20th Meeting of the EC-US Task Force on Biotechnology Research

Follow up on Environmental applications of Synthetic Biology & opportunities for EU-US partnership in this field

Víctor de Lorenzo (CNB-CSIC)
The great input of SB into Env Biotech (i)

Massive genomic refactoring

Feedstock

A → Availability → A → Misrouting → D → Toxicity → Z → Biomass

Z → Product

CO₂ + H₂O
Two systems are orthogonal to each other if they do not influence each other.
Overcoming resistance to implantation of new activities in a pre-existing network
Proposition

The criterion for identifying new scenarios associated to the application of Synthetic Biosystems is not the way the agent is engineered, but the divide between familiar and non-familiar Biology.
Altogether natural

1. Natural isolates
2. Random mutants (NG, insertion)
3. Directed mutants (deletions, alleles)
4. Transgenic variants
5. Synthetic Alleles/transgenes
6. Synthetic genomes
7. Refactored genomes
∞. Alternative genomes

From Genetic Engineering to Synthetic/Non-natural MO
Synthetic DNA fragments

Natural bacterium

Streamlined genome

Viral vectors

Genome-less cells

Plasmid & Transposon vectors

Yeast vectors

Synthetic Genomes
Vesicles/artificial cells

Streamlined genome

• Orthogonal ribosomes
• Alternative/expanded genetic codes
• Proteins with non-natural amino acids

Familiar Biology

Xeno-Nucleic acids (XNAs)

Non-familiar Biology

Alternative information-bearing molecules / genomes

Orthogonal cells

Vesicles/artificial cells

Streamlined genome

• Orthogonal ribosomes
• Alternative/expanded genetic codes
• Proteins with non-natural amino acids
The 10 questions on environmental risks borne by Engineered/synthetic/non-natural microorganisms (SEMs)

1. Can SEMs colonize and eventually takeover natural microbial communities?
2. Is there a chance that SEMs enter new niches that natural bacteria cannot?
3. Might SEMs go into a stage of uncontrolled growth?
4. What are the chances of horizontal transfer of the synthetic genes to novel recipients?
5. Is there a tradeoff between safety and biotechnological efficacy of SEMs?
6. Could traits engineered in SEMs evolve towards virulence or other deleterious behavior?
7. Are there scenarios of SEMs capable of damaging life or property?
8. What is the environmental fate of synthetic genes?
9. Are there chances of malicious misuse of SEMs
10. Should SEMs be endowed with traits to increase their safety and predictability?
The Research Challenges

• Develop tools and methods
• Avoid/manage emergence
• Uncouple growth from activity: engineering long adult life in SMO
• Coordinated population behavior
• Surmounting the complexity pyramid
• Standardization: assembly, manufacture, measurements, descriptive language
EC-US Workshop on Standards in Biotechnology:
Towards Standards in Synthetic Biology

An Exploratory Workshop of the US-EC Task Force in Biotechnology
Parador de Segovia (Segovia, Spain). June 4-6, 2010

Co-Convenors: Drew Endy (Stanford, US)
Víctor de Lorenzo (Centro Nacional de Biotecnología, Spain)
Session I  Functional composition of engineered biological parts and systems

08.30-08.50  **Steve Busby** (Univ Birmingham). Gene expression: from one promoter to one single cell to a whole population.

08.50-09.10  **Reshma Shetty** (Gingko BioWorks, Boston). Promoters, RBS and coding sequences

09.10-09.30  **Christina Smolke** (Stanford Univ). Riboswitches and other RNA elements: integration and insulation.

09.30-09.50  **Sven Panke** (ETH, Basel). Metabolic blocks for engineering catalysts à la carte

Session II  Quantification and measurement of biological functions

11.00-11.20  **Derek Wells** (Genencor, Palo Alto) Industry measurements: current practice and needs.


11.40-12.00  **Richard Kitney** (Imperial College, London). Large-scale characterization of biological parts and devices

12.00-12.20  **Drew Endy** (Stanford, BioFab, Emeryville). Design and measurements towards a first expression operating system.
Session I

Information exchange and language standards

Tom Knight (MIT, Boston). Current state of physical assembly standards.

Archeitect (SEVA) initiative

Victor de Lorenzo (CNB, Madrid). The Standard European Vector

Information encoded as synthetic circuits and commercial angles.

Ralf Wagen (Gernand, Regensburg) State of affairs in a la carte

Session II

Rappoportue x Session Chairs Working Session (leaders of each session)

Biological parts

Randy Retberg (MIT, Boston). Electronic descriptions of standard information supporting synthetic biology research.

Tim Ham (JBEI, Emeryville). Management and exchange of knowledge and circuit design.


Julie Dickerson (Ames, Iowa). Models and information management tools.

Session III

Physical composition of engineered biological systems
Session V  Constraints and bottlenecks to standardization of biological engineering  
Chaired by: Richard Kitney  
Rapporteur: Barry Canton

09.00-09.20  Antoine Danchin (Ceprodi & AMAbiotics, Paris) Molecular traffic jams and emergence of metabolic and regulatory conflicts.

09.20-09.40  Martin Fussenegger (ETH, Basel) Moving synthetic biocircuits from bacteria to animal cells

09.40-10.00  Jim Haseloff (Univ Cambridge) Forward engineering of non-natural traits in plants.

10.00-10.20  Francois Kepes (Genopole, Paris) Dealing with epigenetic phenomena in artificial genetic systems.

11.00-13.30  Session Reports and General Discussion of Outcomes (chaired by D. Endy and V. de Lorenzo)
Point
Adress SB challenges with a historical perspective:

- Learn from past controversies
- Take stock of existing info re GEMs
- Study mistakes and try better
- Do not alarm the public
- Find societal allies
Foster transatlantic collaboration

• Mostly bottom up thus far
• Follow-up standardization issues
• Inspiration from Env Biotech TF
  Mission-oriented sandpits
  Courses and Workshops
  Exchange Fellowships
• Welcome/support joint Projects
• Monitoring misuse
Centro Nacional de Biotecnología (CNB)
Consejo Superior de Investigaciones Científicas (CSIC)

THANKS!

Madrid-Cantoblanco (Spain)