


**Applications in SynBio: Present and Future**




**Industrial Association for Synthetic Biology IASB**

Welcome to the International Association of Synthetic Biology

Activities > Press Area >

ICPS = International Consortium for Polynucleotide Synthesis  
 IASB = International Association Synthetic Biology  
 SBIA = Synthetic Biology International Association  
 IGSC = International Gene Synthesis Consortium  
 ICLS = International Council for the Life Sciences

**Applications in SynBio: Present and Future**





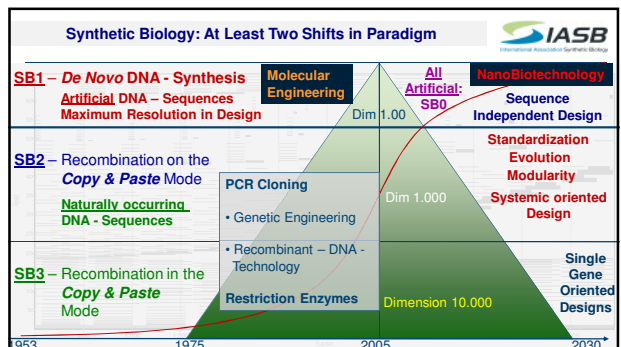
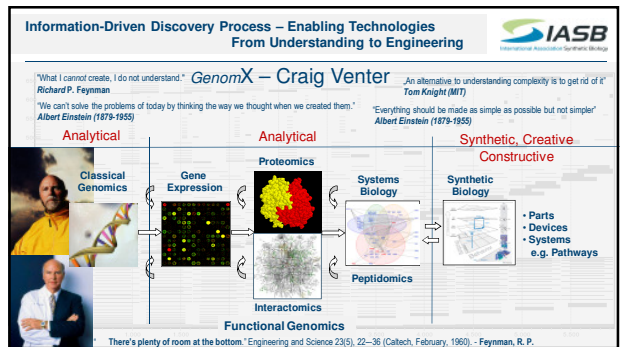
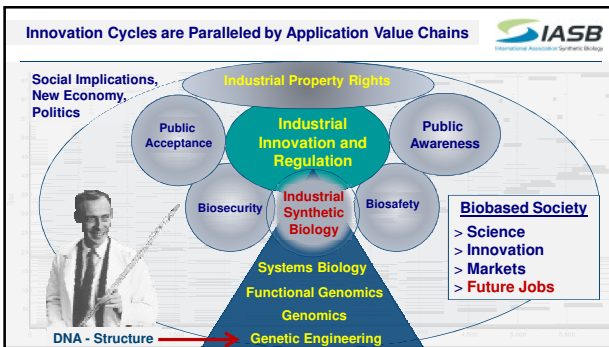
"The field has had its hype phase. Now it needs to deliver!"  
 Martin Fussenegger in Kwok R. (2010) Five hard truths for Synthetic Biology, Nature 463:288ff.

RTG: biosynthetics

www.SB.info

Impact of Synthetic Biology on Integrative Synthetic Biotechnology Projects

Synthetic Biology in Pharma Conference  
 Cambridge, UK  
 March 30-31, 2010

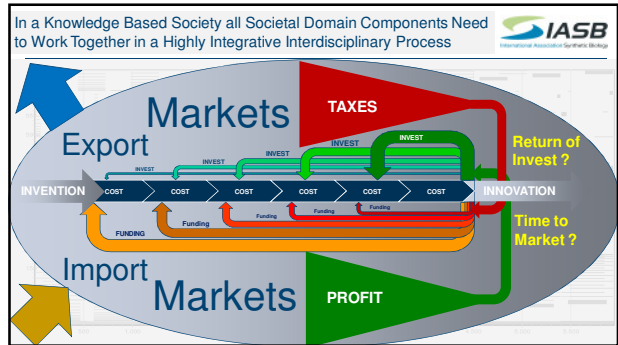




**The Dilemma Between „Science and Market“**

Like all other technology developments - **Synthetic Biology** - is in the tension field of a **dilemma** where on the one hand scientists like to show what is possible and to explore the **borders of knowledge and technology** - but on the other side the markets who always asks:

**Who needs it?** - Is there any benefit for the customers? Is there actually a market?  
**What are the cost?** What are the **return of invest** time-lines and which **profit** can be achieved.

**Synthetic Biology 1:** - has clearly not arrived on the **B2B** nor the **B2C** consumer market.  
**Synthetic Biology 2:** - secondary gene products - small molecules has entered the market  
**Synthetic Biology 3:** - primary gene products (proteins like enzymes, cytokines, biopharmaceuticals etc.) -heterologous expression



**Bottom UP: Idealistic Technology Driven Visionary Phase**

But the real challenge will start when we enter the **synthetic biology phase** of research....This would be a field with...hardly any limitations to building...“synthetic” organisms, like a “new better mouse.” — Waclaw Szybalski, “*In Vivo* and *In Vitro* Initiation of Transcription,” 1974 *versus*

“It can take months if not a year or years to get the network to behave. You have to do an awful lot of tweaking to get your network to work the way you want.”  
 James J. Collins

**Top Down: Realistic Market Driven Phase – Who needs it?**  
 .....means Hard Work of Realizing Products

Sequence Independent Rational Design Principles for Functional Elements

**Principles of Hierarchy in Design:**

- Parts (Module)
- Devices (Function)
- Systems (Application)

**Silicon IT – Technologies** versus **Carbon – IT**  
 → Integrated Carbon Technologies  
 MAC – IT and MAB – IT  
 Integrating Molecular Function of magE – IT

- Abstraction:** Circuitry design – models – simulation – improvement
- Hierarchy:** Different levels of Design
- Modularity:** Parts work together for functional fit in device function
- Standardization:** Documentation of high quality to insure it works
- Decoupling:** of Gene or Pathway Design and DNA-Synthesis → Software vs. Hardware
- Evolution:** Gene Diversification, Shuffling, Functional Optimizations, Selection of Variants
- Orthogonality:** Systems independency no cross-talk
- Reproducibility:** Robustness of function in a defined environment
- Sequence Independency:** Molecular Function Provided
- magE:** Minimal artificial elements Catalysts MACs and Binders MABs as
- From magE-Elements to Minimal Artificial Genomes**
- Programming of Minimal Genetical Cell Systems (MGCS)**

**Sources:**  
 Endy D. (2005) Foundations for engineering biology. Nature Review, 438:449-453  
 Goler et al. (2008) Genetic design: rising above the Sequence. Trends Biotechnol., 26:538-44

**Are There Principaly New Future Synthetic Biology Markets ?**

The Potential Biotech - Markets are The Same for Synthetic Biology :

- Science Market** - heterogeneous - Reagents, Devices, Enabling Technology
- RED** – Biotech – Medical/ Pharma----- Science and R&D Market
- WHITE** – Biotech – Industrial Market-----Science and R&D Market
- GREEN** – Biotech – Agro-Industrial Market-----Science and R&D Market
- BLUE** – Biotech – Nutrition, Pharma, Materials, Enzymes ...

Club of Rome Postulated the Age of Qualitative Growth !

**Rational - From Parts → To Devices → To Systems – Versus Evolutionary Design**

**FFF – Form Follows Function Bauhaus**

**CAD-based Evolutionary Design Optimization with CATIA V5**  
 Oliver König, Marc Wintermantel  
 EVEN - Evolutionary Engineering AG, Zurich, Switzerland

Basic Antipodes of SB – Design of Requirement Specifications

**Flow of Matter in the Metabolism: Directions of Impact**

- Max. Flow – Production** – R<sub>min</sub>. requirement of optimal stoichiometry and
  - low or no complexity in regulation
  - high production yields, high efficiency, high throughput
  - comparable to electrical **strong current** for powering big machines
- Max. Regulation e.g. for Dosage of Drug Delivery**
  - highly regulated** with low throughput – oscillating schemes
  - therapeutics with a high **efficiency on low dose (nM)** R<sub>max</sub> – high regulation
  - comparable with electronics
- Combination of both 1. and 2. means **Max. Regulation of Max. Production**

Regulation of Systems: Genetic Circuits II

**Artificially regulated Genetic Circuits II**

A tunable synthetic mammalian oscillator, Tigges et al. *Nature*, 457, 309-312.  
 A synthetic mammalian electro-genetic transcription circuit, Weber et al. *Nucleic Acids Research*, 37(4) e33.  
<http://oscillatorblog.com/>

Artificial Biosynthetic Pathways – Drugs, bioPharmaceuticals, bioPlastics, Building Blocks, Fine Chemicals...

Synthetic Biology is the **Logic Continuation of Synthetic Chemistry by Means of Biology** - Jay Keasling -

- Self Replicating Systems
- Information Processing
- Compartmentation
- Systems Behavior
- Modularity
- Orthogonality
- Cellular Differentiation

**High Throughput – Specific Molecules**

Design of Requirement Specifications

**Structure and Functional Relationships – Functional Nanoarchitecture**

- Angström to low Nanostructures - Catalysis– Production** – R<sub>min</sub>. requirement of optimal stoichiometry and
  - Turnover (Kinetics)
  - Specificity (Regio-selectivity,
  - Stability (physical: heat, pressure etc.; chemical: solvents etc., biological)
- DNA-Nanostructuring or Microcompartments - Containments e.g. VLPs e.g. for Dosage of Drug Delivery**
  - Self assembly properties
  - Stability (physical: heat, pressure etc.; chemical: solvents etc., biological)
  - Ability to functionalize
- Combination of both 1. and 2. means

Regulation of Systems: Genetic Circuits I

**Artificially regulated Genetic Circuits I**

Tal Danino, Octavio Mondrago n-Palomino, Lev Tsimring & Jeff Hasty (2010) A synchronized quorum of genetic clocks *nature* 463: 326-330

"ssDNA Nanostructuring of Surfaces" – Paul W.K. Rothemund

Periodic structures can be formed. Lattice spacings approach photonic length scales.  
 Few large lattices are formed.

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**DNA Nanotechnology in Ned Seeman's Laboratory**

© Ken Edward Bourafax

**Cleantech Quality Standards in – White Biotech**  
**What makes Synthetic Biology better?**

Classical bioProduction Technologies	Synthetic Biotechnology Production Technologies
• waste of energy	• high energy efficiency
• huge plants	• small and completely new types of plants
• high temperatures	• moderate to low temperatures
• high air pressures - reduced safety	• normal air pressure
• toxic solvents	• solvent water
• reduced production flexibility	• high flexibility in production
• reduced working place safety	• high safety levels achievable
• only economically in huge volumes	• economical production even in smaller volumes

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**Club of Rome Postulated the Age of Qualitative Growth !**

**Plant Synthetic Biology – Discredited by Ideologists**

**Dr. Jim Haseloff**  
 Department of Plant Sciences  
 University of Cambridge  
 Downing Street  
 Cambridge CB2 3EA

**New Standards in Red Biotech – Will future bioProduction Provide Active Pharmaceutical Ingredients and its AutoDosage?**

Classical Pharma Industry based Medical Supply	Synthetic Biology Based Medical Supply
• Small molecules by <b>chemical synthesis</b>	• Sustainably <b>bio-produced small molecules</b>
• Application <b>extracorporeal</b>	• Therapeutic proteins, mAbs, BioLogics bioPharmaceuticals
• invasive therapies (Insuline)	• Application <b>intracorporeal</b>
• oral application multiple	• e.g. sub-cutan
• rectal application multiple	• intravenous single application
• intravenous multiple	• <b>non-invasive therapies – artificial organs</b>
• Block busters – relative unspecificity	• Therapeutic genetic systems
• Many unwanted side effects	• Individualized therapies
• Multiple indications – no specificity	• Low to no adverse effects
• Permanent therapy – <b>no real curing</b>	• Highest efficacy – <b>REAL curing</b>

**Club of Rome Postulated the Age of Qualitative Growth !**

**New Strategies in Health Care e.g. Immunotherapies**

"The future of humanity and microbes will likely unfold as episodes of a suspense thriller that could be titled 'Our Wits Versus Their Genes.'"  
 — Dr. Joshua Lederberg, 1958 Nobel laureate

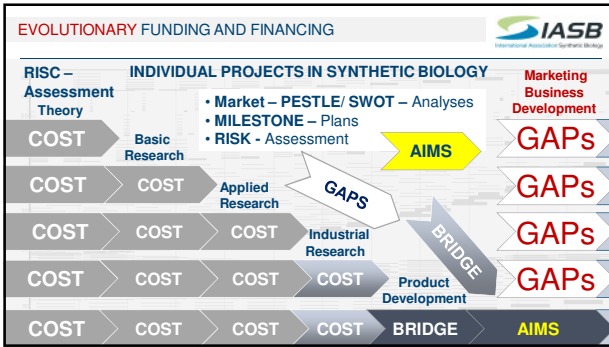
David Baltimore  
 Synthetic Biology 2  
 21 May 2006

**Integrative Synthetic Biotech Projects - High Impact on the Development New Markets on the basis of New Technologies for Future Economy**

**P(t) (Power) = V(Potential) x I(Current)**

**General Technology Transfer Value Chain**

Theory	Basic Research	Applied Research	Industrial Research	Product Development	Marketing Business Development
COST	COST	COST	COST	COST	COST
Universities	Universities	AiF/ ProInno			
Max Planck Organization		Fraunhofer Organization			
					<b>GAPs</b>
					<b>NO TRANSLATIONAL MONEY ???</b>
					BMBF – Federal Ministry of Education and Research



## ***“What can the EU do to promote mental health of older people”***

**Summary of the presentation by Anne-Sophie Parent, Director, AGE-the European Older People’s Platform, 13 June 2008**

Various factors make older people more vulnerable to mental health problems:

- The physiological ageing process which results in an increasing risk of dementia (increased risk both for the ageing individual and partner/carer)
- Adverse effect of overmedication and polypharmacy among the elderly
- Drug-alcohol interaction
- Increasing dependency which results in an increased risk of elder abuse
- The isolation and social exclusion faced by an increasing number of older people today due to modern lifestyles
- Abrupt change from employment to long term unemployment of (early)-retirement (losing sense of purpose in life)
- Lack of professional training in geriatric and gerontology
- Lack of training and support for informal carers
- The gender dimension: very older women are at higher risk

AGE welcomes the EU Pact on Mental Health and commits itself to support all actions implemented to promote better mental health for all.

As part of the Pact on Mental Health, Member States should agree to commit themselves to increase the number of Healthy Life Years by one year in 2013. This would encourage them to adopt a holistic approach to healthy ageing, including the promotion of good mental health in old age.

If the EU is to “foster good health in an ageing Europe” in the period 2008-2013, it should address each of these factors that affect older people’s mental health. In addition to the recommendations listed in the policy brief, EU action is needed in the following fields and the Pact should include to use existing EU instruments to:

### **FP7:**

- Research on old age dementia cause, treatment and prevention. Research should also cover the social and financial impact of old age dementia. (FP 7)
- Research on medication use for the elderly: EMEA should set up a “Geriatric Committee” similar to the “Pediatric Committee” to analyse effect of medication on the elderly, including polypharmacy and overmedication, and share information across the EU with healthcare professionals.

- Raise awareness of care professionals and older citizens/informal carers of potential interaction between medication and alcohol (a problem often overlooked in older people)

### **OMC Social Protection/Social Inclusion**

- Social exclusion of the elderly both in urban and rural/remote areas and examples of good practice across the EU
- EU Strategy to fight against elder abuse: the EU should develop quality guidelines for long term care to help prevent elder abuse (OMC on Social Protection and Social Inclusion)

### **ESF and Lisbon Strategy:**

- Promote active ageing and a more positive of ageing workers;
- Promote health and safety at work including stress reduction;
- Promote more flexible retirement and early preparation for retirement (ESF and Lisbon Strategy)

### **Health Strategy and Grundvig programme**

- Develop geriatric/gerontology training at EU level as exist for paediatrics

This paper was produced for a meeting organized by Health & Consumers DG and represents the views of its author on the subject. These views have not been adopted or in any way approved by the Commission and should not be relied upon as a statement of the Commission's or Health & Consumers DG's views. The European Commission does not guarantee the accuracy of the data included in this paper, nor does it accept responsibility for any use made thereof.