Synthetic biology

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Genomics
Synthetic biology

- Introduction
- Bottom-up approaches
- Top-down approaches
- Semi-synthetic approaches
- Conclusion
Introduction

Definition: design and construction of biological devices and systems

Types

1. DNA-based device construction
2. Genome-driven cell engineering
3. Protocell creation

Bottom-up
Top-down
Semi-synthetic
Bottom-up approaches

- Simple systems are put together, to create more complex systems
  - Construction from basic units of
    - whole genomes
    - cells
Bottom-up: genome synthesis

- Short nucleotide sequences are constructed and assembled


- Partition of a wild M. genitalium genome into 101 cassettes
- Synthesis of 50bp oligonucleotides and assembling
- Assembling of 5-7 kb sequences: 101 cassettes obtained
- Five step assembling and transplantation into yeast
Bottom-up: protocell creation

- **Protocell:**
  - hypothetical precursor structures of the first cells
  - Cell-like construct

- **Two options to create protocells:**
  - Using basic units such as nucleotides and amino acids (bottom-up)
  - Using more complex units such as DNA and enzymes (semi-synthetic)
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Top-down approaches

- Start from a living organism → **TOP**
- Try to make it as simple as possible → **DOWN**

**MINIMAL CELL**
**MINIMAL GENOME**

The notion of “minimal cell”

- containing the minimum and sufficient number of components to be “alive”

**ALIVE**
- self-maintenance
- reproduction
- evolvability

Bioinformatics approach
Experimental approach
Bioinformatics approach

- Compare different genomes:
  - Genes in common → Minimal genome

- First used by Mushegian and Koonin in 1996

Compared the three fully sequenced bacterial genomes available at the time (*Haemophilus influenzae*, *M. genitalium* and *Escherichia coli*)

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**A minimal gene set for cellular life derived by comparison of complete bacterial genomes**

Arcady R. Mushegian and Eugene V. Koonin*  
National Center for Biotechnology Information, National Library of Medicine, National Institutes of Health, Bethesda, MD 20894
Experimental techniques

- Knocking out of genes to see if they are essential for the cell
- Some examples:
  - Global transposon mutagenesis
  - Antisense RNA
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Semi-synthetic approach

- Introduce biomolecules into a synthetic compartment
- **Autopoiesis** (self-producing) is needed

**Theory that describes the behavior of all biological systems**

**It defines the characteristics a synthetic biosystem must have in order to mimic a natural one**
Minimal autopoietic system

- The system is a self-bounded molecular assembly
- Its dynamics are:
  - A and B: components of the environment
  - S and M: components of the cell
  - Y and W: waste material
Semi-synthetic minimal cell

Essential genetic and metabolic compounds are introduced inside vesicles or liposomes.
Conclusion

Applications

- Synthetic systems capable of detecting dangerous substances
- Synthetic communication systems that coordinate cellular response
- Improvement in tissue and organ engineering

- Synthetic biology is becoming a very important field

- Improve our understanding of biology
- Give solutions for global problems
References


