



Project n. 503477

Project acronym: SYMBIONIC

Project title: "Coordinating a neuronal cell simulation initiative with ongoing EU-wide Systems Biology programs"

Instrument: Specific Support Action

Thematic Priority: 1 - "LIFE SCIENCES, GENOMICS AND

BIOTECHNOLOGY FOR HEALTH"

# Final Publishable activity report

Period covered: from 1<sup>st</sup> November 2003 to 31<sup>st</sup> October 2005

Date of preparation: November 2005

Start date of project: 1<sup>st</sup> November 2003 Duration: 24 months

Project coordinator name: Ivan Arisi

Project coordinator organization name: Lay Line Genomics SpA

Revision 1

## Project execution

### Summary description of project objectives

SYMBIONIC is a Specific Support Action funded by the European Commission within the 6<sup>th</sup> Framework Program. It is aimed at establishing a European-wide initiative in the field of the Systems Biology (SB) of the neuronal cell. SYMBIONIC is contributing to create an active European network of scientists developing models and carrying on experimental studies of the neuronal cell. The long-term aim of the project, well beyond its official end, was to be the driving force for a future set-up of a European-based exhaustive and reliable computational model of the neuron. The activity of SYMBIONIC is mainly focused on the training and dissemination area and on the coordination of this Action with other European initiatives in the field of SB, in particular the SSA EUSYSBIO. The main objectives of SYMBIONIC are the following:

- Collaborate and coordinate with other European SB initiatives
- Train a new generation of young scientists in neuronal SB, both in the computational and experimental fields
- Disseminate knowledge about the SB of neuronal cell, even to non-specialized audience
- Raise the awareness of biotech/pharmaceutical and computer industries about the great potential of neuronal SB
- Contribute to standards
- Give birth to more ambitious European research and technological projects.

#### Contractors involved

These are the project contractors:

- Lay Line Genomics SpA (LLG), Rome, Italy
- International School for Advanced Studies (SISSA/ISAS), Trieste, Italy
- University of Barcelona (UB), Dept. of Biochemistry and Molecular Biology, Barcelona, Spain.

Lay Line Genomics is the coordinating partner; it is a biotech SME whose activity is focused on neurodegenerative diseases, intracellular antibodies technology and bioinformatics. SISSA is a post-graduate research institute.

About 20 other institutions and industries from Europe and Israel actively collaborate with the project.

#### Coordinator contact details

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## Work performed

The full title of the project is "Coordinating a neuronal cell simulation initiative with ongoing EU-wide Systems Biology programs", because a key point is to coordinate all the existing efforts towards a broad European SB community, which is also the hope of the funding institution. SYMBIONIC closely collaborates with the SSA EUSYSBIO (EUropean SYStems BIOlogy network, www.eusysbio.org) since the beginning, for the main activities. In particular, joint workshops have been co-organized and scientific collaborations contributed to the courses on computational and experimental SB organized by SYMBIONIC in 2004 and 2005.

The SYMBIONIC training program was aimed at forming a new generation of young scientists in the highly inter-disciplinary field of neuronal SB. It was based on two main courses on computational and experimental methodologies for the neuronal SB and on other collaborations. In particular, SYMBIONIC contributed to a practical course on SB funded by the European Science Foundation (ESF), held in Oxford (UK) in September 2004 and organized by the Oxford Brookes University, and to a lecture course in Gosau (Austria) in March 2005, funded by the Federation of European Biochemical Societies (FEBS) and organized by EUSYSBIO.

The first training activity entirely organized by SYMBIONIC, a practical course on "Computational SB of the Neuronal Cell", was held in Trieste in December 2004. The course topics included methodologies to model neuronal shape and development, temporal-spatial properties of molecular networks, synapses, electrical excitation, signaling pathways and metabolism, molecular transport, genetic networks, and sensory transduction. We provided hands-on computer sessions to introduce some of the main softwares and standards used to model biochemical systems. The second course, "Methods, Data Handling and Standards in Neuronal Systems Biology" was held in the same venue in late summer 2005. It focused on the experimental data that are needed to feed the computational models. Methods to produce high- and medium-throughput experimental data will be illustrated and discussed, along with tools to analyse, integrate and model the same data into more comprehensive frameworks, and with the standardized "languages" in which the data need to be outputted or translated to make it more readable and exploitable by the whole scientific community. Both courses contributed to the creation of an effective European network of neuronal systems biologists, starting from the collaboration that the teachers provided to the courses.

An important event in the dissemination strategy was the workshop on "Industrial Perspectives of Systems Biology" in Heidelberg, Germany, satellite event of the ICSB

2004, where SYMBIONIC and EUSYSBIO invited key representatives from the pharmaceutical, biotech and academic world to discuss the role of SB in current research strategies. Another important chance to meet representatives of the industries was a forward look meeting organized by the ESF in Gosau (Austria) in March 2005. This event focused on strategies for sustained Systems Biology training and research programme development in Europe. SYMBIONIC (LLG and UB) participated in this event and tried to secure inclusion of the neuronal diseases, together with the other major pathologies affecting the human kind, among the problems that SB will address in the next future.

The dissemination activity has been carried out first of all through the web site, where we have advertised all the events organized by SYMBIONIC or related to the project, such as the courses and workshop organized by EUSYSBIO. The web site also provides all the available materials (i.e. presentations) related to these events. One of the most effective dissemination methodology was an e-mailing action: this was done by sending brief but carefully designed and informative messages to most of the European research groups leaders working mainly, but not only, in the SB area, to inform them about the project and all the related events.

Two important publications will contribute to disseminate the ideas that were at the basis of SYMBIONIC. An article entitled "SYMBIONIC: a European initiative on the Systems Biology of the neuronal cell" will be published, at the beginning of 2006, on the journal "Transactions on Computational Systems Biology", as a follow-up of the presentation by LLG at the Conference on "Converging Sciences" held in December 2004 in Trento, Italy (see <a href="http://www.unitn.it/events/consci/">http://www.unitn.it/events/consci/</a>). SYMBIONIC has also funded the publication of a supplement to the online journal BMC Neuroscience and devoted to the neuronal SB. The supplement is a collection of reviews. The volume editors are the SYMBIONIC partners: LLG with the help of SISSA, UB and Italian CNR. Most of the authors had been teachers at the courses organized by SYMBIONIC.

#### **End results**

Our hope was to contribute to the creation of a broad European network of research institutions and industries with interdisciplinary expertise in the SB field, able to be a driving force for future ambitious initiatives in modeling the neuronal cell. Compared with the beginning of the project, in the last months of SYMBIONIC we received hints that the neuronal SB was much more acknowledged as a real research field; by then, in fact, the SB approach to the study of the nervous system had began to be trusted as feasible and promising by the research community. During a workshop in Milan (Italy) in May 2005, some of the participants, including some EUSYSBIO partners, proposed to organize a conference on SB and brain in 2006.

The European network of scientists and research groups created through the SYMBIONIC activities are now likely to generate new and more ambitious research projects in the area of SB. The collaborations started during the project (for example by

inviting scientists that we had not met previously as teachers in the courses) already resulted in new project proposals in FP6, involving the project partners.

Project logo and reference to the project public website

URL: www.symbionicproject.org

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# Annex - Final Plan for using and disseminating the knowledge

In the present annex, an overview of the project training and dissemination activities is presented, together with more detailed information pertaining to the single items of this plan.

A careful dissemination of project original ideas, contents and main activities was the basis for creating a network of effective scientific collaborations throughout Europe and beyond it. Raising the interest of several research groups was the first step towards the birth of a critical mass of scientists for future initiatives in the field of neuronal SB. In turn SYMBIONIC was the first step towards a larger European initiative on the modeling of neuronal mechanisms: some new research proposals have already been submitted that involve SYMBIONIC partners, thanks to the connections established by SYMBIONIC collaborations.

(Please note that Sections 1 and 3 are not relevant to the present project, and are therefore not included in this annex, as indicated in the Guidance notes.)

Section 2 - Dissemination of knowledge

Index of the item	Planned/actual dates	Туре	Type of audience	Countries addressed	Size of audience	Partner responsible
1	August 2004	Project web- site	Academia, research, industry	All	Thousands	1
2	August 2004	Flyer	Academia, research, industry	Europe mainly	Thousands	2
3	1-4 September 2004	Course	Scientific graduate education	All	50	4
4	September 2004	Press release	Research, industry	Italy	Hundreds	1
5	October 2004	Direct e- mailing	Academia, research, industry	Europe mainly	Hundreds	1
6	10 October 2004	Workshop	Academia, research, industry	Europe mainly	100	1
7	6-10 December 2004	Course	Scientific graduate education	Europe mainly	50	2
8	16-17 December 2004	Conference	Academia, research, industry	Europe mainly	150	1
9	12-17 March 2005	Poster	Scientific graduate education	Europe mainly	150	1
10	17-18 March 2005	Workshop	Academia, research, industry	Europe mainly	100	1
11	17 March 2005	Workshop	Academia, research, industry	Europe mainly	50	4
12	17-19 March 2005	Poster	Academia, research, industry	Italy mainly	200	2

13	12-13 May 2005	Workshop	Academia, research	Europe mainly	150	2
14	31 August- 3 September 2005	Course	Scientific graduate education	Europe mainly	50	1
15	5 September 2005	Workshop	Academia, research, graduate education	Europe mainly	150	2
16	Beginning 2006	Publication	Academia, research, industry	All	thousands	1
17	Beginning 2006	Publication	Academia, research, industry	All	thousands	1

Following are details about each item in the table, listed as they appear on the table itself, i.e. in chronological order.

1)The web site for the SYMBIONIC project can be seen at:

http://www.symbionicproject.org/

It is currently used to disseminate information and knowledge about the project and its activities, and about related initiatives and events; it is also meant to act as a repository for didactic material (presentations) from the SYMBIONIC courses and from SYMBIONIC-sponsored events. The web site has been designed to be very "light", that is to occupy very little computer memory so as to allow a very fast access and download, even when connecting by an ordinary telephone line from home. Furthermore, all the links and list of items are in text format, in order to enable visually impaired or blind users, who may not employ any special equipment, to navigate the site. The web portal was designed using ASP and is hosted on a Windows 2003 server at SISSA, one of the SYMBIONIC partners, where it will remain also after the end of the project. The URL of the web site has been circulated among a vast group of scientists (see also "direct e-mailing").

2)A flyer containing an overview of neuronal Systems Biology, describing the aims of the SYMBIONIC project and listing its planned activities was printed in 3,000 copies, to be distributed mostly among European research institutions. Circulation of this leaflet started immediately and has continued throughout the whole project, both in person (at conferences, meetings, courses and other events) and by mailing it to potentially interested parties. Also, the leaflet may be downloaded from the SYMBIONIC web site:

http://www.symbionicproject.org/categories.asp?article\_category\_id=5

3)SYMBIONIC contributed to the ESF course on "Modeling Metabolic and Signal Transduction Networks", held in Oxford, UK, September 1<sup>st</sup>-4<sup>th</sup> 2004. The course took place in the same venue as the XIth Workshop of the BioThermoKinetics Study Group (BTK2004), and immediately preceded it. Within these two events, SYMBIONIC sponsored participation of two students and three lecturers. SYMBIONIC is in fact indicated as a sponsor in the URL of the ESF course: http://btk2004.brookes.ac.uk:8080/BTK2004/ESF-Course%20and%20YBTK

Additionally, three lectures were presented, aiming at integrating the more generally-oriented training activity of the ESF course with more neuronal-related aspects of Systems Biology. Presentations of these lectures, by Ivan Arisi, Nicolas Le Novère and Michel Kerszberg, are linked from the SYMBIONIC web site. SYMBIONIC also sponsored the attendance fee of two speakers at the BTK2004 meeting.

4)A first press release about neuronal Systems Biology and the aims of SYMBIONIC appeared in September 2004 on AREA magazine, a journal published by the AREA Science Park Consortium in Trieste, Italy:

http://www.area.trieste.it/html/press/magazine/31/31 17.htm

5)SYMBIONIC, its aims and activities were also advertised by direct e-mailing to at least 200 interested partied throughout Europe (both individual researchers and scientists, and networks of study on Neurobiology, Neuroscience, Biophysics, Bioinformatics and more). The messages were kept as concise as possible while still retaining relevant information, e.g. indication of relevant SYMBIONIC web pages. Wherever possible, messages were addressed personally (rather than mass e-mailing) to better catch the addressee's attention. This mean was especially used to advertise the SYMBIONIC courses in 2004 and 2005.

6)SYMBIONIC co-organized the first EUSYSBIO-SYMBIONIC joint workshop, held in Heidelberg, Germany, October 10<sup>th</sup> 2004.

This took place as a satellite event of the Fifth International Conference on Systems Biology (ICSB 2004) and focused on "Industrial Perspectives of Systems Biology". The event is posted on the web site of the ICSB 2004:

http://www.icsb2004.org/content.php?pageId=591&lang=de&PHPSESSID=2f435a9817610c0 d4585b67f22f4b852. The program can also be downloaded from the SYMBIONIC events web page at

http://www.symbionicproject.org/categories.asp?article\_category\_id=4. The aim of this workshop was to provide experts' views on the industrial potential of the emerging field of Systems Biology. SYMBIONIC contributed with the following speakers and topics:

- Antonino Cattaneo (SISSA, Trieste): "Systems biology and biotechs"
- Michal Linial (Hebrew University, Jerusalem): "Synapse in action from genes to knowledge"
- Jan Torleif Pedersen (Lundbeck, Copenhagen): "The use of Bayesian networks for the identification of molecular mechanisms driving neuronal inflammation and antiinflammation: Requirements for a general systems biology platform that may be useful for describing molecular processes in the brain.)"
- Georg Casari (CellZome, Heidelberg): "Systems biology and drug discovery"

Antonino Cattaneo is a partner, while Michal Linial and Jan Torleif Pedersen are SYMBIONIC participants. Presentations from the workshop that already received the authorization to be published are available on the SYMBIONIC web site at

http://www.symbionicproject.org/Categories.asp?article\_category\_id\_start=4&article\_category\_id=22 and on the EUSYSBIO web site.

7)SYMBIONIC (LLG and SISSA) organized its first course, on "Computational Systems Biology of the Neuronal Cell", in Trieste, Italy, December 6<sup>th</sup>-10<sup>th</sup> 2004. This activity focused on the modeling of intracellular and membrane processes occurring in neurons. It was targeted to 25 graduate and post-graduate students and researchers from different backgrounds (neuroscience, cell biology, medicine, computer science, bioinformatics, and more). Both lectures and hands-on computer sessions were held. The program tried to encompass a broad range of topics that must be included for a comprehensive overview of all the main issues concerning the modeling of a neuronal cell.

All information pertaining to the course were made available on the SYMBIONIC web site (introductory information, objectives of the course, application forms, general information, course program):

http://www.symbionicproject.org/Categories.asp?article\_category\_id\_start=4&article\_category\_id=22. Also presented lectures and tutorials were made available from the same URL.

Information about the course was circulated very widely (see also "direct e-mailing).

8)SYMBIONIC(LLG) actively participated in the Conference on "Converging Sciences" held in Trento, Italy, 16-17 December 2004: <a href="http://www.unitn.it/events/consci/">http://www.unitn.it/events/consci/</a>. The SYMBIONIC initiative was presented to an academic and industrial audience.

Program and presentations, including the one by SYMBIONIC, are linked from: http://www.unitn.it/events/consci/program.htm

9)A poster describing SYMBIONIC's aims and activities has been presented by LLG at the 1st FEBS Advanced Lecture Course on "Systems Biology: from Molecules & Modeling to cells", March 12-17, 2005 in Gosau, Austria. The course was organized by EUSYBIO. The poster is on the project web site:

http://www.symbionicproject.org/Categories.asp?article\_category\_id\_start=4&article\_category\_id=22.

- 10)SYMBIONIC (LLG and UB) participated in a Forward Look meeting on SB organized and supported by the European Science Foundation (ESF) that took place in the same venue of the FEBS course on March 17-18 2005. This workshop focused on strategies for sustained Systems Biology training and research programme development in Europe.
- 11)Immediately following the FEBS course cited above, SYMBIONIC organized another satellite event, a half-a-day workshop on neuronal SB, in the same venue, on March 17 2005.
- 12)SYMBIONIC (SISSA) presented a poster on the project during the Annual Italian Bioinformatics meeting (BITS) from March 17-19 2005, in Milano, Italy. <a href="http://www.itb.cnr.it/bits2005/abstract\_p.html">http://www.itb.cnr.it/bits2005/abstract\_p.html</a>
- 13)SYMBIONIC (LLG) co-sponsored and international Workshop on Systems Biology from May 12-13 2005 in Milano, Italy. SISSA gave also a seminar on the "Systems Biology of the Neuronal Cell". <a href="http://www.sysbio-italy.org/interno.asp?sez=b">http://www.sysbio-italy.org/interno.asp?sez=b</a>
- 14)The second SYMBIONIC course took place from August 31-September 3 2005 and was devoted to the experimental aspects of neuronal Systems Biology. It was organized by SISSA and LLG, with scientific contributions of UB. The course structure was similar to the first one, was in the same venue and included the use of practical sessions. The course provided the students with an overview of the high-throughput techniques for large-scale data production that are most relevant in view of producing comprehensive *in silico* models of neurons. Also, an overview of the available methods to standardize and structure the output of such high-throughput techniques, for optimal data exchange and mining was presented. All information pertaining to the course were made available on the SYMBIONIC web site (introductory information, objectives of the course, application forms, general information, course program):

http://www.symbionicproject.org/Categories.asp?article\_category\_id\_start=4&article\_category\_id=22. Also presented lectures and tutorials were made available from the same URL.

Also in this case advertisements for the course were circulated very widely (see also "direct emailing) and reached over 200 European research groups working on SB programs.

15)The SYMBIONIC course in Trieste, Italy, was followed by an international workshop on neurogenomics, on September 5 2005, that was also attended by 10 course students. The course was co-organized and co-sponsored by SYMBIONIC. The presentations are available at <a href="http://www.symbionicproject.org/Categories.asp?article\_category\_id\_start=4&article\_category\_id=41">http://www.symbionicproject.org/Categories.asp?article\_category\_id\_start=4&article\_category\_id=41</a>

16)An article entitled "SYMBIONIC: a European initiative on the Systems Biology of the neuronal cell" will be published, probably at beginning 2006 on the journal "Transactions on Computational Systems Biology", as a follow-up of the presentation by LLG at the Conference on "Converging Sciences" held in December 2004 in Trento, Italy (see <a href="http://www.unitn.it/events/consci/">http://www.unitn.it/events/consci/</a>).

17)SYMBIONIC has funded the publication of a supplement to the online journal BMC Neuroscience and devoted to the neuronal SB. The supplement is a collection of reviews. This volume is edited by LLG with the help of SISSA, UB and Italian CNR. Most of the authors had been teachers at the courses organized by SYMBIONIC.