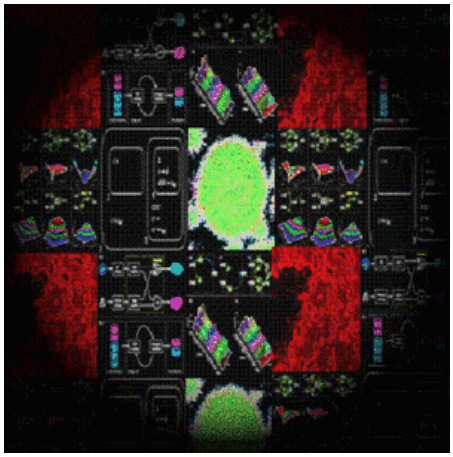
RESEARCH CONFERENCES

ESF-UB Conference in Biomedicine

European Conference on Synthetic Biology (ECSB): Design, Programming and Optimisation of Biological Systems



Hotel Eden Roc, Sant Feliu de Guixols • Spain
24-29 November 2007

Chair: **Alfonso Valencia**, CNIO Madrid, ES
Co-Chairs: **Natalio Krasnogor**, University of Nottingham, UK
- **Sven Panke**, ETH, Zürich Institute of Process Engineering, CH
- **Victor de Lorenzo**, Centro Nacional de Biotecnologia, Madrid, ES

www.esf.org/conferences/07241

SCIENTIFIC REPORT

Introduction (up to 2 pages)

Introduction on the topic in non-specialist terms (especially for highly technical subjects)

The basic premise of synthetic biology is that methods commonly used to design and construct non-biological systems, such as those employed in the computational sciences and the engineering disciplines, could also be used to model and program novel synthetic biosystems. Synthetic biology thus lies at the interface of a variety of disciplines ranging from biology through chemistry, physics, computer science, mathematics and engineering. The field of synthetic biology holds a great promise for the design, construction and development of artificial (i.e. man-made) biological (sub)systems thus offering potentially viable new routes to 'genetically modified' organisms, smart drugs as well as model systems to examine artificial genomes and proteomes. The informed manipulation of such biological (sub)systems could have an enormous positive impact on our societies, with its effects being felt across a range of activities such as the provision of healthcare, environmental protection and remediation, etc.

Although the expression Synthetic Biology (SB) has been present in the scientific and technical literature since 1912, only in more recent times is has come to being an umbrella concept to cover the whole of research developed at the interface between Molecular Biology and sensu stricto the

Computer Sciences and Engineering disciplines. Synthetic Biology is becoming an increasingly inclusive concept, which [i] encompasses new theoretical frameworks that approach biological systems with the conceptual tools and the descriptive language of Computer Science (.e.g. Models, Simulations, Evolutionary Design & Optimisation, etc) [ii] addresses old questions and challenges with fresh approaches inspired in the engineering disciplines (e.g. electric circuitry and chemical processes) and [iii] pursues the creation of new materials with á la carte properties based on the (automated) rational combination of standardized biological parts decoupled from their natural context. In fact, standarization and detailed description of minimal biological parts and their interfaces, to the degree of reliability of the components of modern electronic circuits and the reusability and ubiquity of software components is one of the (dreamt of) trademarks of the whole field.

The basic notion behind SB is that any biological system can be seen as a complex combination of functional, stand-alone elements not unlike those found in man-made devices, and can thus be–deconstructed in a limited number of components and reconstructed in an entirely different configuration for the sake of modifying existing properties or creating altogether new ones. In this context, Engineering and computational modeling and optimal design as disciplines transit from being an analogy of the rational combination of genes made possible by modern Molecular Biology and Biotechnology, to being a *plausible* methodology to construct complex systems and novel properties based on biological components. As any other domain of research, SB has an aspect of developing general-use technological and conceptual tools (biological parts, minimal genomes, artificial cells, DNA synthesis, trustworthy computational methods, etc), addressing hitherto intractable problems (Biosynthesis of complex molecules, breakdown or recycling of toxic chemicals, biological detection of explosives, biological production of H2 and other fuels) and raising utterly novel challenges (DNA computing, design of biological pattern development, targeting bacteria to tumor cells, expanding the genetic code to non-natural amino acids).

Although many activities that would now qualify as Synthetic Biology have been going on for some time in Europe and the USA (protein design, modeling, metabolic engineering, biological nanomachines), it is only now that the immense potential of the field is recognized as one of the most promising pillars of the sustainable and competitive economy of the future. All in all, SB is not primarly about understanding Biological Systems but also about capitalizing such systems as a source of components for creating new devices and properties to solve a variety of problems.

Many of the existing activities in Europe in the field of protein design, metabolic engineering, bio-processing, computational modeling or research on the origin of life and minimal biological systems meet the criteria of SB. Europe has a considerable critical mass of experts in Microbial Metabolism, Bioinformatics, Process Engineering and Ecogenomics, as well as a significant tradition in studies on the Origin of Life and Minimal Biological Systems. Even historically, the term Synthetic Biology was first coined by the frenchman Stéphane Leduc in a 1912 publication.

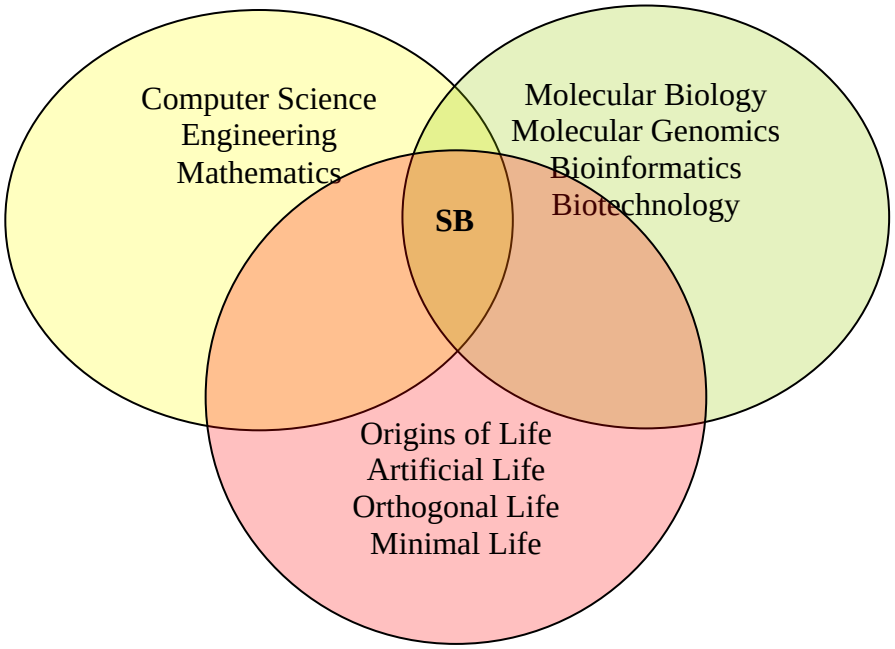


Fig. 1. The 3 pillars of Synthetic Biology in Europe

These credentials more than suffice to assert a specifically European outlook of Synthetic Biology. However, the European expertise in the various fields and the academic and industrial communities needed for boosting SB in our continent has remained typically latent (i.e. not explicit) and fractionated. But now, the international momentum provides a good opportunity for realizing the potential, finding a shared language and identifying synergies. This will require the development of much needed conceptual and material interfaces between the various subjects which are mandatory for the self-recognition of a European community on Synthetic Biology.

I hereby authorize ESF - and/or the University of Barcelona (UB) - to publish the above two-page Introduction on a special page dedicated to 'Conference Highlights' within the Research Conferences website.

Date & Signature: 7/4/2008

■ Scientific Content

▪ Summary of the conference sessions focusing on the scientific highlights

The conference features 4 tutorials, 7 plenary sessions, 2 pannel discussions and 1 poster session. The titles of the talks and brief comments appear below.

Tutorials

Chair: Alfonso Valencia, CNIO, ES

The tutorial day consisted on four tutorials ranging in length between 1 and 2 hours. These

covered a variety of topics representing the many disciplines that impinge in Synthetic Biology. The tutorials imparted where:

S. Panke, ETH, CH
General review and developments on synthetic biology

P. Herdewijn, Katholieke Universiteit, BE
The contribution of nucleic acids chemistry to synthetic biology

N. Krasnogor, University of Nottingham, UK
Computational modelling and optimisation for SB

P.L. Luisi, ETH & Università degli Studi di Roma Tre, IT
What is Life? An outopoiesis perspective

Panke's and Krasnogor's tutorial were of general applicability to the SB practitioner while the tutorials by Herdewijn and Luisi where of a more specific outline.

Session 1 : Biology of Minimal Genomes & Evolution

Chair: Victor de Lorenzo, Centro Nacional de Biotecnologia, ES

Four talks were presented during these session. Two of the dealing with the wet aspect of minimal genomes (Moya and Postfai) and the other two (Ussery and Gouy) focused on computational analysis of very large and complex laboratory data. These talks highlighted the need for a proper integration of wet/in silicon research.

A. Moya
Universidad de Valencia, ES
Genomic "deconstruction": an up-to-down approach to build a cell

D. Ussery
The Technical University of Denmark, DK
Characterization of minimal genomes across bacterial and archael phyla

M. Gouy
Université Claude Bernard - Lyon 1, FR
Non reversible models of evolution

G. Postfai
Hungary Academy of Science, HU
Engineering a Rationally Designed Reduced-Genome Escherichia coli

Session 2 : Showcase of Synthetic Biosystems

Chair: Sven Panke, ETH, CH

This session counted with 4 invited speakers (Danchin, de Lorenzo, Jaramillo and dos Santos) and 2 contributed talks. The first two talks by Danchin and de Lorenzo were fundational in nature and cover both practical, methodological and philosophical aspects of Synthetic Biology's theory and practice. The remaining 4 talks showcased specific cases of engineered synthetic bioentities.

A. Danchin
Institut Pasteur, FR
Will we be able to construct a synthetic bacterium?

V. de Lorenzo
Centro Nacional de Biotecnologia, ES
Engineering vs.evolution of effector specificities in transcriptional factors

M. Hadi
Sandia National Laboratories, US
Synthetic Biology for Biofuels

A. Jaramillo
Ecole Polytechnique, FR

Automatic Design of Genetic Systems

V. dos Santos
Helmholtz Center for Infection Research, DE
Streamlining and reprogramming Pseudomonas putida for biocatalysis

G. Rodrigo
Universidad Politecnica de Valencia, ES
Design of synthetic molecular clocks

Session 3: Simulations

Chair: Christos Ouzounis, Kings College, UK

This session presented two talks on the use of computer models for the analysis of synthetic biology scenarios related to research on the origins of life. The themes presented in this session were later expanded and debated in detail during one of the panel discussions (see below)

D. Lancet
Weizmann Institute of Science, DE
Stability to mutations in simulated prebiotic networks

P.L. Luisi
ETH & Università degli Studi di Roma Tre, IT
Chemical sides of synthetic biology: from the never born proteins to semi-synthetic minimal cells

Session 4: Systems Analysis

Chair: V. de Lorenzo, Centro Nacional de Biotecnologia, ES

Four invited talks made up this session. These covered "system-level" issues ranging from the biological implementation of programmed emergent system-level behaviour (Poyatos) all the way to the computational support tools necessary for systems-synthetic biology.

J. Poyatos
CNIO, ES
Genetic control circuitry at the core of cell fate Determination

S. Brunak
Technical University of Denmark
Interactomes, systems and disease

J. Stelling
ETH, CH
Robustness of engineered genetic circuits

C. Ouzounis
Kings College, UK
Development of computational methods for synthetic biology

Session 5: Infrastructure for Synthetic Biology

Chair: Natalio Krasnogor, University of Nottingham, UK

This session featured 3 invited speakers and 1 contributed talk. The talks centre around the issues of biological, hardware and software platforms, standards and protocols that would be required for the mass scale realisation of synthetic biology projects. Examples of best practices were shown and open-problems discussed.

R. Rettberg
The Registry of Standard Biological Parts, US

iGEM and the Registry of Standard Biological Parts

A. Valencia
CNIO, ES
Bioinformatics infrastructure for synthetic biology

J. Sharpe
Centre for Genomic Regulation, ES
Towards a 4D computer simulation of vertebrate limb development

H. Schwer
Sloning Biotechnology, DE
Slonomics™ - A Unique Platform Technology For Tailoring Genetic Diversity

Session 6: Funding and Industry Links for SB

Chair: Andres Moya, Universidad de Valencia, ES

This session featured non-technical talks related to European and national (UK, in this instance) funding for Synthetic Biology as well as societal impacts and perceptions. The session motivated a lively discussion that clearly indicated the latent vigour of the emergent European SB community. Some of the issues raised were continued during one of the panel discussions.

I. Economidis
European Commission, FP7, ES
Synthetic Biology in the EC and in the transatlantic debate

A. J. Collis
BBSRC, UK
Synthetic Biology: A Funder's Perspective

S. Gaisser
Fraunhofer Institute Systems and Innovation Research, DE
How can Europe be successful in Synthetic Biology?

Session 7: Synthetic Biology and its Future in Europe

Chair: Alfonso Valencia, CNIO, ES

This section concluded the conference with, first, a panel discussion on the worldwide scientific view on SB and then with the business meeting (Discussed in a latter section of this document).

Panel Discussion: "Contrasting Global Opinions on Synthetic Biology"
Chair : V. de Lorenzo ; I. Economidis, Markus Schmidt, Antoine Danchin, Randy Rettberg.

The conference also had a Panel Discussion on artificial life: *"Roadmap to minimal artificial cells"*
Chair : A. Jaramillo ; P.L. Luisi, S. Rasmussen, D. Lancet

There were three poster sessions in which participants showcased their work. The poster sessions were closely monitored and evaluated by a panel of three experts, namely, A. Moya (U. of Valencia), C. Ouzounis (King's College) and A. Wipat (U. Newcastle). They awared the 1st (E250), 2nd (E200) and 3rd (E150) prizes to the best three posters among all sessions. The winners were:

1. Paul Gardner et al for *"Quorum Sensing of Formose by Vibrio Harvery"*
2. Tamas Fehez et al for *"Engineering a Rationally Designed Reduced Genome E. coli"*
3. Javier Carrera et al for *"Modelling and Inference of Genetic Networks from Integration of Transcriptomic Databases"*

▪ Assessment of the results and their potential impact on future research or applications

The conference can be considered to have been highly successful given the arguably fractured nature of the nascent European SB community. 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.

■ Forward Look Plenary Discussion

▪ State-of-the-art in the field

The state of the art in the field was represented throughout the conference with representatives from Europe and the USA. The only other major players missing were the Japanese but we believe this was due to the short time between advertising the conference and its realization.

▪ Emerging topics

The following where 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 chasses 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
Standarization
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

▪ Is there a need for a foresight-type initiative?

Yes.

▪ Outcome of the Business Meeting – Election of the Organising Committee of the next conference

During the conference initially two teams nominated themselves to organize the next *ESF-UB Conference in Biomedicine - European Conference on Synthetic Biology (ECSB): Design, Programming and Optimisation of Biological Systems.* One of the teams was composed of D. Gilbert and A. Jaramillo and the other by S. Gaisser and M. Schmidt. The chairs of ECSB I met with both teams and advised them of logistics aspects of the organisation, the support provided by ESF and other important organizational matters. It was decided that, as to maintain continuity between conferences 2 of the co-chairs of one edition will also co-chair the following one having and so on on subsequent years. As was the case for the 1st edition, a total of 4 co-chairs would be the norm. It was also decided that as the focus of the ECSB series is *science* the chairs should be involved directly on the scientific issues rather than the societal issues. Later on during the conference both teams decided to join forces and it was also agreed that societal issues would be represented by Gaisser and Schmidt in ECSB II. The new team was voted in the last day of

the conference (unopposed) to run ECSB II.

Date & Signature: 7/4/2008