European Commission 6th Framework Programme

NEST – New and Emerging Science and Technology

SYNBIOLOGY

An Analysis of Synthetic Biology Research in Europe and North America

Final Report on Analysis of Synthetic Biology Sector

September 2006

Deliverable D11

FP6-2003-NEST-B4 Project 015357 – SYNBIOLOGY

Sociedade Portuguesa de Inovação

ATG:biosynthetics
Your Partner in Synthetic Biology

UMBC
AN HONORS UNIVERSITY IN MARYLAND

CERES
1994-2004

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EXECUTIVE SUMMARY

This is the Final Report of the Synbiology: An Analysis of Synthetic Biology Research in Europe and North America project. It is provided as Deliverable Number 11 for the project FP6-2003-NEST-B4 Project 015357 – SYNBIOLOGY.

There are many different practical approaches to Synthetic Biology that emanate from different disciplines, which can all claim to represent Synthetic Biology research and engineering.

Synthetic Biology is not primarily a discovery science. It builds on our current understanding of systemic behaviour of biologic systems trying to simplify and optimize some of the complex interactions characteristic in natural biology. The outstanding feature of advanced Synthetic Biology is the standardisation of biological parts in order to create modular molecular tool boxes for the design of artificial molecular systems of biological function. The advantage and promise of this concept is to dramatically reduce the development time of applications based on Synthetic Biology tools compared to classical molecular engineering and molecular biology.

Thus, Synthetic Biology is intentional design based engineering of systems based on artificial biological functions and rules aimed at obtaining new functions which are not present in nature.

The Synbiology project's working definition of Synthetic Biology is as follows: *Synthetic Biology is the engineering of biological components and systems that do not exist in nature and the re-engineering of existing biological elements; it is determined on the intentional design of artificial biological systems, rather than on the understanding of natural biology.*

This Final Report provides an overview of the Synbiology project background and methodology, and brings together the project results. The Report also has the objective of detailing the actions undertaken to disseminate the project results. The Report draws on the previous Synbiology project outputs, including the following:

D3: Synthetic Biology Research – Literature & Statistical Review

D8: Synthetic Biology Research Assessment

D9: Europe/North America Comparative Assessment.

The Report also draws on the information provided in the Synbiology Project Database, which includes 1,100 papers connected to the Synthetic Biology field in peer-reviewed journals published since 1990.

The Report is provided jointly by the consortium led by Sociedade Portuguesa de Inovação. The consortium members are ATG:Biosynthetics, the Center for Economic Research and Environmental Strategy and the University of Maryland Baltimore County.

1. INTRODUCTION

1.1. Note on the Synbiology Project

This is the Final Report of the Synbiology: An Analysis of Synthetic Biology Research in Europe and North America project - FP6-2003-NEST-B4 Project 015357 – SYNBIOLOGY.[1]

The project is co-ordinated by Sociedade Portuguesa de Inovação (SPI). The project partners are:

- University of Maryland Baltimore County (UMBC)
- ATG: Biosynthetics GmbH (ATG)
- Center for Economic Research and Environmental Strategy (CERES).[2]

Recent progress in Synthetic Biology has been significant and wide-ranging. As recognized in the European Commission 6th Framework Programme, a new realm of possibilities for biology-based scientific discovery and innovation is on the horizon.

The nature of the Synthetic Biology sector may result in a number of obstacles to realizing the benefits from Synthetic Biology research. The European Commission NEST (New and Emerging Science and Technology) Programme is one of the key drivers to ensure that scientific research and commercial benefits are maximized in Europe. Thus, in addition to knowledge of the technical research issues, it is vital that the European Commission NEST Programme has a clear understanding of the Synthetic Biology sector.

The first objective of the Synbiology project is thus to provide a sector analysis to assist the European Commission in furthering its understanding of the Synthetic Biology sector, on which are the main actors in the sector, what is the geographic distribution of this research and what funding is currently available. The second objective of the project is to disseminate the sector information and analysis to all interested stakeholders and the general public.

The focus of the Synbiology project's research is Europe and North America.

A Review Panel was initiated for the Synbiology project. This Review Panel were asked to provide brief comments on the project work during the early stages of the project. The Review Panel members are:

- Prof. George Attard – University of Southampton, UK

[1] The European Commission Project Officer for the Synbiology project is Dr. Christian Krassnig.

[2] In addition, Mr. Mark Spinoglio was subcontracted to provide certain tasks for the project.

- Dr. Vitor Martins dos Santos – German Research Centre for Biotechnology
- Prof. Sven Panke – Swiss Federal Institute of Technology
- Prof. Jorge Laborda – University of Castilla-La Mancha, Spain
- Prof. Klaus Palme – Albert Ludwigs University, Freiberg, Germany.

The Synbiology project partners would like to thank the Review Panel members. It should be noted that the Review Panel members are not responsible for the content of the Synbiology project outputs, which are the responsibility and reflect the views of the Synbiology project partners alone. Mistakes also remain the sole responsibility of the project partners.

1.2. Note on the Final Report

This is the Final Report of the Synbiology: An Analysis of Synthetic Biology Research in Europe and North America project. It is provided as Deliverable Number 11 for the project FP6-2003-NEST-B4 Project 015357 – SYNBIOLOGY.

The objective of the Report is to provide an overview of the Synbiology project background and methodology, and bring together all the project results in one document. The Report also has the objective of detailing the actions undertaken to disseminate the project results. The Report thus draws on the previous Synbiology project outputs, including the following:

D3: Synthetic Biology Research – Literature & Statistical Review: A comprehensive discussion of which activities constitute Synthetic Biology research and the current level of understanding in this research

D8: Synthetic Biology Research Assessment: An overview of Synthetic Biology research on a country and regional basis

D9: Europe/North America Comparative Assessment: A comparative analysis of Synthetic Biology research environments, including discussion of funding agencies and the results of the project questionnaire

The Report also draws on the information provided in the Synbiology Project Database, which includes 1,100 papers connected to the Synthetic Biology field in peer-reviewed journals published since 1990.

After this Note on the Final Report, this Introduction chapter includes discussion of the definition of Synthetic Biology.

The Report then includes the following chapters:

- Chapter 2: Key Stakeholders in Synthetic Biology
- Chapter 3: Geographical Analysis of Synthetic Biology Publications
- Chapter 4: Results of the Synbiology Project Survey
- Chapter 5: Policies in Europe and North America
- Chapter 6: European/North American Funding Agencies
- Chapter 7: Dissemination of Synbiology Project
- Chapter 8: Summary.

The Final Report also has four annexes:

- Annex 1: Project Brochure (D1)
- Annex 2: Project Fact Sheet (D5)
- Annex 3: Project Results Brochure
- Annex 4: iGEM and SyntheticBiology 2.0 and 3.0

1.3. Definition of Synthetic Biology

Previous Synbiology project outputs have focused on providing a definition of Synthetic Biology, an extended analysis of literature, as well as positioning Synthetic Biology into other scientific fields and its relationship to different other scientific disciplines.

In this Final Report we provide a brief overview of this heterogeneous but definable scientific field. More detail on the definition of Synthetic Biology, and what activities can be classified as Synthetic Biology, can be found in Output D3: Literature and Statistical Review. Based on its work, the Synbiology consortium is developing a *Consensus Paper* on the definition of Synthetic Biology, which is intended for publication in a peer-reviewed journal. It is expected that this Consensus Paper, which is not a contracted deliverable of the project, will be finalised at the end of 2006.[3]

[3] A draft of the Consensus Paper can be found at http://www.atg-biosynthetics.com/synbiology.html.

It was found that Synthetic Biology can be defined as the boundary between biological sciences and engineering sciences, in which technical approaches are employed to provide future applications.

All currently provided or intended Synthetic Biology applications focus on the design of artificially modified living systems, such as specialized cells for the biobased production of molecules for *in vivo* or *in vitro* use. The key features of Synthetic Biology are on different levels of living systems:

1. Deployment of living systems to engineer complex patterns of artificial biological design containing components of compatible and functional molecular assemblies which are sustainably maintained through continued life cycles.
2. Artificial assemblies of regulators in artificial circuits with designed functions rather than simple single regulator modifications.
3. Deployment of functional assemblies of artificial pathways by modified artificially regulated genes of structural or catalytic function.
4. Production of artificial molecules as primary or secondary gene products

    (a) Macromolecules

        i. RNAs or Proteins, e.g. artificial enzyme catalysts, intracellular or new assemblies in vitro for any biotransformation.

        ii. Artificial biological regulators towards artificial regulating schemes for use in, for instance, molecular medicine.

        iii. Intra- or extra cellular, as molecular sensors for use in, for example, environmental technologies.

        iv. Building blocks for complex subcellular assemblies for nanostructuring of surfaces.

    (b) Small molecules for use as biological drugs, building blocks for chemical synthesis, or for the purpose of nanotechnological engineering of more complex units for different applications

        i. New drugs, starting from design synthesis of Macrolids, Polyketides and non ribosomal peptide synthesis.

        ii. New biobased monomers for the synthesis of macromolecules and towards never seen polymers created by a new deterministic polymer chemistry.

Therefore, the first word "synthetic" in Synthetic Biology describes the synthesis of artificial and natural components forming a new artificial living system. Furthermore, as the techniques for system design, synthesis and optimization mature, we will witness a rapid growth in the capabilities of synthetic systems with a wide-range of applications made possible with the synthesis products of these artificial living systems.

The second intended core competence of Synthetic Biology is the deployment of highly functional artificial assemblies of designed bioregulators and regulatory circuits in combination with redesigned genes, with clearly specified technical and functional requirements for effective and highly controlled bioproduction of natural products, biochemicals and xenobiotica.

The intended applications in Synthetic Biology are fascinating and aim to create and transfer robust behaviour of complex functionality from *in silico* modelling and simulation to *in vivo* and *in vitro* systems with expected identical behaviour. All such applications use parts, building blocks or compounds provided by bioproduction of *in vivo* Synthetic Biology applications.

Only bioambitioned nanotechnology approaches which use parts and building blocks from artificial biologic production for more complex systemic function, such as self-assembly or other self-organizing systems, can be classified accordingly *in vitro* Synthetic Biology. *In vivo* Synthetic Biology therefore is an indispensable prerequisite for providing materials such as artificial designed molecules and material with desired function for *in vitro* Synthetic Biology applications

In the field of *in silico* Synthetic Biology there is a distinction between enabling software, such as traditional bioinformatic software and biological databases, and Synthetic Biology software and algorithms. Sometimes it is difficult to draw this border, since enabling software is mostly the basis for more sophisticated Synthetic Biology computing. Simulating and computer added design algorithms and programs which support design, engineering and creation of Synthetic Biology parts, devices, systems directly resulting in Synthetic Biology applications can be regarded as *in silico* Synthetic Biology. In these, the analysis of systemic behaviour of artificially designed genetic circuits, e.g. modelling of genetic circuits and networks considering noise directly, can be termed as *theoretical* Synthetic Biology.

Synthetic Biology is the deployment of an engineering discipline that is objective driven. It is not primarily a discovery science, as it builds on our current understanding while simplifying some of the complex interactions characteristic of natural biology. Also, it is intentional design based engineering of systems based on biological functions and rules aimed at obtaining new functions which are not present in nature.

The project's working definition is as follows: *Synthetic Biology is the engineering of biological components and systems that do not exist in nature and the re-engineering of existing biological elements; it is determined on the intentional design of artificial biological systems, rather than on the understanding of natural biology.*

2. KEY STAKEHOLDERS IN SYNTHETIC BIOLOGY

2.1. Introduction

This chapter is based upon the identification of Synthetic Biology Key Stakeholders and the publications included in the Synbiology Project Database provided during the project.[4,5]

The Project Database has been developed over the life of the Synbiology Project. This Database provides references to 1,100 papers published in peer-reviewed journals in the Synthetic Biology sector. Each paper in the Database has been assigned an *impact factor*. This is calculated from the importance of the journal in which the paper was published, as measured by the Thomson Scientific Index. These impact factors allow the Database to attach an estimate of the importance to the Synthetic Biology research of each individual paper in the Project Database.

The information in this chapter was previously presented as part of Output D8: Synthetic Biology Research Assessment.

The chapter introduces 50 Key Stakeholders involved in Synthetic Biology research - with a focus on North America and Europe (including the Europe-33 research area countries). These introductions include a short description of their activities and a listing of their papers included in the Synbiology Project Database.[6,7]

It should be noted that the Synbiology Project Database includes links to the relevant organisation and/or personal websites for all the Key Stakeholders introduced in this chapter.

In addition, Annex 4 includes information on two key groups of Synthetic Biology researchers – iGEM (The international Genetically Engineered Machine competition), and the SyntheticBiology2.0 / 3.0 conferences programmes.

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[4] Key Stakeholders are defined in the project as those leading individuals representing Synthetic Biology research, industry and government across Europe and North America.

[5] The Synbiology Project Database is provided as part of Output D2: Project Website - http://www2.spi.pt/synbiology/index.asp

[6] These Key Stakeholders were identified as those with the highest impact weighting separately in North America and Europe applied to their publications in the Synbiology Project Database and through a general assessment by the Synbiology team members of the individuals most involved in the European and North American Synthetic Biology sector. As with all such lists, there remains a significant level of subjectivity in the choice of researchers. The list is in no way intended to represent a ranking of research.

[7] In Output D8: Synthetic Biology Research Assessment, a longer list of Key Stakeholders is provided.

2.2. Key Stakeholder Details – North America

Name	**Institution/Contact Information**
Adam Arkin	Department of Bioengineering, University of California Berkeley

Research Description

Interested in developing a physically-based engineering discipline for cellular and multicellular systems. Such a discipline will lead to a deeper understanding of cellular regulation and development, more efficient discovery of cellular networks, and a better ability to engineer or control cells for industrial or medical purposes. To this end the work develops and applies mathematical theory, computational and experimental approaches to analysis of cellular function.

http://genomics.lbl.gov/People.html

Publications in Synbiology Project Database

"Stochastic kinetic analysis of developmental pathway bifurcation in phage lambda-infected Escherichia coli cells" - Genetics 1998 Aug 149(4):1633-48.

"Stochastic mechanisms in gene expression"- Proc Natl Acad Sci U S A 1997 Feb 4;94(3):814-9.

"Computational functions in biochemical reaction networks" Biophys J 1994 Aug;67(2):560-78.

"A tightly regulated inducible expression system utilizing the fim inversion recombination switch" - Biotechnol Bioeng. 2006 May 5;94(1):1-4.

"Stochastic amplification and signalling in enzymatic futile cycles through noise-induced bistability with oscillations"- Proc Natl Acad Sci U S A 2005 Feb 15;102(7):2310-5

"An allosteric model for transmembrane signalling in bacterial chemotaxis" - J Mol Biol 2004 Oct 15;343(2):291-303.

Name	**Institution/Contact Information**
Frances Arnold	Division of Chemistry and Chemical Engineering, California Institute of Technology

Research Description

Research in the group focuses on evolutionary design methods applied to biological systems - enzymes, metabolic pathways, genetic circuits and ecosystems - and using the results of laboratory evolution experiments to elucidate principles of biological design. The group develops technology for laboratory evolution, including methods for making and characterizing gene libraries, high throughput screening, and hybrid computational-evolutionary optimization strategies.

http://www.che.caltech.edu/faculty/arnold_f/index.html

Publications in Synbiology Database

"Protein stability promotes evolvability" - Proc Natl Acad Sci U S A. 2006 Apr 11;103(15):5869-74.

"Programmed population control by cell-cell communication and regulated killing" - Nature 2004 Apr 22;428(6985):868-71.

"General method for sequence-independent site-directed chimeragenesis" - J Mol Biol 2003 Jul 4;330(2):287-96.

"Protein building blocks preserved by recombination" - Nat Struct Biol 2002 Jul;9(7):553-8.

"Directed evolution of a genetic circuit" - Proc Natl Acad Sci U S A 2002 Dec 24;99(26):16587-91.

"Molecular breeding of carotenoid biosynthetic pathways" - Nat Biotechnol 2000 Jul;18(7):750-3.

Name	**Institution/Contact Information**
Yaakov Benenson	Bauer Center for Genomics Research, Harvard University

Research Description

The group designs molecular systems to process biological information in new ways. They call them "molecular automata" after electromechanical automata that process information encoded in electric pulses. A molecular automaton is a complex, artificially constructed network of interacting biomolecules.

Applications of molecular automata range from complex real-time probing of single cells, to disease diagnostics and treatment with a single-cell resolution, to "reprogramming" cells. The group also hopes, through this work, to uncover fundamental principles pertaining to information processing by living systems in much the same way as the development of a steam engine led to the foundation of thermodynamics

http://www.sysbio.harvard.edu/csb/benenson/

Publications in Synbiology Database

"Stochastic computing with biomolecular automata" - Proc Natl Acad Sci U S A 2004 Jul 6;101(27):9960-5.

Catalytic mechanism of Kdo8P synthase: transient kinetic studies and evaluation of a putative reaction intermediate" - Biochemistry 1998 Nov 17;37(46):16390-9.

An autonomous molecular computer for logical control of gene expression" - Nature 2004 May 27;429(6990):423-9.

DNA molecule provides a computing machine with both data and fuel" - Proc Natl Acad Sci U S A 2003 Mar 4;100(5):2191-6.

Programmable and autonomous computing machine made of biomolecules" - Nature 2001 Nov 22;414(6862):430-4.

Name	**Institution/Contact Information**
Carlos Bustamante	Department of Molecular and Cell Biology, University of California Berkeley

Research Description

Research focuses on the dynamics, structure and kinetics of molecular motors and nucleo-protein assemblies. The tools used are Scanning Force Microscopy (SFM), optical tweezers, magnetic tweezers and fluorescence methods.

http://mcb.berkeley.edu/faculty/BMB/bustamantec.html

Publications in Synbiology Database

"Direct observation of one-dimensional diffusion and transcription by Escherichia coli RNA polymerase" - Biophys J 1999 Oct;77(4):2284-94.

Name	**Institution/Contact Information**
George Church	Harvard-MIT Division of Health Sciences and Technology, Harvard University

Research Description

The mission of the group is to develop broadly distributed, integrated models for biomedical & ecological systems. To make these systems-biology models useful & accurate, they develop biotechnologies suitable for comprehensive yet cost-effective systems measurements and synthesis of designed biosystems. In particular, the group focuses on replication of four systems -- mammalian stem cells, cell-cycle metabolism, microbial ecosystems (e.g. ocean circadian cycles and biofilms), and "in vitro" mini-genomes. Each of these has advantages for developing "systems analysis" tools & each represent existing clinical or commercial practice ripe for improvements (e.g. respectively, stem cell transplants, metabolic engineering, environmental bioremediation, and molecular biology "kits").

http://arep.med.harvard.edu/gmc/

Publications in Synbiology Database

"Sequencing genomes from single cells by polymerase cloning" - Nat Biotechnol. 2006 Jun;24(6):680-6.

"A network of transcriptionally coordinated functional modules in Saccharomyces cerevisiae" - Genome Res 2005 Sep;15(9):1298-306.

"A motif co-occurrence approach for genome-wide prediction of transcription-factor-binding sites in Escherichia coli." - Genome Res 2004 Feb;14(2):201-8.

"On the complete determination of biological systems" - Trends Biotechnol 2003 Jun;21(6):251-4.

"Nucleotides of transcription factor binding sites exert interdependent effects on the binding affinities of transcription factors" - Nucleic Acids Res 2002 Mar 1;30(5):1255-61.

"A statistical model for investigating binding probabilities of DNA nucleotide sequences using microarrays" - Biometrics 2002 Dec;58(4):981-8.

Name	**Institution/Contact Information**
James Collins	Center for BioDynamics and Department of Biomedical Engineering, Boston University

Research Description

Research focuses on developing nonlinear dynamic techniques and devices to characterize, improve and mimic biological function. Specific interests include: (1) modelling, designing and constructing synthetic gene networks; (2) reverse engineering naturally occurring gene regulatory networks; and (3) developing noise-based sensory prosthetics.

http://www.bu.edu/dbin/bme/faculty/?prof=jcollins

Publications in Synbiology Database

"A bottom-up approach to gene regulation" - Nature. 2006 Feb 16;439(7078):856-60.

"RNA synthetic biology" - Nat Biotechnol. 2006 May;24(5):545-54.

"Chemogenomic profiling on a genome-wide scale using reverse-engineered gene networks"- Nat Biotechnol 2005 Mar;23(3):377-83.

"And the noise played on: stochastic gene expression and HIV-1 infection" - Cell 2005 Jul 29;122(2):147-9.

"Programmable cells: interfacing natural and engineered gene networks" - Proc Natl Acad Sci U S A 2004 Jun 1;101(22):8414-9.

"Engineered riboregulators enable post-transcriptional control of gene expression" - Nat Biotechnol 2004 Jul;22(7):841-7.

"Noise in eukaryotic gene expression" - Nature 2003 Apr 10;422(6932):633-7.

"Reverse engineering gene networks: integrating genetic perturbations with dynamical modelling" - Proc Natl Acad Sci U S A 2003 May 13;100(10):5944-9.

"Prediction and measurement of an autoregulatory genetic module" - Proc Natl Acad Sci U S A 2003 Jun 24;100(13):7714-9.

"Synchronizing genetic relaxation oscillators by intercell signaling" - Proc Natl Acad Sci U S A 2002 Jan 22;99(2):679-84.

"Designer gene networks: Towards fundamental cellular control" Chaos 2001 Mar;11(1):207-220.

"Construction of a genetic toggle switch in Escherichia coli" - Nature 2000 Jan 20;403(6767):339-42.

"Noise-based switches and amplifiers for gene expression" - Proc Natl Acad Sci U S A 2000 Feb 29;97(5):2075-80.

Name	**Institution/Contact Information**
Michael Elowitz	Division of Biology, California Institute of Technology

Research Description

The Elowitz Lab is interested in how genetic circuits, composed of interacting genes and proteins, enable individual cells to make decisions, oscillate, and communicate with one another. To learn about these issues, they develop and use several experimental techniques, especially time-lapse movies.

(http://www.elowitz.caltech.edu/)

Publications in Synbiology Database

"An excitable gene regulatory circuit induces transient cellular differentiation" - Nature. 2006 Mar 23;440(7083):545-50.

"Gene regulation at the single-cell level" - Science 2005 Mar 25;307(5717):1962-5.

"Stochastic gene expression in a single cell" - Science 2002 Aug 16;297(5584):1183-6.

"A synthetic oscillatory network of transcriptional regulators" - Nature 2000 Jan 20;403(6767):335-8.

Name	**Institution/Contact Information**
Drew Endy	Department of Biological Engineering, Massachusetts Institute of Technology

Research Description

The group works to enable the design and construction of large scale integrated biological systems. Biology presents a new medium for engineering and contains many domain-specific challenges (e.g., evolution). Still, in getting started, the group makes use of past successful experience in other disciplines. They are currently exploring the application of three past engineering lessons: (1) standardization of components, conditions, and characterization, (2) abstraction as a tool for hiding information and managing complexity, and (3) decoupling of overwhelming, complicated problems into many simpler problems (e.g., design and fabrication).

(http://openwetware.org/wiki/Endy:Research)

Publications in Synbiology Database

"Computation, prediction, and experimental tests of fitness for bacteriophage T7 mutants with permuted genomes" - Proc Natl Acad Sci U S A 2000 May 9;97(10):5375-80.

"Regulated cell-to-cell variation in a cell-fate decision system" - Nature 2005 Sep.

Name	**Institution/Contact Information**
Marvin Frazier	Venter Institute

Research Description

The J. Craig Venter Institute is a not-for-profit research institute dedicated to the advancement of the science of genomics; the understanding of its implications for society; and the communication of those results to the scientific community, the public, and policymakers. Founded by J. Craig Venter, Ph.D., the Institute is home to approximately 200 staff and scientists with expertise in human and evolutionary biology, genetics, bioinformatics/informatics, high-throughput DNA sequencing, information technology, and genomic and environmental policy research.

(http://www.venterinstitute.org/)

Publications in Synbiology Database

N/A

Name	**Institution/Contact Information**
Tim Gardner	Department of Biomedical Engineering, Boston University

Research Description

Microbial organisms are something of a double-edged sword for humankind. They can cause debilitating or fatal infections; but they are also the source of many therapeutic drugs, may be used to detoxify polluted environmental areas, and may even offer solutions to the world's expanding demand for energy. To identify novel treatments that overcome bacterial resistance, and to unlock the full catalytic potential of microbes for bioremediation and energy production, a clearer understanding is needed of the complex systems of genes, proteins and metabolites underlying cell function. The group is currently focused on developing computational and experimental tools for mapping and modelling system-wide properties of gene regulatory networks in microbes. To this end, they have recently developed a network inference method (Network Identification by multiple Regression-the NIR method) and successfully applied it in E. coli.

(http://www.bu.edu/dbin/bme/faculty/?prof=tgardner)

Publications in Synbiology Database

"Construction of a genetic toggle switch in Escherichia coli" - Nature 2000 Jan 20;403(6767):339-42.

"Programmable cells: interfacing natural and engineered gene networks" - Proc Natl Acad Sci U S A 2004 Jun 1;101(22):8414-9.

Name	**Institution/Contact Information**
Terence Hwa	Center for Theoretical Biological Physics & Department of Physics, University of California San Diego

Research Description

Current activities in the lab are focused in the area of quantitative and systemic biology. Progress in this new emerging discipline requires a combination of expertise in biology, chemistry, engineering, and physics. The lab is taking an integrated approach, with efforts both in theory (statistical biophysics and bioinformatics) and experiment (molecular and evolution biology). Experiments are often theory-motivated, yet discoveries made in the lab have inspired fresh theoretical view points. In similar ways, the group's theoretical studies play the dual role of analyzing experimental results and guiding new generation of experiments. The close interaction between theory and experiment allows the theorists to be in contact with the reality of molecular biology, and allows the experimentalists to have a good sense of the power and limitations of quantitative analysis. In this way, the group hopes to train a new generation of scientists who can freely exploit opportunities at the interface between biology and physics.

(http://matisse.ucsd.edu/#Research)

Publications in Synbiology Database

"Nonlinear protein degradation and the function of genetic circuits" - Proc Natl Acad Sci U S A 2005 Jul 5;102(27):9559-64.

"On schemes of combinatorial transcription logic" - Proc Natl Acad Sci U S A 2003 Apr 29;100(9):5136-41.

"Physical constraints and functional characteristics of transcription factor-DNA interaction" - Proc Natl Acad Sci U S A 2002 Sep 17;99(19):12015-20.

Name	**Institution/Contact Information**
Jay Keasling	Department of Chemical Engineering, University of California Berkeley

Research Description

The research in the Keasling Laboratory focuses on the metabolic engineering of microorganisms for degradation of environmental contaminants or for environmentally friendly synthesis. To that end, they have developed a number of new genetic and mathematical tools to allow more precise and reproducible control of metabolism. These tools are being used in such applications as synthesis of biodegradable polymers, accumulation of phosphate and heavy metals, and degradation of chlorinated and aromatic hydrocarbons, biodesulfurization of fossil fuels, and complete mineralization of organophosphate nerve agents and pesticides.

http://cheme.berkeley.edu/people/faculty/keasling/keasling.html

Publications in Synbiology Database

"Engineering Cotton (+)-delta-Cadinene Synthase to an Altered Function: Germacrene D-4-ol Synthase" - Chem Biol. 2006 Jan;13(1):91-8.

"Designed divergent evolution of enzyme function" - Nature. 2006 Feb 22.

"A Salmonella-based, propionate-inducible, expression system for Salmonella enterica" - Gene. 2006 Apr 6.

"Catabolite repression of the propionate catabolic genes in Escherichia coli and Salmonella enterica: evidence for involvement of the cyclic AMP receptor protein" - J Bacteriol 2005 Apr;187(8):2793-800.

"Optimization of DsRed production in Escherichia coli: Effect of ribosome binding site sequestration on translation efficiency" - Biotechnol Bioeng 2005 Oct 24.

"A Propionate-Inducible Expression System for Enteric Bacteria" - Appl Environ Microbiol 2005 Nov;71(11):6856-6862.

"Propionate-regulated high-yield protein production in Escherichia coli" - Biotechnol Bioeng. 2005 Dec 6.

"Mono and diterpene production in Escherichia coli" - Biotechnol Bioeng 2004 Jul 20;87(2):200-12.

"Uranyl precipitation by Pseudomonas aeruginosa via controlled polyphosphate metabolism" - Appl Environ Microbiol 2004 Dec;70(12):7404-12.

"A constructed microbial consortium for biodegradation of the organophosphorus insecticide parathion" - Appl Microbiol Biotechnol 2003 Mar;61(1):77-81.

Name	**Institution/Contact Information**
Thomas Knight	Department of Electrical Engineering and Computer Science, Massachusetts Institute of Technology

Research Description

The Knight lab is developing an engineering technology based on biology. The manufacture of complex structures at the atomic scale requires a fundamental change in approach - a shift from physical to chemical processes. Taking effective engineering control over biochemistry allows us to engineer complex atomic level structures with a precision unmatched by any lithographic technology. The group believes this capability is the key to cost effective nanoscale fabrication, becoming the dominant manufacturing technology of this century.

(http://csbi.mit.edu/members/Members/tknight)

Publications in Synbiology Database

N/A

Name	**Institution/Contact Information**
Wendell Lim	Departments of Cellular and Molecular Pharmacology and Biochemistry and Biophysics, University of California San Francisco

Research Description

The group is interested in understanding the logic by which simple protein components can be used to build complex information processing systems, and is aiming to answer this question at several hierarchical levels.

http://www.ucsf.edu/limlab/people/wendell.html

Publications in Synbiology Database

"The Ste5 Scaffold Allosterically Modulates Signaling Output of the Yeast Mating Pathway" - Science. 2006 Jan 19.

"Domains, Motifs, and Scaffolds: The Role of Modular Interactions in the Evolution and Wiring of Cell Signaling Circuits." - Annu Rev Biochem. 2006 Mar 17.

"A polybasic motif allows N-WASP to act as a sensor of PIP(2) density"- Mol Cell 2005 Jan 21;17(2):181-91.

"A general model for preferential hetero-oligomerization of Lin-2/7 domains: Mechanism underlying directed assembly of supramolecular signaling complexes" - J Biol Chem 2005 Sep 7.

"The role of docking interactions in mediating signaling input, output, and discrimination in the yeast MAPK network" - Mol Cell. 2005 Dec 22;20(6):951-62.

"Sho1 and Pbs2 act as coscaffolds linking components in the yeast high osmolarity MAP kinase pathway" - Mol Cell 2004 Jun 18;14(6):825-32.

"Rewiring MAP kinase pathways using alternative scaffold assembly mechanisms" - Science 2003 Feb 14;299(5609):1061-4.

"Reprogramming control of an allosteric signaling switch through modular recombination" - Science 2003 Sep 26;301(5641):1904-8.

"Optimization of specificity in a cellular protein interaction network by negative selection" - Nature 2003 Dec 11;426(6967):676-80.

"Integration of multiple signals through cooperative regulation of the N-WASP-Arp2/3 complex" - Science 2000 Oct 27;290(5492):801-6.

Name	**Institution/Contact Information**
Chengde Mao	Department of Chemistry, Purdue University

Research Description

The group's research lies at the interface between chemistry, biology, nanotechnology and materials science. It falls into two general themes: 1) developing nanotechnology with biochemical approaches; 2) applying nanotechnology to address fundamental problems in chemistry and biology.

(http://www.chem.purdue.edu/people/faculty/faculty.asp?itemID=46)

Publications in Synbiology Database

"Virus-based toolkit for the directed synthesis of magnetic and semiconducting nanowires" - Science 2004 Jan 9;303(5655):213-7.

"Viral assembly of oriented quantum dot nanowires" - Proc Natl Acad Sci U S A 2003 Jun 10;100(12):6946-51.

"Logical computation using algorithmic self-assembly of DNA triple-crossover molecules" - Nature 2000 Sep 28;407(6803):493-6.

"A nanomechanical device based on the B-Z transition of DNA" - Nature 1999 Jan 14;397(6715):144-6.

Name	**Institution/Contact Information**
Richard Murray	Control and Dynamical Systems, California Institute of Technology

Research Description

The group's research is in the application of feedback and control to mechanical, information, and biological systems. Current projects include integration of control, communications, and computer science in multi-agent systems, information dynamics in networked feedback systems, analysis of insect flight control systems, and synthetic biology using genetically-encoded finite state machines.

(http://www.cds.caltech.edu/~murray/wiki/Main_Page)

Publications in Synbiology Database

"Experimental evolution of mating discrimination in budding yeast." - Curr Biol. 2006 Feb 7;16(3):280-6.

"The centromeric protein Sgo1 is required to sense lack of tension on mitotic chromosomes" Science 2005 Jan 7;307(5706):130-3.

"Identification of xenopus CENP-A and an associated centromeric DNA repeat" - Mol Biol Cell 2005 Apr;16(4):1800-10.

"A small-molecule inhibitor of Mps1 blocks the spindle-checkpoint response to a lack of tension on mitotic chromosomes" - Curr Biol 2005 Jun 7;15(11):1070-6.

"From molecular to modular cell biology." - Nature 1999 Dec 2;402(6761 Suppl):C47-52.

Name	**Institution/Contact Information**
Paul Rabinow	Department of Anthropology, University of California Berkeley

Research Description

Work has consistently centred on modernity as a problem: a problem for those seeking to live with its diverse forms, a problem for those seeking to advance or resist modern projects of power and knowledge. This work has ranged from descendants of a Moroccan saint coping with the changes wrought by colonial and post-colonial regimes, to the wide array of knowledge and power relations entailed in the great assemblage of social planning in France, to my work of the last decade on molecular biology and genomics.

(http://ls.berkeley.edu/dept/anth/rabinow.html)

Publications in Synbiology Database

N/A

Name	**Institution/Contact Information**
Randy Rettberg	Department of Biological Engineering, Massachusetts Institute of Technology

Research Description

Randy Rettberg is Director of the MIT Registry of Standard Biological Parts: BioBricks and a principal research engineer in the biological engineering division at MIT. Previously, he worked for internet pioneer BBN (now Genuity), before moving to Sun Microsystems, where he was CTO for storage systems.

(http://openwetware.org/wiki/The_BioBricks_Foundation:Board_Members)

Publications in Synbiology Database

N/A

Name	**Institution/Contact Information**
Darko Stefanovic	Department of Computer Science, University of New Mexico

Research Description

The Molecular Computing group is a collaboration among chemists, chemical engineers, and computer scientists to understand how computing can occur at the subcellular level in organisms, and to harness computation for diagnostic and therapeutic uses in medicine.

http://www.cs.unm.edu/~darko/

Publications in Synbiology Database

"Deoxyribozyme-Based Three-Input Logic Gates and Construction of a Molecular Full Adder" - Biochemistry. 2006 Jan 31;45(4):1194-1199.

"Deoxyribozyme-based half-adder" - J Am Chem Soc 2003 Jun 4;125(22):6673-6.

"A deoxyribozyme-based molecular automaton" - Nat Biotechnol 2003 Sep;21(9):1069-74.

"Deoxyribozyme-based logic gates" - J Am Chem Soc 2002 Apr 10;124(14):3555-61.

Name	**Institution/Contact Information**
Milan Stojanovic	Division of Clinical Pharmacology and Experimental Therapeutics, Columbia University

Research Description

The group is interested in various devices based on nucleic acids. Some of the molecular devices behave as sensors (1), others release small molecules upon recognition (2), or behave as logic gates that perform Boolean calculations (3). Mixtures of individual devices show aggregate behaviours: some mimic the mammalian olfactory system and fingerprint molecules in solution (4), others perform basic arithmetic operations (5) or simply play games perfectly (6). The Searle Scholarship will allow the group to move into a new area, and study how recognition by assemblies of nucleic acids can be used to achieve directed mechanical movement. Specifically, the group proposes to construct "molecular spiders" which would move on recognition surfaces, and in this process irreversibly change the surface. Over time, the group hopes to learn how to trigger and direct the movement of spiders, with the eventual goal of constructing devices capable of autonomous nano-patterning (for applications in material sciences), building molecular machines able to solve simple mazes ("nanocybernetics"), and achieving insulin release by glucose responsive spiders (medical applications).

http://www.columbia.edu/~mns18/

Publications in Synbiology Database

"Deoxyribozyme-Based Three-Input Logic Gates and Construction of a Molecular Full Adder" - Biochemistry. 2006 Jan 31;45(4):1194-1199.

"Boolean control of aptamer binding states"- J Am Chem Soc 2005 Aug 17;127(32):11348-51.

"Modular aptameric sensors" - J Am Chem Soc 2004 Aug 4;126(30):9266-70.

"Deoxyribozyme-based half-adder" - J Am Chem Soc 2003 Jun 4;125(22):6673-6.

"Cross-reactive arrays based on three-way junctions" - J Am Chem Soc 2003 May 21;125(20):6085-9.

"A deoxyribozyme-based molecular automaton" - Nat Biotechnol 2003 Sep;21(9):1069-74.

"Deoxyribozyme-based logic gates" - J Am Chem Soc 2002 Apr 10;124(14):3555-61.

Name	**Institution/Contact Information**
Craig Venter	Venter Institute

Research Description

The J. Craig Venter Institute is a not-for-profit research institute dedicated to the advancement of the science of genomics; the understanding of its implications for society; and the communication of those results to the scientific community, the public, and policymakers. Founded by J. Craig Venter, Ph.D., the Institute is home to approximately 200 staff and scientists with expertise in human and evolutionary biology, genetics, bioinformatics/informatics, high-throughput DNA sequencing, information technology, and genomic and environmental policy research.

(http://www.venterinstitute.org/)

Publications in Synbiology Database

"Essential genes of a minimal bacterium" - Proc Natl Acad Sci U S A. 2006 Jan 10;103(2):425-30.

"Cell-free cloning using {phi}29 DNA polymerase" - Proc Natl Acad Sci U S A 2005 Nov 14.

"Environmental genome shotgun sequencing of the Sargasso Sea" - Science 2004 Apr 2;304(5667):66-74.

"Generating a synthetic genome by whole genome assembly: phiX174 bacteriophage from synthetic oligonucleotides" - Proc Natl Acad Sci U S A 2003 Dec 23;100(26):15440-5.

"Global transposon mutagenesis and a minimal Mycoplasma genome" - Science 1999 Dec 10;286(5447):2165-9.

Name	**Institution/Contact Information**
Ron Weiss	Electrical Engineering, Princeton University

Research Description

Research focuses on programming new cellular behaviours by designing and embedding synthetic gene networks that perform desired functions in single and multi-cellular environments. The group genetically engineers a variety of cell types including bacteria, yeast, and mammalian stem cells. This nascent field of Synthetic Biology holds promise for a wide range of applications such as programmed tissue engineering, environmental and effecting, biomaterial fabrication, and an improved understanding of naturally biological processes.

http://weisswebserver.ee.princeton.edu/users/rweiss/

Publications in Synbiology Database

"Synthetic biology: new engineering rules for an emerging discipline" - Mol Syst Biol. 2006;2:2006.0028.

"Signal-amplifying genetic circuit enables in vivo observation of weak promoter activation in the Rhl quorum sensing system" - Biotechnol Bioeng 2005 Mar 20;89(6):709-18.

"Ultrasensitivity and noise propagation in a synthetic transcriptional cascade" - Proc Natl Acad Sci U S A 2005 Mar 8;102(10):3581-6.

"A synthetic multicellular system for programmed pattern formation" - Nature 2005 Apr 28;434(7037):1130-4.

"Artificial cell-cell communication in yeast Saccharomyces cerevisiae using signaling elements from Arabidopsis thaliana" - Nat Biotechnol. 2005 Dec;23(12):1551-5.

"Spatiotemporal control of gene expression with pulse-generating networks." - Proc Natl Acad Sci U S A 2004 Apr 27;101(17):6355-60.

Name	**Institution/Contact Information**
Lingchong You	Department of Biomedical Engineering, Duke University

Research Description

Past efforts in engineering robust circuit dynamics have focused on the role of feedback regulation. The group's work focuses on an alternative yet complementary strategy: cell-cell communication. They are particularly interested in quorum sensing the cell-cell communication mechanism by which many bacteria sense and respond to changes in their population density. Using a synthetic population control circuit (You et al, Nature (2004) 428:868), we recently demonstrated that quorum sensing could be coupled with cell killing to generate integrated, robust population dynamics, despite variability among cells in their phenotype. The group is currently investigating whether and to what extent quorum sensing can indeed reduce variability in gene expression, and lead to more robust gene circuit dynamics. Furthermore, the group is interested in exploring mechanisms of cell differentiation and developmental pattern formation by engineering gene circuits to program these phenomena in bacteria.

(http://www.duke.edu/~you/)

Publications in Synbiology Database

"Programmed population control by cell-cell communication and regulated killing" - Nature 2004 Apr 22;428(6985):868-71.

"Modelling biological systems using Dynetica--a simulator of dynamic networks" - Bioinformatics 2003 Feb 12;19(3):435-6.

"Computation, prediction, and experimental tests of fitness for bacteriophage T7 mutants with permuted genomes" - Proc Natl Acad Sci U S A 2000 May 9;97(10):5375-80.

"Long-term monitoring of bacteria undergoing programmed population control in a microchemostat" - Science 2005 Jul 1;309(5731):137-.

2.3. Key Stakeholder Details – Europe (including Europe-33 research area)

Name	**Institution/Contact Information**
Uri Alon	Department of Molecular Cell Biology, Weizmann Institute of Science, Rehovot, Israel

Research Description

Focus on biological networks and circuits using a combined experimental and theoretical approach, aiming to uncover general underlying principles that govern their functioning. The group has defined "network motifs": basic interaction patterns that recur throughout biological networks. The same small set of network motifs appears to serve as the building blocks of transcription networks from bacteria to mammals. Specific network motifs are also found in signal transduction networks, neuronal networks and other biological and non-biological networks.

They have experimentally studied the function of each network motif in the transcription network of E. coli. Each network motifs can serve as an elementary circuit with a defined function: filters, pulse generators, response accelerators, temporal-pattern-generators and more.

Many of these experiments were performed using novel systems for measuring the behaviour of gene circuits within living cells. The group has developed a library of 2000 E. coli strains in which green fluorescent protein reports for the activity of the vast majority of the organisms' promoters. They are also currently developing a system for dynamic monitoring of hundreds of proteins in individual living human cells.

http://www.weizmann.ac.il/mcb/UriAlon/

Publications in Synbiology Database

"Rules for biological regulation based on error minimization" - Proc Natl Acad Sci U S A. 2006 Mar 14;103(11):3999-4004.

"Oscillations and variability in the p53 system" - Mol Syst Biol. 2006;2:2006.0033.

"Optimality and evolutionary tuning of the expression level of a protein" - Nature 2005 Jul 28;436(7050):588-92.

"Spontaneous evolution of modularity and network motifs" - Proc Natl Acad Sci U S A 2005 Sep 20;.

"Environmental selection of the feed-forward loop circuit in gene-regulation networks" - Phys Biol 2005 Jun;2(1-2):81-8.

"The Incoherent Feed-forward Loop Accelerates the Response-time of the gal System of Escherichia coli" - J Mol Biol. 2005 Dec 19.

"Dynamics of the p53-Mdm2 feedback loop in individual cells" - Nat Genet 2004 Feb;36(2):147-50.

"Using a quantitative blueprint to reprogram the dynamics of the flagella gene network" - Cell 2004 Jun 11;117(6):713-20.

"Topological generalizations of network motifs" - Phys Rev E Stat Nonlin Soft Matter Phys 2004 Sep;70(3 Pt 1):0319

"Response delays and the structure of transcription networks" - J Mol Biol 2003 Jun 13;329(4):645-54.

Name	**Institution/Contact Information**
Philippe Bastiaens	European Molecular Biology Laboratory, Cell Biology and Biophysics Unit, Heidelberg, Germany.

Research Description

The Bastiaens group focuses on the understanding of reaction-diffusion properties of protein reaction networks that generate spatial patterns of protein reaction states in cells, and how these reaction patterns regulate cellular signal transduction and morphogenesis. They develop optical microscopic approaches to image elementary protein reactions, such as interactions, post-translational modifications and conformational changes within the intact cell, thereby maintaining network interconnectivity and spatial organisation.

http://www-db.embl.de/jss/EmblGroupsOrg/per_1686.html

Publications in Synbiology Database

"EGFR activation coupled to inhibition of tyrosine phosphatases causes lateral signal propagation" - Nat Cell Biol 2003 May;5(5):447-53.

Name	**Institution/Contact Information**
Hamid Bolouri	Science & Technology Research Centre, University of Hertfordshire, UK

Research Description

Hamid Bolouri leads the BioComputation group at the Science & Technology Research Centre. He is also a Visiting Associate in the Division of Biology and in Control and Dynamical Systems at the California Institute of Technology (Caltech)

He focuses on the study of biological systems to learn how information is processed in biological systems, and how these systems have evolved. At Caltech his group are unravelling the genetic regulatory circuit underlying early cell differentiation in sea urchin embryos using qualitative modelling, macroarrays, and regulatory-sequence pattern searching. He also leads the development of the Systems Biology Workbench as part of the ERATO Kitano Systems Biology Project at Caltech.

http://strc.herts.ac.uk/bio/hamid/

Publications in Synbiology Database

"Transcriptional noise and cellular heterogeneity in mammalian macrophages" - Philos Trans R Soc Lond B Biol Sci. 2006 Mar 29;361(1467):495-50

"A method for estimating stochastic noise in large genetic regulatory networks" - Bioinformatics 2005 Jan 15;21(2):208-17.

"Control of internal and external noise in genetic regulatory networks" - J Theor Biol 2004 Oct 7;230(3):301-12.

Name	**Institution/Contact Information**
Erez Braun	Department of Physics, Technion-Israel Institute of Technology, Haifa, Israel

Research Description

Erez Braun is focused on experimental biophysics and nanotechnology, the interface between molecular biology and nanoelectronics, organic chemistry, electronic transport in small scale devices, and nonlinear dynamics of systems out of equilibrium

He leads the group's work to harness the power of DNA to create a self-assembling nanoscale transistor that can be switched on and off by applying voltage to it. This is seen as a crucial step in the future development of devices such as tiny computers with vastly increased speed and memory, and sensors to perform diagnostic tests in healthcare.

http://physics.technion.ac.il/~site/wisw/info_page.php?userid=erez

Publications in Synbiology Database

"DNA-templated carbon nanotube field-effect transistor" - Science 2003 Nov 21;302(5649):1380-2.

"DNA-templated assembly and electrode attachment of a conducting silver wire" - Nature 1998 Feb 19;391(6669):775-8.

Name	**Institution/Contact Information**
Hermann Bujard	Zentrum für Molekulare Biologie Heidelberg, University of Heidelberg, Germany.

Research Description

The merozoite surface protein 1 (MSP-1) of P.falciparum is for a number of reasons considered a promising candidate for a vaccine against Malaria tropica, the most severe form of human malaria. MSP-1 constitutes the major protein component at the surface of the erythrocyte-invading form (merozoite) of the parasite, and even though we still lack information on its exact function, it now is clear that MSP-1 plays a pivotal role during invasion of erythrocytes by merozoites.

Hermann Bujard's laboratory's work focuses on (1) Development of a vaccine based on full size MSP-1, (2) Exploration of the human immune response against MSP-1, and (3) Definition of structural and functional parameters of MSP-1. The laboratory is also developing methodological improvements for Tet regulation in vivo.

http://www.zmbh.uni-heidelberg.de/Bujard/default.shtml

Publications in Synbiology Database

"Dissecting the functional program of Escherichia coli promoters: the combined mode of action of Lac repressor and AraC activator" - Nucleic Acids Res 2001 Sep 15;29(18):3873-81.

"Independent and tight regulation of transcriptional units in Escherichia coli via the LacR/O, the TetR/O and AraC/I1-I2 regulatory elements" - Nucleic Acids Res 1997 Mar 15;25(6):1203-10.

"Tetracycline-controlled transcription in eukaryotes: novel transactivators with graded transactivation potential" - Nucleic Acids Res 1997 Jul 15;25(14):2723-9.

"Tight control of gene expression in mammalian cells by tetracycline-responsive promoters" - Proc Natl Acad Sci U S A 1992 Jun 15;89(12):5547-51.

"Stringent doxycycline-dependent control of gene activities using an episomal one-vector system" - Nucleic Acids Res 2005;33(16):e137.

"Optimal design of a single recombinant adeno-associated virus derived from serotypes 1 and 2 to achieve more tightly regulated transgene expression from nonhuman primate muscle" - Mol Ther 2004 Mar;9(3):410-8..

Name	Institution/Contact Information
Cees Dekker	Kavli Institute of Nanoscience, Section Molecular Biophysics, Delft University of Technology, Delft, Netherlands.

Research Description

Cees Dekker is one of the leaders of the Molecular Biophysics group at Delft University of Technology. The group's research focuses on single-molecule biophysics. The group employs magnetic and optical tweezers, AFM, STM, sensitive electrical measurements, and nanofabricated structures to study biomolecular systems and foster new nanotechnology. Current research lines include (1) Carbon nanotubes, electronic fundamentals and electrochemical sensors, (2) Local-probe studies of single enzymes acting on DNA and RNA, (3) DNA and biomolecular motors confined to nanofabricated structures, and (4) Ionic systems on the nanoscale

http://www.mb.tn.tudelft.nl/user/dekker/index.html

Publications in Synbiology Database

Molecular sorting by electrical steering of microtubules in kinesin-coated channels. Science. 2006 May 12;312(5775):910-4.

Name	Institution/Contact Information
Mans Ehrenberg	Department of Cell & Molecular Biology, Uppsala University, Sweden.

Research Description

The Ehrenberg group focuses on protein synthesis, protein synthesis in biotechnology and systems biology. The goal of their research in protein synthesis is to understand the mechanisms of termination of protein synthesis, recycling of ribosomes from termination back to initiation, initiation of protein synthesis, elongation of proteins, accuracy of tRNA and release factor selection by the messengerRNA coded ribosome, toxicity of mini-genes and drop-off of peptidyl-tRNA. In protein synthesis in biotechnology, their goal is to constitute an in vitro system for bacterial protein synthesis which can be used to (i) produce any conceivable protein in large scale starting from its gene sequence (ii) synthesise proteins which are isotope labeled in chosen regions to facilitate structural analysis with NMR (iii) develop new, powerful techniques for combinatorial design of oligo-peptides and proteins and apply these methods to obtain new antibiotics, new protein biosensors and new catalysts.

In the area of systems biology, the group explores (1) Stochastic modelling of copy number control for plasmids, with special reference to plasmids ColE1 and R1, (2) General features of noise in intracellular control systems, (3) Regulation of protein synthesis, adaptation and growth control in bacteria, (4) Action of antibiotics and mechanisms for antibiotic resistance in bacteria, and (5) Development of numerical methods for stochastic descriptions of intracellular reaction-networks including diffusion-reaction couplings.

http://www.icm.uu.se/molbio/mans.html

Publications in Synbiology Database

"Near-critical phenomena in intracellular metabolite pools" - Biophys J 2003 Jan;84(1):154-70.

"Fast evaluation of fluctuations in biochemical networks with the linear noise approximation" - Genome Res 2003 Nov;13(11):2475-84.

"Comparison of repressor and transcriptional attenuator systems for control of amino acid biosynthetic operons" - J Mol Biol 2001 Nov 9;313(5):941-54.

"Stochastic focusing: fluctuation-enhanced sensitivity of intracellular regulation" - Proc Natl Acad Sci U S A 2000 Jun 20;97(13):7148-53.

"Fluctuations and quality of control in biological cells: zero-order ultrasensitivity reinvestigated" - Biophys J 2000 Sep;79(3):1228-36.

Name	**Institution/Contact Information**
Nir Friedman	School of Computer Science and Engineering, Hebrew University, Jerusalem, Israel.

Research Description

The Nir Friedman Research group focuses on molecular biology and probabilistic models. The research areas include probabilistic graphical models (representation and inference in probabilistic graphical models and learning probabilistic graphical models), computational biology (computational analysis of gene expression data, reconstructing regulatory networks and phylogentic inference), machine learning and belief change and nonmonotonic reasoning).

Nir Friedman is also Associate Editor: of the Journal of Artificial Intelligence Research and ACM Transactions on Computational Biology and Bioinformatics. He is on the Editorial Board of the Journal of Machine Learning Research.

http://www.cs.huji.ac.il/~nirf/

Publications in Synbiology Database

"Precise temporal modulation in the response of the SOS DNA repair network in individual bacteria" - PLoS Biol 2005 Jul;3(7):e238.

"Module networks: identifying regulatory modules and their condition-specific regulators from gene expression data" - Nat Genet 2003 Jun;34(2):166-76.

Name	**Institution/Contact Information**
Martin Fussenegger	Institute for Chemical and Bio-Engineering (ICB), Swiss Federal Institute of Technology, ETH Hoenggerberg, Zurich, Switzerland

Research Description

Martin Fussenegger's multinational biotechnology and bioengineering group is dedicated to high leverage research in the fields of antibiotic screening, tissue engineering, the development of viral vectors, gene regulation systems for gene therapy as well as biopharmaceutical manufacturing..

It's research focuses on novel gene regulation systems for gene therapy and tissue engineering (E.REX,PIP Novel antibiotic discovery technology: MAST TM), 3D artificial tissue cultivation, gene therapy approaches in animal models and new strategies for enhanced protein production in mammalian cells.

http://www.fussenegger.ethz.ch/people/martinf/

Publications in Synbiology Database

"Therapeutic protein transduction of mammalian cells and mice by nucleic acid-free lentiviral nanoparticles" - Nucleic Acids Res. 2006 Jan 30;34(2):e16.

"A genetic redox sensor for mammalian cells" - Metab Eng. 2006 Feb 10.

"Improved transgene expression fine-tuning in mammalian cells using a novel transcription-translation network" - J Biotechnol. 2006 Feb 17.

"Xbp1-based engineering of secretory capacity enhances the productivity of Chinese hamster ovary cells" - Metab Eng. 2006 Apr 3.

"Engineered Streptomyces quorum-sensing components enable inducible siRNA-mediated translation control in mammalian cells and adjustable transcription control in mice" - J Gene Med 2005 Apr;7(4):518-25.

"Quorum-sensing-based toolbox for regulatable transgene and siRNA expression in mammalian cells" - Biotechnol Prog 2005 Jan-Feb;21(1):178-85.

"Hysteresis in a synthetic mammalian gene network" - Proc Natl Acad Sci U S A 2005 Jul 5;102(27):9517-22.

"In vivo transduction of HIV-1-derived lentiviral particles engineered for macrolide-adjustable transgene expression"- J Gene Med 2005 Jul 6.

"A novel mammalian expression system derived from components coordinating nicotine degradation in arthrobacter nicotinovorans pAO1" - Nucleic Acids Res 2005;33(12):e107.

"Autoregulated, bidirectional and multicistronic gas-inducible mammalian as well as lentiviral expression vectors" - J Biotechnol 2005 Jul 15.

Name	**Institution/Contact Information**
Ernst Gilles	Max Planck Institute for Dynamics of Complex Technical Systems, Magdeburg, Germany.

Research Description

Ernst Gilles is the Foundation Director of the Max Planck Institute for Dynamics of Complex Technical Systems. His research interests include control engineering, systems biology, modelling, system dynamics and network theory of chemical and biological processes.

He is head of the Systems Biology Research group at the Institute for Dynamics of Complex Technical Systems. The group is composed of researchers from different disciplines. All activities are based on a close cooperation with external biological groups. The group has built up a fermentation laboratory to perform experiments with isogenic mutant strains of E. coli and other microorganisms. The quantitative determination of important parameters, such as metabolite concentrations in fermentation experiments is a major task for the set up and validation of the mathematical model. Here, experimental methods for sampling, sample preparation and sample analysis are being developed. The functional units under investigation are mainly focused on global control and signal-transduction systems.

http://www.mpi-magdeburg.mpg.de/people/gilles/gilles_e.html

Publications in Synbiology Database

"A domain-oriented approach to the reduction of combinatorial complexity in signal transduction networks" - BMC Bioinformatics. 2006 Jan 23;7(1):34.

"A methodology for the structural and functional analysis of signaling and regulatory networks" - BMC Bioinformatics. 2006 Feb 7;7(1):56.

"A benchmark for methods in reverse engineering and model discrimination: problem formulation and solutions" - Genome Res 2004 Sep;14(9):1773-85.

"Mathematical modelling of complex regulatory networks" - IEEE Trans Nanobioscience 2004 Sep;3(3):172-9.

"Modular modelling of cellular systems with ProMoT/Diva" - Bioinformatics 2003 Jun 12;19(9):1169-76.

Name	**Institution/Contact Information**
Heinrich Reinhart	Department of Theoretical Biophysics, Institute of Biology, Humboldt-University, Berlin, Germany.

Research Description

Heinrich Reinhart is a Professor at the Department of Theoretical Biophysics. His research interests are (1) Modelling metabolic networks and metabolic control theory, (2) Modelling of signal transduction networks, (3) Evolutionary optimization and design of cellular networks, (4) Nonlinear dynamics as applied to biological systems, and (5) Protein translocation, lipid translocation,vesicular transport, DNA repair.

http://itb.biologie.hu-berlin.de/~herzel/

Publications in Synbiology Database

"Stoichiometric design of metabolic networks: multifunctionality, clusters, optimization, weak and strong robustness" - Bull Math Biol 2003 Mar;65(2):323-57.

Mathematical models of protein kinase signal transduction" - Mol Cell 2002 May;9(5):957-70.

Name	**Institution/Contact Information**
Hanspeter Herzel	Institute for Theoretical Biology, Humboldt University, Berlin, Germany.

Research Description

Hanspeter Herzel is a Professor in the Institute for Theoretical Biology. His research interests focus on molecular evolution (statistics of DNA and protein sequences, DNA chips, modelling signaling cascades and gene regulation), and nonlinear dynamics (modelling the voice, bioacoustics, heart modelling, time series analysis, and Lyapunov exponents in stochastic systems).

http://itb.biologie.hu-berlin.de/~herzel/

Publications in Synbiology Database

"EGFR activation coupled to inhibition of tyrosine phosphatases causes lateral signal propagation" - Nat Cell Biol 2003 May;5(5):447-53.

Name	**Institution/Contact Information**
Ulrich Gerland	Department of Physics, University of Munich, Germany.

Research Description

With a background in theoretical condensed matter physics, Ulrich Gerland's research is at the interface between physics and biology. From a physics perspective, his work can be described as "Statistical physics of single biomolecules and their interactions", while the biological significance is to develop a "Physical underpinning for Quantiative Biology".

His main research interests are gene regulation, single molecule biophysics and molecular evolution.

http://www.theorie.physik.uni-muenchen.de/lsfrey/index.php?option=content&task=view&id=56

Publications in Synbiology Database

"DNA as a programmable viscoelastic nanoelement" - Biophys J 2005 Sep 30.

"Physical constraints and functional characteristics of transcription factor-DNA interaction" - Proc Natl Acad Sci U S A 2002 Sep 17;99(19):12015-20.

Name	Institution/Contact Information
Ehud Keinan	Department of Chemistry, Institute of Catalysis Science and Technology, Technion, Israel.

Research Description

Ehud Keinan is Dean of the Faculty of Chemistry at Technion – Israel Institute of Technology and Adjunct Professor at the Department of Molecular Biology and the Skaggs Institute of Chemical Biology, the Scripps Research Institute.

In 1991 he established an independent laboratory at the Scripps Research Institute, focusing on catalytic antibodies, synthetic enzymes and synthesis of antitumor agents. His group has developed a combinatorial synthetic approach to Annonaceous acetogenins, have demonstrated the first use of catalytic antibodies in the total synthesis of natural products, proved that antibodies in an aqueous medium can catalyze reactions which are strongly disfavoured in water, and showed that antibodies can perturb the coordination geometry of a transition metal complex.

He was the founder and first Head of the Institute of Catalysis Science and Technology (ICST) at Technion. His research interests include biocatalysis with antibodies and with synthetic enzymes, organic synthesis, organometallic chemistry, molecular computing devices, synthetic receptors and molecular machines, and drug discovery (anti-cancer agents, anti-arrhythmic drugs, anti-asthma drugs).

http://chemistry.technion.ac.il/staff/keinan/

Publications in Synbiology Database

"Parallel biomolecular computation on surfaces with advanced finite automata" - J Am Chem Soc 2005 Mar 23;127(11):3935-43.

"Programmable and autonomous computing machine made of biomolecules" - Nature 2001 Nov 22;414(6862):430-4.

Name	Institution/Contact Information
Victor de Lorenzo	Centro de Investigaciones Biologicas Consejo Superior de Investigaciones Científicas, Madrid, Spain.

Research Description

The de Lorenzo Laboratory is committed to understanding how bacteria which inhabit natural niches sense and process multiple environmental signals into distinct transcriptional responses.

Their preferred experimental system involves the strain KT2440 of the soil and plant root colonizer Pseudomonas putida bearing the plasmid pWW0, which allows growth on toluene as the only C and energy source. The biotechnological side of this biological question is the possibility of programming bacteria for deliberate environmental release aimed at biodegradation of toxic pollutants or as biosensors for monitoring the presence or absence of given chemicals.

http://www.cnb.uam.es/groups-en/DBM/lineas__dpto2/victor_de_lorenzo

Publications in Synbiology Database

"The upstream-activating sequences of the sigma54 promoter Pu of Pseudomonas putida filter transcription readthrough from upstream genes" - J Biol Chem. 2006 Apr 28;281(17):11940-8.

"Transcriptional regulators a la carte: engineering new effector specificities in bacterial regulatory proteins" - Curr Opin Biotechnol. 2005 Dec 13.

"Metabolic engineering of bacteria for environmental applications: construction of Pseudomonas strains for biodegradation of 2-chlorotoluene" - J Biotechnol 2001 Feb 13;85(2):103-13.

"Engineering of quasi-natural Pseudomonas putida strains for toluene metabolism through an ortho-cleavage degradation pathway" - Appl Environ Microbiol 1998 Feb;64(2):748-51.

"Engineering of alkyl- and haloaromatic-responsive gene expression with mini-transposons containing regulated promoters of biodegradative pathways of Pseudomonas" - Gene 1993 Aug 16;130(1):41-6.

Name	**Institution/Contact Information**
Dietmar Manstein	Institut fur Biophysikalische Chemie, Medizinische Hochschule Hannover, Hannover, Germany.

Research Description

The objective of Dietmar Manstein's work is the identification and characterization of molecular motors and proteins that regulate dynamic changes of cytoskeletal and membranous structures. Using transient kinetics in combination with cell biological, molecular genetic, and structural approaches, his work has led to the structural and functional characterization of several unconventional myosins, dynamin-related proteins, and regulators of small GTPases. The development of a high through-put method for the determination of atomic structures by X-ray crystallography is in progress.

Current projects include (1) Molecular engineering principles are applied to generate molecular motors with specifically altered properties, (2) Single molecule approaches are used for the identification of interacting proteins and for the development of new in vitro assay systems for cytoskeletal proteins and proteins involved in membrane trafficking, (3) Determination of the X-ray structure of full length dynamin and improvement of the current EM reconstructions of the dynamin ring complex by the use of cryo-methods, and (4) Characterisation of the role of molecular motors in cell adhesion and the formation of cell surface extensions

http://www.bpc.mh-hannover.de/manstein/

Publications in Synbiology Database

"Molecular engineering of a backwards-moving myosin motor" - Nature 2004 Feb 5;427(6974):558-61.

Name	**Institution/Contact Information**
Jens Nielsen	Center for Microbial Biotechnology, BioCentrum-DTU, Technical University of Denmark, Lyngby, Denmark.

Research Description

Jens Nielsen, the Head of Section of Biotechnology and Bioinformatics at BioCentrum – DTU, focuses his research on fermentation physiology and metabolic engineering, metabolic flux analysis, metabolite profiling, DNA arrays, metabolite production by S. cerevisiae, enzyme production by fungi, production of antibiotics, and morphology of filamentous fungi.

In addition he is the Associate Editor of Bioprocess and Biosystems Engineering (an international forum to facilitate discussions between engineers and biological scientists seeking efficient solutions in the development and improvement of bioprocesses).

http://www.cpb.dtu.dk/staff/jn.html

Publications in Synbiology Database

"Improvement of Galactose Uptake in Saccharomyces cerevisiae through Overexpression of Phosphoglucomutase: Example of Transcript Analysis as a Tool in Inverse Metabolic Engineering" - Appl Environ Microbiol 2005 Nov;71(11):6465-72.

"Microbial isoprenoid production: an example of green chemistry through metabolic engineering" - Adv Biochem Eng Biotechnol 2005;100:19-51.

"In silico aided metabolic engineering of Saccharomyces cerevisiae for improved bioethanol production" - Metab Eng. 2005 Nov 9.

"Evolutionary programming as a platform for in silico metabolic engineering" – BMC Bioinformatics. 2005 Dec 23;6:308.

"Integration of gene expression data into genome-scale metabolic models" - Metab Eng 2004 Oct;6(4):285-93.

"Genome-scale reconstruction of the Saccharomyces cerevisiae metabolic network." - Genome Res 2003 Feb;13(2):244-53.

"Metabolic engineering of the morphology of Aspergillus oryzae by altering chitin synthesis" - Appl Environ Microbiol 2002 Apr;68(4):1827-36.

"An expanded role for microbial physiology in metabolic engineering and functional genomics: moving towards systems biology" - FEMS Yeast Res 2002 May;2(2):175-81.

"The role of metabolic engineering in the improvement of Saccharomyces cerevisiae: utilization of industrial media" - Enzyme Microb Technol 2000 Jun 1;26(9-10):785-792.

"Increasing galactose consumption by Saccharomyces cerevisiae through metabolic engineering of the GAL gene regulatory network" - Nat Biotechnol 2000 Dec;18(12):1283-6.

Name	**Institution/Contact Information**
Bela Novak	BUTE Faculty of Chemical and Bioengineering, Budapest, Hungary.

Research Description

Bela Novak is the head of the Molecular Network Dynamics Research group at the BUTE Faculty of Chemical and Bioengineering.

His main research interests are the creation of a expanded version of the fission yeast cell cycle model, the provision of different models to create a generic cell cycle model, modelling of the meiotic -mitotic switch of fission yeast cells, investigating microtubule dynamics, modelling of the morphogenesis of fission yeast, modelling of fission yeast septation and the mammalian cell cycle model.

http://cellcycle.mkt.bme.hu/people/bnovak/bnovak.htm

Publications in Synbiology Database

"A model for restriction point control of the mammalian cell cycle" - J Theor Biol 2004 Oct 21;230(4):563-79.

"Modelling the controls of the eukaryotic cell cycle" - Biochem Soc Trans 2003 Dec;31(Pt 6):1526-9.

"A stochastic, molecular model of the fission yeast cell cycle: role of the nucleocytoplasmic ratio in cycle time regulation" - Biophys Chem 2001 Aug 30;92(1-2):1-15.

"Modelling the fission yeast cell cycle: quantized cycle times in wee1- cdc25Delta mutant cells" - Proc Natl Acad Sci U S A 2000 Jul 5;97(14):7865-70.

"Modelling the control of DNA replication in fission yeast" - Proc Natl Acad Sci U S A 1997 Aug 19;94(17):9147-52.

Name	**Institution/Contact Information**
Sven Panke	Institute of Process Engineering, Swiss Federal Institute of Technology, ETH Hoenggerberg, Zurich, Switzerland.

Research Description

Sven Panke is an Assistant Professor for Bioprocess Engineering at the Institute of Process Engineering. He focuses on new and generic solutions for the integrated manufacturing of fine chemicals and biopharmaceuticals

Research of the Bioprocess Laboratory is grouped around the topics of "From Process to Product", From Basic Concepts to Technology Platforms, and From Systems Biology to Synthetic Biology

http://www.ipe.ethz.ch/laboratories/bpl/people/panke/bio

Publications in Synbiology Database

"Engineering of quasi-natural Pseudomonas putida strains for toluene metabolism through an ortho-cleavage degradation pathway" - Appl Environ Microbiol 1998 Feb;64(2):748-51.

"Putative regulatory sites unraveled by network-embedded thermodynamic analysis of metabolome data" - Mol Syst Biol. 2006;2:2006.0034.

"In silico genome-scale reconstruction and validation of the Staphylococcus aureus metabolic network" - Biotechnol Bioeng 2005 Sep 9.

"Pilot-scale production of (S)-styrene oxide from styrene by recombinant Escherichia coli synthesizing styrene monooxygenase" – Biotechnol Bioeng 2002 Oct 5;80(1):33-41.

Name	Institution/Contact Information
George Schulz	Institut fur Organische Chemie und Biochemie, Albert-Ludwigs-Universitat Freiburg, Freiburg, Germany

Research Description

The Shulz group are interested in the modifications of enzyme catalysis (for example in changing the product spectrum in a cyclodextrin generating enzyme), in the characteristics of the membrane-channel of porines and in changing the manner in which proteins associate (to build up protein networks).

Their special interests are in the field of membrane proteins. Because of their large hydrophobic surfaces specific difficulties arise with purification and crystallization. In order to prevent aggregation of the protein, carefully selected detergents have to be added. The second atomic structure of a membrane protein was solved in the group in 1989. Furthermore the group has solved the structures of two other bacterial porins as well as the structures of squalen-hopene-cyclase, OmpA and OmpX.

http://www.structbio.uni-freiburg.de/schulzgroup

Publications in Synbiology Database

"Self-assembly of proteins into designed networks" - Science 2003 Oct 3;302(5642):106-9.

Name	Institution/Contact Information
Luis Serrano	European Molecular Biology Laboratory, Structures and Biocomputing, Heidelberg, Germany

Research Description

The group is interested in understanding how proteins acquire a 3D structure and the relationship between structure and function. The group has moved from the analysis of protein folding to the development of computer algorithms that could be used for protein design. Currently, they are mainly focused on a particular aspect of the folding problem: aggregation and amyloid formation. They continue to develop an automatic protein design algorithm, FoldX, and have recently modified it so that it can predict protein–DNA interactions. Regarding the misfolding studies and based on the experimental analysis of several hundred peptides, they have developed two algorithms, Tango and AmyScan, that predict aggregation and amyloid tendency in protein sequences.

The group has started a new line of research centred on systems biology, believing that the combination of theoretical and experimental approaches is the most fruitful way to address such a complicated field. On the one hand the group designed and tested small gene networks while on the other developed a software tool, SmartCell, that could be used to study the dynamics of biological networks. Recently the group also developed a system that allows the engineering and analysis of special networks in a controlled in vitro system, and we use it to study patterning. Similarly, they have developed a system to engineer spatial distributions of modified cells to study cell–cell interactions.

http://www-db.embl.de/jss/EmblGroupsHD/per_397.html

Publications in Synbiology Database

"The Ubiquitin Domain Superfold: Structure-based Sequence Alignments and Characterization of Binding Epitopes"- J Mol Biol. 2006 Jan 27;355(4):821-4.

"Protein aggregation and amyloidosis: confusion of the kinds?" - Curr Opin Struct Biol. 2006 Jan 21.

"Engineering gene networks to emulate Drosophila embryonic pattern formation" - PLoS Biol 2005 Mar;3(3):e64.

"Space as the final frontier in stochastic simulations of biological systems" - FEBS Lett 2005 Mar 21;579(8):1789-94.

"Positive feedback in eukaryotic gene networks: cell differentiation by graded to binary response conversion" - EMBO J 2001 May 15;20(10):2528-35.

"Engineering stability in gene networks by autoregulation" - Nature 2000 Jun 1;405(6786):590-3.

Name	**Institution/Contact Information**
FriedrichSimmel	Center for NanoScience, Ludwig-Maximilian-University Munich, Germany

Research Description

The Simmel group is a young investigator group working on the boundary between biophysics and nanoscience. Their goals are (1) The utilization of the unique properties of biomolecules for the construction of artificial nanostructures and nanodevices and imitation of biological principles of structure formation, and (2) The application of advanced micro- and nanolithographic techniques for the realization of tailored on-chip environments for biophysical studies.

In the first research area, the group currently aims at the construction of artificial molecular machines based on DNA (molecular machinery) and the fabrication of complex DNA networks (biomolecular nanostructures). The latter may serve as templates for the deposition of functional materials or for the arrangement of nanocomponents such as quantum dots (self-assembly and self-organization).

The second research area contains all the group's efforts to utilize modern chip fabrication techniques for biophysical investigations (biophysics on a chip). For example, bioelectronic hybrid systems have many potential applications as biosensors or in the context of "labs on-a-chip". Furthermore, tailoring the physical environment of a biological system can also help to gain insight into fundamental processes.

http://www.nano.physik.uni-muenchen.de/nanobio/group/fritz.html

Publications in Synbiology Database

"A modular DNA signal translator for the controlled release of a protein by an aptamer" - Nucleic Acids Res. 2006 Mar 17;34(5):1581-7.

"Periodic DNA nanotemplates synthesized by rolling circle amplification" - Nano Lett 2005 Apr;5(4):719-22.

"Using DNA to construct and power a nanoactuator" - Phys Rev E Stat Nonlin Soft Matter Phys 2001 Apr;63(4 Pt 1):0419.

Name	**Institution/Contact Information**
Victor Sourjik	Zentrum für Molekulare Biologie Heidelberg, Heidelberg, Germany.

Research Description

The goal of Victor Sourjik's laboratory is to understand the functioning of the chemotaxis pathway as a whole system. To complement existing genetic and biochemical data, we use fluorescence microscopy and fluorescence resonance energy transfer (FRET) to measure localization and interactions of chemotaxis proteins in the cell. FRET allows the laboratory to monitor the changes in interactions of all proteins upon chemotactic stimulation in real time in vivo. They also use FRET as a pathway activity reporter to analyze integration and amplification of different stimuli by the sensory complexes, as well as to study cross-talk between chemotaxis and other signalling and metabolic pathways in the cell. These quantitative data can be used directly for computer modelling. Additionally, they are interested in understanding the formation of the chemosensory complex in the cell and in investigating the role of the cell-to-cell variation in the numbers of chemotaxis proteins ("gene expression noise") in the signalling.

http://www.zmbh.uni-heidelberg.de/Sourjik/default.shtml

Publications in Synbiology Database

"Design principles of a bacterial signalling network" - Nature. 2005 Nov 24;438(7067):504-7.

Name	**Institution/Contact Information**
Jörg Stelling	Institute of Computational Science, Swiss Federal Institute of Technology, ETH Hoenggerberg, Zurich, Switzerland.

Research Description

Jörg Stelling is an Assistant Professor for bioinformatics. His current research interests are focused on the analysis and synthesis of biological networks using - and further developing - methods from systems theory and computer science. The highly interdisciplinary character of the research projects is reflected by an (international) network of collaborators from different disciplines.

He is a member of the Computational Systems Biology group. This group focuses on structural network analysis, systems dynamics of cellular regulation and synthetic biology.

http://csb.inf.ethz.ch/people/stelling.html

Publications in Synbiology Database

"Robustness properties of circadian clock architectures" - Proc Natl Acad Sci U S A 2004 Sep 7;101(36):13210-5.

"Mathematical modelling of complex regulatory networks" - IEEE Trans Nanobioscience 2004 Sep;3(3):172-9.

Name	**Institution/Contact Information**
Jens Timmer	Physics Institute, University of Freiburg, Freiburg, Germany.

Research Description

Jens Timmer's group focuses on Data Analysis and Modelling of Dynamic Processes in the Life Sciences. The work is based upon dynamic processes, which are ubiquitous in the life sciences. They can be found from the regulation in cells up to oscillations in tremor. Malfunction of these dynamic processes can be a cause or a sign of diseases. In interdisciplinary projects, the group develops and applies mathematical methods to analyse and model these processes based on measured data.

The final aim of the group is to help to turn the life sciences from a qualitative descriptive into a quantitative predictive science

http://webber.physik.uni-freiburg.de/~jeti/

Publications in Synbiology Database

"Estimating rate constants from single ion channel currents when the initial distribution is known" - Eur Biophys J 2005 Jun;34(4):306-13.

"Computational processing and error reduction strategies for standardized quantitative data in biological networks" - FEBS J. 2005 Dec;272(24):6400-11.

"Design principles of a bacterial signalling network" - Nature. 2005 Nov 24;438(7067):504-7.

Name	**Institution/Contact Information**
James Uney	Department of Medicine, University of Bristol, UK.

Research Description

The overall aims of James Uney's research are to study some of the pathways underlying neurodegenerative processes; to develop adenoviral, adeno-associated and lentiviral vector technologies to facilitate in vivo and in vitro studies into neuronal gene function and to allow gene therapy strategies to be evaluated in the CNS (Crystallography & NMR System).

http://www.cnb.uam.es/groups-en/DBM/lineas__dpto2/victor_de_lorenzo

Publications in Synbiology Database

"Switching transgene expression in the brain using an adenoviral tetracycline-regulatable system" - Nat Biotechnol 1998 Jun;16(6):553-5.

Name	**Institution/Contact Information**
Olaf Wolkenhauer	Department of Computer Science, University of Rostock, Rostock, Germany.

Research Description

The Wolkenhauer group is interested in the development of systems- and control methodologies, using mathematical modelling, simulation and statistical data analysis applied to complex dynamic systems. Although the methodologies are generic, the group is particularly interested in applications to molecular- and cell biology (systems biology and bioinformatics).

http://www.systemsbiology.umist.ac.uk/people_wolkenhauer.html

Publications in Synbiology Database

"A hybrid systems framework for cellular processes" - Biosystems 2005 Jun;80(3):273-82.

"A systems- and signal-oriented approach to intracellular dynamics" - Biochem Soc Trans 2005 Jun;33(Pt 3):507-15.

"Modelling and simulation of intracellular dynamics: choosing an appropriate framework" - IEEE Trans Nanobioscience 2004 Sep;3(3):200-7.

"Investigations into the analysis and modelling of the TNF alpha-mediated NF-kappa B-signaling pathway" - Genome Res 2003 Nov;13(11):2413-22.

"Analysis and modelling of signal transduction pathways in systems biology" - Biochem Soc Trans 2003 Dec;31(Pt 6):1503-9.

"Mathematical modelling in the post-genome era: understanding genome expression and regulation--a system theoretic approach" - Biosystems 2002 Feb;65(1):1-18.

3. GEOGRAPHICAL ANALYSIS OF SYNTHETIC BIOLOGY PUBLICATIONS

3.1. Introduction

The information in this chapter was previously presented as part of Output D8: Synthetic Biology Research Assessment.

One of the objectives of the Synbiology project is to identify the countries which provide the most published Synthetic Biology research. In this chapter, we identify these countries through assessing the location of the authors' affiliated organizations of the published Synthetic Biology research which is detailed in the Synbiology Project Database.[8,9,10]

As discussed above, the Project Database includes approximately 1,100 papers in Synthetic Biology. In identifying the location of Synthetic Biology research, we focus on those 680 papers which have been classified as *in vivo*, *in vitro* and *theoretical* in the Database.

It should be noted that the Synbiology Project Database only includes papers published in English. Thus papers published in other, and especially Asian, languages are not included in this assessment.

The Database includes a very high number of papers and was developed using a consistent and logical method. However, as with any database of publications, it is not possible to be certain that it includes all relevant papers and authors. Thus, the information included in this chapter, whilst informative, should be considered in conjunction with the lists and assessments of Key Stakeholders, institutions and funding agencies provided in the Synbiology project.

The analysis is provided in two parts. Firstly, the analysis focuses solely on the number of papers in published Synthetic Biology. This is termed the *unweighted analysis*. In the second part, the *weighted analysis*, each paper is assigned an impact factor, dependent upon the importance of the journal in which the paper is published, as calculated by the Thomson Scientific Index. The

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[8] In this chapter, we define the location of the author(s) as the country in which the organization to which they are affiliated is located.

[9] For papers with more than one author, the locations of the affiliation of the first and last authors have been used. To ensure precision (to eliminate unknown inter-temporal movements) and to avoid biases, papers with individual authors for which multiple affiliations are identified, and for which the paper does not identify a specific affiliation for this author, have been excluded.

[10] In the case where an individual author had different affiliations for different papers, the author location is only included for those papers in which that author's affiliation was specifically mentioned.

papers are then weighted by this impact factor, ensuring that the analysis of each country's importance in Synthetic Biology published research is weighted by a proxy for the importance of each publication.

3.2. Unweighted Analysis

Global Analysis

As expected, the Synthetic Biology papers identified in the Project Database are overwhelmingly provided by authors in the US. In total, just under two-thirds of papers are authored by those in the US, emphasizing that the focus of Synthetic Biology research is to be found in the US.[11] Just under one-fifth (19%) of papers in the Project Database were published by authors in the EU-25 countries, with authors in Japan, Israel, Switzerland, Canada and South Korea, with a collective share of approximately 15% of published papers in the Project Database, also providing important Synthetic Biology published research. This global overview is illustrated in Figure 1.

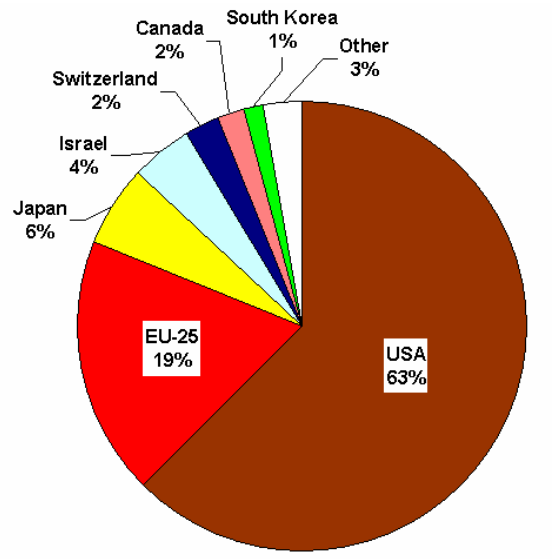


Figure 1: Global Overview of Synthetic Biology Publications - Unweighted

European Analysis

Within the EU-25 area, authors located in Germany are responsible for the highest country-proportion of published papers – contributing over one-third of papers with authors located

within the EU-25 area. Authors located in the UK and France also provide significant contributions, with over 10% of all papers recorded in the Project Database with authors located in the EU-25 countries. Together, these three countries represent two-thirds of papers with EU-25 authors in the Synbiology Project Database.

Further, authors located in the Denmark, the Netherlands and Spain, each with between 6% and 9% of the EU-25 published research in the Project Database, also provide a notable contribution to Synthetic Biology published research.

Figure 2 illustrates the EU-25 countries with the highest contributions to Synthetic Biology publications.

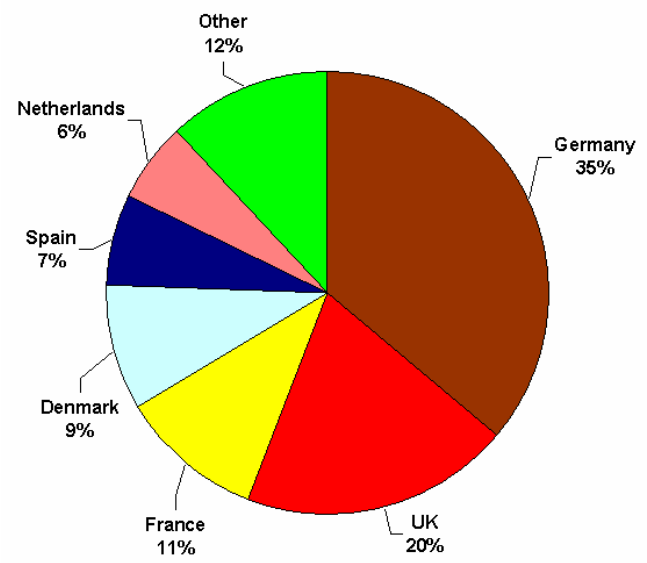


Figure 2: EU-25 Overview of Synthetic Biology Publications - Unweighted

This result is largely in accordance with overall research investment within the EU-25 countries. In particular, the countries with the highest contributions to Synthetic Biology publications (Germany, France and the UK) also have the highest Gross Domestic Expenditure on general R&D. However, the medium-sized countries, for instance Belgium, Austria and Ireland have lower relative contributions to Synthetic Biology publications than their Gross Domestic Expenditure on general R&D, would suggest. Of these medium-sized countries, the Netherlands and, in particular, Denmark provide a higher contribution to Synthetic Biology publications than the relative amount invested in general R&D.

It is also of interest to assess the results for countries in the Europe-33 research area. The agreement between the Europe-33 countries and the European Commission allows the Europe-33 research area countries access to the EU Framework Programme for RTD, and hence allows

them to play a role in identifying future priorities. In addition, there is significant actual and potential research cooperation and networking between the EU-25 and associated Europe-33 research area countries as a result of their geographical proximity and cultural affinity.

Of the eight additional countries included in the Europe-33 area, Israel and Switzerland are the main contributors. Figure 3 below provides a map that illustrates the relative contribution of Europe-33 research area countries to papers included in the Project Database.

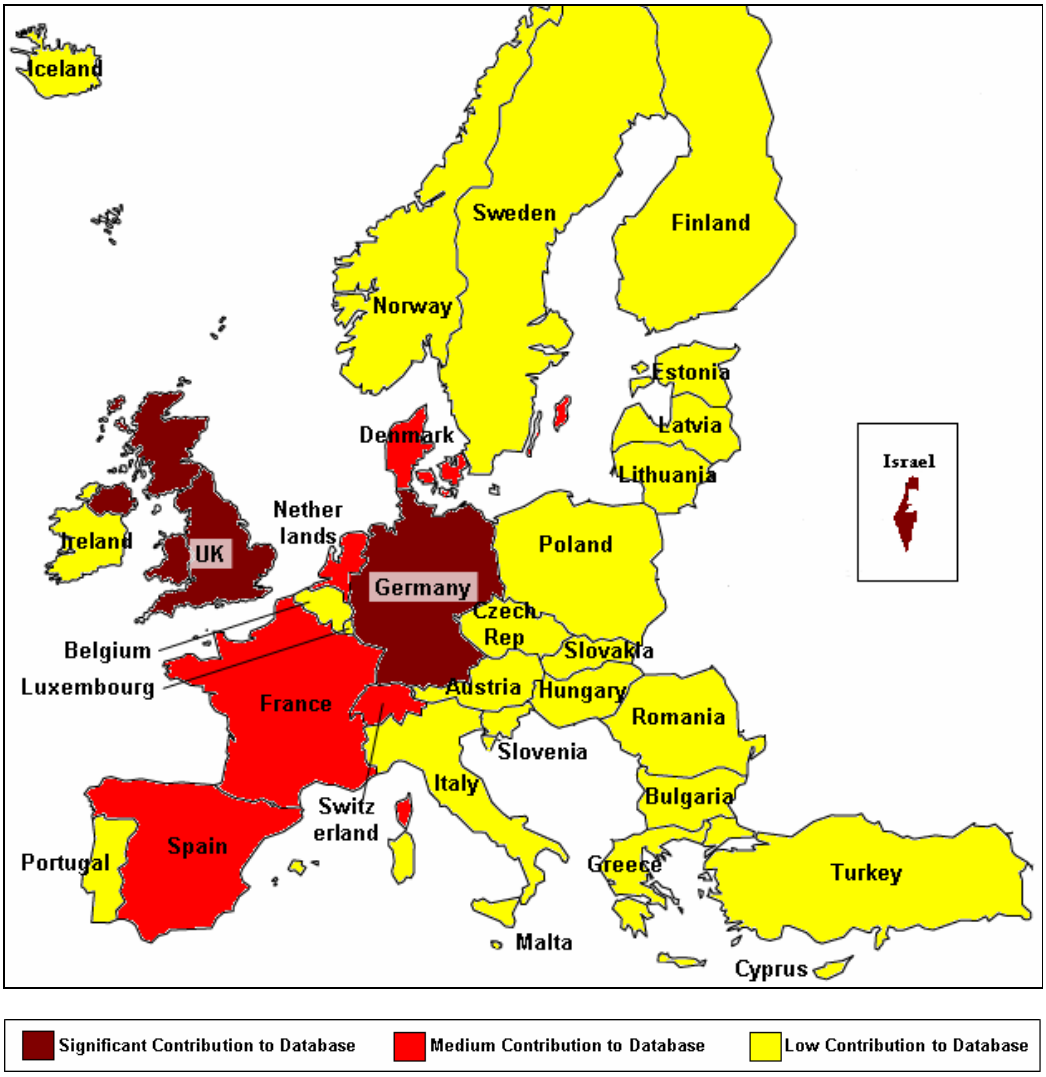


Figure 3: Europe-33 Overview of Synthetic Biology Publications - Unweighted

The map shows that authors located in Germany, the UK and Israel provide a significant contribution to the papers in the Project Database, defined as more than 10% of the papers published by Europe-33 located authors. In addition, authors located in Denmark, France, Spain

and Switzerland provide a medium contribution to the papers in the Project Database, defined as between 4%-10% of the papers published by Europe-33 research area located authors.

3.3. Weighted Analysis

The impact of each of the publications included in the Project Database can vary considerably. Hence, it is informative to provide an assessment of the importance of individual papers, and hence an effort was made to attribute impact weightings. These weightings were based on the importance of the journal in which the papers were published, as measured by the Thomson Scientific Index.[12,13]

Global Analysis

Figure 4 shows the weighted contribution of authors located in each of the major countries and areas.

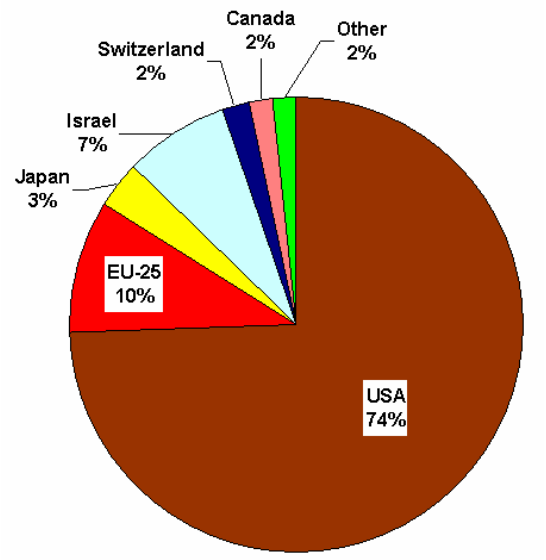


Figure 4: Global Overview of Synthetic Biology Publications - Weighted

[12] In the case where an author has more than one affiliation (in different countries) in different papers, the impact is calculated exclusively for the author's articles in which the author's affiliation was specifically mentioned.

[13] In the case where an author has two affiliations (in different countries) in the same paper, it is assumed that 50% of the impact of the paper should be added to one country and 50% to the other.

This enriched assessment shows that the gap between the contribution to published research between the EU-25 and the USA increases if the effect of the impact of publications is included. In particular, the importance of papers published by authors based in the EU-25 is reduced (to approximately 10% of the total weight of impact of papers in the Project Database) and the importance of papers published by authors based in the USA is increased (to just under three-quarters of the total impact weight of papers in the Project Database) when compared to the un-weighted analysis. This emphasizes the importance of Synthetic Biology published research in the USA.

European Analysis

As with the unweighted analysis, authors located in Germany contribute the most Synthetic Biology published research in the EU-25, with approximately 30% of the total weight of impact of papers authored in the EU-25 in the Project Database.

Authors located in Denmark join those in the UK and France in each contributing over 10% of the total weight of impact of papers authored in the EU-25 in the Project Database. This indicates that the papers published by the authors located in Denmark are assigned a higher impact factor than is average over the whole Project Database, increasing the perceived relevance of this research in the EU-25. The importance of papers published by Swedish-affiliated authors also increases under the weighted analysis.

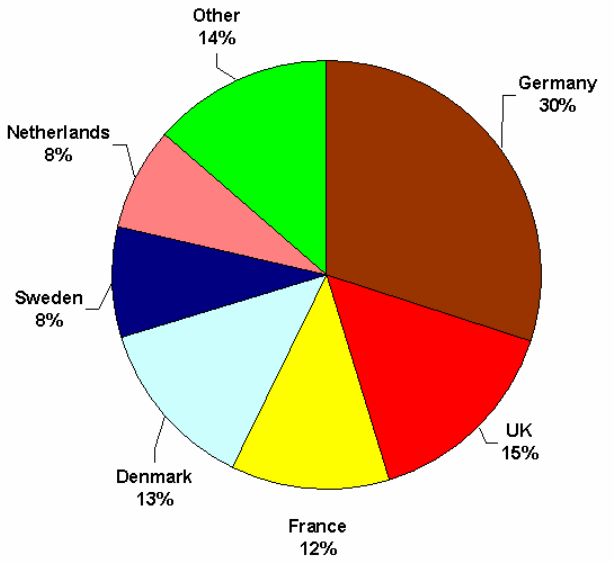


Figure 5: EU-25 Overview of Synthetic Biology Publications - Weighted

The most significant change between the unweighted and weighted analysis in the Europe-33 research area concerns Israel. When weighted by the impact factor, papers with authors located in Israel account for nearly 40% of the total impact weight of papers from the Europe-33 research area in the Project Database. It is likely that this increase results from the tendency of these authors to publish in the best-known, and highest rated, US journals. When weighted by the impact factor, the importance of publications by Swiss-affiliated authors also increases to over 10% of total impact weight of papers from the Europe-33 area in the Project Database.

Figure 6 below provides a map that illustrates the relative contribution, using impact weighting, of Europe-33 research area countries to papers included in the Project Database.

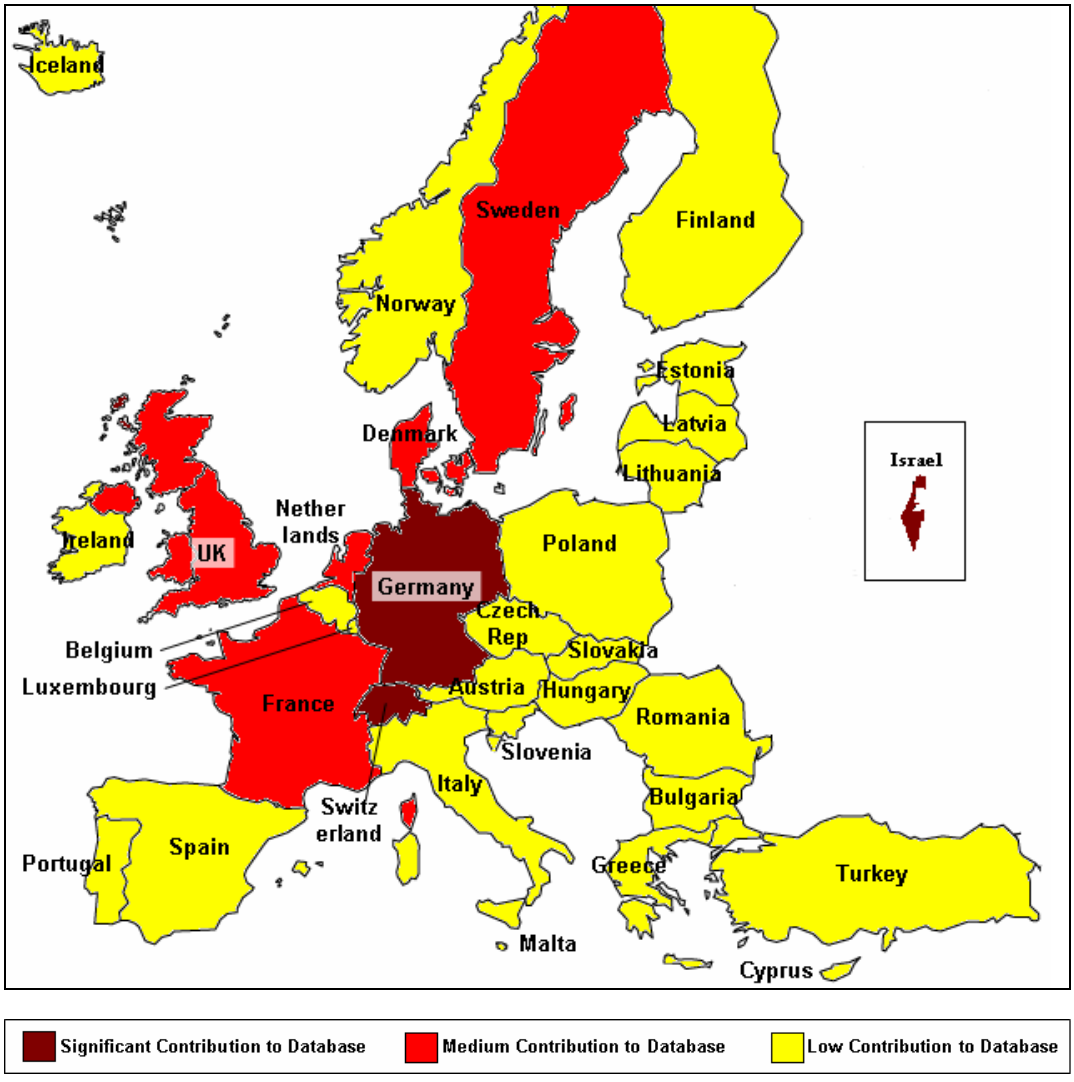


Figure 6: Europe-33 Overview of Synthetic Biology Publications - Weighted

3.4. Summary

This geographical assessment of author location of Synthetic Biology publications provides the following conclusions:

1. The USA is the most important source of research results in Synthetic Biology. In quantitative terms, nearly two-thirds of all papers are published with authors located in the USA. If impact weightings of papers are included, based on the Thomson Scientific Index of the relevant journal, the importance of papers published by authors based in the USA is even more increased and accounts for three-quarters of the total impact weight of papers in the Synbiology Project Database.

2. The number and importance of Synthetic Biology publications from the EU-25 countries follow the USA at a considerable distance. Within the EU-25 area, publications from authors based in Germany, the UK and France represent two-thirds of Synthetic Biology papers. In addition, authors located in the Denmark, the Netherlands and Spain also provide notable contributions. If impact weightings of papers are included, then papers by authors affiliated to organizations based in Denmark show increased importance.

3. Outside of the USA and EU-25, authors based in Switzerland, Israel, Canada and Japan provide significant contributions to Synthetic Biology publications. This is especially the case for authors based in Israel when the impact factor of papers is considered.

4. RESULTS OF THE SYNBIOLOGY PROJECT SURVEY

4.1. Introduction

The information in this chapter was previously presented as part of Output D9: Europe/North America Comparative Assessment.

This chapter provides an overview of the results from the survey undertaken as part of the project. This survey provides an important source of information from Key Stakeholders, and was carried out via online questionnaire. At the start of the project, the Synbiology team identified over 200 Synthetic Biology sector participants to which the questionnaire could be sent. These sector participants included researchers at universities and other research organizations, private and public funding agencies and researchers in private sector companies.

The questionnaire was developed and provided on-line in November 2005 to the identified sector participants.

The questionnaire is accessible at http://www.spi.pt/synbiology/survey.asp.

The questionnaire included four main elements, as follows:

- Definition of Synthetic Biology and Synthetic Biology activities – To elicit the respondents' general understanding of what Synthetic Biology research includes. Also to allow the respondents to describe, in detail, the activities that are provided under Synthetic Biology
- Funding and commercialisation – To enable the respondents to provide information on how their Synthetic Biology work is funded and the potential commercialization of their and others' work
- Satisfaction with available infrastructure, funding and facilities in the Synthetic Biology sector – To elicit respondent's opinions on how satisfactory are these elements in the Synthetic Biology sector
- European/North American relationship – To enable the respondents to comment on the nature of links between Europe and North America in the Synthetic Biology sector.

A total of 41 questionnaires were completed and returned, with an even split of respondents between Europe and North America. The information collected from the questionnaires was centrally harmonized, ensuring accuracy and providing for rich levels of comparisons in the Synthetic Biology field. The results from the questionnaire analysis were first presented at the Project Dissemination Seminar held on May 30th 2006 at the European Commission, Brussels.

4.2. Results and Analysis

(i) Definition of Synthetic Biology and Synthetic Biology Activities

The respondents were provided with three possible definitions of Synthetic Biology and asked to comment on them:

- Synthetic Biology is the "designed-based engineering" of systems based on biological functional rules aimed at obtaining new functionalities not present in nature
- Synthetic Biology is the engineering of biological components and systems that do not exist in nature and the re-engineering of existing biological elements; it is determined on the intentional design of artificial biological systems, rather than on the understanding of natural biology
- Synthetic Biology is rational engineering and design of complex systems with novel functionalities that do not exist in Nature.

As Table 1 shows, there was no consensus among the respondents on which of these three options best defined Synthetic Biology. In addition, respondents provided a number of other possible definitions, emphasizing the difficulty in specifying a single definition of Synthetic Biology.

Table 1: Definition of Synthetic Biology

Definition	European Respondents	North American Respondents
Synthetic Biology is the "designed-based engineering" of systems based on biological functional rules aimed at obtaining new functionalities not present in nature	45%	45%
Synthetic Biology is the engineering of biological components and systems that do not exist in nature and the re-engineering of existing biological elements; it is determined on the intentional design of artificial biological systems, rather than on the understanding of natural biology	40%	45%
Synthetic Biology is rational engineering and design of complex systems with novel functionalities that do not exist in Nature	15%	25%

Respondents were provided with a classification of Synthetic Biology activities developed at the start of the Synbiology project. This classification had seven fields:

- Concepts and political strategy
- Theoretical bio-engineering *in silico*
- Biological inspired nanotechnology *in vitro*
- Practical engineering *in vivo*
- Applications of Synthetic Biology (related and enabling technologies)
- Products
- Others.

More details of the classification in the questionnaire are provided on the following page in Figure 7.

Figure 7: Synthetic Biology Classification Details

1. Concepts and political strategy

2. Theoretical bio-engineering *in silico*
   - *Modeling of natural systems*
     - *Genome, Proteome, Metabolone analysis*
     - *Analysis and modelling of molecular networks*
     - *Metabolic profiling*
   - *Modeling of synthetic systems*
     - *Design principles of systems and networks*
     - *Noise in systems and components*
     - *Information processing and control theory*

3. Biological inspired nanotechnology *in vitro*
   - *Biomimetics, Nanobionics, Evolutionary Nanotechnology*
     - *Computation using biological components and principles*
     - *Selfassembling, biomimetic, biomaterials, bioelectronics*
     - *Single molecule manipulation and/or measurement methods*
     - *Reporters and sensors*
     - *Molecular machines, actuators and device*
   - *Artificial Life*

4. Practical engineering *in vivo*
   - *Engineering of structural function*
     - *Molecular engineering (rational design)*
       - *DNA/RNA/PNA*
       - *Proteins*
     - *Artificial evolution and evolutionary optimization strategies (irrational design)*
       - *DNA/RNA/PNA*
       - *Proteins*
     - *Semisynthetic design (rational + irrational design)*
   - *Engineering of regulatory function*
     - *Biochemical or genetic network design*
     - *Riboswitches*
   - *Parts fabrication, characterization, assembly*
     - *The BioBricks strategy*
     - *Programmable organisms or systems*

5. Applications of Synthetic Biology (related and enabling technologies)
   - *Molecular Biology Methodology in general*
     - *Genome-, Chromosome-, Genetic Engineering, Molecular Evolution methodologies*
     - *DNA-, Gene synthesis*
   - *Analytics*
     - *Diagnostics*
     - *Microarrays, Biochips, Microfluidic devices, Nanotechanalytic*
       - *Microfluidics*
     - *Analytical chromatography, spectroscpical methodologies, bioimaging, high throughput bioassays*
     - *Chromatography for molecule and cell enrichment, purification, isolation*
   - *Computing*
     - *Biocomputing, Bioinformatic, Systems Biology*
     - *System Sciences, Informatics, Computing Technologies*
   - *Biological chemicals*
     - *Building blocks, fine chemicals*
     - *Biocatalysis, biotransformations*
   - *Biopharmaceuticals*
     - *Small molecule and Macromolecule drugs*
     - *Delivery systems*
   - *Biomaterials*
     - *Biopolymers, colloids and nanoparticles*
     - *Biocomposites*
   - *Cell technology*
     - *Cell culture, Transfection*
     - *Stem Cell technology*
   - *Tissue and Organ engineering, Transplantation*
   - *Reproduction Technologies, In Vitro Fertilisation*
   - *Transgenic plants and animals*
   - *Bio-energy sources*
     - *Bio-fuels, biogas*
     - *Bioelectricity*

6. Products
   - *Small molecular drugs, bio-drugs, bio-agents*
   - *Flavors, fragrances, colors, pigments, commodities*
   - *Biopolymers, biocomposites*
   - *Cell culture, Stem Cells*
   - *Tissues, organs, organisms*
   - *Bio-fuels, bio-electricity*
   - *Biomimetic, biocomputers*

7. Others

Respondents were asked to comment on the coverage, structure, interdisplinarity and future for these activities under Synthetic Biology.[14] Figure 8 provides the results, segregated between European and North American stakeholders.

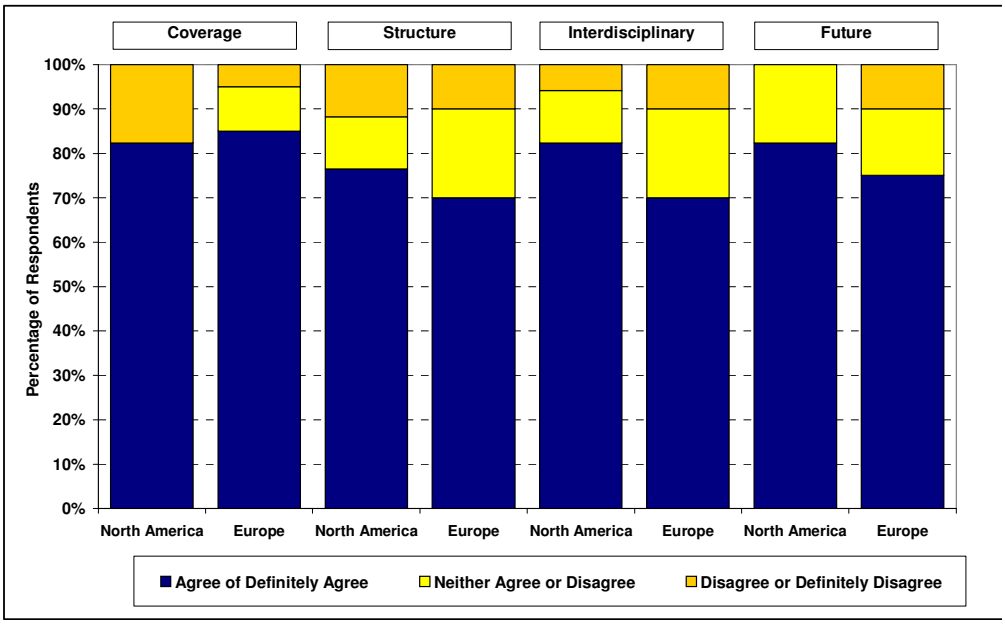


Figure 8: Synthetic Biology Classification

Figure 8 shows that there was broad agreement between the respondents on the classification of Synthetic Biology activities. However, there were a number of respondents which believed that the classification needed to be updated. In particular, the following points were highlighted:

- Modelling of natural systems should not be included as it not the essence of Synthetic Biology, but rather more associated with systems biology. It was also noted that although Synthetic Biology definitely benefits from advances in modelling of natural systems, it is more a natural part of biology and biochemistry.

[14] **Coverage –** Whether the description covers all aspects of synthetic biology research.

Structure – Whether the organization of activities into 7 groups and subgroups accurately represent the synthetic biology field.

Interdisciplinarity – Whether the description of synthetic biology activities fully takes account for the links between synthetic biology and other scientific activities.

Future – Whether the description is sufficiently flexible to account for likely future developments and activities in synthetic biology.

- Applications of Synthetic Biology (related and enabling technologies) should be excluded, for instance as several applications are too complex to be controlled, such as cell technology, and tissue and organ engineering. It was also noted that these refer to technologies that can be developed in *in vivo* and *in vitro* research.

(ii) Funding and Commercialisation

The availability of public and private funding clearly has a significant impact on the development of the Synthetic Biology sector. Respondents were first asked to comment on the most important project elements (including relevance, potential impact, calibre of the participants and organisation and management) required to access public and private finance in the Synthetic Biology sector.[15] The results are reported in Figure 9 below.

[15] **Relevance** - The importance of the objectives and the extent to which the proposed project addresses desired objectives

Potential impact - The extent to which: (a) the goals of the network are suitably ambitious; (b) there is clear added value in carrying out the work; (c) there is an effective plan for exploiting results

Calibre of the participants - The extent to which: (a) the participants are currently conducting leading research relevant to the topic of the network or are capable of important contributions; (b) the participants are well suited to the tasks assigned to them; (c) the participants have the necessary critical mass of expertise and resources to carry out the programme of activities successfully

Organisation and management - The extent to which: (a) the organisational structure provides a secure framework; (b) the management is demonstrably of high quality

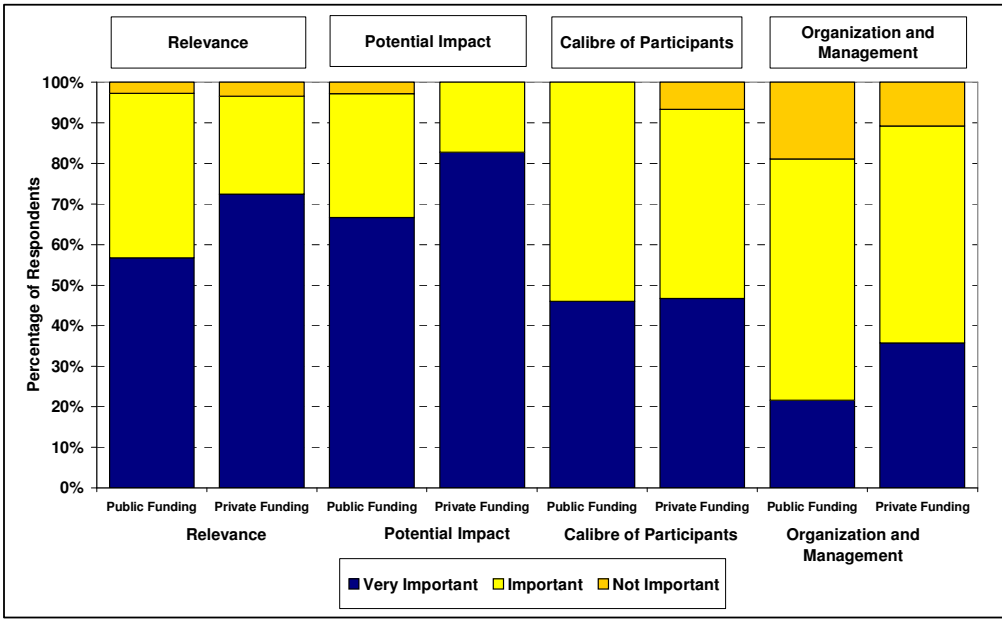


Figure 9: Importance of Criteria in Gaining Funding

The Figure illustrates that the relevance, potential impact and calibre of participants were thought to be either very important or important by the vast majority of respondents. In particular, the relevance and potential impact were regarded as very important by over 50% of respondents – in particular for accessing private financing. A number of respondents emphasized the importance of a project's potential impact in short and medium run commercial terms – especially for accessing private financing.

There is evidence of differences between the importance of criteria between European and North America respondents, especially in the allocation of public funding. Respondents from North America tended to state that the relevance of the project is not as important as its potential impact or calibre of participants. Also, a number of North American respondents highlighted the need for projects to be very innovative to attain public funds. Whereas in Europe, respondents tended to value the importance of the calibre of participants less highly to the project's relevance or potential impact. This is as an important difference for eligibility criteria. In particular, discussion during the Project Dissemination Seminar highlighted the idea that in the US funding "goes after" the best researchers, not the other way round.

(iii) Satisfaction with Synthetic Biology Sector

Respondents were asked to express the level of their satisfaction with the following elements in the Synthetic Biology sector.

- Accessibility to results of previous research
- Ability to patent research results
- National/Regional interest in field
- Availability of funding for research
- Availability of specialized and qualified staff
- Affordability of research
- Adequacy of Government policies
- Availability of core facilities (labs and research centres)
- Availability of post-doc training
- Availability of funding for commercialization
- Transferability of research into products
- Adequacy of legal processes
- Transferability of research to the business sector.

The results are provided below in Figure 10.

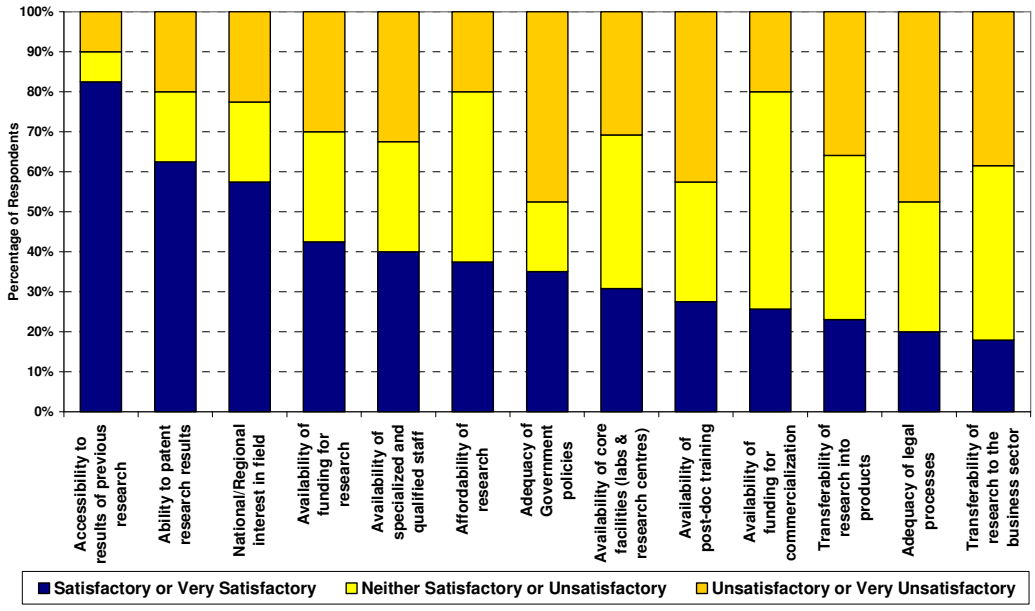


Figure 10: Satisfaction with Synthetic Biology Sector

There are significant variations between the respondents' levels of satisfaction with the elements of the Synthetic Biology sector. In particular:

- Elements such as the accessibility of previous research, ability to patent results and general national/regional interest in Synthetic Biology were mainly rated as very satisfactory, whilst

- Respondents stated that there are significant problems with the commercialization processes – including the availability of funding for commercialization of results, the transferability of research into products and to the business sector, and adequacy of processes to solve legal issues.

There was evidence of differences between the levels of satisfaction between European and North American respondents for a number of the elements. In particular, nearly half of all North American respondents perceived the availability of specialized and qualified staff and the availability of core facilities (labs and research centres) as very satisfactory or satisfactory. However under one-fifth of European respondents thought that these elements were very satisfactory or satisfactory.

Conversely, 40% of European respondents perceived that the adequacy of government policies in the Synthetic Biology sector was very satisfactory or satisfactory. However, less than half of this proportion in North America thought that the adequacy of government policies very satisfactory or satisfactory. The availability of funding for research and the affordability of the research were also thought to be more satisfactory in Europe than North America.

(iv) Europe/ North American Relationship

Respondents were asked to comment on the current and future relationship between European and North American Synthetic Biology research. The majority (80%) of respondents also believed there is an opportunity for joint funding schemes from European and North American funding agencies (either public or private non-profit) to fund Synthetic Biology research activities; either within the next 5 years (55% of respondents), or after 5 years (25% of respondents).

However, the majority (over 80%) of respondents also believed that existing infrastructures and protocols to share research materials between Europe and North America are not efficient. As discussed in the Synbiology Project Dissemination Seminar (May 30th 2006), there is a general belief that a number of barriers exist which limit future joint funding schemes from European and North American funding agencies in Synthetic Biology.

In particular, many stakeholders believe that differences in research culture form a barrier, for instance the North American area is more open to competition, while Europe is more focused on collaborations. Also, it was mentioned that a substantial proportion of prospective projects in the US are military driven, and thus maybe less open to joint work with European researchers. Other identified barriers were the distance, as periodical face-to-face meetings are still very fruitful, and the fact that such joint funding schemes may require significant bureaucracy, and could depend upon political decisions.

5. POLICIES IN EUROPE AND NORTH AMERICA

5.1. Introduction

The information in this chapter was previously presented as part of Output D9: Europe/North America Comparative Assessment.

In this chapter we provide an overview of policies in the Synthetic Biology field. As described in the chapter, there are few policies specifically designed for the sector. Thus, the discussion also includes a focus on general policies in the research sector which can have an effect on Synthetic Biology.

5.2. Policies in North America

This section focuses on the US. There are no US Government policies or guidelines that specifically address the field of Synthetic Biology. This is a very new field where the debate is just emerging in terms of the risks potentially associated with these scientific activities. Such public debate is being fostered by the researchers themselves in a model similar to the Asilomar 1975 Conference where the first biotechnologists met to agree on self-denying principles that went a long way to establishing their credentials as responsible individuals.[16] This Asilomar Conference was key to prevent the development of hasty government legislation that could possibly stifle the growth of what has become a true breakthrough scientific field with a safe record up to the present time.

This public debate on Synthetic Biology was furthered at a recent meeting on Synthetic Biology (SB2.0) held in May 2006 at the University of California-Berkeley. At the meeting, Nobel laureate and key Asilomar Conference figure David Baltimore reminded everyone that "nature is a very tough critic" and of how our depth of knowledge today is so contextually different from the Asilomar days. A discussion document has been issued from the Berkeley conference.[17] Also of

[16] Asilomar International Conference on Recombinant DNA Molecules, February 1975. In this conference, 140 biologists and physicians met in the presence of four lawyers and 16 science writers to consider the potential dangers of biological research. At the end of the conference, the scientists adopted guidelines under which research on splicing DNA could resume, subject to safety procedures that took into account the magnitude of risk associated with each experiment.

[17] Available at http://openwetware.org/wiki/Synthetic_Biology/SB2Declaration.

note is that the Sloan Foundation has provided funding for a report due out soon on the risks and social implications of Synthetic Biology.[18]

Several US government agencies have formulated initiatives that play a major role in the development of scientific research in the United States. One of such initiatives is the National Institutes for Health (NIH) Roadmap.[19] The NIH Roadmap provides a framework for the priorities NIH as a whole must address in order to optimize its entire research portfolio. It identifies the most compelling opportunities in three main areas: new pathways to discovery, research teams of the future, and re-engineering the clinical research enterprise. The NIH roadmap represents an integrated vision that deepens the understanding of biology, stimulates interdisciplinary research, and reshapes clinical research to accelerate medical discovery and improve people's health.

Another recent initiative from a US government agency is the Critical Path Initiative by the US Food and Drug Administration (FDA). The FDA has issued such initiative as a means to address the growing concern of moving basic discoveries to the market where they can be made available to the patients.[20] In order to meet the goal of advancing new drug products to reach the patients, a product developer has to successfully progress along a multidimensional critical path leading from the discovery or design stage to final commercial marketing. This critical path includes three main dimensions:

1. Assessing safety, showing that the product is adequately safe for each stage of development
2. Demonstrating medical utility, showing that the product benefits people
3. Industrialization, going from a laboratory concept or prototype to a manufacturable product

The FDA is stimulating advancements along these three scientific and technical dimensions by working with academia and industry in a variety of opportunities that can lead to new medical products reaching the market more expeditiously while preserving safety and efficacy.

Another major strategic initiative has been the creation of Engineering Research Centers (ERC) by the National Science Foundation (NSF). ERC's focus on the definition, fundamental understanding, development, and validation of technologies needed to realize a well-defined class of engineering systems with the potential to spawn whole new industries or radically transform

[18] To be presented in November 2006.

[19] http://nihroadmap.nih.gov

[20] www.fda.gov/oc/initiatives/criticalpath/whitepaper.html

the product lines, processing technologies, or service delivery methodologies of current industries.[21] ERC's involve faculty, students, and industry partners in an integrated discovery and learning effort within an interdisciplinary environment that reflects the complexities and realities of real-world technology. Of major significance to the Synthetic Biology field is the recent award of an ERC led by the University of California-Berkeley on Synthetic Biology.[22]

As a final example of a US government agency initiative, it is important to highlight the recent Multi-Year Program Plan (2007-2012) on Biomass by the US Department of Energy/Office of the Biomass Program.[23] The Program approach involves a combination of fundamental core research on feedstocks, sugars and thermochemical conversion platforms, and biobased products to create the scientific and technological underpinnings of the new bioindustry, and the application of these technologies by development of integrated biorefineries through public-private partnerships. The Program drives its momentum from the Energy Policy Act of 2005 signed into law on August 8, 2005. As part of the Act, is funding specifically targeted at improving the technology associated with biomass systems and increasing the amount of biopower, biofuels, and bioproducts used in the US. This is an area where Synthetic Biology may play an important role in the future.

5.3. Policies in Europe

In order to understand the current and potential policies for Synthetic Biology it is important to understand the crucial features of the European research system. These features include the following:

1. There is a substantial gap in the relationship between Gross Expenditure on R&D and overall GDP when compared to the same relationship in the US and Japan. This gap is more pronounced when Industry-Financed or Business-Executed R&D are considered. The presence of these gaps between Europe and the US/Japan indicate that there is, in general, less research in Europe, and the research undertaken is comparatively more relevant in the public than in the business sector.
2. Only about 2% of total EU research expenditure is funded centrally at the EU level, with the remaining expenditure financed out of national budgets.

[21] www.nsf.gov/eng/eec

[22] www.synberc.org

[23] http://www1.eere.energy.gov/biomass/pdfs/mypp.pdf

3. Foresight exercises in most advanced technologies have demonstrated that the EU is lagging behind or losing competitive positions in new technologies. Explicit policies aiming at reversing the situation have been adopted, which position research very prominently in the political agenda. However, their implementation has provided only limited success as yet.

There are no explicit Synthetic Biology policies at the national level. Most Synthetic Biology research, teaching and funding in the EU is concentrated in Germany and the UK. However, in neither of these countries is there an explicit national policy or priority area. Instead, the sector is driven by the concentration of researchers and funding opportunities:

In the UK there are three important funding sources:

- The Research Councils (Medical Research Council, Biotechnology and Biological Sciences Research Council, Natural Environment Research Council)
- The Wellcome Trust
- The Leverhulme Trust.

In addition, several universities have emerging activities and the Synthetic Biology Teaching Course (Organizer: Bioinformatics and Genomics Lab, Cambridge University) is among the activities of importance.[24]

In Germany there are a wide number of universities undertaking Synthetic Biology research and there is also funding from the Federal Ministry. It is also noteworthy that most of the companies identified to undertake Synthetic Biology research in Europe are in Germany.[25]

Outside of the EU, Synthetic Biology research in Switzerland includes that of the Swiss Federal Institute of Technology (ETH) which provides funding and undertakes research.[26] It will also host Synthetic Biology 3.0, the first international conference in Synthetic Biology to be held in Europe.

Other explicit policy initiatives have been undertaken in some international European organisations.

[24] http://www.plantsci.cam.ac.uk/Haseloff/syntheticbiology/index.html

[25] Details of many of the German companies are provided in Section 6.3.

[26] http://www.ivuk.ethz.ch/laboratories/bpl/research/index

The European Molecular Biology Organization (EMBO) and Nature Publishing Group (NPG) are editing the on-line journal: *Molecular Systems Biology*, the first journal dedicated solely to the emerging fields of molecular systems biology and synthetic biology.[27]

The European Union: The EU finances, through the European Commission NEST (New and Emerging Science and Technology) Pathfinder initiative, Synthetic Biology projects. The objective of the initiative is to bring together high level research groups in Europe with the long term goal of creating artificial systems based on biological engineering principles. These systems will foster unprecedented benefits in applications such as health, energy, environment or materials.

The projects funded by the programme include the following:

- BIOMODULARH2 - Engineered Modular Bacterial Hydrogen Photoproduction of Hydrogen
- BIONANO - SWITCH - A Biological Nanoactuator as a Molecular Switch for Biosensing
- CELLCOMPUT - Biological computation built on cell communication systems
- COBIOS - Engineering and COntrol of BIOlogical Systems: a new way to tackle complex diseases and biotechnological innovation
- EMERGENCE - Setting the bases for Synthetic Biology in Europe
- EUROBIOSYN - A modular platform for biosynthesis of complex molecules
- FuSyMEM - Functional Synthetic Membranes for GPCR based Sensing
- HYBLIB – Human monoclonal antibodies from a library of hybridomas
- NANOMOT - Synthetic Biomimetic Nanoengines: A Modular Platform for Engineering of Nanomechanical Actuator Building Blocks
- NEONUCLEI - Self-assembly of synthetic nuclei: key modules for semibiotic
- NETSENSOR - Design and Engineering of gene networks to respond to and correct alterations in signal transduction pathways.
- ORTHOSOME - An orthogonal episome: An artificial genetic system based on a novel type of nucleic acids
- PROBACTYS – Programmable Bacterial Catalysts.
- SynBioComm - Towards a European Synthetic Biology Community.
- SYNBIOLOGY - An Analysis of Synthetic Biology Research in Europe and North America.
- SYNBIOSAFE - Safety and Ethical Aspects of Synthetic Biology.
- SYNTHCELLS - Approaches to the bioengineering of synthetic minimal cells
- TESSY - Towards a European Strategy for Synthetic Biology

[27] http://www.embo.org/publications/msb.html

6. EUROPEAN/NORTH AMERICAN FUNDING AGENCIES

6.1. Introduction

The information in this chapter was previously presented as part of Output D9: Europe/North America Comparative Assessment

The chapter focuses on the funding of activities in Synthetic Biology. It starts with Section 6.2, in which descriptions of funding agencies including Federal Government agencies, venture capital funds, foundations and private companies in North America is provided. In Section 6.3 public funding agencies and private companies which fund and/or provide some Synthetic Biology research are described.

6.2. Funding Agencies in North America

Although there is some new discussion about possible general calls for proposals in the Synthetic Biology subject field (e.g. by the US Department of Energy), there are no significant centralized funding initiatives in the Synthetic Biology sector in North America. Instead, financing in the sector focuses on a bottom up approach, in which individual investigators provide proposals for funding to relevant funding agencies.

In this section, we detail the most relevant of these funding agencies, including identifying a number of the Key Stakeholders within the sector to whom they have provided financial support. The list of funding agencies has been developed through use of the Synbiology Project Database and through the amalgamation of information from the Project Questionnaire and discussions with Key Stakeholders.

In questionnaires and discussion with Key Stakeholders, a number of relevant points were made in regard of financing Synthetic Biology in the US. These include the following:

Training: Funding for post-docs and for Synthetic Biology training courses is especially required if the sector is to expand from its current base of researchers. Training is also required to increase the Synthetic Biology expertise for reviewers in funding agencies, patent examiners and legal counsel.

Funding Cycle: Synthetic Biology research tends to be expensive and long term – project cycles of 5 years are the norm, resulting in the need for long-term funding contracts. This long-term nature emphasizes the need for collaboration among a number of parties, and thus such partnerships should be encouraged with funding for large consortia, especially in

international projects. In addition, results can be achieved most effectively within a long-term project if the funding arrangements allow the researchers flexibility to allocate their funds within the overall grants to the specific priorities which they perceive to be the most important.

Synthetic Biology Funding Groups: Funding agencies are very hard-pressed for funds. Thus it would be helpful if senior administrators in the funding agencies were able to create special funding/groups for Synthetic Biology. In addition, it would be beneficial if such funding groups organise joint meetings between North America and Europe.

The main funding agencies in North America can be classified into the following groups:

- Federal government agencies
- Venture capital funds
- Foundations
- Private companies.

Federal Government Agencies

The (US) Federal Government Agencies include the following elements:

- National Institutes of Health
- Department of Energy
- National Science Foundation
- Department of Defense (Defense Advanced Research Projects Agency)
- National Aeronautics and Space Agency
- National Cancer Institute
- Office of Naval Research (United States Navy)
- National Institute of Allergy and Infectious Diseases.

These are described below.

National Institutes of Health	
Institution Description	
The National Institutes of Health (NIH) are the principal health research agency of the Federal Government; it is a component of the Department of Health and Human Services. With headquarters in Bethesda, Maryland, the NIH is a large, complex organization composed of 27 distinct institutes and centres. The NIH awarding institutes use three major instruments to provide funds to organizations outside the NIH to accomplish program goals--grants, cooperative agreements, and contracts. (http://www.nih.gov)	
Investigators/Companies Funded	
Terence Hwa	Donald Doyle
Roger Brent	A. Michael Sismour
Wendell Lim	Adam P. Arkin
David Lynn	Homme Hellinga

US Department of Energy	
Institution Description	
The Department of Energy's overarching mission is to advance the national, economic, and energy security of the United States; to promote scientific and technological innovation in support of that mission; and to ensure the environmental cleanup of the national nuclear weapons complex. The Department of Energy offers programs to assist research and development efforts, including cooperative partnerships, technology transfer, and financial awards. (http://www.doe.gov)	
Investigators/Companies Funded	
Terence Hwa	David Lynn
Roger Brent	

National Science Foundation	
Institution Description	
The National Science Foundation (NSF) is an independent federal agency created by Congress in 1950 "to promote the progress of science; to advance the national health, prosperity, and welfare; to secure the national defense…". With an annual budget of about US$5.5 billion, they are the funding source for approximately 20% of all federally supported basic research conducted by US colleges and universities. In many fields such as mathematics, computer science and the social sciences, the NSF is the major source of federal backing. (http://www.nsf.gov)	
Investigators/Companies Funded	
Terence Hwa	Chengde Mao
Roger Brent	A. Michael Sismour
Wendell Lim	Mehmet Sarikaya
Darko Stefanovic	Milan N. Stojanovic

Department of Defense (Defense Advanced Research Projects Agency)	
Institution Description	
The mission of the Department of Defense (DoD) is to provide the military forces needed to deter war and to protect the security of our country. Grants are provided to fund basic and applied research that has the potential to further this mission. The Defense Advanced Research Projects Agency (DARPA) is the central research and development organization for the DoD. It manages and directs selected basic and applied research and development projects for DoD, and pursues research and technology where risk and payoff are both very high and where success may provide dramatic advances for traditional military roles and missions. http://www.dod.gov) (http://www.darpa.mil)	
Investigators/Companies Funded	
Terence Hwa	Chengde Mao
Roger Brent	A. Michael Sismour
Wendell Lim	Mehmet Sarikaya
Darko Stefanovic	Milan N. Stojanovic

National Aeronautics and Space Agency
Institution Description The National Aeronautics and Space Agency (NASA) is a federal agency that's responsible for aeronautical exploration. It concentrates its resources in four distinct areas: aeronautics, exploration systems, science, and space operations. (http://www.nasa.gov)
Investigators/Companies Funded A. Michael Sismour

National Cancer Institute
Institution Description The National Cancer Institute (NCI) is a component of the National Institutes of Health (NIH), one of eight agencies that compose the Public Health Service (PHS) in the Department of Health and Human Services (DHHS). The NCI, established under the National Cancer Act of 1937, is the Federal Government's principal agency for cancer research and training. They support and coordinate research projects conducted by universities, hospitals, research foundations, and businesses throughout this country and abroad through research grants and cooperative agreements. (http://www.nci.nih.gov)
Investigators/Companies Funded Thomas A. Spratt

Office of Naval Research
Institution Description The Office of Naval Research (ONR) coordinates, executes, and promotes the science and technology programs of the United States Navy and Marine Corps through schools, universities, government laboratories, and nonprofit and for-profit organizations. It provides technical advice to the Chief of Naval Operations and the Secretary of the Navy and works with industry to improve technology manufacturing processes. (http://www.onr.navy.mil)
Investigators/Companies Funded Adam P. Arkin Homme Hellinga

National Institute of Allergy and Infectious Diseases
Institution Description The National Institute of Allergy and Infectious Diseases (NIAID) conducts and supports basic and applied research to better understand, treat, and ultimately prevent infectious, immunologic, and allergic diseases. For more than 50 years, NIAID research has led to new therapies, vaccines, diagnostic tests, and other technologies that have improved the health of millions of people in the United States and around the world. (http://www3.niaid.nih.gov)
Investigators/Companies Funded Coda Genomics

Venture Capital Funds

Venture capital funds include the following:

- Khosla Ventures
- Flagship Ventures
- Kleiner Perkins Caufield & Byers
- Mohr Davidow Ventures
- Draper Fisher Jurvetson
- Alloy Ventures
- Tech Coast Angels

These are described below.

Khosla Ventures	
Institution Description	
Khosla Ventures offers venture assistance, strategic advice and capital to entrepreneurs. The firm helps entrepreneurs extend the potential of the Internet to new markets such as mobile and supports breakthrough scientific work such as bio refineries. The partners have been involved in founding or growing billion dollar businesses such as Sun Microsystems, Juniper Networks and AOL and pioneering scientific work such as the first complete sequencing of a plant genome. The firm's capital comes entirely from its own partners and a portion of all profits are donated to charitable causes, with an emphasis on micro-finance and affordable housing. Khosla Ventures is based in Menlo Park, California. (http://www.khoslaventures.com/)	
Investigators/Companies Funded	
Amyris Biotechnologies	LS9

Flagship Ventures
Institution Description
Flagship Ventures is an early-stage venture capital firm focused on creating, financing, and building innovative companies in the Life Science and Technology sectors. Headquartered in Cambridge, MA, Flagship Ventures was founded in 1999 and manages US$700 million in capital. Prior to its founding. (http://www.flagshipventures.com/)
Investigators/Companies Funded
Codon Devices

Kleiner Perkins Caufield & Byers
Institution Description
A well-known venture capital firm based in Menlo Park, CA. (http://www.kpcb.com/)
Investigators/Companies Funded
Codon Devices

Mohr Davidow Ventures
Institution Description Mohr Davidow Ventures (MDV) invests in innovative entrepreneurs with deep expertise in energy and materials, Internet services; life sciences, semiconductor and software and systems. Their venture capital team engages very early in the life of a company to impact its long-term success. For more than 20 years, their mission as an early stage venture capital firm has been to identify, invest in, mentor and develop venture-backed companies that redefine how organizations and individuals apply new technologies and scientific advances.
Investigators/Companies Funded DNA Repair

Draper Fisher Jurvetson
Institution Description Draper Fisher Jurvetson is a venture capital firm with global presence through a network of affiliated funds, with offices in more than 30 cities around the world and approximately US$3.5 billion in capital commitments. DFJ's mission is to identify, provide capital for, and serve extraordinary entrepreneurs anywhere who want to change the world. Over the past 20 years, DFJ has been backed approximately 300 companies across a range of sectors. (http://www.dfj.com/)
Investigators/Companies Funded Synthetic Genomics

Alloy Ventures
Institution Description Alloy Ventures is an early-stage venture capital firm. Overall, their partners have entrusted Alloy Vemtures with over US$1 billion in capital. Ally Ventures are currently investing out of their 5th fund - a $368 million limited partnership raised in June 2005. Each year they invest in a small number of entrepreneurial ideas and young companies, and aim to achieve long-term relationships with our entrepreneurs and executives. (http://www.alloyventures.com/)
Investigators/Companies Funded Codon Devices

Tech Coast Angels
Institution Description Tech Coast Angels (TCA) attempts to help fuel the growth of the most innovative companies and entrepreneurs in Southern California. TCA has 270 members to help companies grow and succeed. (http://www.techcoastangels.com/)
Investigators/Companies Funded Coda Genomics

Foundations

Foundations with links to Synthetic Biology funding in North America include the following:

- The Ellison Medical Foundation
- The Howard Hughes Medical Institute
- The Packard Foundation
- The Seaver Foundation
- The Keck Foundation
- The Burroughs Wellcome Foundation
- The Alfred P. Sloan Foundation
- The John D. and Catherine T. MacArthur Foundation
- The Bill and Melinda Gates Foundation

These are described below.

Ellison Medical Foundation
Institution Description The Ellison Medical Foundation supports basic biomedical research on aging relevant to understanding aging processes and age-related diseases and disabilities. The Foundation particularly wishes to stimulate new, creative, research that might not be funded by traditional sources or that is often under-funded in the U.S. The Foundation fosters research by means of grants-in-aid on behalf of investigators to universities and laboratories within the United States. (http://www.ellisonfoundation.org/)
Investigators/Companies Funded Roger Brent

Howard Hughes Medical Institute	
Institution Description	
The Howard Hughes Medical Institute (HHMI) is a nonprofit medical research organization that employs hundreds of leading biomedical scientists working at the forefront of their fields. In addition, through its grants program and other activities, HHMI is helping to enhance science education at all levels and maintain the vigour of biomedical science worldwide. (http://www.hhmi.org/about/)	
Investigators/Companies Funded	
David Lynn	Adam P. Arkin

Packard Foundation
Institution Description
Guided by the business philosophy and values of our Founders, the Packard Foundation invests in and takes smart risks with innovative people and organizations to improve the lives of children, enable creative pursuit of science, advance reproductive health, and conserve and restore earth's natural systems. (http://www.packard.org/)
Investigators/Companies Funded
David Lynn

Seaver Foundation	
Institution Description	
The Seaver Foundation supports projects on a variety of topics including the arts, private education, youth, health concerns, public affairs, the disabled, literacy, and science. Seed grants are awarded for projects that offer the potential for a significant advancement in their fields. Funded projects should incorporate state-of-the-art scientific research, exceptional educational development, unique approaches to the creative arts, and the ramifications of shifting societal realities. (http://www.compact.org/grants/grants.php?viewgrant=897)	
Investigators/Companies Funded	
David Lynn	Donald Doyle

Keck Foundation
Institution Description In recent years, the Foundation has focused on five broad areas: Science and Engineering Research; Undergraduate Science and Engineering; Medical Research; Liberal Arts; and Southern California. Each of their grant programs invests in people and programs that are making a difference in the quality of life, now and for the future. (http://www.wmkeck.org/)
Investigators/Companies Funded Pamela Silver

Burroughs Wellcome Foundation
Institution Description The Burroughs Wellcome Fund is an independent private foundation dedicated to advancing the medical sciences by supporting research and other scientific and educational activities. (http://www.bwfund.org/)
Investigators/Companies Funded Michael Elowitz

Alfred P. Sloan Foundation
Institution Description The Alfred P. Sloan Foundation is a philanthropic nonprofit institution. The Foundation's programs and interests fall into the following areas: science and technology, standard of living and economic performance, education and careers in science and technology, and selected national issues. (http://www.sloan.org/)
Investigators/Companies Funded Bioethics Consortium spearheaded by the Venter Institute

John D. and Catherine T. MacArthur Foundation
Institution Description The John D. and Catherine T. MacArthur Foundation is a private, independent grantmaking institution dedicated to helping groups and individuals foster lasting improvement in the human condition. Through the support it provides, the Foundation fosters the development of knowledge, nurtures individual creativity, helps strengthen institutions, helps improve public policy, and provides information to the public, primarily through support for public interest media. (http://www.macfound.org/)
Investigators/Companies Funded Michael Nacht - Policy Standards Development

Bill and Melinda Gates Foundation	
Institution Description Guided by the belief that every life has equal value, the Bill & Melinda Gates Foundation works to reduce inequities and improve lives around the world. In developing countries, it focuses on improving health, reducing extreme poverty, and increasing access to technology in public libraries. In the United States, the Foundation seeks to ensure that all people have access to a great education and to technology in public libraries. (http://www.gatesfoundation.org/)	
Investigators/Companies Funded	
University of California Berkeley	Amyris Biotechnologies
Institute for OneWorld Health	

Private Companies

Companies that fund Synthetic Biology research in North America include the following:

- Microsoft Research
- Research Corporation

These are described below.

Microsoft Research
Institution Description Microsoft Research aims to create new technology that will help define the computing experience, with the objective to innovate in computer science. To that end, they collaborate with universities, submit papers for peer review, and partner with product groups to bring our research to the public. (http://research.microsoft.com/)
Investigators/Companies Funded Currently soliciting grant applications

Research Corporation
Institution Description Research Corporation is an active, hands-on foundation that stimulates advances in science. Its mission is one of partnership rather than ownership. The major activities of Research Corporation are associated with grants activities operated through five major programs: the Development Awards, the Cottrell College Science Awards, the Research Innovation Awards, the Cottrell Scholar Awards, and the Research Opportunity Awards. (http://www.rescorp.org/)
Investigators/Companies Funded Donald Doyle

6.3. Funding Agencies in Europe

In this section, we detail the most relevant funding agencies that provided part or full finance for some of the papers included in the Synbiology Project Database. These include the following.

Alexander von Humboldt Foundation (Germany)
Institution Description
Non-profit foundation established by the Federal Republic of Germany for the promotion of international research cooperation. It enables highly qualified scholars not resident in Germany to spend extended periods of research in Germany and promotes the ensuing academic contacts. The Humboldt Foundation promotes an active world-wide network of scholars. Individual sponsorship during periods spent in Germany and longstanding follow-up contacts have been the focus of much of the foundation's work since 1953. (http://www.humboldt-foundation.de/en/stiftung/stiftung.htm)

Belgium National Fund for Scientific Research - FWO
Institution Description
Founded in 1928, the FWO finances basic research which is aimed at moving forward the frontiers of knowledge in all disciplines. Basic research is carried out in the universities of the Flemish Community and in affiliated research institutes. (http://sun.fwo.be/page1en.php?lang=en#top)

Danish Natural Science Research Council
Institution Description
One of five scientific research councils under the Danish Councils for Independent Research. The Council covers research within the classical disciplines of astronomy, physics, chemistry, mathematics, computer science, molecular biology, biochemistry/biophysics, biology, geology and aspects of geography that relate to natural science. (http://forsk.dk)

Deutsche Forschungsgemeinschaft (German Research Foundation)
Institution Description
Central, self-governing research organisation that promotes research at universities and other publicly financed research institutions in Germany. Promoting research includes supporting individual projects and research cooperation, awarding prizes for outstanding research achievements as well as funding scientific infrastructure and encouraging contacts in science and research. (www.dfg.de)

Engineering and Physical Sciences Research Council - EPSRC (UK)
Institution Description
UK Government's leading funding agency for research and training in engineering and the physical sciences. (www.epsrc.ac.uk)

European Molecular Biology Laboratory - EMBL (Germany)
Institution Description
Non-profit organisation and basic research institute funded by public research monies from 18 member states. Research is conducted by approximately 80 independent groups covering the spectrum of molecular biology. The cornerstones of EMBL's mission are to perform basic research in molecular biology, to train scientists, students and visitors at all levels, to offer vital services to scientists in the member states, and to develop new instruments and methods in the life sciences, and technology transfer. (http://www.embl-heidelberg.de/)

Fonds der Chemischen Industrie (Germany)
Institution Description
Research funds provided by the Chemical Industry Federation, based in Frankfurt. Provides funds for many complementary and supporting measures. In the area of University support awards for research are given means for renowned scientists and up-and-coming researchers. Within the scope of the project "school partnership of chemistry", the fund promotes experimental lessons at schools. (www.vci.de/fonds/)

French National Center for Scientific Research - CNRS
Institution Description
Publicly-funded research organization with the mission to produce knowledge and making it available to society. CNRS has 26,000 employees. The 1,260 CNRS service and research units are spread throughout the country and cover all fields of research. CNRS has mission to evaluate and provide research, contribute to the application and promotion of research results, develop scientific information, support training for and through research and participate in the analysis of the national and international scientific climate. (www.cnrs.fr)

Fonds zur Förderung - FWF (Austrian Science Fund)
Institution Description Austria's central body for the promotion of basic research. Its responsibilities are to promote high-quality scientific research, education and training through research, knowledge transfer and the establishment of a science-friendly culture via an exchange between science and other areas of society, and public relations in the field of scientific research (www.fwf.ac.at)

German-Israeli Project Cooperation - DIP
Institution Description Established in 1997 by the German Federal Ministry for Education and Research (BMBF), with the aim of devoting funds to a substantial support of joint projects in highly competitive areas of academic research. There are no limitations regarding the topics chosen. Projects within this program are selected through annual competition and funded for up to five years. Eligible for the submission of proposals are the six Israeli universities and the Weizmann Institute. BMBF has charged the International Bureau (IB) of the DLR (German Aerospace Center) with responsibility for the administration of the program and the guidance of applicants. (http://www.internationales-buero.de/de/787.php)

Institut National de la Santé et de la Recherche Médicale (France)
Institution Description Created in 1964, Inserm is a public institution with a scientific and technical vocation, under the dual auspices of the Ministry of Health and the Ministry of Research. It is the only French public research body entirely dedicated to human health. Its researchers are committed to studying all diseases through their work in the fields of biology, medicine and public health. Inserm's principal mission is to facilitate exchange between basic research, clinical research, therapeutic or diagnostic research, and public health research, aimed at gaining a better understanding of health mechanisms, notably through the study of particular population groups. (http://www.inserm.fr/fr/home.html)

Israel Academy of Sciences
Institution Description The Academy's principal objectives are to enlist as its members distinguished scholars and scientists resident in Israel, to cultivate and promote scholarly and scientific endeavour, to advise the government on activities relating to research and scientific planning of national significance, to maintain contact with parallel bodies abroad, to ensure the representation of Israel scholarship and science at international institutions and conferences and to publish writings calculated to promote scholarship and science. The Academy founded and administers the Israel Science Foundation (www.isf.org.il), with an annual budget of $53 million, took part in the establishment of a National Research Council and an active Forum for National Research and Development Infrastructure, helped initiate the US$300 million Israel Nanotechnology Program, and facilitated the participation of Israeli scientists in cutting-edge research at international high-energy physics (CERN) and synchrotron radiation (ESRF) mega-facilities. (http://www.academy.ac.il/)

Israel Science Foundation - ISF
Institution Description Israel's predominant source of competitive grants funding for basic research. Its roughly US$60 million annual budget funds 1,300 grants a year, providing two-thirds of all such funds. The ISF awards grants in all fields of Exact Sciences and Technology, Life Sciences and Medicine, and Humanities and Social Sciences to researchers at Israeli universities, other centres of higher education, research centres and medical centres. Most funds (96%) are provided by the Government of Israel via the Planning and Budgeting Committee (PBC) of the Israel Council for Higher Education. (http://www.isf.org.il/)

L'Association Francaise contre les Myopathies - AFM (France)
Institution Description Created in 1958 by a group of patients and their families, and recognized as being of public utility in 1976, AFM (French Muscular Dystrophy Association) has the single objective : to defeat neuromuscular diseases which are devastating muscle-wasting diseases. It has set itself two missions: curing neuromuscular diseases and reducing the disabilities they cause. (http://www.afm-france.org/afm-english_version/ewb_pages/d/decouvrirafm_missions_strategie.php)

Schweizerischer Nationalfonds - SNSF (Switzerland)
Institution Description Swiss institution for the promotion of scientific research. It supports research in all disciplines, from philosophy and biology to the nanosciences and medicine. Established in 1952 as a foundation under private law, it has the autonomy it needs to promote independent scientific research. The SNSF funds research and promotes application oriented-research in various scientific fields. The main task of the SNSF is to evaluate the quality of research proposals submitted by scientists and to provide funding on the basis of priorities and available financial resources. (www.snf.ch)

UK Biotechnology and Biological Sciences Research Council - BBSRC
Institution Description The UK's principal funder of basic and strategic biological research. To deliver its mission, the BBSRC supports research and research training in universities and research centres throughout the UK, including BBSRC-sponsored institutes, and promotes knowledge transfer from research to applications in business, industry and policy, and public engagement in the biosciences. The BBSRC, a non-departmental public body, is one of eight Research Councils supported through the Science Budget by the Department of Trade and Industry. (http://www.bbsrc.ac.uk/about/Welcome.html)

Private Companies

In addition there are a number of private sector organizations in Europe that fund and provide research which includes work in the Synthetic Biology field. The following includes a sample of such organizations, along with a specific contact at each organization with strong links to the Synthetic Biology Sector.

ALTANA Pharma AG
Institution Description ALTANA Pharma AG is the pharmaceutical division of ALTANA AG, headquartered in Konstanz, Germany. ALTANA Pharma is an international pharmaceutical group with about 9,000 employees and over 30 subsidiaries in Europe, North and Latin America, Asia, South Africa and Australia. It concentrates on innovative pharmaceutical products in therapeutics, imaging (contrast media) and OTC medication. Therapeutics, the most important business area, is based on prescription drugs for gastrointestinal and respiratory diseases. Contact: Dr. Wurst (http://www.altanapharma.com/)

AMGEN
Institution Description A leading human therapeutics company in the biotechnology industry. Amgen pioneered the development of novel products based on advances in recombinant DNA and molecular biology and launched the biotechnology industry's first blockbuster medicines. Today, as a Fortune 500 company serving millions of patients, Amgen continues to be an entrepreneurial, science-driven enterprise. (http://www.amgen.com/)

Bayer CropScience AG
Institution Description Bayer CropScience is one of the world's leading innovative cropscience companies in the area of crop protection, non agricultural pest-control, seeds and plant biotechnology. The company is structured into six Business Operations units: four regional crop protection units and two units responsible for Environmental Science and BioScience - offering an outstanding range of products and extensive service backup for modern, sustainable agriculture as well as for non-agricultural applications. Contact: Dr. Bayer Kesisoglu and Dr.Manfred Kern (http://www.bayercropscience.com/bayer/cropscience/cscms.nsf/id/Our-Company)

Degussa AG

Institution Description

Rentschler Biotechnologie are committed to R&D as a basis of profitable growth. Around 2,300 Degussa employees work in R&D at over 35 research locations all over the world, and are involved in over 200 cooperative projects with universities as a means of swiftly introducing scientific knowledge into the company. Approximately 20% of sales are based on products and technologies that are less than five years old. The Science to Business Center Nanotronics (which develops nanomaterials-based system solutions for the electronics industry) and the new Science to Business Center Bio (white biotechnology) are the latest research operations.

Contact: Dr. Gröger Harald

(http://www.degussa.com/degussa/en/company/)

febit biotech GmbH

Institution Description

febit biotech develops and manufactures innovative technologies for DNA analysis. GENIOM is a high-tech device unique on the global market, featuring benchmark performance in DNA microarray analysis. High-ranking molecular biology and medical research institutions often choose GENIOM for its high flexibility, speed and data security.

Contact: Dr. Peer Stähler

(http://www.febit.com/europe/en/unternehmen/index.cfm)

GENEART AG

Institution Description

GENEART provides integrated system solutions for DNA engineering and processing based on the gene synthesis technology platform to deliver improved drugs and biotech products. Companies and research institutions from both the pharmaceutical and biotech industries make use of GENEART's expertise in the development and production of DNA- and protein-based drugs and vaccines, and in identifying improved biocatalysts (enzymes). The GENEART service portfolio ranges from the production of optimized synthetic genes and the generation of gene variants and combinatorial biology (directed evolution) right through to the production of DNA-based agents.

Contact: Dr. Graf Marcus

(http://www.geneart.com/)

Henkel KgaA and EUCODIS GmbH

Institution Description

Henkel KGaA and EUCODIS GmbH and have funded a joint collaboration that focuses on developing a biocatalyst for Henkel's Laundry & Home Care business sector. EUCODIS will apply in vivo recombination technology. EUCODIS GmbH is a biotechnology company with headquarters and main laboratories in Vienna, Austria, which applies technologies of in vivo recombination and somatic hypermutation, generating projects and partnerships in two business areas: "red biotechnology", focusing on (bio-) pharmaceuticals and human antibodies, and "white biotechnology", comprising projects partnered to leading life science companies on novel enzymes and fermentation optimisation.

Contact: Dr. Karl-Heinz Maurer

(http://www.henkel.com)

(http://www.eucodis.com)

Hybrigenics SA

Institution Description

Hybrigenics identifies new drug targets and therapeutic molecules using a combination of high throughput protein interaction mapping, in-depth functional validation and leading-edge chemical screening technologies. Its mission is to discover and develop small molecule drug candidates that address unmet medical needs, primarily in Oncology.

(http://www.hybrigenics.com/index.html;jsessionid=FF2ED43737A0421BFD2968DD3F68DF41)

Lonza AG

Institution Description

Lonza is a chemical and biotechnology company driven by the life sciences. Headquartered in Switzerland, Lonza operates 22 production and R&D sites around the world. Lonza is one of the leading custom manufacturers of chemical intermediates, active ingredients and biopharmaceuticals for the pharmaceutical and agrochemical industries. On the basis of organic and performance chemicals, and biotechnology platforms, Lonza creates value-added solutions for the nutrition, hygiene and personal care, wood and water treatment and industrial specialty markets. Lonza also offers polymer intermediates, resins and compounds.

Contact: Dr. Hans-Peter Meyer

(http://www.lonza.com/group/en/company.html)

Proto Life
Institution Description
ProtoLife develops automated, high-throughput methods for designing complex chemical systems. ProtoLife methodologies may be used for discovery of new materials as well as new chemical reactions. Their current focus is on soft matter chemistry and self-assembly processes, including optimizing functional properties of structures such as liposomes, vesicles, and micro-bubbles. Contact: Dr. Norman Packard (http://www.protolife.net/company/profile.php)

Sanofi-Aventis
Institution Description
Sanofi-aventis is the world's 3rd largest pharmaceutical company, ranking number 1 in Europe. It aims to develop leading positions in seven major therapeutic areas: cardiovascular disease, thrombosis, oncology, diabetes, central nervous system, internal medicine, and vaccines. Contact: Prof. Andreas Busch (cardiovascular) and Dr. Juergen Dedio (molecular and cell biology) (http://www.sanofi-aventis.us/index.html)

Syngenta International AG
Institution Description
Syngenta is a world-leading agribusiness committed to sustainable agriculture through innovative research and technology. The company is a leader in crop protection, and ranks third in the high-value commercial seeds market. They focus on improving crop solutions, with the goal of being the leading global provider of innovative solutions and brands to growers and the food and feed chain. (http://www.syngenta.com/en/index.aspx)

Strathmann Biotec GmbH & Co.
Institution Description
Strathmann Biotec is an expanding biotechnology company based in Hamburg, Germany. Founded in 1987 as Pharma Biotechnologie Hannover, it was one of the first manufacturers of recombinant proteins in Germany. Since 1997 it has been part of the Strathmann group, a leading mid-sized pharmaceutical company in Germany. Today, Strathmann Biotec employs about 100 experts for the development and manufacturing of biopharmaceuticals working together in interdisciplinary teams. (http://www.biotec-ag.de/de/company/comphome.shtml)

7. DISSEMINATION OF SYNBIOLOGY PROJECT

7.1. Introduction

This chapter provides an overview of the Synbiology project dissemination activities. These activities include the providing the project deliverables:

- D1: Project Brochure
- D2: Project Website
- D5: Fact Sheet
- D7: Synthetic Biology Research Survey Workshop
- D10: Synthetic Biology Research Seminar

In addition, a Project Results Brochure was provided. These dissemination activities are further described below.

7.2. D1: Project Brochure

The Project Brochure was developed and a total of 250 full-colour copies were printed, which were distributed during the project meetings. The Brochure was also uploaded onto the Project Website.

The Brochure, which is included as Annex 3 to this Report, included information on the project's participants, strategic objectives, benefits, inputs and outputs, and dissemination activities.

7.3. D2: Project Website

The Project Website was put on-line at the start of the project, and continually updated during the project's life. The Website can be found at www.spi.pt/synbiology.

The Website is the central source of public information on the project. It provides information on the project's objectives and benefits, its methodology and activities, and provides links to the project partners' home websites. It also provides other interesting links in the Synthetic Biology field, including to the European Commission NEST (New and Emerging Science and Technology) website, the SB2.0 Conference website and the Report of the Synthetic Biology: Applying Engineering to Biology - NEST High-Level Expert Group.

In addition, the Website includes access to all the project documents, including reports and presentations from the project meetings. The Website was also used to provide the questionnaire used in the project survey (see Section 4 above).

In Figures 11 and 12 we provide example screenshots of the Website.

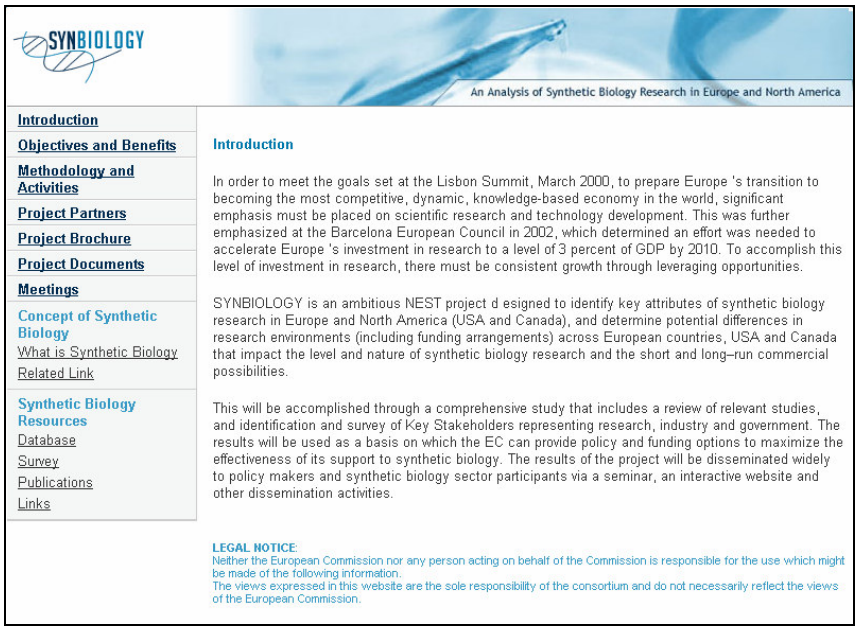


Figure 11: Home Page of Project Website

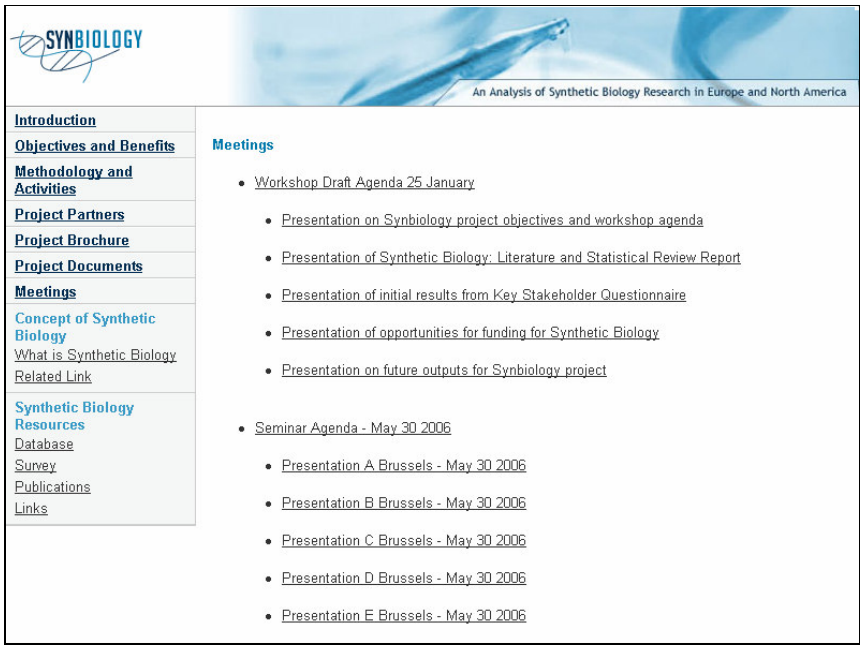


Figure 12: Meetings Page of Project Website

Synbiology Project Database

The Synbiology Project Database is included in the Project Website. The Database has been developed over the life of the Synbiology Project and provides references to 1,100 papers published in peer-reviewed journals in the Synthetic Biology sector.

Originally 1.5 million abstracts, dating from 1990, in the life sciences field were downloaded. The abstracts of these papers were then searched using algorithms based on keywords relating to Synthetic Biology that had been selected by the Synbiology team. The purpose of this search was to identify papers with most relevance to the Synthetic Biology field.

Further, abstracts of papers authored by known Synthetic Biology researchers, including those in the European Commission High-Level Expert Group, but which had not been identified in the automatic search were then added.

In this way, a total of 1,100 papers were identified as being part of the Synthetic Biology field, and thus included in the Project Database as Synthetic Biology publications.

Each paper in the Database has been assigned an *impact factor*. This is calculated from the importance of the journal in which the paper was published, as measured by the Thomson Scientific Index. These impact factors allow the Database to attach an estimate of the importance to the Synthetic Biology research of each individual paper in the Project Database

The Database also includes links to the relevant organisation and/or personal websites for all the papers' authors.

Figures 13 and 14 below provide example screenshots of the Database.

Figure 13: Example Screen-Shot of Synbiology Project Database (1)

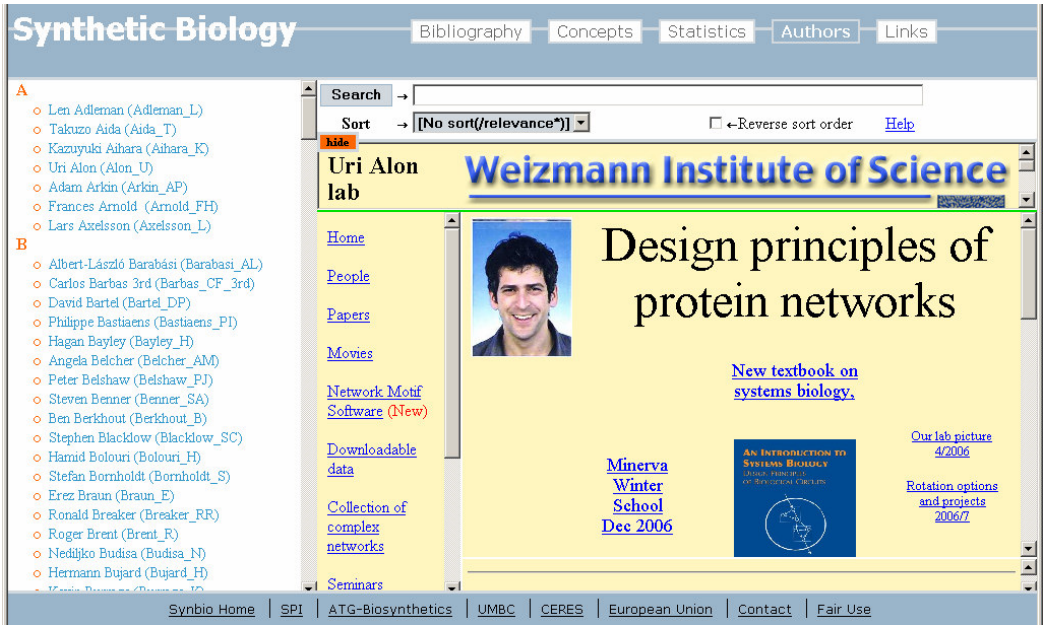


Figure 14: Example Screen-Shot of Synbiology Project Database (2)

7.4. D7: Synthetic Biology Research Survey Workshop

The Synthetic Biology Research Survey Workshop was held on 25th January 2006 at the European Commission in Brussels. The Workshop lasted one day and focused on the following:

- Presentation of D3: Synthetic Biology Research – Literature & Statistical Review
- Introduction to the preliminary results of the project survey
- Discussion of funding opportunities in North America and Europe.

The Workshop was chaired by Dr. Christian Krassnig from the European Commission and was attended by all project partners and the following invitees:

- Prof. Dr. Alexander Steinbüchel - Institut für Mikrobiologie, Westfälische Wilhems-Universität Münster, Germany
- Dr. Ulrich Commandeur - Institute for Biology VII, RWTH Aachen University, Germany
- Prof. Dr. Frank Seela - Universität Osnabrück, Institut für Chemie, Germany
- Dr. Adrian Dubock - Syngenta International AG, Switzerland
- Dr. Peer Stähler - Febit ag, Germany
- Prof. Sven Panke - ETH Zurich, Bioprocess Engineering, Switzerland
- Dr. Kristian Müller - Institut für Pharmazeutische Chemie, Germany
- Dr. Vitor A.P. Martins dos Santos - German Research Centre for Biotechnology, Germany
- Prof. Klaus Palme - Universität Freiburg, Germany
- Prof. Donald F. Doyle - Georgia Institute of Technology, School of Chemistry and Biochemistry, USA
- Dr. Randy Rettberg - Massachusetts Institute of Technology, USA

7.5. D10: Synthetic Biology Research Seminar

The Synthetic Biology Research Seminar was held on 30th May 2006 at the European Commission in Brussels.

The Seminar lasted one day and focused on the following:

- Definition of Synthetic Biology activities
- Discussion of funding of Synthetic Biology in North America and of human capital and funding mechanisms supporting Synthetic Biology in Europe
- Discussion of results of the project survey
- Introduction to the Synbiology Project Database.

The Workshop was chaired by Dr. Christian Krassnig from the European Commission and was attended by all project partners and the following invitees:

- Prof. George Attard - University of Southampton, UK
- Eng. Vitor A.P. Martins dos Santos - German Research Centre for Biotechnology, Germany
- Dr. Keith Firman - School of Biological Sciences, University of Portsmouth, UK
- Dr. Andrei Kuznetsov - IMTEK-Institut für Mikrosystemtechnik, Albert-Ludwigs-Universität Freiburg, Germany
- Brigitte Tempelmaier - Life Science Austria (LISA) Vienna Region, Austria
- Dr. Vitor de Lorenzo - Centro Nacional de Biotecnologia, CSIC, Spain
- Prof. Dr. Frank Breitling - German Cancer Research Center, Germany
- Prof. Rudolf K. Allemann - School of Chemistry, Cardiff University, UK
- Markus Schmidt - Organisation for International Dialogue and Conflict Management, Austria
- Andrew Hessel – iGEM Ambassador.

7.6. Project Results Brochure

In addition to the above dissemination activities, the project has provided a Project Results Brochure. This Brochure is available on the Project Website and is included as Annex 3 to this Report. The Brochure includes information on the project's participants, details the dissemination activities such as the Project Website, Database and meeting, and describes the project reports.

8. SUMMARY

This is the Final Report of the Synbiology: An Analysis of Synthetic Biology Research in Europe and North America project. It is provided as Deliverable Number 11 for the project FP6-2003-NEST-B4 Project 015357 – SYNBIOLOGY.

The objective of the Final Report is to provide an overview of the Synbiology project background and methodology, and bring together all the project results in one document. The Report also has the objective of detailing the actions undertaken to disseminate the project results.

In **Chapter 1**, the Report provided a brief overview of this heterogeneous but definable scientific field. It was found that Synthetic Biology can be defined as the boundary between biological sciences and engineering sciences, in which technical approaches are employed to provide future applications. The Chapter also defined the project's working definition is as follows: *Synthetic Biology is the engineering of biological components and systems that do not exist in nature and the re-engineering of existing biological elements; it is determined on the intentional design of artificial biological systems, rather than on the understanding of natural biology.*

Chapter 2 introduced 50 Key Stakeholders involved in Synthetic Biology research - with a focus on North America and Europe (including the Europe-33 research area countries). These introductions include a short description of their activities and a listing of their papers included in the Synbiology Project Database.

In **Chapter 3**, a geographical assessment of author location of Synthetic Biology publications was provided. The assessment led to the following conclusions

- The USA is the most important source of research results in Synthetic Biology and the number and importance of Synthetic Biology publications from the EU-25 countries follow the USA at a considerable distance
- Within the EU-25 area, publications from authors based in Germany, UK and France represent the majority of Synthetic Biology papers. Authors located in the Denmark, the Netherlands and Spain also provide notable contributions
- Outside of the USA and EU-25, authors based in Switzerland and Israel provide significant contributions to Synthetic Biology publications.

Chapter 4 provided an assessment of the results from the survey of Key Stakeholders undertaken as part of the Synbiology project, including an assessment of the differences between responses from North America and Europe were found.

In particular:

Gaining Project Funding: Respondents from North America tended to state that the relevance and level of innovation of a particular research project is not as important as its potential impact or calibre of participants in gaining project funding. In Europe, respondents tended to value the importance of the calibre of participants less highly to the project's relevance or potential impact. This can be seen as is as an important difference for eligibility criteria. In particular, discussion it may highlight an idea discussed during the project that in the US funding "goes after" the best researchers, not the other way round.

Satisfaction with Facilities: Nearly half of all North American respondents perceived the availability of specialized and qualified staff and the availability of core facilities (labs and research centres) as very satisfactory or satisfactory. However under one-fifth of European respondents thought that these elements were very satisfactory or satisfactory.

Europe/North American Relationship: The majority of respondents believed there is an opportunity for joint funding schemes from European and North American funding agencies (either public or private non-profit) to fund Synthetic Biology research activities. However, the majority also believed that existing infrastructures and protocols to share research materials between Europe and North America are not sufficiently efficient. In particular, some believed that differences in research culture form a barrier, for instance the North American area being more open to competition, while Europe is more focused on collaborations.

Chapter 5 presented an overview of policies in the Synthetic Biology field. There are few policies specifically designed for the sector. Thus, the chapter's discussion also included a focus on general policies in the research sector which can have an effect on Synthetic Biology.

Chapter 6 gave an overview of the funding of activities in Synthetic Biology. Descriptions of funding agencies including Federal Government agencies, venture capital funds, foundations and private companies in North America were provided, before details of public funding agencies and private companies which fund and/or provide some Synthetic Biology research in Europe were provided.

In **Chapter 7**, the Synbiology projects dissemination activities were detailed, including the Project Brochure, Project Website, Synthetic Biology Research Survey Workshop, Synthetic Biology Research Seminar and Project Results Brochure.

ANNEXES

This Final Report includes the following four annexes:

Annex 1: Project Brochure (D1)

Annex 2: Project Fact Sheet (D5)

Annex 3: Project Results Brochure

Annex 4: iGEM and SyntheticBiology 2.0 and 3.0

ANNEX 1: D1: PROJECT BROCHURE


The dissemination and promotion activities are designed to exploit the project results within Europe and North America.
Project Website
Project Brochure
Database of Synthetic Biology Research
International Workshop
International Seminar
Report on Analysis of Synthetic Biology Sector
PROJECT DISSEMINATION
PARTICIPANTS:
WWW.SPI.PT/SYNBIOLOGY
SYNBIOLOGY
An analysis of Synthetic Biology Research in Europe and North America

STRATEGIC OBJECTIVES:

Synthetic biology is an emerging scientific discipline, but it is unclear exactly what research in this area is taking place in Europe and North America.

SYNBIOLOGY is supported by the European Commission. It aims to provide the 'big picture' of synthetic biology, and show how this emerging science can be fostered, encouraged and strengthened. The project will identify:

- What synthetic biology research is being performed
- Which are the main actors - organizations and individuals - in the sector
- How is research information disseminated
- What funding and support services are available

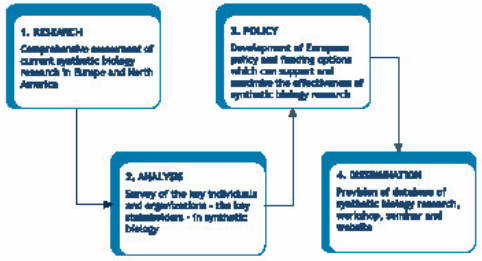
By surveying key stakeholders in Europe and North America, the project will assess the main drivers and barriers for effective research and for developing the discipline of synthetic biology further.

Findings will be communicated to European policymakers so they can consider how to build Europe's strengths in the field. This will be done through providing a workshop and seminar, a synthetic biology research database, a project website and a series of other dissemination activities.

BENEFITS INCLUDE:

- Identification of synthetic biology research activities in Europe and North America
- Analysis of methods to improve synthetic biology funding
- Strengthening of partnerships between European and North American synthetic biology communities
- Inputs into further development of European policy for supporting synthetic biology research

METHODOLOGY:



INPUTS AND OUTPUTS:

The project inputs are drawn from scientific and technical expertise, including many relevant efforts from research projects sponsored by the European Union. The project consortium is made up of two research and innovation consultancies, a synthetic biology company and a US university.

The project outputs will identify and assess synthetic biology research and funding opportunities. They will provide a far-reaching impact on the future of synthetic biology in Europe. The project will highlight various factors. These factors include mechanisms that impact the level and nature of research in this area and the short and long-term commercial possibilities.

The project outputs will give national and European policy-makers essential information from which they can develop plans to establish synthetic biology research in support of technological progress in the 21st century.

ANNEX 2: D5: PROJECT FACT SHEET

NEST Pathfinder

SYNBIOLOGY

SYNTHETIC BIOLOGY

The project aims to provide the 'big picture' of synthetic biology in Europe and North America. © Thomas Jones

A European perspective on synthetic biology

Synthetic biology is an emerging scientific discipline, but it is unclear exactly what research in this area is taking place in Europe. SYNBIOLOGY aims to identify the organisations where synthetic biology research is, or could be, taking place. By surveying key stakeholders in Europe and North America the project intends to discover the main drivers and barriers for effective research and for developing this discipline further. Findings will be communicated to national and European policy-makers so they can consider how to build Europe's strengths in this field.

Engineers and designers often take inspiration from nature. Whether it is self-cleaning paint, Velcro or morphing aeroplane wings, many technological advances are based on designs that have existed in the natural world for millions of years. Recognising nature's incredible engineering and problem-solving skills, scientists often integrate aspects of biology into their research projects. Indeed, entire scientific disciplines are emerging that merge biology with previously unrelated fields such as electronics.

Synthetic biology is one of these new disciplines, using biological research in a wide range of technology and engineering applications. The idea is to design and produce simple biological components that can be 'plugged together' like electronic components. These constructed, artificial systems do not exist in the natural world; they are designed for specific functions ranging from protein engineering to computation.

Looking for details

Only a small number of research centres, mainly outside Europe, explicitly use the term 'synthetic biology' to describe their work. Yet Europe has a wealth of expertise in molecular biology, genetics, mathematics, and other disciplines which form the foundations for synthetic biology research.

In fact, some synthetic biology is certainly taking place in Europe, scattered between a host of different organisations. This fragmentation means that the overall state of research and its future potential across Europe is unclear. The SYNBIOLOGY project will therefore conduct the first ever survey of this new discipline. It aims to qualify the key attributes of synthetic biology research in Europe and North America, and identify differences across European countries, the USA and Canada. From this analysis it should be possible to highlight various factors, such as funding mechanisms, that could impact the level and nature of research in this area and its short and long-term commercial possibilities.

The project consortium is made up of two research and innovation consultancies, a synthetic biology company and a US university. Together they will first attempt to identify all the existing and potential actors in synthetic biology research (e.g. universities, research institutes, research companies and production companies) along with their geographic distribution. A selection

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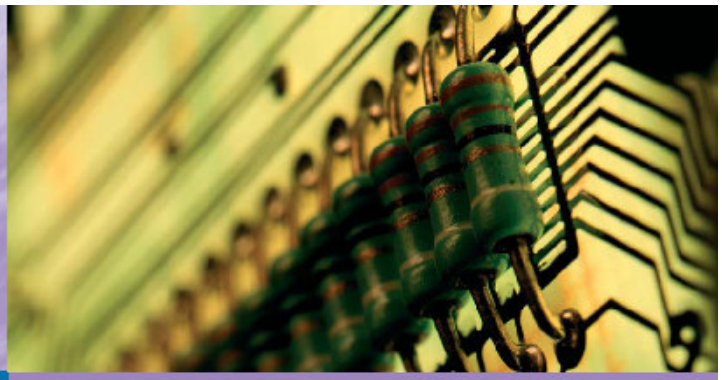

Entire scientific disciplines are emerging that merge biology with previously unrelated fields such as electronics.

SYNBIOLOGY

AT A GLANCE

Official title
An Analysis of Synthetic Biology Research in Europe and North America

Coordinator
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Partners
- Greece: Centre for Economic Research and Environmental Strategy
- Germany: ATG:Biosynthetics
- USA: University of Maryland Baltimore County

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Duration
15 months

Project Cost
€ 226 200

EU Funding
€ 226 200

Project reference
Contract No 15357 (NEST)

Web: http://www.cordis.lu/nest

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of key stakeholders – leading individuals representing the synthetic biology research community, industry and government – will then be contacted for more details on the nature of the research, how it is disseminated, and what funding and support services are currently available.

Building a framework

SYNBIOLOGY is a support action complementing the more technology-focused projects within the NEST Synthetic Biology PATHFINDER initiative. As such, it aims to provide the 'big picture' of synthetic biology in Europe and North America, and show how this emerging science can be fostered, encouraged and strengthened. At the national level, for example, key stakeholders will act as the primary 'disseminators' within their respective countries. They are ideally positioned to communicate the findings of SYNBIOLOGY to the national policy-makers who may have influence over the future of their country's synthetic biology research.

> Synthetic biology aims to design and produce simple biological components that can be 'plugged together' like electronic components.

The results of this project will also be used by the Commission. The project will highlight how European policy and funding options could also support the development and maximise the effectiveness of this research domain.

Questionnaires and surveys do not look like the kind of ground-breaking, high-risk science one usually associates with NEST projects. Yet SYNBIOLOGY has the potential to produce a far-reaching impact on the future of synthetic biology in Europe. Its insights will give national and European policy-makers essential information from which they can base their plans to build up synthetic biology research to support technological progress in the 21st century.

SIXTH FRAMEWORK PROGRAMME

ANNEX 3: PROJECT RESULTS BROCHURE


The dissemination and promotion activities were designed to exploit the project results within Europe and North America.
Project Website
Project Brochure
Project Questionnaire
Database of Synthetic Biology Research
International Workshop
International Seminar
Report on Analysis of Synthetic Biology Sector
PROJECT DISSEMINATION
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SYNBIOLOGY
AN ANALYSIS OF SYNTHETIC BIOLOGY RESEARCH IN EUROPE AND NORTH AMERICA
WWW.SPI.PT/SYNBIOLOGY
Project Reference
Contract: 15357 (NEST)
European Commission Framework Programme
NEST - New and Emerging Science and Technology

WEBSITE:

The Synbiology website is found at www.spi.pt/synbiology

The website is the central source of information on the project, providing links to:

- Project brochures
- Project reports
- Project questionnaire
- Meeting presentations
- Project database
- Other Synthetic Biology organizations and activities

PROJECT DATABASE:

The Project Database includes over 1,000 papers connected to the field of Synthetic Biology published since 1990. The papers are organised into four main categories - in vivo engineering, in vitro engineering, theoretical research and enabling infrastructure. These categories are then further broken down into detailed components.

The abstracts of the papers are fully searchable, and a link to the homepage of each of the authors in the Database is provided.

MEETINGS:

The project outputs were discussed and disseminated in two meetings, both held at the European Commission in Brussels

- International Workshop – held on 25th January 2006 - in which discussion with the US and European attendants focused on defining Synthetic Biology activities and identifying the Key Stakeholders

- International Seminar – held on 30th May 2006 - in which the project results were introduced and discussed

REPORTS:

The project results were provided in four reports:

Synthetic Biology Research - Literature & Statistical Review: A comprehensive discussion of which activities constitute Synthetic Biology research and the current level of understanding of this research.

Synthetic Biology Research Assessment: An overview of Synthetic Biology research on a country and regional basis.

Europe / North America Comparative Assessment: A comparative analysis of Synthetic Biology research environments, including discussion of funding agencies and the results of the project questionnaire.

Final Report on Analysis of Synthetic Biology Sector: The final report, bringing all the project's work together.

ANNEX 4: IGEM AND SYNTHETICBIOLOGY 2.0 AND 3.0

iGEM - The international Genetically Engineered Machine competition[28]

iGEM addresses the question: Can simple biological systems be built from standard, interchangeable parts and operated in living cells? Or is biology simply too complicated to be engineered in this way?

The only way to answer this is to actually try to engineer biological devices.

The iGEM competition facilitates this by providing a library of standardized parts (called parts BioBricks) to students, and asking them to design and build genetic machines with them. Students are welcome to make their own BioBricks as well.

Information about BioBricks, and a toolkit to make and manipulate them, is provided by the Registry of Standard Biological Parts (the Registry). This is a core resource for the iGEM program, and one that has been evolving rapidly to meet the needs of the program.

Beyond trying to answer the question above, iGEM's broader goals include:

- To enable the systematic engineering of biology
- To promote the open and transparent development of tools for engineering biology
- To help construct a society that can productively apply biological technology.

In its three years, iGEM teams have managed to partially or completely build a variety of systems, from biosensors to biological photographic film. Thus it seems that engineering biology is possible.

History of iGEM:

2003: During the 2003 Independent Activity Periods (IAP), students designed biological oscillators coupled to fluorescent reporters. These genetic blinkers were intended to improve on Elowitz's Repressilator. One team coupled two oscillators to even out the oscillations. Another used cell-cell signaling to coordinate the oscillators in a colony.

2004: During MIT's IAP, MIT-based teams designed genetic systems to create cellular patterns varying from bull's-eyes to polka dots, and even dynamic designs where cells would swim together. From these designs, many standard biological parts (BioBricks) were designed and synthesized.

[28] The information on iGEM is sourced from http://parts2.mit.edu/wiki/index.php/Main_Page.

2004 also marked the first true Synthetic Biology Competition. Teams from five schools competed to build cellular state machines and counters. The teams came together for a jamboree in early November to compare their results. The most graphic project was "photographic biofilm" that could capture an image (now called coliroid film).

2005: In the summer of 2005, the iGEM competition became an international event. A record 13 teams worked on projects involving chemotaxis regulation systems, cell-cell genetic communications systems, cellular/biological wires, thermometers, biological sketch pads (drawing systems), cellular relay races, a digital counter, and more.

iGEM Ambassador Program:

iGEM ambassadors were added to the competition in 2006. They are charged with helping each team, but in particular teams new to the program, have a successful experience. While team needs vary greatly, ambassadors generally maintain communications, visit, and provide tutorials or assistance as required. Behind the scenes, they help support both the *Parts Registry* and the *iGEM wiki*.

The following are the official iGEM 2006 ambassadors and their general regional assignments:

- James Brown - Northeastern United States, Cambridge
- Andrew Hessel - Canada, US Midwest and South
- Melissa Li - Western and Southeastern United States
- Jonas Nart - European schools
- Robin Künzler - European schools
- Tamara Ulrich - European schools
- Reshma Shetty - Asia
- Meagan Lizarazo - Latin America.

SyntheticBiology 2.0 and 3.0[29]

The Second International Conference on Synthetic Biology (SB2.0) took place on 20th-22nd May 2006, at the University of California, Berkeley. The conference brought together a diverse group of participants from a variety of disciplines, including some of the world's leaders in biological engineering, biochemistry, quantitative biology, biophysics, molecular and cellular biology, bioethics, policy and governance, and the biotech industry. A collaborative effort of Berkeley Lab, MIT, UC Berkeley, and UCSF, the conference sought to promote and guide the further, constructive development of the field.

SB2.0 began with two days of plenary talks and discussions focused on five research areas: energy, chemistry, health, materials, and foundational technologies. The third day of the conference focused on four key societal issues associated with synthetic biology: safety and security, public understanding and perception, ownership, and community organization.

The SB2.0 community is developing a written statement describing some principles for advancing this new field in a safe and effective way, based on the third day of discussions and input from conferees.

The Third International Conference on Synthetic Biology (SB3.0) will take place on 24th-27th June 2007 at the ETH Zurich in Switzerland. The conference will capitalize on the EU's SYNBIOCOMM program, which provides support for synthetic biology through research proposals from the European Commission NEST.

The goals of SB3.0 are:

- To have an enthusiastic and inspiring scientific meeting
- To make the meeting attractive in particular for young reasearchers (i.e., travel grants)
- To strengthen the development of Synthetic Biology in Europe
- To present a forum for the European Synthetic Biology research projects
- To present a platform for communicating and discussing the societal issues accompanying Synthetic Biology (IPR, ethics, public perception).

[29] The information on SyntheticBiology 2.0 and 3.0 is sourced from http://pbd.lbl.gov/sbconf/