	2008	2009	2010	2011	'08-'11	2012	'08-'12
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 were 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.

### Allocation of SystemsX.ch Funds 2008-2018

All CHF 119.7 million (CHF 120.1 million including interest) of the first period 2008-2012 was allocated by November 30, 2012, as decreed by the SERI. The entire amount of CHF 218.5 million (CHF 219.0 million including interest) of the whole period 2008–2016 was allocated by December 31, 2015, as decreed by the SERI. Allocated funds may be used until the end of 2018, and for administrative tasks until 2019.. Table 7 shows SystemsX.ch Funds allocated fund, income and balance 2008-2018.

**Table 7:** SystemsX.ch fund expenses 2008-2018 as allocated up to December 2015 (top), income 2008-2018 (middle) and balance 2008-2018 (bottom).

Expenses 2008-2018	allocated 2008-2016		corr(+) allocat 2016	corr(-) allocat 2016
RTD	131'549'704	60.2%	-	-308'409
MRD	18'587'695	8.5%	-	-
SyBIT	17'549'500	8.0%	-	-
TPdF a)	8'977'706	4.1%	8'297	-1'017
IPhD a)	18'652'270	8.5%	6'013	-93'431
Special Opportunity	3'097'335	1.4%	-	-
Transfer Project	2'097'716	1.0%	-	-
Internat Activities	2'997'528	1.4%	-	-
IPP	3'435'371	1.6%	-	-20'331
BIP	1'843'336	0.8%	-	-22'568
High Tech Funds	1'440'087	0.7%	-	-
SNSF	1'796'400	0.8%	-	-
Event/Workshops/Conf b)	1'665'306	0.8%	-	-4'440
Management Office b)	4'830'271	2.2%	-	-
Repayment pool	450'196	0.2%	-	-
<b>Total</b>	<b>218'970'420</b>	<b>100%</b>	<b>14'310</b>	<b>-450'196</b>

Income 2008-2018			
Source	income total		income 2008-2016
SERI (ETH domaine & CUS)	218'498'800	99.8%	218'498'800
Interests	486'258	0.2%	486'258
<b>Total</b>	<b>218'985'058</b>	<b>100%</b>	<b>218'985'058</b>

Balance 2008-2018			
Item			
Total allocation	218'520'225	99.8%	
Total income	218'985'058	100.0%	
<b>Difference</b>	<b>464'834</b>	<b>0.2%</b>	

a) subject to changes in salary and social taxes

b) plan; changes may occur due to event approval of the SEB and MO personnel fluctuation

## 5.2 Financial report 2008-2016

### SystemsX.ch Funding Income

**Table 8** shows all federal payments made to and from the two SystemsX.ch open accounts for 2016 and summarized over the calendar years 2008–2016, including interest. The payments to SystemsX.ch were made by the SUC and ETH-Board via SNSF.. As of December 2016, the SystemsX.ch open accounts show a cumulated surplus in the amount of CHF 21.8 million.

**Table 8.** 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 2016	SystemsX.ch		01.01.2008 - 31.12.2016	SystemsX.ch	
	Payments	yearly balance		Payments	Total balance
<b>Total Open accounts</b>					
SNSF payments SUK	12'000'000	12'000'000	SNSF payments SUK	108'561'300	108'561'300
SNSF payments ETH-Rat	12'500'000	24'500'000	SNSF payments ETH-Rat	109'937'500	218'498'800
Open account interest	0	24'500'000	Open account interest	486'258	218'985'058
Total payments	-27'357'863	-2'857'863	Total payments	-197'229'840	21'755'218
<b>Total</b>	<b>-2'857'863</b>	<b>-2'857'863</b>	<b>Total</b>	<b>21'755'218</b>	<b>21'755'218</b>

### Approved project funds, payments

SNSF decisions, allocations by the MO and payments for 2016 and summarized over the calendar year 2008-2016 are given in **Table 9**. In 2016, a total of CHF 27.4 million was paid from SystemsX.ch to the partner institutions (including MO and SNSF). Up to December 2016, the SNSF decided on a total amount of CHF 194.3 million, which adds up to CHF 215.6 million, including decisions made by the SEB (2008-2016).

**Table 9.** SNSF-decisions and allocations for SystemsX.ch Funds per project type

Year 2016	SystemsX.ch			01.01.2008 - 31.12.2016	SystemsX.ch		
	SNSF decisions	MO act. Allocation	Payments		SNSF decisions	MO act. Allocation	Payments
Management		600'500	600'500	Management	-	4'118'771	4'118'771
Events (alle Events)		144'584	171'822	Events (alle Events)		1'541'830	1'441'568
SNSF review & admin cost		-	200'000	SNSF review & admin cost		-	1796'400
RTD	-	-423'791	11'940'247	RTD	132'426'309	131'434'322	123'546'441
RTD-HT	-	-	-	RTD-HT	-	1'440'087	1'440'087
SIP	-	-	1'360'000	SIP	17'824'000	17'549'500	16'109'500
IPhD	-	-156'265	2'354'472	IPhD	15'881'857	18'583'423	15'700'438
IPP	-	-20'331	-20'331	IPP	-	3'435'371	3'435'371
BIP	-	-33'068	-22'568	BIP	-	1'843'336	1'843'336
TPdF	-	-99'856	2'013'501	TPdF	6'871'261	8'870'570	7'674'713
SpecOp	-	-15'376	697'037	SpecOp	-	3'081'959	2'636'592
TF	-	-	390'314	TF	2'097'716	2'097'716	2'097'716
IntAct	-	-	1'038'897	IntAct	659'322	2'997'528	2'053'005
MRD	-	-	6'633'972	MRD	18'587'697	18'587'696	13'335'902
<b>Total</b>	-	<b>-3'603</b>	<b>27'357'863</b>	<b>Total</b>	<b>194'348'162</b>	<b>215'582'108</b>	<b>197'229'840</b>

All the budgeted and expended funds for 2016 are given in **Table 10** according to project type, including the MO and the SNSF service fee each as a separate item. The amounts budgeted and reported in 2016 (see in the tables column “Budget” and “Reported”) differ by an over expenditure of +3%. Overall, the initiative has a significant surplus of 11%. 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 2016, SystemsX.ch released a total of CHF 28.3 million for the project types RTD, SIP, IPhD, TPdF, SpecOpp, TF and IntAct and CHF 1.0 million for the Management Office (MO), the Swiss National Science Foundation and Events. The total released amount was CHF 27.4 million. On the other hand, the overall amount of reported SystemsX.ch Funds was CHF 27.6 million. At the end of 2016 there was a balance of CHF 21.8 million.

### **Report of used resources**

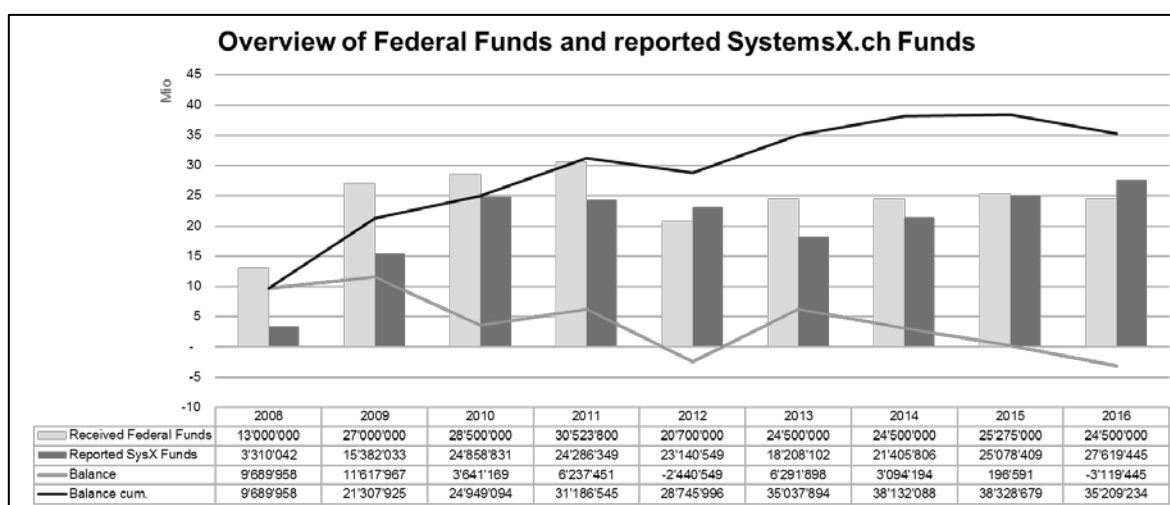
Comparing the cash flow (annual balance) of the Federal Funds to the reported use of funds from projects (all expenditures), one notices that as of yet, aside from the “leap year” in 2012, 2016 is the only other year in which more spending was reported than SystemsX.ch received from the SNSF (see Figure 4).

From 2008–2016, SystemsX.ch received a total of CHF 218.5 million in Federal Funds, whereas within the same time frame, a total of CHF 183.3 million SystemsX.ch Funds were used and reported.

**Table 10. Funding categories per project type (incl. Management, Events, SNSF)**

Year 2016	SystemsX.ch		Own Contribution	Third P	Total
	Budget	Reported	Reported	Reported	Reported
Management	128'500	560'661	458'668	-	1'019'329
Events (all)	411'500	225'492	-	23'871	249'363
SNSF fee	200'000	200'000	-	-	200'000
RTD	13'442'336	12'516'557	16'843'095	716'703	30'076'355
RTD-HT	-	-752	752	-	-
SIP	1'360'000	1'120'988	485'063	-	1'606'052
IPhD	1'675'713	2'481'457	2'554'834	115'731	5'152'021
IPP	-	-154'577	31'330	-	-123'247
BIP	-	-4'593	46'670	-	42'077
TF	315'628	450'682	490'716	529'688	1'471'086
TPdF	964'797	2'403'241	1'135'438	-	3'538'678
SpecOpp	692'413	836'697	850'698	-	1'687'395
IntAct	921'762	750'341	351'121	-	1'101'461
MRD	6'633'972	6'233'252	7'127'760	-	13'361'012
<b>Total</b>	<b>26'746'622</b>	<b>27'619'445</b>	<b>30'376'144</b>	<b>1'385'993</b>	<b>59'381'582</b>

01.01.2008 - 31.12.2016	SystemsX.ch		Own Contribution	Third P	Total
	Budget	Reported	Reported	Reported	Reported
Management	5'689'500	4'390'063	3'151'120	34'135	7'575'318
Events (all)	1'441'500	1'428'961	41'278	204'460	1'674'699
SNSF fee	1'801'000	1'796'400	-	-	1'796'400
RTD	126'395'039	116'533'205	172'176'452	11'448'474	300'158'131
RTD-HT	6'000'000	1'440'087	421'183	-	1'861'270
SIP	16'144'000	16'117'468	5'913'396	60'615	22'091'478
IPhD	14'778'942	14'790'716	15'293'636	270'803	30'355'155
IPP	3'499'178	3'416'827	2'355'178	38'500	5'810'505
BIP	1'882'242	1'843'335	1'420'422	1'119'355	4'383'112
TF	2'097'716	1'863'850	1'399'539	1'911'217	5'174'607
TPdF	6'745'464	6'728'455	3'905'671	-	10'634'126
SpecOpp	2'729'635	2'285'947	1'722'360	-	4'008'307
IntAct	2'252'912	1'355'233	985'976	-	2'341'209
MRD	13'335'902	9'299'022	12'429'087	52'000	21'780'109
<b>Total</b>	<b>204'793'029</b>	<b>183'289'567</b>	<b>221'215'299</b>	<b>15'139'561</b>	<b>419'644'427</b>



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

Over the nine years from 2008–2016, about CHF 123.5 million in SystemsX.ch Funds was paid out to the 34 RTD Projects, CHF 16.1 million to the two SIPs, CHF 15.7 million to 87 IPhD Projects and CHF 13.3 million to 9 MRD Projects. The Management Office, including Events, received CHF 5.6 million and all other project types (including SNSF) CHF 23.0 million (see **Table 11**).

All Own Contributions amount to CHF 221.2 million. The SystemsX.ch community reported the acquisition of more than CHF 15.1 million in 3<sup>rd</sup> Party Funds (plus CHF 5.5 million from FMI and IBM), and CHF 34.4 million in competitive research grants with a synergy and/or collateral benefit (2<sup>nd</sup> Party Funds) for SystemsX.ch.

**Table 11.** Reported use of SystemsX.ch Funds and Own Contributions in CHF for 2008-2016 (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	4'390'063	3'151'120
Events	1'428'961	41'278
SNSF review & admin costs	1'796'400	-
RTD	116'533'205	172'176'452
RTD-HT	1'440'087	421'183
SIP	16'117'468	5'913'396
IPhD	14'790'716	15'293'636
IPP	3'416'827	2'355'178
BIP	1'843'335	1'420'422
TF	1'863'850	1'399'539
TPdF	6'728'455	3'905'671
SpecOpp	2'285'947	1'722'360
IntAct	1'355'233	985'976
MRD	9'299'022	12'429'087
<i>Total</i>	<i>183'289'567</i>	<i>221'215'299</i>

**Table 11 (cont.).** Reported use of SystemsX.ch Funds and Own Contributions in CHF for 2008-2016 (a) per project type, and (b) per cost type.

b)

<i>Cost Type</i>	<i>Reported SystemsX.ch Funds</i>	<i>Reported Own Contributions</i>
Personnel	135'899'914	167'799'643
Consumables	27'315'788	12'251'405
Miscellaneous	8'975'194	5'242'118
Equipment	10'460'905	23'800'812
Infrastructure	-	12'020'700
Various	637'766	100'621
<i>Total</i>	<i>183'289'567</i>	<i>221'215'299</i>

The SystemsX.ch Funds allocated and released to each partner institution are shown in **Table 12**. Please note that selection criteria for SystemsX.ch proposals are “scientific quality” and “added value to Systems Biology”. **Table 12** shows how the CHF 197.2 million paid out are distributed to the SystemsX.ch partner institutions. By December 31, 2016, CHF 183.3 million of SystemsX.ch Funds and CHF 221.2 million of Own Contributions were used and reported.

**Table 12.** allocations and payments of SystemsX.ch Funds and reported Own Contributions per SystemsX.ch partner 2008-2016.

Year 2016	SystemsX.ch		01.01.2008 - 31.12.2016	SystemsX.ch	
	MO act. allocation	Payments		MO act. allocation	Payments
Management	600'500	600'500	Management	4'118'771	4'118'771
Events (all)	103'934	156'322	Events (all)	1'219'942	1'151'330
SNSF fee	-	200'000	SNSF fee	-	1'796'400
EPFL	-380'344	3'166'456	EPFL	29'162'826	26'744'385
ETHZ	-1'405'636	7'293'654	ETHZ	64'142'764	58'759'662
FMI	-32'011	471'640	FMI	4'496'081	4'180'374
PSI	-	105'587	PSI	791'925	738'920
SIB	1'341'513	971'408	SIB	9'398'396	8'535'281
UniBE	-58'589	1'058'763	UniBE	9'190'801	8'147'327
UniBS	11'777	2'884'486	UniBS	27'449'601	25'037'483
UniFR	47'553	619'158	UniFR	2'993'630	2'751'696
UniGE	-514'442	2'535'034	UniGE	16'267'398	14'676'838
UniL	28'899	1'477'956	UniL	11'646'030	10'446'969
UniNE	-	-	UniNE	162'381	162'381
USI	-	232'605	USI	749'877	498'594
UZH	253'242	5'282'159	UZH	32'516'121	28'814'184
ZHAW	-	184'235	ZHAW	847'431	346'411
IBM	-	102'600	IBM	307'800	205'200
others	-	15'300	others	120'333	117'633
RTD-HT undefined	-	-	RTD-HT undefined	-	-
<b>Total</b>	<b>-3'603</b>	<b>27'357'863</b>	<b>Total</b>	<b>215'582'108</b>	<b>197'229'840</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
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