ERASys*APP*
ERA-Net for Applied Systems Biology

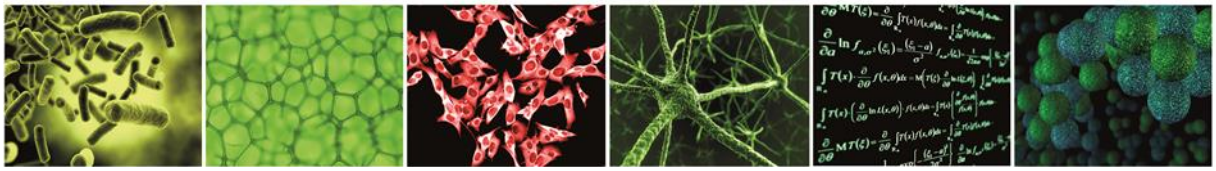

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Table of Contents

Executive summary

Systems biology is a promising research area with the potential to fundamentally change the life sciences. Systems biology can provide answers to major ecological, economic and medical challenges of our time. Using an interdisciplinary approach, systems biology combines cutting-edge experimental methods in biology with knowledge and technologies from the fields of mathematics, computer science, physics and engineering in order to map complex biological processes.

ERASys*APP* is an ERA-NET funded by the European Commission in the 7th Framework Programme from January 2013 to December 2015. It brings together 16 funding and/or management organisations from 13 countries with important activities in the field of systems biology. The central idea of ERASys*APP* was to promote the robust development of systems biology by structuring and coordinating national efforts and investments. Following a period of basic research in systems biology, ERASys*APP* has taken a major step forward by funding research projects addressing industry-relevant issues in order to increase the use of systems biology in industrial research.

Twelve transnational research projects have been funded in two ERASys*APP* calls comprising 71 research groups from 10 countries with a budget of 16,9 Mio € in total for a project duration of three years between October 2014 and December 2018. The ERA-NET consortium organized two **ERASys*APP* Exchange Days** to enhance information exchange on the funded projects, networking of the involved scientists and to encourage them to share existing resources. The modelling of biological systems is based on integration and cross linking of diverse data sets. ERASys*APP* aimed for a data management strategy to provide the funded research projects with support in cross cutting issues related to data handling and storing. **Data management issues** were integrated in ERASys*APP* calls in an early stage ensuring implementation of a solid data management in the research projects funded under ERASys*APP*. In collaboration with the ESFRI ISBE – Infrastructure for Systems Biology Europe ERASys*APP* assisted to establish a data and model management project called **FAIRDOM**. This project (www.fair-dom.org) was funded to support the ERASys*APP* research groups. It represents a single platform which bundles data and model management expertise and offers support in this field. Through FAIR research assets (**F**indable, **A**ccessible, **I**nteroperable, **R**e-usable) applied also in research projects funded by ERASys*APP* a maximum impact can be reached by allowing research assets to be exchanged and re-used more easily between researchers.

By elaborating **a catalogue of currently 89 master- and PhD programs in Europe** with a focus on systems biology and defining a **core curriculum** for a master's program in systems biology, ERASys*APP* contributed to a harmonized education of future systems biologists and to a more transparent educational landscape. By the establishment of an overview of existing web-based learning tools relevant for systems biology and an event calendar ERASysAPP further contributed to education and training in the field of systems biology. By organising six summer courses and five data management related workshops ERASysAPP added to the professional development of nearly 240 researchers.

ERASys*APP* performed a substantial work on **mapping activities** compiling several inventories of **R&D organisations, initiatives and companies related to the field of systems biology**. Another important activity was the organization of four workshops to **enhance the networking between systems biology centers and between academia and industry**. The strategic research agenda based on the ERASysBIO vision paper published in 2008 has been updated. The aim of the "**Systems biology in Europe - Strategic research agenda: an update since 2008**" is to offer a vision on the development of systems biology as a key component of the life sciences in Europe until 2025.

Summary description of the project context and objectives

Systems biology is a promising research area with the potential to fundamentally change the life sciences. Systems biology can provide answers to major ecological, economic and medical challenges of our time. Using an interdisciplinary approach, systems biology combines cutting-edge experimental methods in biology with knowledge and technologies from the fields of mathematics, computer science, physics and engineering in order to map complex biological processes. The experimental findings are used to create quantitative mathematical models, which are tested and validated in iterative cycles of laboratory experiments.

ERASys*APP* is an ERA-NET funded by the European Commission in the 7th Framework Programme from January 2013 to December 2015. It brings together 16 funding and/or management organisations from 13 countries with important activities in the field of systems biology. The central idea of ERASys*APP* was to promote the robust development of systems biology by structuring and coordinating national efforts and investments, taking past successful developments and achievements into account, e.g. ERASysBio and its spin-offs ERASysBio+, SysMO and SysMO2. Following a period of basic research in systems biology, ERASys*APP* has taken a major step forward by funding application-oriented research projects addressing industry-relevant issues in order to increase the use of systems biology in industrial research.

The main objectives in the course of the project were:

1. Setting up joint transnational calls with a focus on translational systems biology and applications to tackle questions on complex biological processes in microorganisms, plants and animals, which are of current and broad interest in the life sciences.
2. The exploration and support of mechanisms to strengthen the academic-industrial links in systems biology in the ERA.
3. The organisation and execution of transnational systems biology networks in the ERA. Whenever possible, networks from outside the ERA shall be approached and integrated to convert ERA networks to global systems biology networks.
4. Execution and organisation of optimised educational and training measures for scientists, PhD students and students in systems biology in the ERA including a scientific exchange programme.
5. The support and adaption of data management systems, data management standards and “good practices” rules for data sharing in the ERA.
6. The establishment, support and maintenance of systems biology research structures in a larger number of countries in the ERA (and worldwide) than in the past to help execute the ongoing and proclaimed paradigm shift towards systems biology in the life sciences while supporting the Knowledge-Based Bio Economy concept.

Description of the main S&T results

Funding of transnational research projects and supporting collaboration

Funding of transnational research projects was one of the most important activities of ERASys*APP*. In its project duration ERASys*APP* implemented two joint transnational calls with a focus on translational aspects of systems biology research relevant for industrial application. In the 1st joint transnational call (JTC-1) in 2013 applied systems biology research on microorganisms, plants and animals including human was addressed by a bottom-up funding approach while in the 2nd joint transnational call (JTC-2) in 2014 applied systems biology research on microorganisms, plants and animals excluding human was addressed by nine broad scientific areas. The proposals covered a wide spectrum of topics within the area of life sciences and biotechnology. In total, 44 proposals were submitted to the two calls involving 244 research groups from 15 countries. Following a one-step evaluation procedure including a rebuttal step **12 projects** were selected to fund **71 research groups from 10 countries with a budget of 16,9 Mio € in total**. The funded research projects run for three years between October 2014 and December 2018.

The modelling of biological systems is based on integration and cross linking of diverse data sets. A key problem is that even if data is available, it tends to be poorly annotated. Therefore, it is unclear how it has been acquired and under what conditions, making re-use for others difficult if not impossible. A solid data management plan is fundamental for the success of systems biology projects. ERASys*APP* aimed for a strategy in the context of data management to provide the funded research projects with support in cross cutting issues related to data handling and storing. **Data management issues** were integrated in ERASys*APP* calls in an early stage ensuring implementation of a solid data management in the research projects funded under ERASys*APP*. A series of webinars were held during the submission phase of both JTCs with the aim to inform the applicants on data management issues, to make clear what is needed in the data management part of the proposal. A short video produced in the ERASys*APP* project contributes to an increased awareness about the benefits of efficient data management. In collaboration with the ESFRI ISBE – Infrastructure for Systems Biology Europe ERASys*APP* assisted to establish a data and model management project called **FAIRDOM**. This project (www.fair-dom.org) was funded to support the ERASys*APP* research groups. It represents a single platform which bundles data and model management expertise and offers support in this field. Moreover, FAIRDOM aims for training of future data managers and coordination of further tool developments in data management systems.

Additionally to the implementation of transnational joint calls a **match making platform** was established to support the formation of project consortia as well as to draft the first stage of a proposal. This tool has been used and appreciated by the applicants in both calls. The Technology Exchange Platform will not be closed at the end of the ERASys*APP* project, it is further available at http://uefiscdi-direct.ro/ERASysAPP/main/index.php.

Since networking between scientists working on projects funded under the ERASys*APP* calls was considered as an important element among the activities aiming to strengthen the systems biology scientific community, the ERA-NET consortium organized two **ERASys*APP* Exchange Days**. Project coordinators introduced their projects or gave an overview on their first achievements. Poster sessions and diverse activities during the breaks provided plenty of possibilities for networking. By organizing these events the ERA-NET consortium contributed not only to exchange information on the funded projects and networking of the involved scientists, but encouraged them to share existing

resources. The reports of both ERASys*APP* Exchange Days can be found on the ERASys*APP* website www.erasysapp.eu/index.php?index=106 and www.erasysapp.eu/index.php?index=121. The ERASys*APP* consortium supported the idea of having additional ERASys*APP* Exchange Days to enhance the networking of the participating scientists beyond the ERASys*APP* project duration. The first steps to prepare a third Exchange Day were taken.

Education and training of the next generation of systems biology researchers

Other important activities were undertaken to promote the **education and training of the next generation of systems biology researchers** and to facilitate the **transfer of well-established scientists to the interdisciplinary field of systems biology**.

A **catalogue of currently 89 master- and PhD programs in Europe** with a focus on systems biology was elaborated. Intentionally, not only study programs on pure systems biology were added, but also related programs that set an important focus on systems biology, e.g. bioinformatics with a major in systems biology. By widening the focus the intention was to reflect the need for interdisciplinary trained life scientists and to create a list that is of interest to a broader target group. Thanks to filtering options, such as main focus of the program, country or language, appropriate offers can easily be found. The Graduate Study Program webpage can be accessed via the following link: www.erasysapp.eu/training-and-exchange/graduate-study-programs. In order to ensure a sustainable investment and to avoid duplication of work that has already been done, ERASys*APP* hands this catalogue over to ISBE, who already embedded the list into the ISBE Community webpage community.isbe.eu/content/graduate-study-programs-catalogue.

The increasing number of masters' programs on systems biology differs a lot in their content und focus. To develop common views on systems biology education and to add to a harmonized educational landscape, ERASyS*APP* determined main criteria of a **systems biology curriculum at master's level**, together with ISBE and the education strategy team of the Gothenburg Centre for Systems Biology. A manuscript entitled '**Strategies for structuring interdisciplinary education in Systems Biology'** was elaborated based on the outcome of two workshops involving representatives of 20 higher education representatives. This paper contains (a) a list of expected competences and skills of student that passed a Systems Biology Masters' program, (b) educational methods and approaches to acquire those skills and (c) possible career paths for graduates of such a program. In order to disseminate the recommendations and make them available to a broad community, the manuscript was submitted to the open-access online journal of the Nature Group, npj Systems Biology and Applications, in October 2015 and will be published online most probably in March 2016.

The interdisciplinary nature of systems biology proposes a challenge to the education and training of future systems biologists. Up to now there is still a lack of qualified teachers who are able to cover the bandwidth of systems biology education and training. The fact that only few adequate text books on systems biology education have been published so far adds to this issue. As a first step, ERASys*APP* set up an overview of existing educational websites on topics relevant for systems biology. Altogether 22 **web-based learning tools**, such as comprehensive online portals, e-courses or video lectures are listed under the following link: www.erasysapp.eu/training-and-exchange/web-based-learning-tools. Each tool was categorized and compared by its type (video lecture, reading material, e-course, audio lecture, and workshop material) and topics (e.g. systems biology, bioinformatics, genetics). As a next step the Systems Biology Educational portal SBEDU was set up at www.sbedu.eu to promote the **sharing and exchange of educational material** and to attract new teachers from disciplines related to

systems biology. The 'sort by' function allows for fast search of relevant article. Transparency regarding the quality of educational material is given by the possibility to evaluate posts. For a long-term visibility of this portal it was added to the "Tools and Resources" section of the ISBE Community website. In addition, an **event calendar** to collect open-access events for researchers was embedded in the ERASys*APP* webpage.

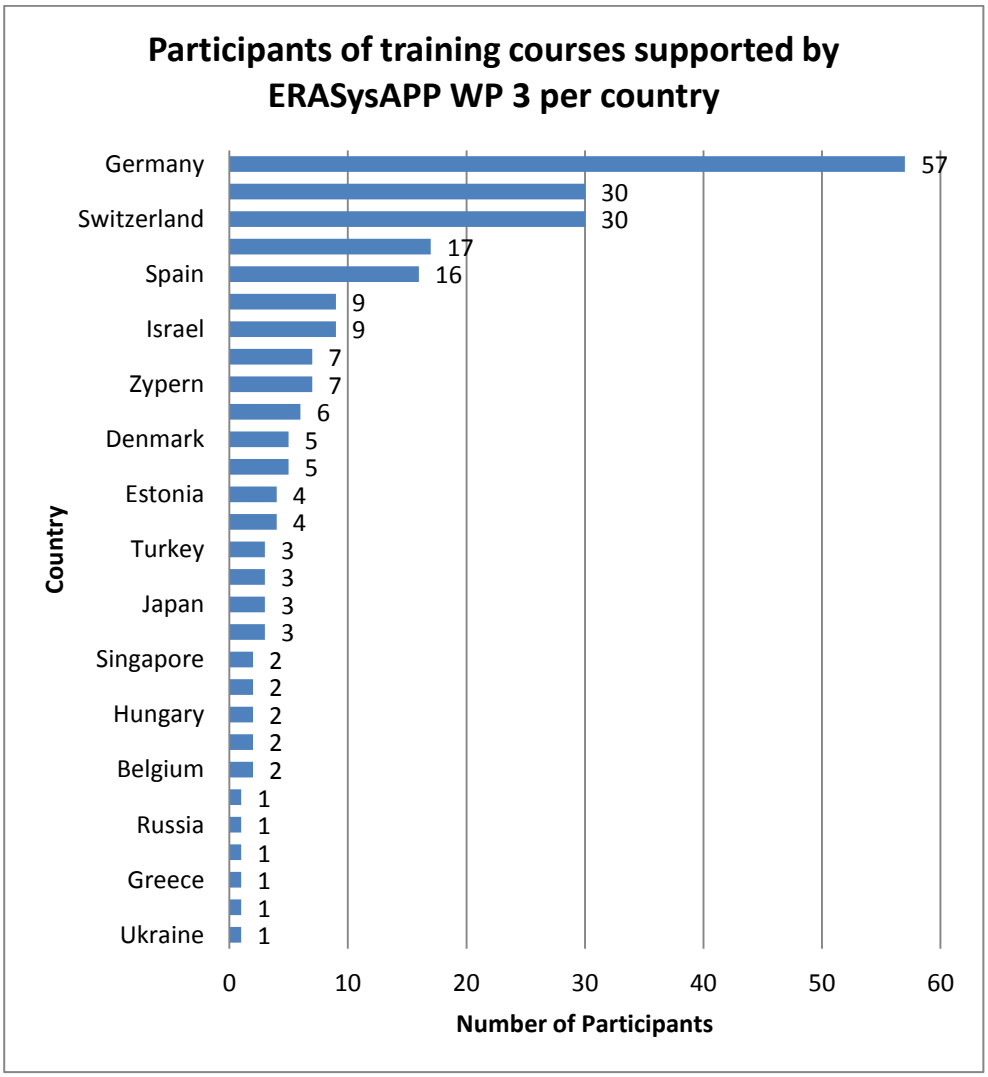
A variety of courses including **six summer schools** and **five data management related workshops** were held. The topics of these events were defined based on an online survey among 270 systems biology researchers and comprised data integration and modelling, reproducible and citable data and models and data management. Mainly PhD students and postdocs attended the courses which bridged the gap between scientists from different disciplines and imparted new knowledge necessary for interdisciplinary research.

Summer School	**Date**	**Location**
Modeling for Systems Biology 2013	9.-14.6.2013	Barcelona, Spain
International Course in Yeast Systems Biology	3.-10.6.2013	Göteburg, Sweden
Advanced Lecture Course on Systems Biology	2.-8.3.2014	Innsbruck, Austria
Stoichiometric and Kinetic Modelling of Biochemical Networks	6.-10.10.2014	Larnaca, Cyprus
Data Integration in the Life Sciences	2.-6.2.2015	Leiden, Netherlands
7th International Practical Course in Systems Biology	1.-12.6. 2015	Göteburg, Sweden
Workshop	**Date**	**Location**
Tutorial-Workshop „Modelling and Simulation of Biological Models"	14.09.2014	Melbourne, Australia
Systems Biology Data Management Foundry: A meeting for practitioners	6-7.10.2014	Heidelberg, Germany
Data Management Information Workshops	Submission period of JTC-1 and JTC-2	webinars
Reproducible and Citable Data and Models Workshop	14-16.09.2015	Rostock-Warnemünde, Germany

The **ERASys*APP* Mobility Program** encouraged ERASys*APP* scientists to make use of the wide variety of knowledge of 71 research groups involved in ERASys*APP* funded research projects. The program supported PhD students, postdocs, technicians and engineers in arranging short-term visits for training purposes to one of the research groups funded by ERASys*APP*. An online survey confirmed

that participants acquired new skills, the collaboration between project partners was significantly improved and progress towards the goals of the projects could be achieved. As hosts encouraged a continuation of the program, ERASysAPP compiled a list or research groups in Europe who are willing to host young researchers for a short period. This list was published online on the ERASysAPP webpages (https://www.erasysapp.eu/training-and-exchange/mobility-of-researchers) and intends to motivate for self-organized laboratory visits in order to foster networking and knowledge-exchange between scientists.

Altogether, ERASys*APP* added to the **professional development of 234 researchers from 29 different countries**. The distribution of participants per country is presented in the Graph 1.



Graph 1:Participants of ERASySAPP supported courses per country

Systems biology in Europe

Besides the usual dissemination activities ERASys*APP* performed a substantial work on **mapping activities** compiling several inventories of **R&D organisations, initiatives and companies related to the field of systems biology**. Another important activity was the organization of four workshops to **enhance the networking between systems biology centers and between academia and industry**. The purpose of the workshops was not only to establish networks of research centers, but also to design new and improved formats for such links. Topics on model systems, collaboration schemes, data exchange and standards, and intellectual property rights were discussed. The main outcomes of these networking workshops served as valuable input for the strategic research agenda of ERASys*APP*.

The strategic research agenda based on the ERASysBIO vision paper published in 2008 has been updated. It reflects back on the progress over the last 10 years in the field of systems biology and gives an overall future vision by formulating recommendations for the next 10 years. The aim of the "**Systems biology in Europe - Strategic research agenda: an update since 2008**" is to offer a vision on the development of systems biology as a key component of the life sciences in Europe until 2025. It is written for scientists, funders, policy makers and industry and aims to provoke, focus discussions and help plan the future. After an overview of the present situation an analysis of how to move forward and what challenges must be faced is followed by concrete recommendations on topics about funding of collaborative research, partnership of academia and industry, management of results of research projects (data, procedures, models, maps, etc.), education and training and the role of European research infrastructures.

Sustainable funding concept

Systems biology and synthetic biology have developed wide intersections with biotechnology within the last two decades. The ERASysAPP consortium joined its efforts with the ERASynBio, the ERA-NET on synthetic biology and ERA-IB2, the ERA-NET for industrial biotechnology to broaden the scientific and technological spectrum of these three ERA-NETs. A workshop on "Future RTD collaborations in Horizon 2020: Needs and expectations of the stakeholders for a long-term sustainable cooperation framework on SB research" was organized to address for the first time the whole value chain of bio-based production and the modern underlying platform technologies. The workshop took place in Berlin, on 6 Nov 2014.

Within the Horizon 2020 Work Programme 2016 - 2017 the European Commission published the topic BIOTEC-1-2016 addressing an **ERA-NET Cofund on Biotechnologies**. In response to this, most of the partners from the ERA-NETs ERASys*APP*, ERASynBio and ERA-IB2 as well as new research funders have joined forces to form the **CoBioTech Consortium** and applied to this call. The consortium will take on the challenge addressed in the topic to "speed-up research and innovation in industrial biotechnology establishing systems biology and synthetic biology as technology drivers" by bringing together a critical mass of funding through a co-funded call.

Potential impact, main dissemination activities and exploitation of results

Twelve transnational research projects have been funded in two ERASys*APP* calls comprising 71 research groups from 10 countries with a budget of 16,9 Mio € in total for a project duration of three years between October 2014 and December 2018. This represents a leverage factor of 8,5-fold for the EC funding of 2 Mio €. All research projects involve an industrial partner which ensures the application-oriented research approach addressing issues relevant for industry. For an efficient exploitation of results a technology transfer office is involved in each research project. It is expected that successfully finished projects will promote the market potential of systems biology.

The joint transnational calls are considered to be a valuable opportunity for **transnational collaboration in the field of systems biology**. Even researchers from countries not participating in the joint transnational call were attracted to join ERASys*APP* applications which indicates the high visibility of ERASys*APP* and the overall interest in the research field and the well-connected scientific community. The transnational collaborations were further enhanced by the networking possibilities provided by ERASys*APP* such as match making platform, mobility programme and ERASys*APP* Exchange Days. Hence, the ERA-NET contributed to the strengthening of the systems biology scientific community in a long term.

By elaborating **a catalogue of currently 89 master- and PhD programs in Europe** with a focus on systems biology and defining a **core curriculum** for a master's program in systems biology, ERASys*APP* contributed to a harmonized education of future systems biologists and to a more transparent educational landscape. By incorporating systems biology in master-level education and postdoctoral training a new generation of researchers will be educated who are able to apply systems biology approaches in the field of life sciences and biotechnology. In a long term it will ensure the success of systems biology leading to more efficient research due to use of computational modelling in the experimental design. ERASys*APP* contributes to the training of systems biology researchers in a practical manner by making available the webpages Graduate Study Program and SBEDU for wider scientific community through the ISBE webpage and by maintaining the established lists beyond the duration of the ERASys*APP* project.

Through close collaboration with the FAIRDOM project **a solid data management system** is applied by the research projects funded under the ERASys*APP* calls, the use of FAIR research assets are encouraged. Research assets of FAIR quality are

- **F**indable: can be searched for after publication
- **A**ccessible: can be read/downloaded by others
- **I**nteroperable: understood clearly in the context of the original experiment
- **R**e-usable: can be used by other researchers.

The science community's attitude to the publication of data has been changed. Instead of coming up with own solutions for the citing of data, FAIRDOM and thus the ERASysAPP data management is intensely cooperating with open access and open data initiatives such as F1000-Research and OpenAire. Citing of data is a part of the ERASysAPP data management, implemented in the FAIRDOM software openSEEK. Furthermore, ERASys*APP* supports the development and usage of community standards for systems biology. A systems biology standards community evolved and became highly self-driven by a cross-section of researchers who focus on standards development from a model

centric view. COMBINE, an initiative that coordinates the development of community standards and formats for computational models and FAIRDOM work closely together to further enhance this field. ERASys*APP* supports the use of standards provided by COMBINE and FAIRDOM in the frame of research projects funded by ERASys*APP*.

Through application of such a comprehensive data management system a maximum impact of investments can be reached allowing research assets to be exchanged and re-used more easily between researchers.

In the future some important activities such as training, education and data management will be addressed by ISBE – Infrastructure Systems Biology Europe and the FAIRDOM project representing a sustainable maintenance of the activities initiated by ERASys*APP*.

The ERASys*APP* consortium members confirmed through their funding commitments that collaboration of funding agencies is a key element in establishing transnational funding programmes. Through the CoBioTech Consortium the development of systems and synthetic biology into a technology driver approach will be promoted in industrial biotechnology. With this the impact of the methodological toolbox of life sciences will be strengthened; systems biology will become used in a wide area of applications positively influencing the economic development in Europe.

Project website and contact details

www.erasysapp.eu

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