



## RESEARCH CONFERENCES

# ESF-UB Conference in Biomedicine ECSB II: DESIGN, PROGRAMMING AND OPTIMISATION OF BIOLOGICAL SYSTEMS

Hotel Eden Roc, Sant Feliu de Guixols (Costa Brava) • Spain  
**29 March – 03 April 2009**

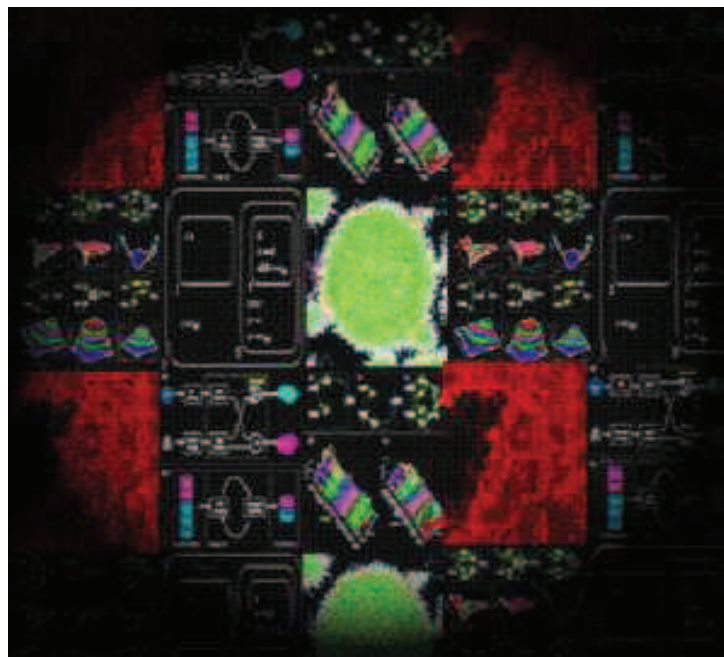
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Co-Chairs: **Alfonso Jaramillo**, Ecole Polytechnique, FR  
**Natalio Krasnogor**, University of Nottingham, UK  
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### Highlights & Scientific Report



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## Conference Highlights

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*Please provide a brief summary of the conference and its highlights in non-specialist terms (especially for highly technical subjects) for communication and publicity purposes. (ca. 400-500 words)*

The European Conference on Systems Biology ECSB 2009 ([www.esf.org/index.php?id=5386](http://www.esf.org/index.php?id=5386)) was the second conference in the series, the first having been held in November 2007. The focus of the conference was on the field of Synthetic Biology which holds great promise for the design, construction and development of biological systems (artificial or modified), by offering viable new routes to 'genetically modified' organisms, smart drugs and hybrid computational-biological devices. The informed manipulation of such biological 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 to the construction of smarter more ubiquitous bio-integrated computing systems, etc.

Although the term Synthetic Biology (SB) has been present in the scientific and technical literature since 1912, only in more recent times it has come to being an umbrella concept to cover the whole of research developed at the interface between Molecular Biology and 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 à la carte properties based on the (automated) rational combination of standardized biological parts decoupled from their natural context. In fact, standardization 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 premise of Synthetic Biology is that methods commonly used to build non-biological systems, such as those employed in the computational sciences and the engineering disciplines that can deal with large and complex systems, can also be used to specify, design, implement, test and deploy novel synthetic biosystems. Synthetic biology lies at the interface of a variety of disciplines ranging from biology through chemistry, physics, computer science, mathematics and engineering. Two communities are emerging within Synthetic Biology, namely top-down - i.e. knocking out or modifying functions of existing cells, and bottom-up - that is construction of artificial systems from first principles, protocells, etc.

The aim of this conference was to generate new and vigorous interactions between the disciplines that impinge on and contribute to Synthetic Biology, and to bring together in the same context top-down and bottom-up researchers. It comprised invited talks by internationally known scientists who are leaders in their fields, tutorials to introduce young researchers to Synthetic Biology, contributed talks and posters. The conference was limited to around 100 participants, in a venue whose environment was highly conducive to networking and scientific interactions.

The topics presented in the conference included DNA sequencing and synthesis, designing and engineering chemical and biological networks, computational techniques for synthetic biology, minimal genomes, evolution (natural, directed and simulated), origins of life, biological systems, cell cycles and circuits, minimal cells, applications to medicine and computational infrastructures for synthetic biology. There were also three tutorials on genetic tools, computational tools and societal aspects as well as a session on the support for the development of European Synthetic

**Biology.**

A key aspect of the conference was the deliberate mixing of topics in the programme -- top-down 'biology', bottom up 'chemistry' as well as computation, engineering and applications -- with the intention of breaking down the barriers between different approaches to and interpretations of Systems Biology. Coupled with the small and relaxed location, and a group visit to Girona in the middle of the week, this created an ideal atmosphere for debate and the fruitful exchange of views. The conference was very enjoyable for the participants, and the feedback indicated that they found the event very useful in terms of discussing issues with scientists from a wide range of disciplines, as well as evaluating their own scientific views in the context of Synthetic Biology.

Overall there were 36 invited speakers and chairs, and 60 participants of whom 80% were young researchers and 31% were female; grants were allocated to 40% of the participants. The attendance was from over 18 countries, with Spain, France and the UK topping the list; speakers were from France, Germany, Israel, Spain, Switzerland, UK, and the USA.

The unanimous request from participants was for the conference series to be continued, and the Chair and organizing committee were elected for ECSBIII which is to be held in 2011.

I hereby authorize ESF – and the conference partners to use the information contained in the above section on 'Conference Highlights' in their communication on the scheme.

## Scientific Report

### Executive Summary

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(2 pages max)

The European Conference on Systems Biology ECSBII 2009 was the second conference in the series, the first having been held in November 2007. Continuity was ensured by the active participation of some members of the first conference committee in the organisation and running of ECSBII. The focus of the conference was on the field of Synthetic Biology, which has been defined as aiming to “design and engineer biologically based parts, novel devices and systems as well as redesigning existing, natural biological systems.” [Report from the Royal Academy of Engineering UK, May 2009]. The field is of great potential scientific, humanitarian and commercial interest, with applications including the development of viable new routes to ‘genetically modified’ organisms, smart drugs and hybrid computational-biological devices.

Synthetic biology lies at the interface of a variety of disciplines ranging from biology through chemistry, physics, computer science, mathematics and engineering. Two communities are emerging within Synthetic Biology, namely top-down, biochemical approach involving knocking out or modifying functions of existing cells, and a bottom-up approach based in chemistry involving the construction of artificial systems from first principles, protocells, etc.

Although the expression Synthetic Biology (SB) has been present in the scientific and technical literature since 1912, only in more recent times it 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, standardization 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 aim of this conference was to generate new and vigorous interactions between the disciplines that impinge on and contribute to Synthetic Biology, and to bring together in the same context top-down and bottom-up researchers. It comprised invited talks by internationally known scientists who are leaders in their fields, tutorials to introduce young researchers to Synthetic Biology, contributed talks and posters. Overall there were 96 attendees -- 36 invited speakers and chairs, and 60 participants of whom 80% were young researchers and 31% were female. Grants were allocated to 40% of the participants.

The topics presented in the conference included gene design and synthesis, mobile genetic elements, molecular components, intra-cellular networks, inter-cellular networks, chassis, minimal cells, artificial vesicles synthetic cells, reconstruction of life, computer science and synthetic biology, software engineering and standards, and applications to medicine. There were tutorials on genetic tools, computational tools and societal aspects as well as a session on the support for

## the development of European Synthetic Biology.

A key aspect of the conference was the deliberate mixing of topics in the programme -- top-down 'biology', bottom up 'chemistry' as well as computation, engineering and applications -- with the intention of breaking down the barriers between the different approaches of the participants to Systems Biology. This worked very well, and was facilitated by the relaxing location which provided an ideal mixture of 'work', restful environment and excellent food! Coupled with the good number of participants (not too many or too few), the high proportion of young researchers, and a group visit to Girona in the middle of the week, this created an ideal atmosphere for debate and the fruitful exchange of views. The conference was very enjoyable for the participants, and the feedback indicated that they found the event very useful in terms of discussing issues with scientists from a wide range of disciplines, as well as evaluating their own scientific views in the context of Synthetic Biology. There was unanimous agreement for another conference in the future.

Some suggestions for activities that the community would like to see supported included a European registry of parts and public licences, promotion of educational activities and the exchange of scientific personnel, encouraging the participation of industry in Synthetic Biology, and the establishment of a set of Grand Challenges in Synthetic Biology.

In order to preserve some snapshot of the current state of the field, we have invited speakers to deposit versions of their materials on the conference website which is hosted by the ESF. We also have an agreement with Springer Verlag to publish a special issue of the Journal of Systems and Synthetic Biology which will contain articles by speakers at the conference which will act as at least a partial record of the current state of Synthetic Biology.

Conference website: <http://www.esf.org/index.php?id=5386>

## Scientific Content of the Conference

(1 page min.)

- Summary of the conference sessions focusing on the scientific highlights
- Assessment of the results and their potential impact on future research or applications

The topics presented in the conference included gene design and synthesis, mobile genetic elements, molecular components, intra-cellular networks, inter-cellular networks, chassis, minimal cells, artificial vesicles synthetic cells, reconstruction of life, computer science and synthetic biology, software engineering and standards, and applications to medicine. There were tutorials on genetic tools, computational tools and societal aspects as well as a session on the support for the development of European Synthetic Biology.

The programme comprised 26 invited talks, 12 short contributed talk (annotated '[S]'), 3 tutorials, one session European landscape perspectives, one session on futures, and 47 posters (in 2 poster sessions). The final programme, list of participants, and list of posters are on the conference website: <http://www.esf.org/index.php?id=5386>. Speakers have been invited to deposit the abstracts and slides of their talks on at: <http://www.esf.org/activities/esf-conferences/details/2009/confdetail294/presentations-abstracts.html>.

### Gene design & synthesis

This topic covered the design and synthesis of biological components at the nucleotide level, and contributions were about DNA in this conference. The approaches considered ranged from consideration of existing DNA sequences from the point of view of compaction, as well as that of

synthesis via shuffling to de-novo synthetic gene design and synthesis:

- DNA compaction: auto-organisation, prebiotic chemistry and in vivo condensed forms of DNA; Alain Thierry (CNRS / BIO-RAD, Montpellier) [S]
- DNA shuffling: a dynamic model for novel gene synthesis; Maude David (E. Centrale de Lyon)
- Gene Design, Gene Synthesis, Synthetic Gene Libraries and Beyond: Catalyst of Innovative Biotechnology; Ralf Wagner (Gene Art)
- Recursive construction of perfect DNA molecules from imperfect building blocks; Gregory Linshiz (Weizmann Institute) [S]

### **Mobile genetic elements**

An interesting view was presented on the analysis of mobile elements in existing gene sequences, with some implications regarding synthesis of biological systems via modifications using mobile elements.

- Showing restraint: bacterial mobile genetic elements are designed not to perturb their host genome; Didier Mazel (Institute Pasteur Paris)

### **Molecular components**

The design, engineering and use of sub-cellular components at the molecular level were the topic of several talks. These components ranged from proteins in many guises (enzymes, regulatory proteins and receptors) to larger molecules such as plasmids:

- Designer cellulosomes: creating novel types of multi-enzyme complexes; Edward Bayer (Weizmann Institute)
- Designing artificial regulatory proteins for novel transcriptional control circuits; Gonzalo Durante (CIB, Madrid) [S]
- Engineering amyloid assemblies through ligand-modulated protein conformational switches; Rafael Giraldo (CIB, Madrid)
- Engineering membrane receptors, reporter enzymes, and DNA Nano-structures as parts for synthetic signaling Kristian Müller (U. Freiburg) [S]
- Engineering of tunnels in proteins with buried active sites Jiri Damborsky (Masaryk University)
- Plasmids and plasmid modules as orthogonal devices in Synthetic Biology, Fernando de la Cruz (U. Cantabria)

### **Intra-cellular networks**

Intra-cellular networks are a step up from molecular components both in terms of scale as well as the complexity required for design and analysis. The networks considered in this group of talks included transcriptional, metabolic and oscillatory:

- A systems chemical biology approach to infer and design metabolic networks; Jean-Loup Faulon (Genopole Evry)
- Engineered Genetic Oscillations; Jeff Hasty (UCSD)
- Engineering of mammalian gene networks; Martin Fussenegger (ETH Zurich)
- Experimental reconstruction of single cell metabolism and its implication in synthetic biology; M. Eugenia Guazzaroni (Instituto de Catálisis, CSIC) [S]
- Global transcriptional optimization; François Képès (Genopole Evry)
- Heterogeneous timing in bacterial gene control; Ulrich Gerland, U. Cologne
- Rewiring metabolic networks in bacteria through intracellular expression of camel VHH domains; Jose-Ignacio Jimenez (CNB, Madrid) [S]
- Synthetic alternatives to canonical metabolism; Philippe Marliere (Isthmus SARL)
- The TOL logicome tunes m-xylene degradation to the core metabolic network of

*Pseudomonas putida*; Rafael Silva-Rocha (CNB-CSIC, Madrid) [S]

- Towards orthogonal biochemical networks; Sven Panke (ETH, Basel)

### **Intercellular networks**

The design and implementation of networks at the inter-cellular level are an emerging theme in Synthetic Biology, and were the subject of one presentation by Professor Camara:

- Emerging themes in bacterial cell-cell communication networks; Miguel Camara (University of Nottingham)

### **Chassis**

The choice of which *chassis* (organism) on which to install or implement synthetic systems is very topical; in this meeting the *E. coli* was presented as the example chassis in two talks:

- Proteomic level characterisation of an *E. coli* synthetic biology chassis; Phillip Wright (Sheffield University)
- Re-engineering *E. coli* chassis under dynamic environments; Javier Carrera (IBMCP CSIC-UPV) [S]

### **Minimal cells**

The creation and analysis of minimal biological cells (and hence often minimal genomes) is of great interest not only in terms of promoting our understanding of what is needed for life at the cellular level, but also as a means to create lean and cut-down chassis for installation and experimentation of synthetic systems:

- Artificial promoters and minimal cells for whole cell biocatalysis; Anton Glieder (TU Graz) [S]
- Learning from minimal natural cells; Andres Moya (University of Valencia)
- Removal of the flexible gene pool of *E. coli* is accompanied by loss of adaptability; Tamas Feher (Hungarian Academy of Sciences) [S]

### **Artificial vesicles & Synthetic cells**

The 'bottom-up' approach to Synthetic Biology requires the development of techniques to engineer artificial vesicles and more ambitiously synthetic cells, which exhibit some of the characteristic behaviour of 'natural' (biological) cells:

- Artificial vesicles as biomimetic compartments and templates; Peter Walde (ETH Zurich)
- CompuBioTic, a methodology for de novo design of vesicles performing programmed tasks; Stephanie Rialle (CNRS, Montpellier) [S]
- Lipid vesicles as cellular models: from self-reproduction to semi-synthetic minimal cells; Pasquale Stano (RomaTre)

### **Computer science & BioSystem synthesis**

Techniques from computer science have the potential to make a very powerful contribution to the field of Synthetic Biology. These can include the design and exploitation of advanced algorithms, which are then coupled with genetic engineering approaches:

- Beyond BioBricks: Synthetizing synergistic biochemical systems from the bottom-Up; Mark Bedau (Reed College, Oregon)
- Computational design of bacterial systems for new functionalities; Alfonso Jaramillo (Ecole Polytechnique, Paris)
- Inductive logic programming and machine learning for Synthetic Biology; Stephen Muggleton (Imperial College, London)

### **Software engineering and standards**

The field of Synthetic Biology is highly reliant on the use and availability of software in some open form (i.e. the software is itself open and freely available, or at least it operates over some standard

data formats), and this was covered in one presentation by Herbert Sauro:

- The role of software and standards in the design and construction of synthetic networks; Herbert Sauro (U. Washington)

## Reconstruction of life

The study of the emergence of living systems is an extremely important topic, because it can give insights and some guidance to the design of synthetic biological systems.

- Maxwell's demon's genes; Antoine Danchin (Institute Pasteur Paris),
- Mechanisms of emergence in the prebiotic world; Irene Chen (Harvard University)
- Reconstruction of (bio)chemical life by interpolation from modern sequences to zero time; Edward Trifonov (University of Haifa)

## Applications

If Synthetic Biology is to become an established scientific field, then there must be some applications of the topic that illustrate its usefulness and advantages over traditional genetic engineering. One such talk was by the KU Leuven iGEM (internationally Genetically Engineered Machines) team from the 2008 competition, which described a medical application:

- Modeling for Dr. Coli: a synthetic biology approach to intelligent bacterial drug delivery; Inge Thijs (KU Leuven) [S]

## Tutorials

There were 3 tutorials which were designed to enable participants to learn about techniques from genetic and computer science which can be used in Synthetic Biology, as well as a tutorial ethical and legal issues:

- Tutorial 1: Genetic tools for Synthetic Biology; Victor de Lorenzo (CNB, Madrid)
- Tutorial 2. Computational tools for Synthetic Biology; Natalio Krasnogor (University of Nottingham); David Gilbert (Brunel University)
- Tutorial 3. Societal aspects of Synthetic Biology; Markus Schmidt (IDC Vienna)

## Futures

Two forward-looking sessions were held: one about the opportunities and directions for future development of Synthetic Biology in Europe, and the other on future topics that could be covered in the conference series.

- Synthetic biology landscape in Europe: Sibylle Gaisser (Fraunhofer ISI) Context conditions, actors and leading countries in SB ; Benedicte Callan (OECD) International governance Opportunities and Challenges ; Berthold Rutz (European Patent Office) IP regimes in the future and their impact on SB research and development ; Ioannis Economidis (European Commission) SB strategy in the European Commission and in FP7 ; Sophia Abbasi (BBSRC, UK) UK strategy in Synthetic Biology
- Forward Looking Plenary Discussion – this covered many topics including the use of viruses as vesicles, biological complexity, modularization at the level of protein structure, social legal and ethical issues, a European registry of parts and public licences, education and the exchange of scientific personnel, how to encourage the participation of industry, and a suggestion for Grand Challenges in Synthetic Biology.

## Project meetings

- Targeting environmental pollution with engineered microbial systems, Sectorial meeting of the TARPOL Network

## Posters

1 Bikard David. The Synthetic Integron: An in vivo genetic shuffling device



- 2 Billerbeck Sonja. Orthogonalization of a dihydroxyacetone-phosphate producing biotransformation module: Systematic search for ATP sinks in cell free extracts
- 3 Blakes Jonathan. An integrated development environment for synthetic biology models
- 4 Calles Belén. Re-writing metabolic pathways: a transposon tool tailored for production of conditional enzymes
- 5 Camsund Daniel. Synthetic Biology in Cyanobacteria – Tools and parts development and characterization
- 6 Carrera Javier. Re-engineering E. coli chassis under dynamic environments
- 7 Ceroni Francesca. LacI operator sites for regulated promoter standard assembly
- 8 Damborsky Jiri. Engineering of Tunnels in Proteins with Buried Active
- 9 de las Heras Aitor. Designing regulatory networks to increase the response of a whole-cell biosensor
- 10 Delaye Luis José. Engineering the genome of *Synechococcus elongatus*: towards a minimum photoautotrophic cell
- 11 Dietz Sven. Constructing minimal cells by genome reduction and selection: A synthetic biology approach
- 12 Durante Gonzalo. Designing artificial regulatory proteins for novel transcriptional control circuits
- 13 Feher Tamas. Removal of the flexible gene pool of E. coli is accompanied by loss of adaptability USA
- 14 Glieder Anton. Artificial promoters and minimal cells for whole cell biocatalysis
- 15 Grünberg Raik. Biobrick applications and management (in everyday research)
- 16 Guazzaroni María. Eugenia EXPERIMENTAL RECONSTRUCTION OF SINGLE CELL METABOLISMS AND ITS IMPLICATION IN SYSTEM BIOLOGY
- 17 Jimenez Jose Ignacio. Rewiring metabolic networks in bacteria through intracellular expression of camel VHH domains
- 18 Kirov Boris. Minimal Oscillator
- 19 Leprince Audrey. *Pseudomonas putida* KT2440: genome minimization project
- 20 Linshiz Gregory. Recursive construction of perfect DNA molecules from imperfect building blocks
- 21 Liu Xuan. A computational platform to support the design and construction of synthetic biological systems
- 22 Lopo Miguel. Parts and modules for H<sub>2</sub> production in a *Synechocystis* sp. PCC 6803 “chassis”
- 23 Michel Klaus-Peter. FORSYS and FORSYS-Partner: German Research Units for Systems Biology
- 24 Mohamed Zuki Fathiah. Bacterial adhesion: XDLVO Theory and Numerical Analysis on Geometrical Effect
- 25 Montagud Arnau. Construction and analysis of a genome scale metabolic model for the cyanobacteria *Synechocystis* sp. PCC6803
- 26 Müller Kristian. Engineering Membrane Receptors, Reporter Enzymes, and DNA Nano-Structures as Parts for Synthetic Signaling
- 27 Neverov Konstantin V. A composition containing photosensitizer and perfluorocarbons: photodynamic properties and impact on cell cultures
- 28 Noirel Josselin. Validation of Mixture Model on Graphs on yeast
- 29 Pacheco Catarina. Parts and modules for H<sub>2</sub> production in a *Synechocystis* sp. PCC 6803 “chassis”
- 30 Panke Sven. Orthogonality in metabolic networks
- 31 Pasotti Lorenzo. Construction and validation of logic functions in a biological chassis
- 32 Paun Andrei. DISCRETE NONDETERMINISTIC MODELING OF AN APOPTOSIS PATHWAY
- 33 Pinto Filipe. Parts and modules for H<sub>2</sub> production in a *Synechocystis* sp. PCC 6803 “chassis”
- 34 Rialle Stephanie. CompuBioTic, a methodology for de novo design of vesicles performing programmed tasks
- 35 Rizk Aurelien. Towards a general computational method for robustness analysis
- 36 Rodrigo Guillermo. Towards the hydrogen production in cyanobacteria using oxygen consuming pathways
- 37 Rouilly Vincent. Design of Experiments Applied to Stochastic Gene Expression Simulations: Steady-state diagnostic and Sensitivity Analysis
- 38 Ruiz Raúl. Deciphering the transcriptional regulatory network of conjugative plasmid R388
- 39 Silva-Rocha Rafael. The layout of the TOL logicome tunes m-xylene degradation to the core metabolic network of *Pseudomonas putida* mt-2
- 40 Smaldon James. Liposome Logic – Compartmentalised Computing
- 41 Strelkowa Natalja. Robust synthetic gene network for sequential pathways regulation

- 42 Tanaka Kosei. A combined experimental/theoretical approach to reduce the bacterial genome  
43 Thierry Alain. NANOSTRUCTURES UNVEIL A GENERAL SELF-ORGANIZATION OF NUCLEIC ACIDS: Implications to prebiotic chemistry to in vivo DNA condensation  
44 Thijs Inge. Modeling for Dr. Coli: a synthetic biology approach to intelligent bacterial drug delivery  
45 Trybilo Maciej. A Rational Design Framework of Orthologous miRNA/target site Pairs for Synthetic Biology  
46 Venken Lyn. Facilitating ChIP-chip-based reconstruction of regulatory networks by combining omics data  
47 Wu Bian. Enzymatic synthesis of enantiopure  $\alpha$ - and  $\beta$ -amino acids by phenylalanine aminomutase-catalyzed amination of cinnamic acid derivatives

## Forward Look

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(1 page min.)

- *Assessment of the results*
- *Contribution to the future direction of the field – identification of issues in the 5-10 years & timeframe*
- *Identification of emerging topics*

### Assessment of the results

The conference was highly successful given the different scientific camps which still make up the framework of the emerging European SB community. Thus the meeting enabled the participants to gain a very good understanding of the current state of the field of Synthetic Biology, how the different approaches could interplay, who are the major players in Europe and an understanding of some of the drivers for the future development of Synthetic Biology. There have been many discussions and interactions, and the meeting has contributed to continuing the establishment of a scientific community Systems Biology in Europe. A particular important element in this is the active participation of young researchers who will play an active role in shaping the direction of research and applications in Systems Biology as their careers mature. The conference was very enjoyable for the participants, and the feedback indicated that they found the event very useful in terms of discussing issues with scientists from a wide range of disciplines, planning research projects, finding out how to obtain funding, as well as evaluating their own scientific views in the context of Synthetic Biology.

In order to preserve a snapshot of the current state of the field, we have invited speakers to deposit versions of their materials on the conference website which is hosted by the ESF: <http://www.esf.org/activities/esf-conferences/details/2009/confdetail294/presentations-abstracts.html>

We also have an agreement with Springer Verlag to publish a Special Conference Issue of the Journal of Systems and Synthetic Biology which will contain articles by speakers at the conference which will act as at least a partial record of the current state of Synthetic Biology. The current planned date for the publication is in Spring 2010.

### Contributions to the future direction of the field – identification of issues in the 5-10 years timeframe

The following topics emerged as being important in the mid to long term timeframe for the Systems Biology agenda in Europe:

1. The development of sound, tried and tested techniques for modelling, designing and implementing synthetic biological systems. This involves scientifically sound approaches to the definition and use of biological parts as well as 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.

2. Maintaining a healthy balance between mission-oriented research, with a serious perspective of application within a reasonable period of time, and blue-sky research for which immediate applications are not evident, e.g. Origin and re-Creation of Life, minimal life, etc.
3. The pursuit of societal allies for the support of the use of the new technology, rather than becoming embroiled in 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 the contribution of SB to the economic globalization agenda. A re-enactment of the GMO controversy must be deliberately avoided for SB.

Critical issues which could help to catalyse the development of Synthetic Biology include

- The establishment of Grand Challenges in Synthetic Biology.
- The identification and publicizing of high-profile examples of successful applications of Synthetic Biology which have obvious humanitarian benefit
- The establishment of a secure funding stream for Synthetic Biology in Europe
- The establishment of European education and research collaboration and interchanges in Synthetic Biology.

Specific issues to be tackled in the timeframe include:

#### **The development of enabling technologies, including**

- Computational design, programming, modelling, validation and optimisation of Biological systems at all levels of scale (molecular, intracellular, intercellular, tissue to organism)
- 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\$ or less, fast genome synthesis
- Large-scale DNA synthesis
- Massive DNA sequencing
- Methods for Chromosomal replacement and chromosome engineering
- DNA-free cells: vesicles and maxicells
- Standardization
- Accurate definition of the boundaries of biological functions
- Development of consensus criteria for Biological Standards
- Development of standard computational models for standard biological parts
- Infrastructures
- Biocomputing
- European Institute of Biological Standards

#### **Societal and acceptance issues**

- Involvement multiple stakeholders, Identify end-users
- Making links to Medicine and Human Health

- Establishment of training Programs and undergraduate education: an European CV in SB
- Community building initiatives (for example an “iGEM Europe”)
- Attracting senior IPs to SB
- Philosophical implications of SB, Safety and security of SB
- The human factor: anticipating societal reactions

## Identification of emerging topics

Emerging topics and themes identified in the Forward Looking Plenary Discussion included:

- Synthetic Biology at the intracellular level and beyond
- Biological complexity
- The use of viruses as vesicles
- Modularization at the level of protein structure
- The possible establishment of a European registry of parts and public licences,
- Education and the exchange of scientific personnel
- The establishment of Grand Challenges in Synthetic Biology.
- Industrial participation
- Applications of SB
- Computational methodologies for SB.
- 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

### ■ Is there a need for a foresight-type initiative?

Yes, Synthetic Biology is an important area in which rapid scientific and technological advances are expected to be made, and which could have a great impact on the quality of life and society in Europe and the world in general. The major international player is arguably the USA, but European scientists are also very active.

## Business Meeting Outcomes

- *Election of the Organising Committee of the next conference*
- *Identified Topics*
- *Next Steps*

The organizing committee for the next conference (ECSBIII) with a suggested date in 2011 was elected: Chair – Didier Mazel (Institut Pasteur, Paris), Co-chairs include Fernando de la Cruz (University of Cantabria, Spain), Pasquale Stano (RomaTre, Italy), and in order to ensure continuity with ECSBII: David Gilbert (Brunel University, UK), Alfonso Jaramillo (Ecole Polytechnique / Université d'Evry – France).

This is in accordance with the agreements made at the first conference ECSBI that in order 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, and 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.

Areas suggested for specific emphasis include: Biological complexity; Synthetic Biology at the intracellular level and beyond; contributions from computer science; Applications. Other identified topics: including DNA sequencing and synthesis, designing and engineering chemical and biological networks, computational techniques for synthetic biology, minimal genomes, evolution (natural, directed and simulated), origins of life, biological systems, cell cycles and circuits, minimal cells, computational infrastructures for synthetic biology. We also plan to have tutorials on selected topics, and meetings for scientific projects.

The next steps: Virtual meeting of the committee, allocation of tasks, coordination with ESF for the date, creation of timetable leading up to the conference, suggestions for and selection of speakers, fund raising.

## **Atmosphere and Infrastructure**

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▪ *The reaction of the participants to the location and the organization, including networking, and any other relevant comments*

A key aspect of the conference was the deliberate mixing of topics in the programme -- top-down 'biology', bottom up 'chemistry' as well as computation, engineering and applications -- with the intention of breaking down the barriers between the different approaches of the participants to Systems Biology. This worked very well, and was facilitated by the relaxing location which provided an ideal mixture of 'work', restful environment and excellent food! Coupled with the good number of participants (96 – not too many or too few), the high proportion of young researchers, and a group visit to Girona in the middle of the week, this created an ideal atmosphere for debate and the fruitful exchange of views. The conference was very enjoyable for the participants, and the feedback indicated that they found the event very useful in terms of discussing issues with scientists from a wide range of disciplines, as well as evaluating their own scientific views in the context of Synthetic Biology. There was unanimous agreement for another conference in the future.

However there was one major complaint from all of the attendees: the wifi connections were so poor throughout the entire meeting that there was no effective useable internet connection. Many were unable to carry out crucial time-critical activities such as meeting funding deadlines, doing scientific paper reviews, project reviews etc. The majority of attendees agreed to attend on the understanding that they could access the internet in order to carry on with normal academic business. The concern is that unless a better wifi service can be guaranteed at Eden Roc or an alternative location, many members of the community will simply refuse to attend the next meeting, and the hard work and investment that has been put into establishing this community will have gone to waste. We note that this complaint was also made at the last conference ECSBI, and that the wifi service has not practically improved since then.