

Basic Principles of Synthetic Biology

Engineering Biology for Innovation

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Course Overview

Today's Learning Objectives:

- Define synthetic biology and its core principles
- Understand key engineering approaches in biology
- Explore standardization and modularity concepts
- Examine commercial applications and market potential
- Discuss ethical considerations and future directions



What is Synthetic Biology?

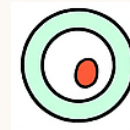
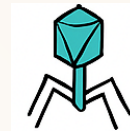
- Definition: Engineering approach to biology that applies engineering principles to biological systems
- Goal: Design and construct new biological parts, devices, and systems
- Approach: Redesign existing natural biological systems for useful purposes
- Interdisciplinary field: Combines biology, engineering, computer science, and chemistry
- Bottom-up construction: Building biological systems from well-characterized parts

Source: Nature Reviews Molecular Cell Biology (2016)

Historical Context and Key Milestones

Key Milestones:

- 1970s: Recombinant DNA technology foundations
- 2000: First synthetic genome (ϕ X174 bacteriophage)
- 2003: BioBricks and standardized parts concept
- 2010: First synthetic bacterial genome (*Mycoplasma mycoides*)
- 2016: Synthetic yeast chromosome project
- 2020s: CRISPR integration and advanced gene circuits



Core Principle 1: Engineering Design Cycle

Traditional Engineering Approach:

- Design: Specify system requirements
- Build: Construct the system
- Test: Measure performance
- Learn: Analyze results and iterate

Applied to Biology:

- Design: Define biological function
- Build: Assemble genetic circuits
- Test: Measure biological output
- Learn: Optimize and redesign

Source: Nature Biotechnology (2018)

Core Principle 2: Standardization

- BioBricks: Standardized biological parts with defined interfaces
- RFC Standards: Request for Comments defining part specifications
- Interchangeable components: Parts that work together predictably
- Characterization: Quantitative description of part behavior
- Registries: Databases of characterized biological parts

Source: iGEM Foundation, Registry of Standard Biological Parts

Core Principle 3: Modularity

Hierarchical Organization:

- **Parts:** Basic functional units (promoters, genes, terminators)
- **Devices:** Combinations of parts with specific functions
- **Systems:** Multiple devices working together
- **Chassis:** Host organisms containing the systems

AI-generated modular system diagram

Core Principle 4: Abstraction

- Physical Layer: DNA sequences, proteins, metabolites
- Device Layer: Functional units (sensors, actuators, logic gates)
- System Layer: Complete biological programs
- Application Layer: Real-world functions and purposes
- Benefit: Enables specialists to work at different levels without understanding all details

Source: Molecular Systems Biology (2017)

Genetic Circuits and Logic Gates

Boolean Logic in Biology:

- AND gates: Multiple inputs required
- OR gates: Any input sufficient
- NOT gates: Inverter circuits
- Toggle switches: Bistable systems
- Oscillators: Periodic behavior

Applications:

- Biosensors for environmental monitoring
- Therapeutic circuits in medicine
- Metabolic pathway control
- Cell fate determination

Source: Science (2013) - Genetic logic circuits

Chassis Organisms

- *Escherichia coli*: Most common, well-characterized, fast growth
- *Saccharomyces cerevisiae*: Eukaryotic system, post-translational modifications
- *Bacillus subtilis*: Gram-positive, protein secretion capabilities
- *Pichia pastoris*: High protein expression levels
- Mammalian cells: Complex protein folding, human-compatible
- Minimal cells: Reduced genomes for predictable behavior

AI-generated comparison of different chassis organisms

Synthetic Biology Toolbox

DNA Assembly Methods:

- BioBrick assembly
- Gibson assembly
- Golden Gate assembly
- SLIC (Sequence and Ligation Independent Cloning)
- CPEC (Circular Polymerase Extension Cloning)

Characterization Tools:

- Flow cytometry
- Fluorescence microscopy
- RNA sequencing
- Proteomics
- Metabolomics

Source: Nature Methods (2019)

CRISPR Integration in Synthetic Biology

- Programmable gene editing: Precise DNA modifications
- CRISPRa/CRISPRi: Activation and interference systems -Base editing: Single nucleotide changes without double-strand breaks
- Prime editing: Precise insertions, deletions, and substitutions
- Multiplexed editing: Simultaneous modification of multiple targets

Source: Nature Reviews Genetics (2020)

Metabolic Engineering Principles

Pathway Design Strategies:

- Heterologous pathway expression: Introducing foreign pathways
- Pathway optimization: Balancing enzyme levels
- Cofactor engineering: Managing cellular resources
- Compartmentalization: Organizing reactions spatially
- Dynamic regulation: Responsive pathway control

AI-generated metabolic pathway diagram

Protein Design and Engineering

- Directed evolution: Laboratory-based protein evolution
- Rational design: Structure-based protein modification
- De novo design: Creating proteins from scratch
- Protein-protein interactions: Engineering binding specificity
- Allosteric regulation: Designing responsive proteins

Source: Nature Chemical Biology (2018)

Biosafety and Containment

Physical Containment:

- Laboratory biosafety levels
- Specialized equipment and facilities
- Training and protocols
- Waste management procedures

Biological Containment:

- Auxotrophic strains (nutrient dependencies)
- Kill switches and terminator genes
- Orthogonal biological systems
- Genetic firewalls

AI-generated biosafety illustration

Commercial Example 1: Ginkgo Bioworks

Business Model:

- “Organism company” - designs custom microbes
- Automated strain engineering platform
- Applications in pharmaceuticals, agriculture, food
- Partnerships with major corporations
- Valuation: \$15+ billion (2021)

Key Technologies:

- High-throughput DNA assembly
- Automated testing and optimization
- Machine learning for design
- Standardized biological parts

Source: Ginkgo Bioworks company materials

Commercial Example 2: Synthetic Spider Silk

- Companies: Bolt Threads, Spiber, Modern Meadow
- Product: Recombinant spider silk proteins in microorganisms
- Properties: Stronger than steel, biodegradable, lightweight
- Applications: Textiles, medical devices, protective equipment
- Market potential: \$1.3 billion by 2027

Source: Nature Materials (2019)

Commercial Example 3: Biofuels and Chemicals

Zymergen (acquired by Ginkgo): Amyris:

- Microbial strain optimization
 - Machine learning-guided engineering
 - Focus on specialty chemicals
- Synthetic artemisinin production
 - Renewable chemicals from sugar
 - Cosmetics and fragrance ingredients

AI-generated biofuel production flowchart

Commercial Example 4: Synthetic Biology in Medicine

- CAR-T cell therapy: Engineered immune cells for cancer treatment
- Biosynthetic insulin: Recombinant human insulin production
- Synthetic antibiotics: Novel antimicrobial compounds
- Personalized medicine: Tailored therapeutic approaches
- Market size: \$39 billion by 2027

Source: Nature Biotechnology (2020)

Commercial Example 5: Food and Agriculture

Applications:

- Impossible Foods: Plant-based meat with synthetic heme
- Perfect Day: Animal-free dairy proteins
- Motif FoodWorks: Designer food ingredients
- Crop enhancement: Improved yield and nutrition