

European Science Foundation
Standing Committee for Life, Earth and Environmental Sciences (LESC)



ESF LESC EXPLORATORY WORKSHOP

Synthetic Biology: Constructing and Deconstructing Life
An Exploratory Workshop of the European Science Foundation
Castillo de Magalia (Avila, Spain)
October 13-16 2005

EW04-68

Convenors:

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1. Executive summary

The pursuit of Synthetic Biology is both the design and fabrication of biological components and systems that do not exist in the natural world as well as the re-design and fabrication of already existing biological systems. Ultimately, it is envisioned to build up cellular components and even cells from scratch to create living devices and use them either as molecular-scale factories, to detect chemical weapons, clean up pollutants, make simple computations, diagnose disease, deliver vaccines, produce water for water or sunlight, or to create new, hybrid materials. This vision has, thus, a tremendous scientific, technological and economical impact. However, Synthetic Biology is, as yet, at a very preliminary stage.

Knowledge is highly scattered and, despite of the strong tradition of European science in the various relevant areas Europe (Microbial Metabolism, Bioinformatics, Process Engineering and Ecogenomics, as well as a significant tradition in studies on the Origin of Life and Minimal Biological Systems), lags clearly behind US or Japan.

The goal of this workshop, was to bringing together experts in the various fields of this highly interdisciplinary, emerging science and set a forum for discussion on the possibilities of Synthetic Biology, on its needs and its boundaries with focus on biocatalysis and biodegradation. It was aimed at setting a transnational, European-wide framework for future cooperative projects that bundle the diverse expertises and concertedly work towards the translation of this joint know-how into concrete technological and economical developments.

The workshop itself consisted of a mixture of longer review/perspective talks on the various main topics, shorter talks on specific subjects related to the session topics and panel discussions. The sessions constitute subject modules that form the backbone of Synthetic Biology.

The meeting was the very first in this field in Europe and became a milestone in Synthetic Biology research at the continent. The broad scope, the quality and expertise of the speakers and the environment created, promoted lively and deep discussions, and enabled the identification of critical points and avenues for the development of the field and helped to set the basis of a road map for further endeavours.

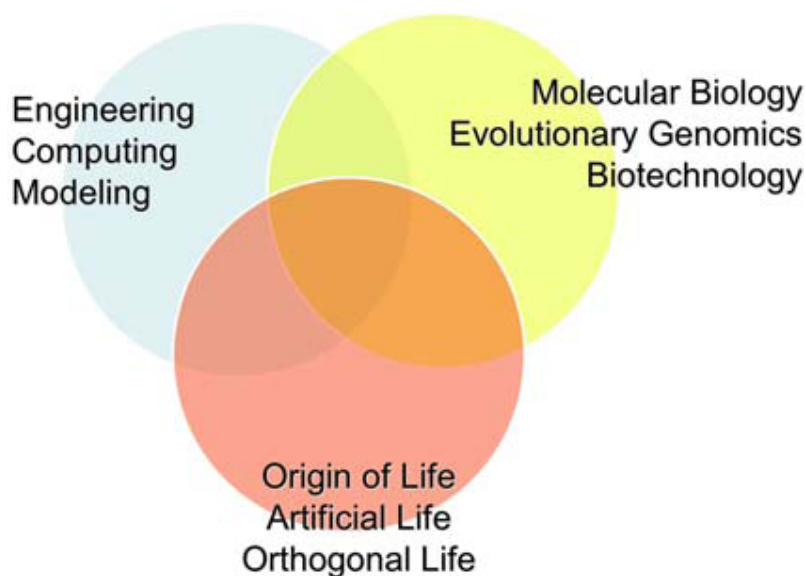


Figure 1 - The 3 pillars of Synthetic Biology in Europe

Albeit still in its infancy, synthetic biology builds upon and adopts structures that have proven transformative in industrial history; by analogy, synthetic biology will materialize the enormous benefits long promised by biotechnology. This ambitious goal, and the success of synthetic biology as a field, will depend on a number of demanding scientific and technical questions. The identification of these was the one of the main deliverables of this exploratory workshop. The other main result was the establishment of an informal network of researchers that would help in raising the profile of this exciting discipline in Europe.

Keywords: Synthetic & Digital Biology, Artificial Cells, Genetic Circuit Design & Assembly, Genome Synthesis & Minimization, Biocatalysis & Biodegradation

2. Scientific content of the event

The workshop consisted of a mixture of longer review/perspective talks (including those by the three US participants) on the various main topics (according to session headings, see program below), shorter talks on specific subjects related to the session topics and panel discussions. The sessions constitute subject modules that form the backbone of Synthetic Biology.

The first talk in each session (review/perspective) was a 30 min one plus 15 min discussion. The remaining contributions were 15 minutes talk plus 15 minutes discussion format. The panel discussions were held on especially relevant themes. The final session on Day 4 (see above) involved a discussion among the scientists present on how to put together the various issues discussed throughout the meeting to enable the assembly of a draft framework on Synthetic Biology. Special emphasis was put on stimulating discussion and on fostering contacts for future collaborations in the form of project proposals and research interactions.

3. Assessment of the results, contribution to the future direction of the field, outcome

The workshop was very successful in bringing the different “schools” and perspectives together and at creating a forum for discussion on the potential, methods, needs and pitfalls of the current and future endeavors in Synthetic Biology. The attendees identified the following points as desirable features for the future of SB in Europe.

[i] The rigorous adherence to scientifically sound descriptive language (rather than provocative or misleading jargon). This may require an effort to define what is a biological part and even pose a research agenda (see forward looking discussions) to bring natural biological modules to the degree of context-independence that would be needed for serious engineering. Alternatively, if this –at the end- is shown to be unfeasible then devise robust and sound methodologies for coping with the inherent complexity of biological parts as they are, that is, embracing their noisy nature, non-linear interactions, etc.

[ii] Keep a healthy balance on mission-oriented research, with a serious perspective of application within a reasonable period of time, while at the same time making allowances for blue-sky research for which immediate applications are not evident, e.g., research on the Origin and re-Creation of Life, minimal life, etc.

[iii] The pursuit of societal allies for the celebration of the new technology, rather than calling for noisy controversies. Many Europeans experience some anxieties about creating non-natural life forms, the possible effect of novel biological materials if released into the environment and -not the least- the contribution of SB to the economic globalization agenda. A re-enactment of the GMO controversy must be deliberately avoided for SB.

Emerging topics

The following were the topics/themes identified during the closing forward looking plenary discussion

Projection of stochastic phenomena of single cells into community behaviour

Non-DNA information-bearing macromolecules
Orthogonality and orthogonal systems in Biology
Constraints in natural and engineered biological systems
Auto-optimizing systems
Design principles of natural and artificial Biological systems
Artificial nucleic acids and associated enzymes
Minimal Biological Systems: metabolism, replication, translation
Fully artificial abiotic (orthogonal) organisms.
Transitions from abiotic to biological systems
Ancestral Biological Systems
Autopoiesis vs. Epipoiesis
Artificial Life and Origins of Life

Visions for the future of the research field – identification of issues in the 5-10 years & timeframe

To address the long term scientific issues mentioned above the following specific issues must be tackled:

Enabling technologies

Computational design, programming, modelling, validation and optimisation of Biological systems
Automation of the Molecular Biology Laboratory
Technologies for Single-cell omics
Robust genomic chassis for White and Environmental Biotech
New procedures for multi-scale directed evolution (genes, genomes, populations)
Multi-scale imaging (single molecules, single cells, populations)
Intelligent Molecular Decision Systems
Branch-cutting of Metabolic modules
Orthogonal regulatory modules
Towards a 1000 \$ genome synthesis
Methods for Chromosomal replacement and chromosome engineering
DNA-free cells: vesicles and maxicells

Standardization

Define accurately the boundaries of biological functions
Development of consensus criteria for Biological Standards
Development of standard computational models for standard biological parts
Infrastructures
Large-scale DNA synthesis
Massive DNA sequencing
Biocomputing
European Institute of Biological Standards

Societal and acceptance issues

Involve multiple stakeholders, Identify end-users
Make links to Medicine and Human Health
Training Programs and undergraduate education: an European CV in SB
Community building initiatives (~iGEM?), Attract senior IPs to SB
Philosophical implications of SB, Safety and security of SB
The human factor: anticipating societal reactions

4. Final Programme

Day 1. Thursday, October 13

- 09.00-14.00 Arrival to the Residencia de Estudiantes, CSIC, Madrid
14.00-15.30. Lunch at the Residencia de Estudiantes
- 16.00-17.30. Transportation to the *Castle of Magalia* (Navas del Marqués, Avila). Bus departs by the fence of Serrano 117 at sharp 16.00 h
- 17.30-18.30 Check-in and Tea
- 18.30-19.00. Welcome and presentation of the Workshop by **the Organizers**
- Session I** *Chaired by Sven Panke*
- 19.00-20.00 Keynote talk. **Luis Serrano**. European Molecular Biology Laboratory (EMBL). *SmartCell and FOLD-X two tools to design networks in living systems.*
- 20.00-22.0. Dinner & Bar discussion

Day 2. Fri, October 14

- Session II** *Chaired by Eric Smith*
- 09.00-09.30. **Juan Pérez-Mercader**. Centro de Astrobiología (CSIC-INTA). *Synthetic Biology and Astrobiology*
- 09.30-10.00. **Sven Panke**. Institute for Process Engineering ETH-Zentrum. *Artificial pathways*
- 10.00-10.30. **Peter Walde**. Institut für Polymere, ETH-Hönggerberg. *From simple lipid vesicles to enzyme-containing nanoreactors.*
- 10.30-11.00. Coffee break
- 11.00-11.30. **Drew Endy**. Massachusetts Institute of Technology. *Engineering integrated biological systems*
- 11.30-12.00. **Jörg Stelling**. Institut für Computational Science. *Robustness of engineered genetic circuits*
- 12.00-12.30. **Hans Westerhoff**. Free University of Amsterdam. *Systems Biology and the Life to be 'de'constructed*
- 12.30-13.00. **Martin Fussenegger**. Institut für Biotechnologie. ETH Hönggerberg. *Combining transgene control systems to synthetic mammalian gene networks*
- 13.00-15.00 Lunch
- Session III** *Chaired by Vitor Martins dos Santos*
- 15.00-15.30.** **Vitor Martins dos Santos**. German Research Centre for Biotechnology (GBF). *Programmable Bacterial Catalysts*

- 15.30-16.00. **François Taddei.** Génétique Moléculaire Evolutive et Médicale. INSERM. *Extending E. coli Genetics :extended phenotypes, extended environment and extended inheritance*
- 16.00-16.30. **Ehud Shapiro.** Weizmann Institute of Science. *Computers made of biological molecules*
- 16.30-17.00. **Eric Smith.** Santa Fe Institute. *Metabolism from first principles*
- 17.00-17.30. Coffee break
- 17.30-18.00. **ESF representative.** European Science Foundation Headquarters, Strasbourg *The ESF and its mission in Frontier Research in Europe*
- 18.00-18.30 **Stenbjörn Styring.** Uppsala University. *From natural to artificial photosynthesis. Hydrogen from sun to water*
- 18.30-19.00. **Frank Breitling.** Deutsches Krebsforschungszentrum. *Generation of a hybridome library*
- 19.00-19.30. **Alfonso Valencia.** Protein Design Group CNB-CSIC. *The organization of the known biodegradation network*
- 20.00-22.00. Dinner & Bar discussion

Day 3. Sat, October 15

Session IV *Chaired by Martin Fussenegger*

- 09.00-09.30. **Christoph Adami.** Keck Graduate Institute, California, USA. *Digital genetics: unravelling the genetic basis of evolution*
- 09.30-10.00. **Tom Knight.** MIT. *Simplifying the organism Mesoplasma florum for engineering purposes*
- 10.00-10.30. **Rene Wijffels.** Wageningen University. The Netherlands. *Photosynthetic cell factories*
- 10.30-11.00. Coffee break
- 11.00-11.30. **J. J. Heijnen.** Delft University of Technology. *In vivo kinetics of metabolism in cell factories*
- 11.30-12.00 **Doron Lancet.** Weizmann Institute of Science. *Lipid world: evolving protocells without RNA*
- 12.00-12.30. **Peter J. Bentley.** University College London. *Understanding embodied computation through evolution and development*
- 12.30-13.00 **Victor de Lorenzo.** National Center for Biotechnology (Madrid). *Evolving transcriptional regulators from recombinant antibodies*
- 13.00-15.00 Lunch

Session V *Chaired by Victor de Lorenzo*

- 15.00-15.30 **Norman Packard.** CEO, Protolife, Italy. *Co-evolution of chemistry and self-assembly*
- 15.30-16.00 **Marcello Barbieri.** Univ. Ferrara. *A model of embryonic development.*

- Can we build an epigenetic machine?*
- 16.00-17.00 Concluding talk. **Jay Keasling**. University of California. *Building microbial chemical factories*
- 17.00-17.30. **Sven Panke**. Institute for Process Engineering ETH-Zentrum. *Briefing on the First European Synthetic Biology Conference*
- 17.30-18.00. Coffee break
- 18.00-19.30. **All participants**. *Brainstorming and plans for action: a transatlantic scientific agenda in Synthetic Biology?* (chaired by the Organizers)
- 20.00-22.00. Dinner & Bar discussion

Day 4. Sun, October 16

- 07.30 Departure of Bus back to Madrid and Madrid Airport

5. Full List of Participants (including full title, address, tel, fax, email)

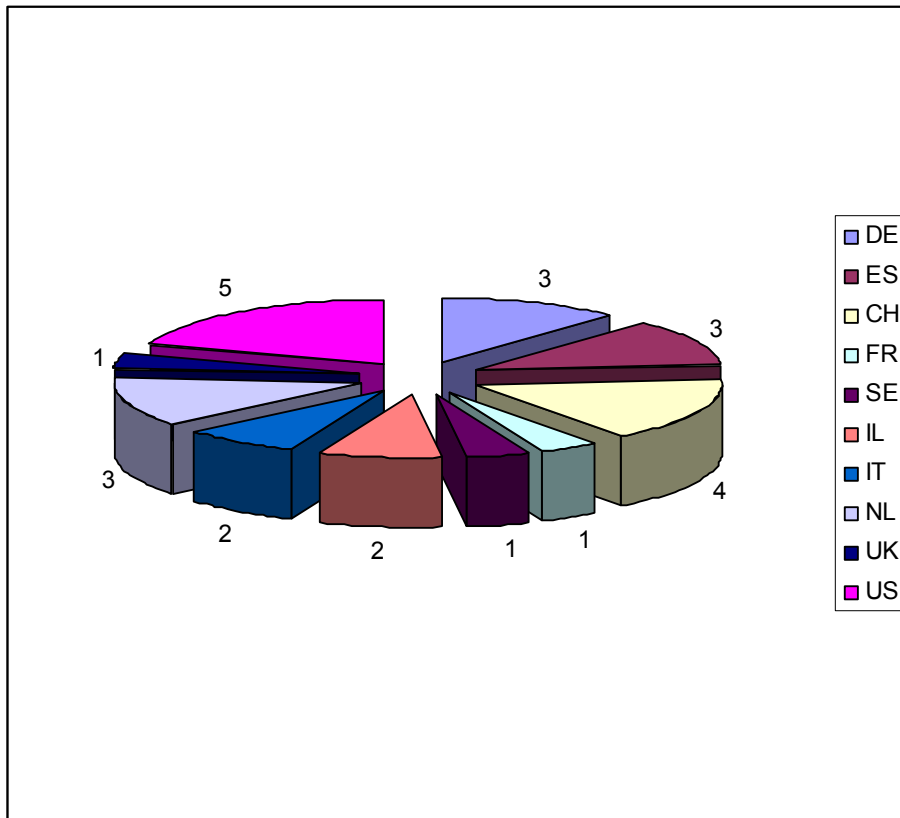
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6. Statistical information on participants (age bracket, countries of origin, etc)

Distribution of the participants per country of origin



Note: three of the US attendees were subsidised by the Centre for AstroBiology, a NASA-associated centre in Madrid. The reason for the presence of a relatively large number of US participants was because the field is more developed in the USA and, being the first workshop in Europe in this field, it was pivotal to have a sound and varied contribution from experts.

Distribution of the participants per age categories

About half of the participants were between 35 and 45, and the other between 45 and 55.

Distribution of the participants per age categories

All participants were male. Unfortunately, at the time, it was not possible to balance gender in the relevant areas.

Group photograph
(at the castle's court)



Addendum post-report

The workshop helped to create a core network of researchers that had previously not had any contact with each other. Therefore, it strongly contributed to spin off a number of activities in the field. Several EU project applications in the field of SB were triggered by this meeting and various were successfully granted.

These are:

- PROBACTYS: Programming Bacterial Catalysts (www.probactys.eu), a FP6-NEST, 7-partner STREP project coordinated by V. Martins dos Santos and with the participation of V. de Lorenzo.
- EMERGENCE: Fostering a Community of Knowledge in Synthetic Biology (www.emergence.ethz.ch/), a FP6-NEST Coordination Action coordinated by S. Panke and involving 10 partners including A. Valencia, V. Martins dos Santos, V. de Lorenzo
- HYBLIB: Human monoclonal antibodies from a library of hybridomas, (<http://www.synbiosafe.eu/index.php?page=hyblib>) a FP6-NEST, 5-partner STREP project coordinated by F. Breitling
- TARPOL: Targeting environmental pollution with engineered microbial systems á la carte. A FP7 EU – KBBE Coordination Action involving 18 Partners that include V. Martins dos Santos, V. de Lorenzo, S. Panke: (www.helmholtz-hzi.de/de/forschergruppen/molekulare_biotechnologie/system_und_synthetische_biologie/projekte/tarpol/)
- NANOMOT: Synthetic Biomimetic Nanoengines: a Modular Platform for Engineering of Nanomechanical Actuator Building Blocks, a FP6-NEST, 5-partner STREP project in which S. Panke participates (<http://www.synbiosafe.eu/index.php?page=nanomot>)
- NETSENSOR: Design and Engineering of gene networks to respond to and correct alterations in signal transduction pathways, a FP6-NEST, 5-partner STREP project coordinated by L. Serrano (<http://netsensor.org.es/>).
- COBIOS: Engineering and Control of Biological Systems: a New Way to Tackle Complex Diseases and Biotechnological Innovation, a FP6-NEST, 5-partner STREP project in which M. Fussenegger and J. Stelling participate. (<http://lnx.cobios.net/>)

Furthermore, a proposal theme targeting a community of about 250 researcher in Europe has been submitted to the EUROCORES program of the ESF.

In addition to this series of projects, a large number of meetings of different formats and addressing various aspects of Synthetic Biology across Europe have been organized across Europe and beyond since the Workshop.

The list is quite extensive but a particularly relevant one is:

EUROPEAN CONFERENCE ON SYNTHETIC BIOLOGY (ECSB): DESIGN, PROGRAMMING AND OPTIMISATION OF BIOLOGICAL SYSTEMS, a ESF-UB Conference in Biomedicine, organised by S. Panke, A. Valencia, N. Krasnogor and V. de Lorenzo (<http://www.esf.org/conferences/07241>).

This conference has thus been a follow up of the exploratory workshop and has been now set as a series.

Thus in conclusion, the objectives and impact of the exploratory workshop were reached fully.