CHEMBIO 18.3.2015

SYNTHETIC BIOLOGY - SYNTEETTINEN BIOLOGIA

Chair Jussi Jäntti, PhD, VTT Technical Research Centre of Finland, BTNK

9.30-9.50 What is synthetic biology?

Jussi Jäntti, PhD

VTT Technical Research Centre of Finland, BTNK

9.50-10.40 Advantages of modularity for synthetic biology - from engineering logic functions into cells to the design of new protein folds

Professor Roman Jerala, PhD

Department of Biotechnology, national Institute of Chemistry, Slovenia

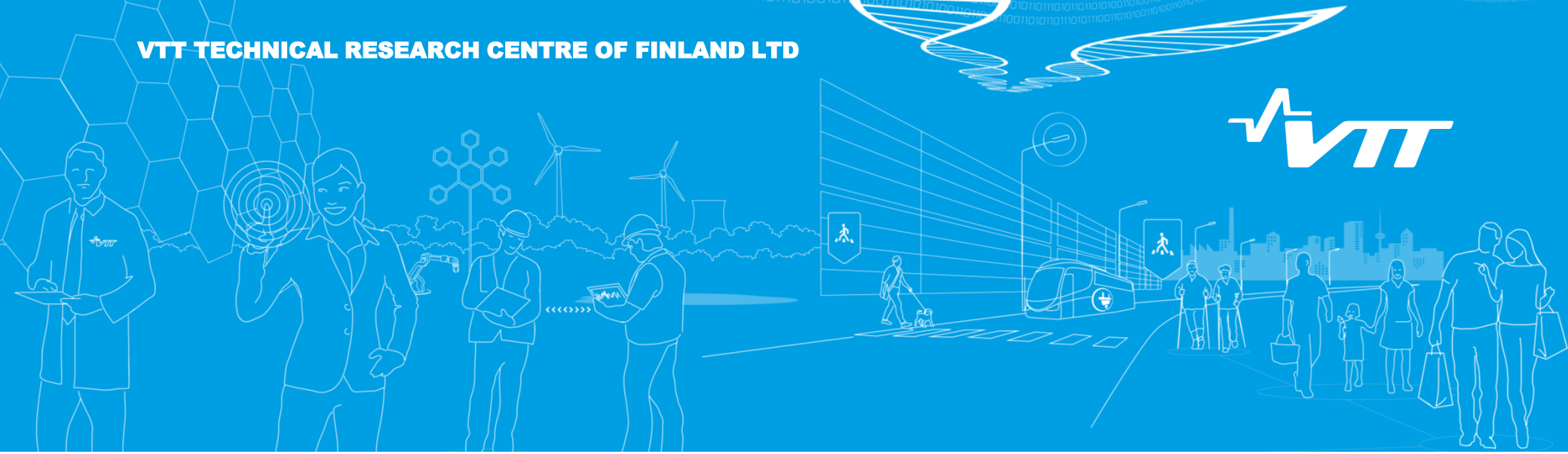
10.40-11.30 Industrial perspective on Synthetic Biology

Professor Roel Bovenberg, PhD

Honorary professor Synthetic Biology and Cell Engineering, University of Groeningen

Corporate Scientist, Biotechnology DSM, Netherlands

11.30-12.30 Lunch break - Lounastauko

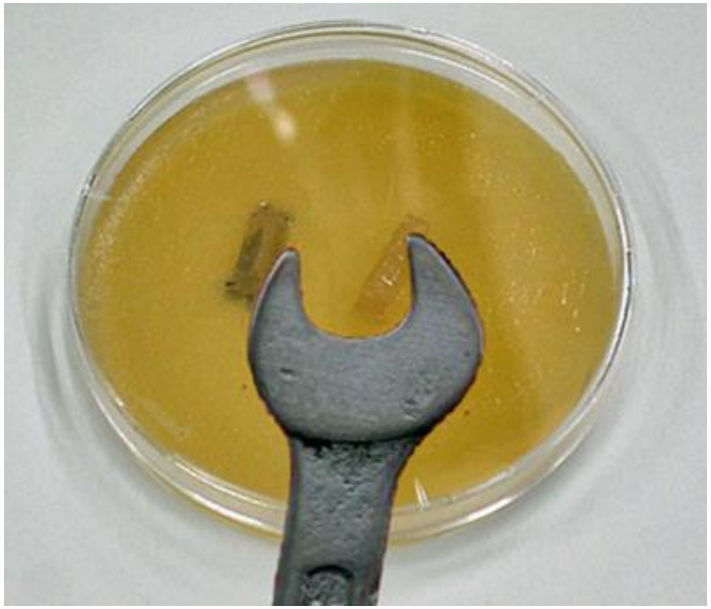


What is synthetic biology?

Jussi Jäntti

VTT Technical Research Centre of Finland Ltd
Advisory Board on Biotechnology/
Biotekniikan neuvottelukunta

Synthetic biology:



- “Synthetic biology” term coined by Stéphane Leduc (1853–1939)
    - Théorie physico-chimique de la vie et générations spontanées, 1910
    - La Biologie Synthétique, 1912

- Geneticist Waclaw Szybalski,1974
    - Control elements and control circuits, modules, new genomes

Synthetic biology definition (https://www.erasynbio.eu/):

- Based on principles elucidated from biology and engineering, the deliberate design/redesign and construction of novel biological and biologically based parts, devices and systems to perform new functions for useful purposes

A practical definition of synthetic biology

- **Making biology easier to engineer:** “Engineering of biology remains complex because we have never made it simple” (Thomas F Knight, MIT/Gingko Bioworks)

- **Applying engineering principles to biological systems:**

    - Design
    - Modelling
    - Abstraction
    - Characterization

<u>Key enabling technologies:</u> The design and synthesis of DNA

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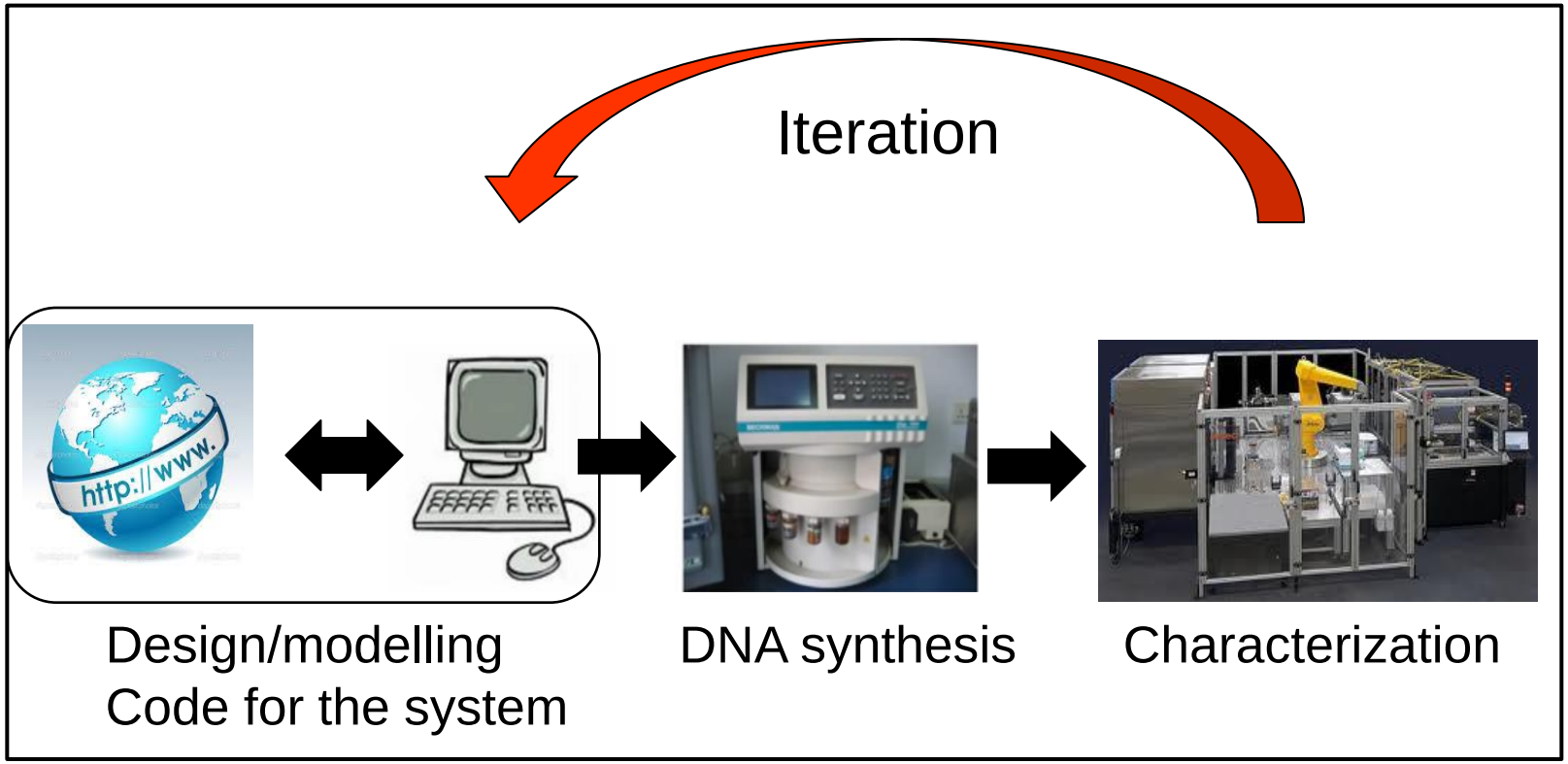
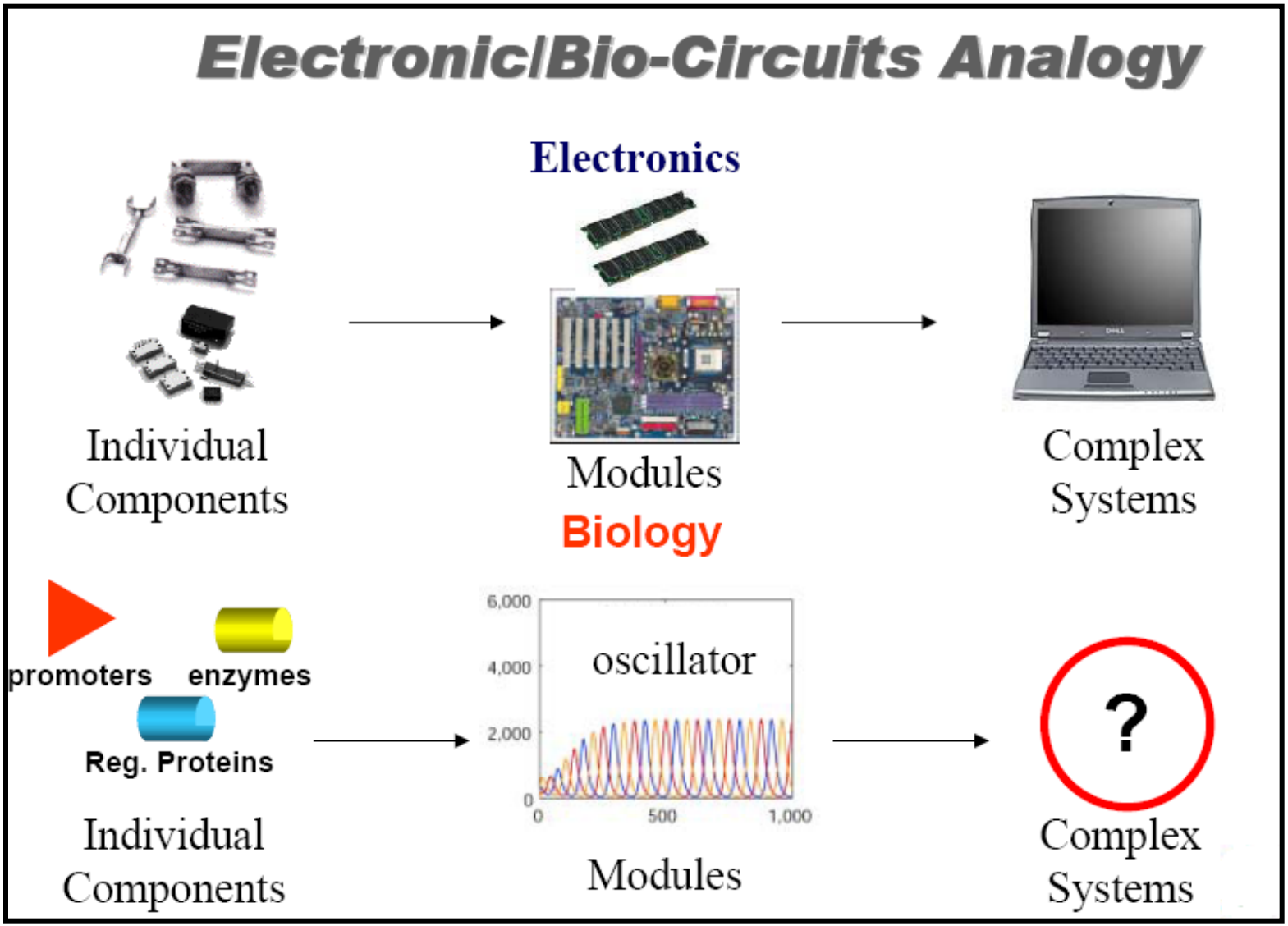


Engineering principles in biology:



http://parts.mit.edu/

Multidiciplinarity required for establishment of biological systems

Code writing & modeling
- DNA synthesis
- Mathematical modeling

Engineering of biological parts devises and systems
- Molecular machineries with desired functions
- Regulatory elements
- Interplay of molecular systems

In vitro systems
- Test beds
- Reduced complexity

→ ”Novel biology”

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- Genome assembly

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→ ”*De novo* cell”

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→ ”*De novo* cell”

What is life?

…so where is the field now….

Some examples

Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome

Daniel G. Gibson,[1] John I. Glass,[1] Carole Lartigue,[1] Vladimir N. Noskov,[1] Ray-Yuan Chuang,[1] Mikkel A. Algire,[1] Gwynedd A. Benders,[2] Michael G. Montague,[1] Li Ma,[1] Monzia M. Moodie,[1] Chuck Merryman,[1] Sanjay Vashee,[1] Radha Krishnakumar,[1] Nacyra Assad-Garcia,[1] Cynthia Andrews-Pfannkoch,[1] Evgeniya A. Denisova,[1] Lei Young,[1] Zhi-Qing Qi,[1] Thomas H. Segall-Shapiro,[1] Christopher H. Calvey,[1] Prashanth P. Parmar,[1] Clyde A. Hutchison III,[2] Hamilton O. Smith,[2] J. Craig Venter[1,2]*

We report the design, synthesis, and assembly of the 1.08–mega–base pair *Mycoplasma mycoides* JCVI-syn1.0 genome starting from digitized genome sequence information and its transplantation into a *M. capricolum* recipient cell to create new *M. mycoides* cells that are controlled only by the synthetic chromosome. The only DNA in the cells is the designed synthetic DNA sequence, including "watermark" sequences and other designed gene deletions and polymorphisms, and mutations acquired during the building process. The new cells have expected phenotypic properties and are capable of continuous self-replication.

crude *M. mycoides* or *M. capricolum* extracts, or by simply disrupting the recipient cell's restriction system (*8*).

We now have combined all of our previously established procedures and report the synthesis, assembly, cloning, and successful transplantation of the 1.08-Mbp *M. mycoides* JCVI-syn1.0 genome, to create a new cell controlled by this synthetic genome.

Synthetic genome design. Design of the *M. mycoides* JCVI-syn1.0 genome was based on the highly accurate finished genome sequences of two laboratory strains of *M. mycoides* subspecies *capri* GM12 (*8*, *9*, *11*). One was the genome donor used by Lartigue *et al.* [GenBank accession CP001621] (*10*). The other was a strain created by transplantation of a genome that had been cloned and engineered in yeast, YCpMmyc1.1-Δ*typeIIres* [GenBank accession CP001668] (*8*). This project was critically dependent on the accuracy of these sequences. Although we believe that both fin-

- Changing *Mycoplasma capricolum* cells to *M. genitalium* with JCVI syn1.0 genome (2010).
- One species changed to another with the use of a synthetic genome – "Synthetic cell" (>40 M$)
- **One single nucleotide deletion (dnaA-DNA replication) caused a severe delay for the project**

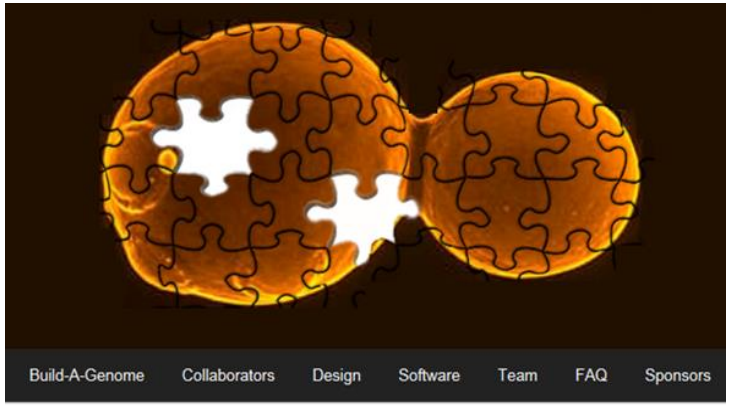
RESEARCH ARTICLES

Total Synthesis of a Functional Designer Eukaryotic Chromosome

Narayana Annaluru,[1*] Héloïse Muller,[1,2,3,4*] Leslie A. Mitchell,[2,5] Sivaprakash Ramalingam,[1] Giovanni Stracquadanio,[2,6] Sarah M. Richardson,[6] Jessica S. Dymond,[2,7] Zheng Kuang,[2] Lisa Z. Scheifele,[2,8] Eric M. Cooper,[2] Yizhi Cai,[2,9] Karen Zeller,[2] Neta Agmon,[2,5] Jeffrey S. Han,[10] Michalis Hadjithomas,[11] Jennifer Tullman,[6] Katrina Caravelli,[2,12] Kimberly Cirelli,[1,12] Zheyuan Guo,[1,13] Viktoriya London,[1,13] Apurva Yeluru,[1,13] Sindurathy Murugan,[6] Karthikeyan Kandavelou,[1,14] Nicolas Agier,[15,16] Gilles Fischer,[15,16] Kun Yang,[2,6] J. Andrew Martin,[2,6] Murat Bilgel,[13] Pavlo Bohutski,[13] Kristin M. Boulier,[12] Brian J. Capaldo,[13] Joy Chang,[13] Kristie Charoen,[13] Woo Jin Choi,[13] Peter Deng,[11] James E. DiCarlo,[13] Judy Doong,[13] Jessilyn Dunn,[13] Jason I. Feinberg,[12] Christopher Fernandez,[12] Charlotte E. Floria,[12] David Gladowski,[12] Pasha Hadidi,[13] Isabel Ishizuka,[12] Javaneh Jabbari,[12] Calvin Y. L. Lau,[13] Pablo A. Lee,[13] Sean Li,[13] Denise Lin,[12] Matthias E. Linder,[12] Jonathan Ling,[13] Jaime Liu,[13] Jonathan Liu,[13] Mariya London,[12] Henry Ma,[13] Jessica Mao,[13] Jessica E. McDade,[13] Alexandra McMillan,[12] Aaron M. Moore,[12] Won Chan Oh,[13] Yu Ouyang,[13] Ruchi Patel,[13] Marina Paul,[12] Laura C. Paulsen,[13] Judy Qiu,[13] Alex Rhee,[13] Matthew G. Rubashkin,[13] Ina Y. Soh,[12] Nathaniel E. Sotuyo,[12] Venkatesh Srinivas,[13] Allison Suarez,[13] Andy Wong,[13] Remus Wong,[13] Wei Rose Xie,[12] Yijie Xu,[13] Allen T. Yu,[12] Romain Koszul,[3,4] Joel S. Bader,[2,6] Jef D. Boeke,[2,11,5]† Srinivasan Chandrasegaran[1]†

Synthetic Yeast 2.0

Building the world's first synthetic eukaryotic genome together



http://syntheticyeast.org/sc2-0/

Science 2014 Apr 4;344(6179):55-8

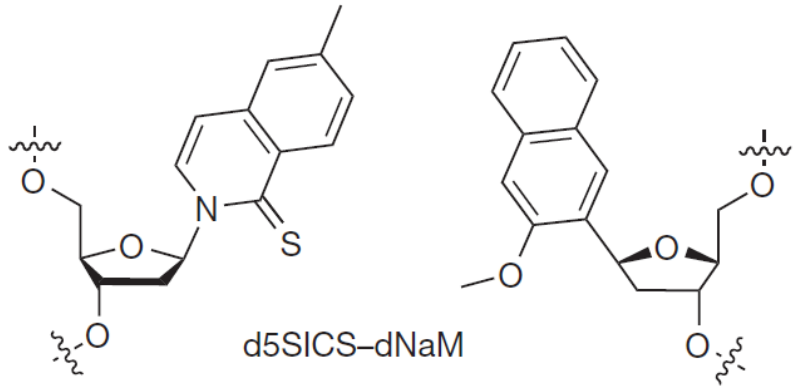
LETTER

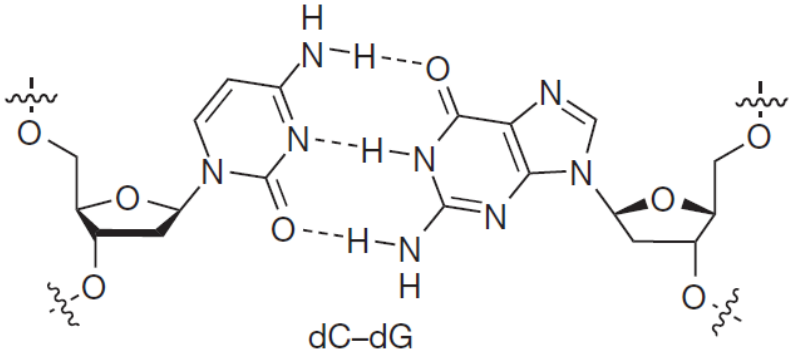
Nature. 2014 May 15
doi:10.1038/nature13314

A semi-synthetic organism with an expanded genetic alphabet

Denis A. Malyshev[1], Kirandeep Dhami[1], Thomas Lavergne[1], Tingjian Chen[1], Nan Dai[2], Jeremy M. Foster[2], Ivan R. Corrêa Jr[2] & Floyd E. Romesberg[1]

- Hydrophobic nucleobases d5SICS and dNaM
- Pairing mediated by hydrophobic interactions
- Only one of each molecule was incorporated into an extrachromosomal DNA
- The novel nucleotides were not recognized as lesions by the cellular DNA repair pathway
- The unnatural-base-pair-containing DNA is replicated, without *E. coli* cell growth being significantly affected





LETTER

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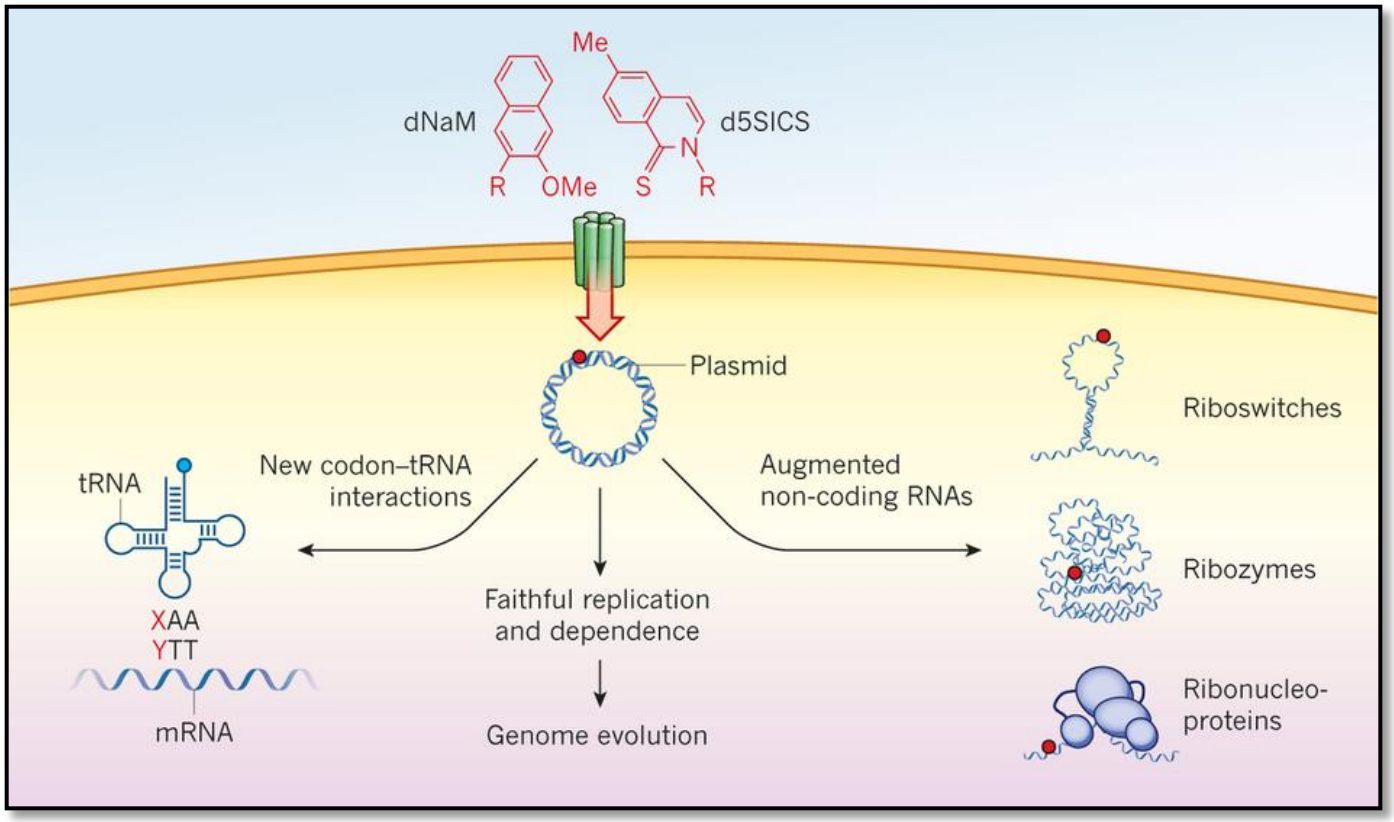


Synthetic biology: New letters for life's alphabet
Thyer & Ellefson
Nature 509, 15 May 2014

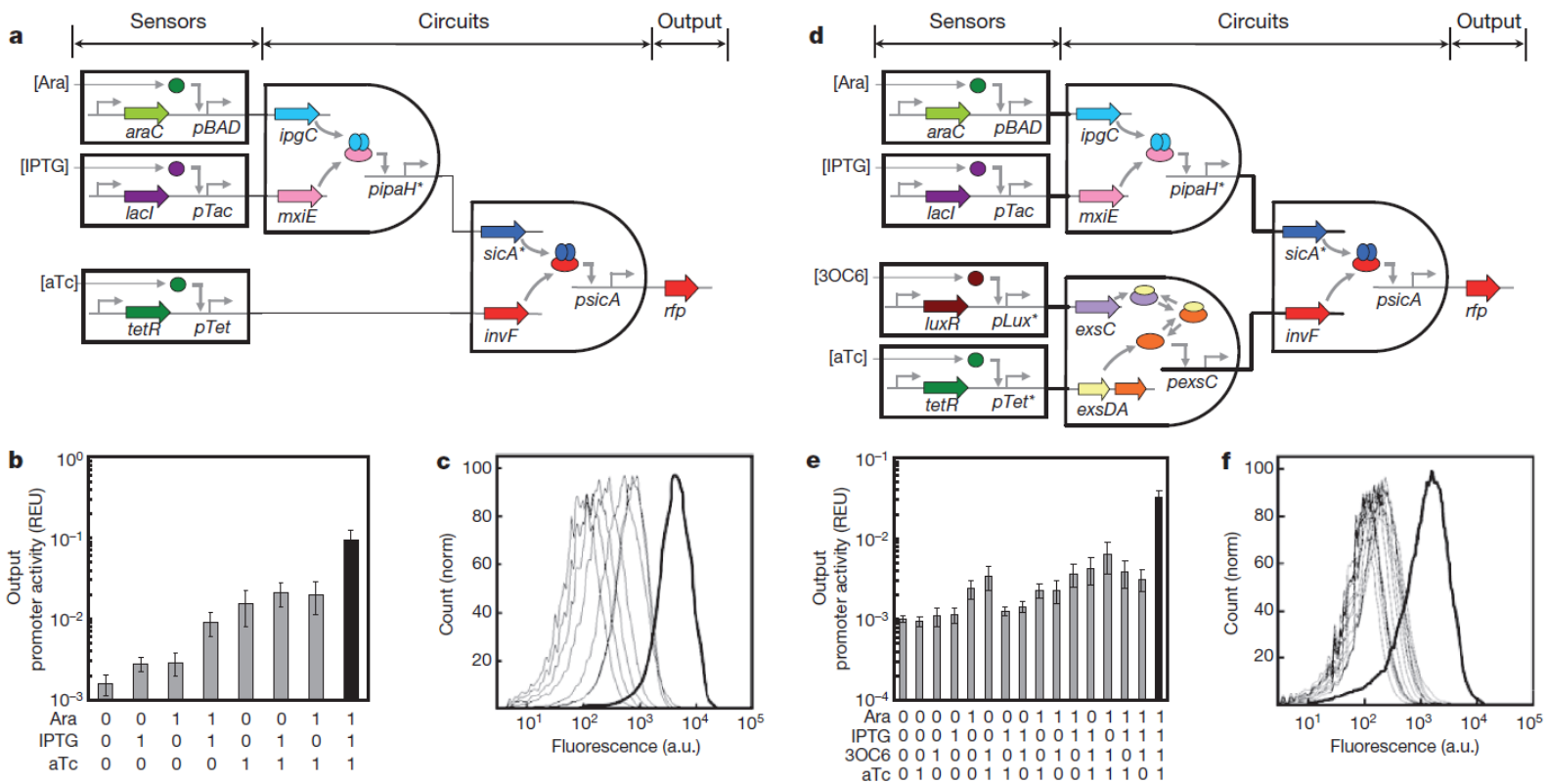
LETTER

Nature. 2012 491:249-53

doi:10.1038/nature11516

Genetic programs constructed from layered logic gates in single cells

Tae Seok Moon[1]†, Chunbo Lou[1], Alvin Tamsir[2], Brynne C. Stanton[1] & Christopher A. Voigt[1]



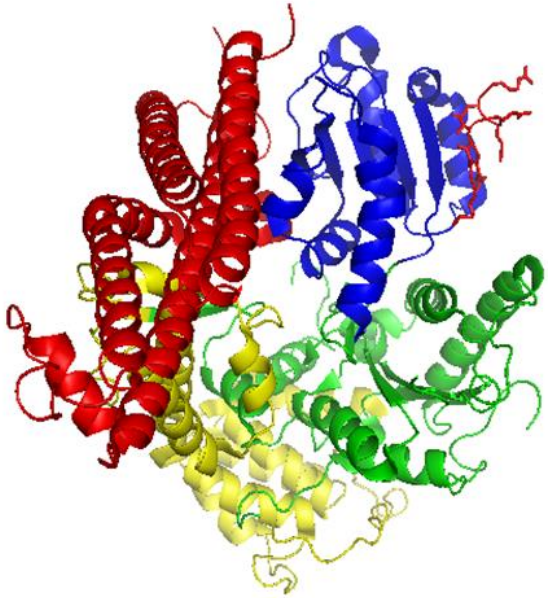
Challenges in Synthetic biology

1) Methodological development at an relatively early stage
   - Currently, design and establishment of a biological system is a major research project, not just a design and engineering task.

2) Evolution/stability of the established systems

3) The ownership and usability of established biological parts
   - Establishment of biological standards

4) Biosafety and ethics



Current and future application areas of Synthetic biology

1) Industrial biotechnology and bioenergy

- Biotechnological production of chemicals, fuels and pharmaceuticals
- Conversion of light energy to a storable form

2) Medical

- Novel types of biology inspired materials (e.g. for regenerative medicine)
- New antimicrobials
- Diagnostics in animal and human health

3**) Environmental**

- Waste water treatment
- Aggriculture: sensing and remediation

4**) Novel bioengineering technologies**

- New biological functions
- New research tools

https://www.erasynbio.eu/

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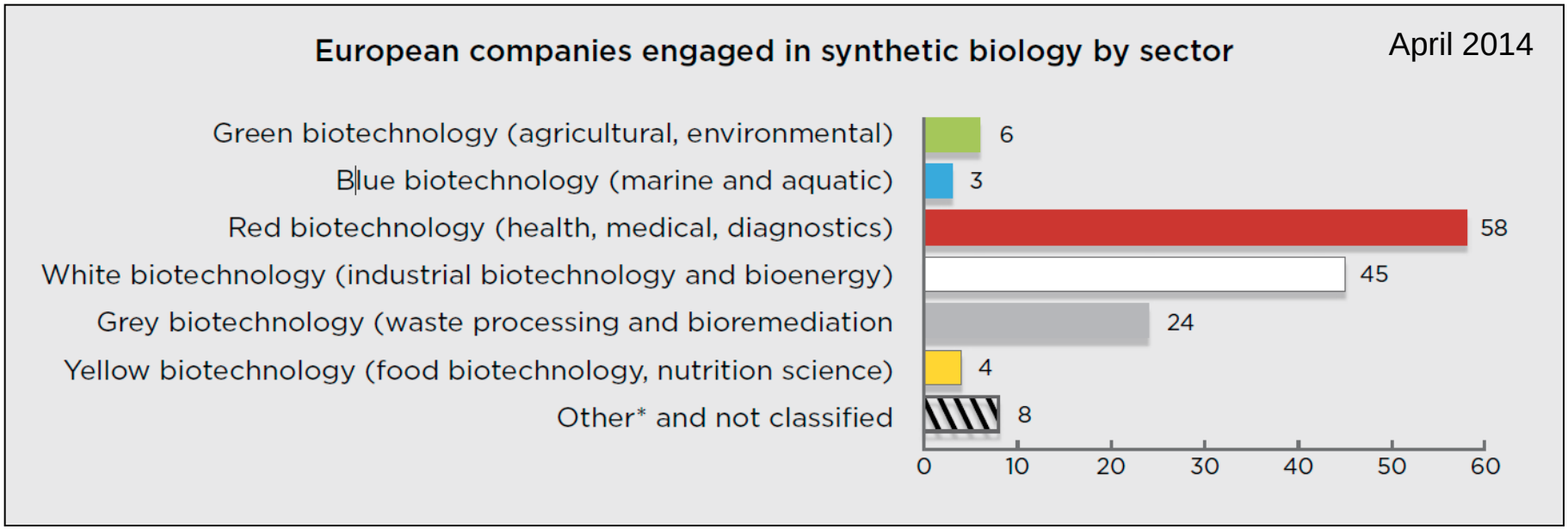


European synthetic biology companies by sector. Companies were classified according to their primary area of R&D interest (https://www.erasynbio.eu/ Strategic vision).

Advantages of modularity for synthetic biology - from engineering logic functions into cells to the design of new protein folds

Roman Jerala

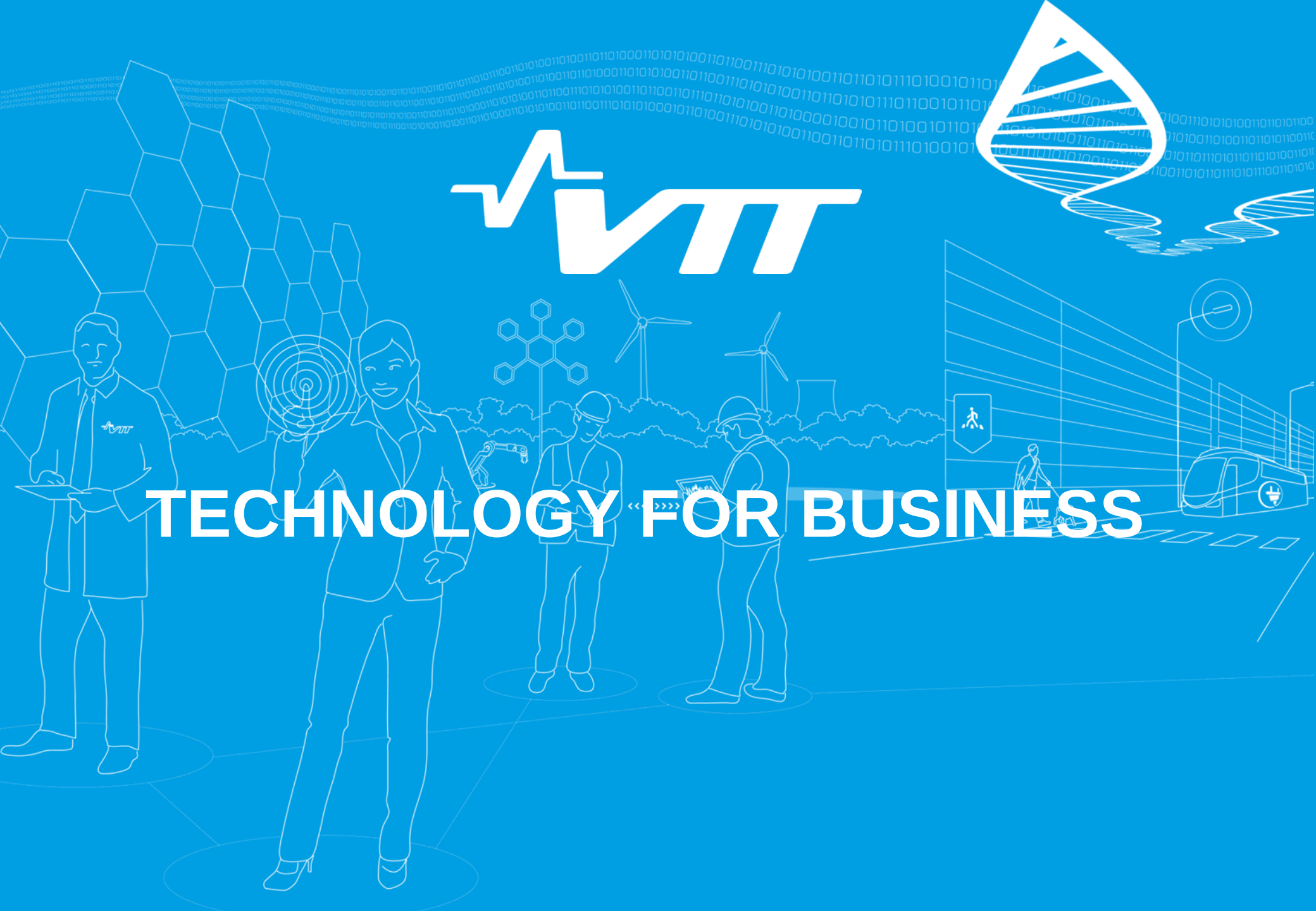
Professor, Department of Biotechnology
National Institute of Chemistry, Slovenia

An industrial perspective on Synthetic Biology

Roel Bovenberg

DSM corporate scientist, Netherlands

Honorary Professor of Synthetic Biology and Cell Engineering, University of Groningen, Netherlands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TECHNOLOGY FOR BUSINESS