AL-FARABI KAZAKH NATIONAL UNIVERSITY FACULTY OF BIOLOGY AND BIOTECHNOLOGY
DEPARTMENT OF BIOTECHNOLOGY

INTRODUCTION TO BIOLOGICAL ENGINEERING

LECTURE 6.

MODERN TRENDS IN BIOLOGICAL ENGINEERING:

CURRENT DEVELOPMENTS AND FUTURE PERSPECTIVES

PhD., Acting Associate
Professor Doktyrbay Gulina

Lecture Plan

1. Engineering biology in 2026
2. AI and machine learning
3. Automation and biofoundries
4. Genome-scale engineering
5. Cell-free systems
6. Synthetic cells
7. Living medicines and diagnostics
8. Engineered microbial communities
9. Sustainable biomanufacturing
10. Governance and future directions

Learning Outcomes

By the end of this lecture, students should be able to:

LO1 Summarize major current trends in biological engineering.

LO2 Explain how AI, automation and high-throughput experimentation change engineering workflows.

LO3 Describe emerging platforms such as cell-free systems, synthetic cells and living medicines.

LO4 Recognize current directions in sustainable biomanufacturing and engineered communities.

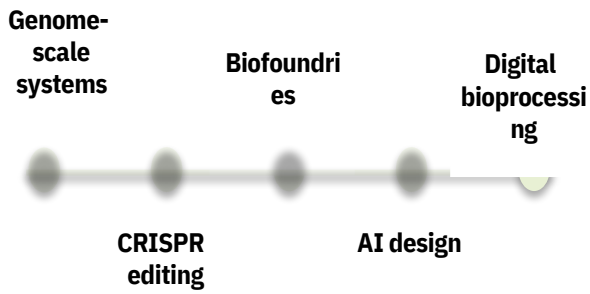
LO5 Evaluate benefits and limitations of emerging technologies.

LO6 Discuss governance, dual-use and responsible innovation in future engineering biology.

Why the field is changing rapidly

Biological engineering is moving from isolated experiments toward integrated, data-rich, automated design platforms.

- Lower-cost DNA synthesis and sequencing expand the scale of design space that can be explored.
- High-throughput measurement, robotics and machine learning shorten iteration cycles.
- At the same time, translation pressures are increasing attention to manufacturability, governance and sustainability.
- A useful engineering representation separates controllable variables from disturbances and constraints.



Progression across scales or stages

AI for biological design

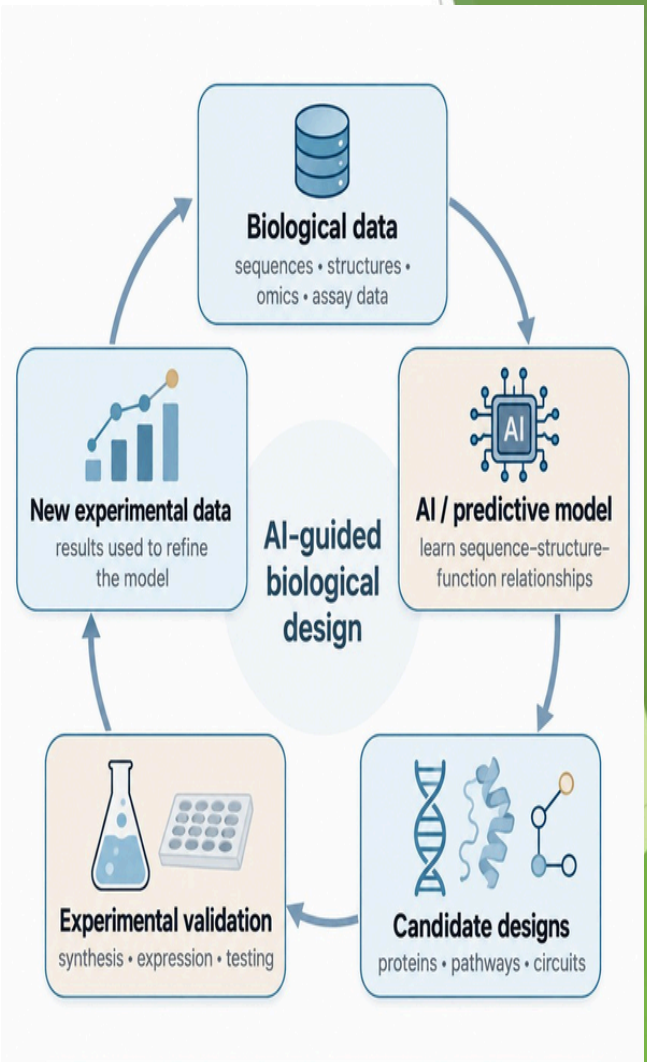
Artificial intelligence is transforming biological engineering from a predominantly experimental discipline into a more predictive design process, where computational models help identify promising molecules, sequences and engineering strategies before laboratory testing.

•**Machine-learning models** are increasingly used for protein structure and function prediction, sequence design, metabolic pathway optimization and experimental prioritization. **Generative AI models** can propose novel proteins, enzymes and regulatory sequences with desired properties, dramatically expanding the accessible biological design space.

Computational predictions do **not replace experimental validation**: candidate designs must still be tested for biological activity, stability, safety and manufacturability.

Model performance depends strongly on the **quality, diversity and relevance of training data**, especially when predictions are transferred to new organisms or experimental conditions.

The most reliable strategies combine **data-driven prediction, mechanistic knowledge and iterative experimentation**in a closed engineering loop.



Protein design revolution

Structure prediction and generative models allow engineers to explore sequence- structure-function relationships at unprecedented scale.

•Modern computational models can connect **amino-acid sequence, three-dimensional structure and biological function**, allowing engineers to explore much larger design spaces than conventional experimental screening alone. **Structure-prediction tools** help identify folding patterns, active sites, binding interfaces and regions that may influence protein stability or activity. **Generative models** can propose novel protein sequences optimized for properties such as catalytic activity, binding affinity, specificity, thermostability or expression. Applications include the engineering of **enzymes, therapeutic proteins, antibodies, biosensors and molecular binders**.

Computational predictions substantially reduce the number of candidates that must be tested, but **experimental validation remains essential** because expression, folding, activity and stability depend on the real biological environment.

The most effective workflow is therefore iterative: experimental results are returned to the computational model to guide the **next generation of improved protein designs**.

Automated DBTL cycles

Robotic platforms can assemble DNA, culture strains, run assays and capture structured data with reduced manual variation.

•In the **Design** stage, computational tools define genetic constructs, pathways or experimental conditions that should be tested.

During **Build**, automated DNA assembly, strain construction and liquid-handling platforms convert digital designs into physical biological systems.

The **Test** stage uses high-throughput assays, sensors and analytical instruments to measure growth, expression, activity, product formation and other performance metrics.

In the **Learn** stage, experimental data are analyzed using statistical models or machine learning to identify important variables and improve subsequent designs.

Automation increases **throughput, reproducibility and traceability**, while reducing manual variability and enabling much larger design spaces to be explored.

Advanced biofoundries increasingly operate as **closed-loop systems**, where test results can automatically guide the selection of the next experiment.

DESIGN
select sequences, pathways, targets
↓
BUILD
DNA assembly • strain construction
↓
TEST
high-throughput assays • measurements
↓
LEARN
data analysis • ML • model updating

Biofoundries

Biofoundries are highly automated biological engineering facilities that integrate computational design, robotic experimentation, high-throughput analytics and standardized data management within a unified Design–Build– Test–Learn workflow.

•Biofoundries automate repetitive laboratory operations such as **DNA assembly, liquid handling, microbial cultivation, screening and sample analysis**. Standardized protocols improve **reproducibility, traceability and comparability** between experimental runs and across research teams. High-throughput platforms allow hundreds or thousands of biological variants to be constructed and evaluated in parallel, greatly expanding the accessible **design space**.

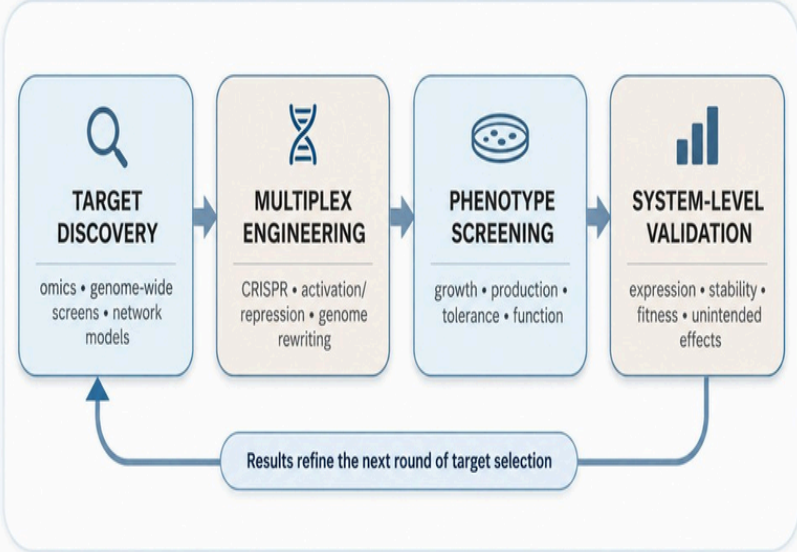
Integrated software connects experimental planning with robotics, analytical instruments and laboratory information-management systems, creating a continuous **digital–physical workflow**.

Biofoundries are particularly valuable for rapid prototyping of **engineered strains, metabolic pathways, genetic circuits, enzymes and therapeutic biomolecules**. Their main engineering challenge is not automation alone, but the integration of **reliable protocols, quality control, standardized data and meaningful decision criteria**.

Genome-scale engineering

DNA target Genome-scale engineering expands the design space from individual genes to interacting pathways and resource networks.

- **CRISPR-based genome engineering** enables precise gene deletion, insertion, activation and repression, while multiplex approaches allow many loci to be modified simultaneously.
- **Genome-wide perturbation screens** systematically connect genetic changes with measurable phenotypes and help identify genes, pathways and regulatory interactions that control system performance.
- Large-scale genome rewriting can include **genome recoding, chromosome restructuring, pathway refactoring and removal of non-essential genetic elements**.
- Because genes operate within interconnected regulatory and metabolic networks, modifying multiple loci can generate **epistasis, compensatory responses and unexpected phenotypes**.
- Successful genome-scale engineering therefore requires validation at several levels: **DNA sequence, gene expression, cellular phenotype, growth, stability and system-level function**.
- The engineering objective is not simply to create more edits, but to identify a **minimal and coordinated set of genomic changes** that produces the desired phenotype while maintaining cellular robustness.



Cell-free synthetic biology

Cell-free platforms accelerate prototyping by removing barriers of cell viability and transport.

Cell-free platforms **decouple biochemical synthesis from cell growth and viability**, allowing engineering objectives to be optimized without maintaining an intact living organism.

Direct access to DNA, RNA, enzymes, ribosomes, metabolites and cofactors enables **rapid prototyping, flexible reaction design and precise control of reaction conditions**.

Because there is no requirement to preserve cellular survival, cell-free systems can support the synthesis or testing of **toxic compounds, difficult proteins and non-natural biochemical pathways**.

Lyophilized cell-free reactions can be stored and activated when needed, creating opportunities for **portable biosensors, decentralized diagnostics and field-deployable manufacturing**.

Major engineering challenges include **extract variability, reagent cost, energy regeneration, reaction lifetime, product recovery and scale-up**.

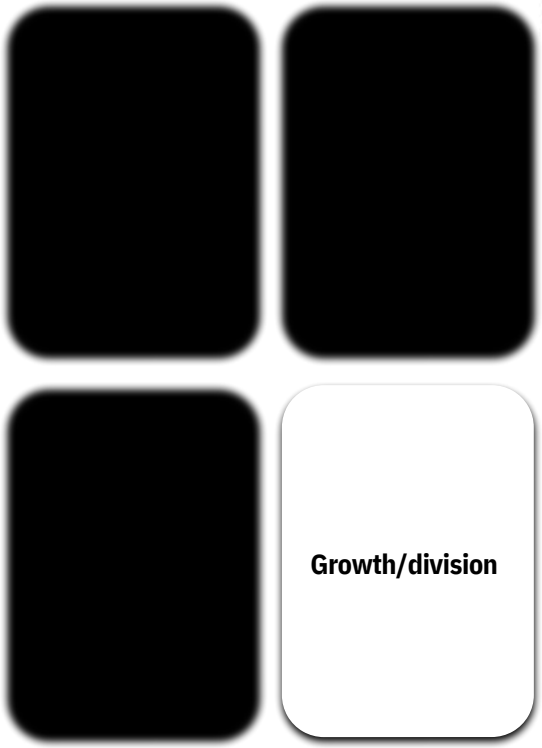
For translation beyond laboratory prototyping, performance must therefore be evaluated in terms of **yield, stability, reproducibility and manufacturing economics**.

DNA / RNA template
↓
Cell-free extract
ribosomes • enzymes • transcription/translation machinery
↓
Energy + cofactors + substrates
↓
Cell-free reaction
↓
Protein / metabolite / biosensor signal

Synthetic cells

Bottom-up synthetic cells aim to assemble cell-like functions from defined components.

- They help study minimal requirements for life and may become programmable microreactors or delivery systems.
- Synthetic-cell research asks which components are minimally sufficient for functions such as compartmentalization, metabolism, information processing and replication.
- Key challenges include energy regeneration, membrane growth, information replication and coordinated division.
- The field also raises conceptual questions about how much cellular complexity is necessary for useful function.
- Engineering value comes from controlled simplification, which can reveal design principles that are difficult to isolate in natural cells.



Living medicines

Engineered bacteria, immune cells and other living therapeutics can sense disease signals and respond locally.

Living therapeutics can be built from **engineered bacteria, immune cells and other cellular platforms** designed to operate directly within the patient or at a specific disease site.

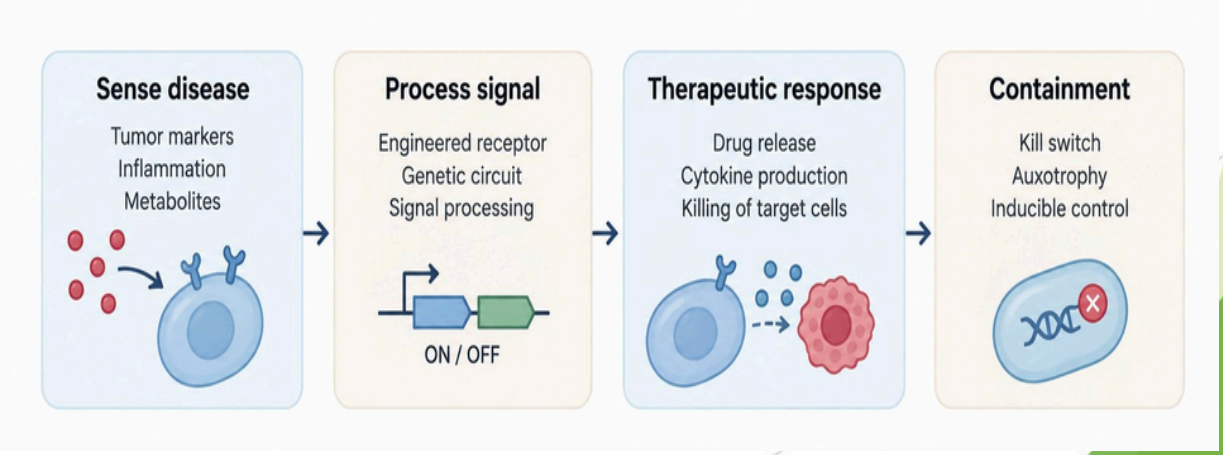
Their functions may include **targeted drug delivery, cytokine production, metabolic conversion, immune modulation and destruction of diseased cells**.

Unlike conventional small-molecule drugs, living medicines can **respond dynamically to their environment**, change activity over time and, in some cases, proliferate or persist after administration.

A major design goal is to achieve **high therapeutic activity while limiting uncontrolled growth, off-target effects and excessive persistence**.

Safety strategies include **genetic kill switches, auxotrophy, inducible circuits, spatial containment and external control mechanisms**.

Because living systems can evolve and change phenotype, product characterization must consider **identity, potency, stability, persistence, containment and patient-to-patient variability**.



Advanced biosensing

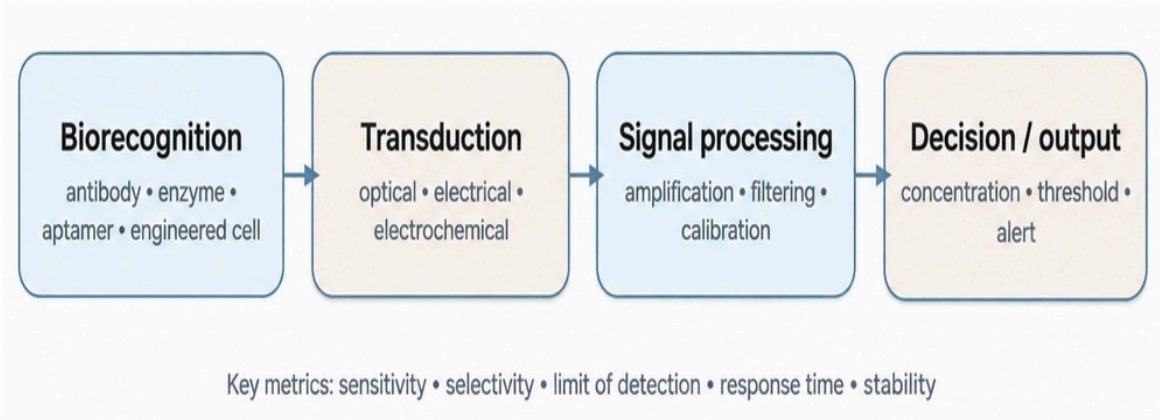
Engineered cells and molecular circuits can transform biological recognition into readable signals.

Biosensing begins with a **recognition element** such as an antibody, enzyme, nucleic-acid probe, receptor, engineered cell or synthetic genetic circuit that selectively responds to the target analyte. The recognition event must then be converted through **signal transduction** into a measurable optical, electrical, electrochemical or mechanical output.

Modern biosensors increasingly integrate **microfluidics, wearable platforms, implantable devices and wireless electronics** to enable continuous or near-real-time measurements. **Multiplexed sensing** allows several biomarkers to be measured simultaneously, improving biological context but increasing requirements for calibration, normalization and signal interpretation.

Performance must be evaluated using engineering metrics such as **sensitivity, selectivity, limit of detection, response time, dynamic range, reproducibility and stability**.

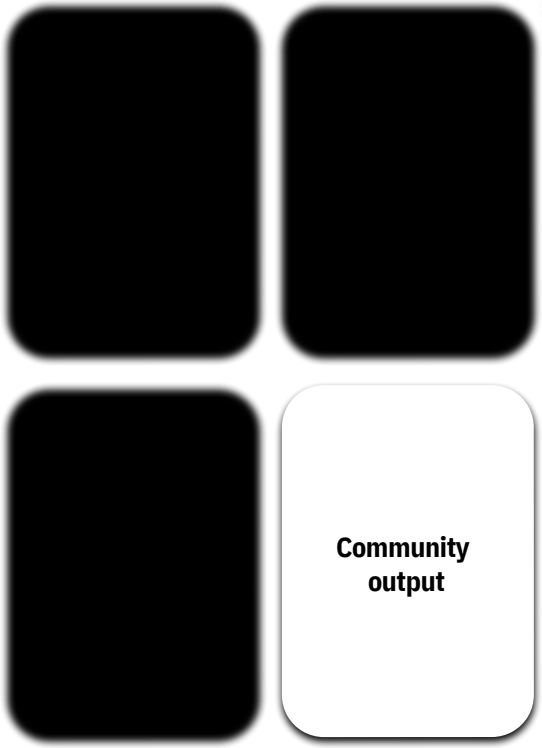
Real-world deployment requires robustness to **complex biological samples, temperature variation, fouling, interfering molecules and user-dependent conditions**.



Engineered microbial communities

Community engineering distributes metabolic tasks across different organisms, reducing burden on single strains.

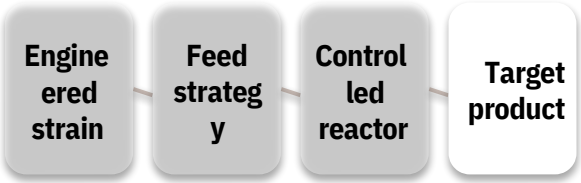
- Synthetic ecology can exploit cross- feeding, spatial organization and division of labor.
- Community-level function emerges from interactions such as cross-feeding, competition, inhibition and spatial organization.
- Community stability is difficult because population dynamics and evolution can change composition over time.
- New modelling and control approaches are needed for predictable multispecies systems.
- Composition alone is not enough to predict performance; interaction strength, environmental context and ecological stability must also be considered.



Precision fermentation

Precision fermentation produces defined proteins, fats, flavors and ingredients using engineered microorganisms.

- Industrial performance is determined by the interaction of strain design, medium composition, reactor operation and downstream recovery.
- Its growth is driven by food, materials and specialty-chemical applications.
- Competitive processes require high yield, low-cost feedstocks, efficient recovery and reliable scale-up.
- Claims of sustainability must be supported by life-cycle analysis and realistic energy assumptions.
- The most productive strain under one condition may not provide the lowest-cost or most robust manufacturing process at scale.

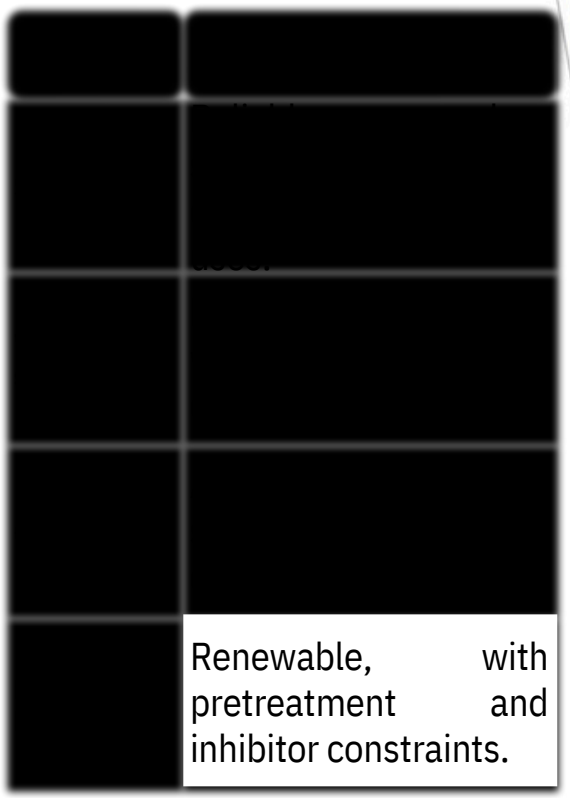


Conceptual workflow

Alternative feedstocks

Engineering is expanding from refined sugar toward lignocellulosic hydrolysates, waste gases, methanol, formate and CO2-derived intermediates.

- Sustainability should be treated as a quantitative design objective.
- New feedstocks can reduce competition with food resources but introduce toxicity, impurity and metabolic challenges.
- C1 biomanufacturing seeks to use one-carbon substrates through natural or engineered pathways.
- Feedstock choice influences both strain design and reactor technology.
- Carbon source, water demand, energy intensity, waste generation and downstream separations can shift environmental burden between process stages, so local yield alone is not...



Continuous biomanufacturing

Continuous upstream and downstream processing can increase equipment utilization and reduce process footprint.

In continuous operation, **fresh medium is supplied while product-containing material is removed continuously**, allowing the process to operate for extended periods without repeated batch shutdowns.

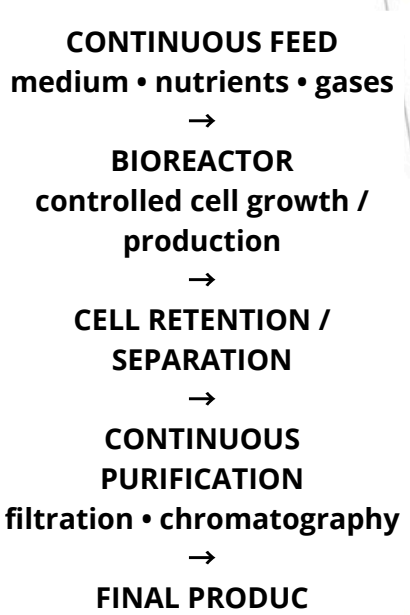
Maintaining a stable process requires tight control of **cell density, nutrient supply, dissolved oxygen, pH, temperature and product concentration**.

Continuous production can improve **facility utilization and volumetric productivity** while reducing equipment size and downtime between production campaigns.

Integration with continuous downstream operations such as **cell retention, filtration, chromatography and product concentration** can create an end-to-end manufacturing platform.

Process Analytical Technology (PAT) and online sensors are essential for detecting deviations early and maintaining operation within an acceptable control region.

Key challenges include **contamination risk, long-term cell-line stability, equipment fouling, process disturbances and coordinated control of upstream and downstream units**.



Organs-on-chips and microphysiological systems

Microengineered tissue models reproduce selected human physiological functions under controlled flow and mechanical cues. Microphysiological systems integrate **human cells, extracellular matrix and microfluidic architecture** to reproduce specific tissue-level functions in a controlled experimental environment. Dynamic perfusion provides continuous delivery of **nutrients, oxygen, signaling molecules and drugs**, while simultaneously removing metabolic waste.

Mechanical cues such as **shear stress, stretching, compression and cyclic deformation** can be incorporated to mimic physiological conditions experienced by tissues in vivo.

Organ-on-chip systems are increasingly used for **disease modelling, drug efficacy testing, toxicity assessment and mechanistic studies**, often providing greater human relevance than conventional static cell culture.

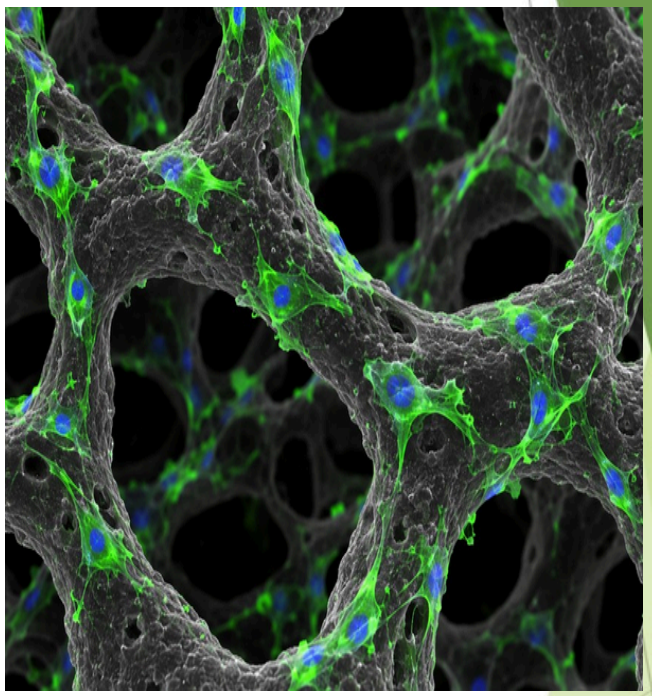
Integration of **embedded sensors and real-time imaging** enables continuous monitoring of barrier integrity, metabolism, electrical activity and other functional readouts.

Major challenges include **standardization, reproducibility, long-term cell stability, scaling between tissues and validation against clinical physiology**.

Engineered living materials

Living cells embedded in matrices can produce pigments, minerals, polymers or repair functions in situ.

- Engineered living materials couple a structural matrix with cells that sense, respond, produce or repair.
- Genetic programs can couple environmental sensing to material response.
- Applications are emerging in construction, textiles, coatings and biomedical devices.
- Containment, durability and control of growth are key design constraints.
- Performance therefore depends on both material properties and biological state, creating design trade-offs between mechanical function, viability, containment and long-term...



Biomaterials by design

Computational and modular approaches increasingly link molecular composition to mechanical, transport and biological properties.

•Biomaterial performance depends not only on chemical composition, but also on **microstructure, porosity, surface chemistry, stiffness, viscoelasticity and degradation behaviour**.

Hydrogels and bioinks can be engineered with tunable mechanics, cross-link density, ligand presentation and mass transport to reproduce selected features of native extracellular matrices.

Computational and modular design approaches enable researchers to explore **structure–property–function relationships** and identify combinations of material parameters that produce a desired biological outcome.

4D biomaterials extend conventional design by changing shape, mechanics or biochemical function over time in response to stimuli such as temperature, pH, enzymes or cellular activity.

At the cell–material interface, material properties influence **adhesion, migration, proliferation, differentiation and immune response**, making biological performance an integral design criterion.

Translation requires materials to maintain their intended properties after **manufacturing, sterilization, storage and scale-up**, with reproducible characterization across batches.

AI-enabled bioprocessing

Machine learning can estimate hidden process states, detect anomalies and optimize feed or control policies.

Modern bioprocesses generate continuous data from **pH, dissolved oxygen, temperature, biomass, spectroscopy, metabolite and product-quality measurements**.

Machine-learning models can transform these measurements into **soft sensors**, estimating variables that are difficult or slow to measure directly, such as biomass concentration, substrate consumption or product titer.

Anomaly-detection algorithms can identify abnormal trajectories before conventional alarm limits are reached, supporting earlier process intervention.

Hybrid models combine mechanistic knowledge with data-driven learning, improving prediction while preserving biological and engineering constraints.

Digital twins can simulate alternative feeding, aeration or control strategies before they are applied to the physical process.

Reliable deployment requires careful attention to **data quality, model validation, distribution shift, interpretability and continuous performance monitoring**.

PROCESS
bioreactor / production system
↓
SENSORS & PAT
pH • DO • spectroscopy • metabolites
↓
DATA LAYER
cleaning • integration • historical data
↓
AI / HYBRID MODEL
state estimation • prediction • anomaly detection
↓
DECISION & CONTROL
feed • aeration • temperature • harvest timing

Sustainability as a design loop

Future engineering biology increasingly uses life-cycle and techno-economic metrics during early design.

Early-stage design should consider not only biological performance, but also **feedstock demand, energy use, water consumption, downstream processing, waste generation and product recovery**.

Life-cycle assessment (LCA) evaluates environmental impacts across the full system, from raw-material production and manufacturing to product use and end-of-life treatment.

Techno-economic analysis (TEA) complements environmental assessment by estimating production cost, capital requirements, utilities and major economic bottlenecks.

A pathway with a high biological yield may still perform poorly at system level if it requires **expensive feedstocks, intensive purification, large energy inputs or difficult waste treatment**.

Sustainable biological engineering therefore uses **multi-objective optimization**, balancing productivity, cost, resource efficiency and environmental impact rather than maximizing a single variable.

Results from LCA and TEA should feed back into earlier design decisions, allowing engineers to modify the **host, pathway, feedstock, process conditions or recovery strategy** before scale-up.

Convergence with electronics and robotics

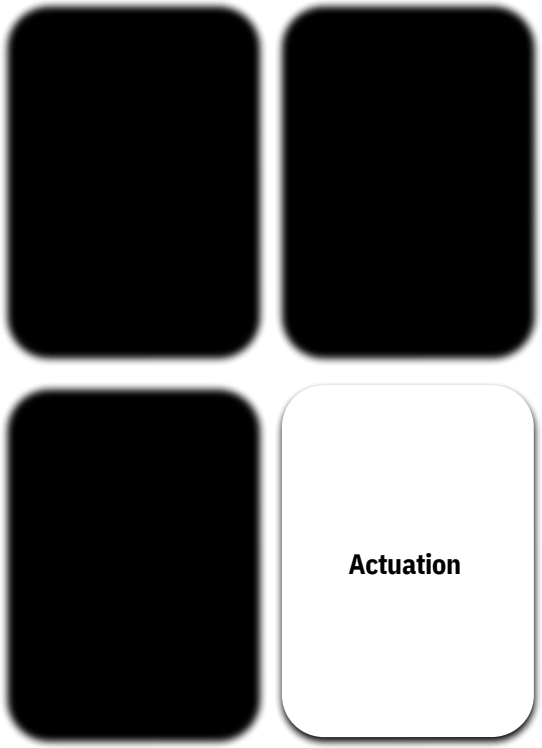
Biological components can provide highly specific **sensing, adaptation and self-organization**, while electronics contribute rapid signal processing, communication and precise control.

Examples include **biohybrid soft robots, neural interfaces, smart prosthetic systems, automated organ- on-chip platforms and cell-based sensing devices**. Microfluidics and embedded sensors make it possible to connect living biological systems with **real-time measurement, feedback control and automated decision-making**.

Robotic actuation can translate biological signals into physical actions, enabling systems that **move, release compounds, adjust environmental conditions or interact with surrounding tissues**.

A major engineering challenge is the interface between **wet biological components and dry electronic hardware**, including sterility, packaging, signal conversion, power supply and long-term stability.

Reliable deployment requires the complete hybrid system to be tested under **realistic mechanical, environmental and biological conditions**, not only under ideal laboratory settings.



Open science and standards

Shared data schemas, reference materials and standardized protocols improve interoperability and reproducibility.

•Standardized experimental protocols and **reference materials** make it possible to compare biological measurements across instruments, laboratories and research groups.

Structured **metadata** should describe not only the result, but also the biological system, operating conditions, measurement method, calibration and data-processing workflow.

Shared repositories and machine-readable formats enable experimental datasets, genetic designs and computational models to be **reused, combined and independently validated**.

Version-controlled workflows improve **traceability**, allowing researchers to reconstruct how a dataset, model or design changed during a project.

Community standards support interoperability, but they should preserve **biological context**, because measurements obtained under different hosts, media or environmental conditions may not be directly comparable.

Reproducibility should therefore be treated as an **engineering property of the complete information pipeline**, rather than only as a requirement for scientific reporting.

Dual-use and governance

Powerful tools can be beneficial or misused, so responsible engineering must include risk awareness.

•Biological engineering can generate major benefits in **medicine, agriculture, manufacturing and environmental applications**, but the same capabilities may also introduce biosafety, biosecurity or societal risks.

Dual-use assessment considers not only the intended application, but also **how a technology could behave outside its intended context, who can access it and what consequences misuse could create**. Governance can include **institutional biosafety review, DNA synthesis screening, access control, cybersecurity, traceability and regulatory oversight**.

AI-enabled design and increasingly automated biological workflows expand technical capability, making **secure data handling, model access and experimental authorization** increasingly important.

Risk management should be **proportionate to the level of hazard and uncertainty**, allowing beneficial research to continue while applying stronger safeguards where consequences could be greater. Governance is most effective when incorporated **before deployment**, because safety, monitoring and compliance requirements can influence the design itself.

INTENDED BENEFIT
health • food • manufacturing • environment
↓
DUAL-USE ASSESSMENT
hazard • exposure • misuse potential • uncertainty

TECHNICAL SAFEGUARDS
containment • access control • monitoring • fail-safe design
и
GOVERNANCE MEASURES
review • standards • screening • regulation
↓
RESPONSIBLE DEPLOYMENT

Future workforce

Modern biological engineers need biology, quantitative modelling, process thinking, data literacy and communication skills.

•Strong foundations in **molecular biology, genetics, biochemistry and cell biology** remain essential for understanding biological mechanisms and experimental limitations.

Engineering practice increasingly requires **quantitative modelling, process design, systems thinking, transport analysis and scale-up reasoning**.

Data-rich biological research makes **programming, statistics, machine learning and data interpretation** increasingly important professional skills.

No single engineer can master every relevant technology,
making **interdisciplinary teamwork and communication**central to modern biological engineering.

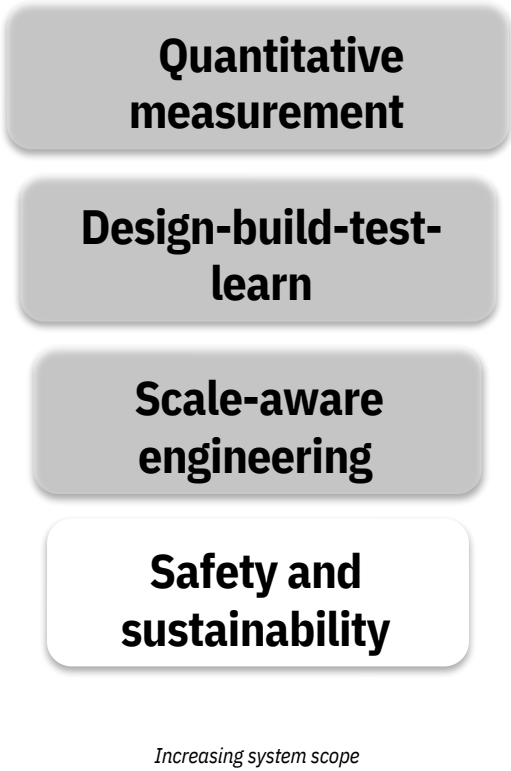
Engineers must be able to evaluate **uncertainty, evidence quality and model limitations**, rather than simply apply the newest computational or experimental tools.

Ethics, biosafety, regulation and responsible innovation are becoming core engineering competencies because technical decisions increasingly affect clinical, environmental and societal systems.

What is likely to persist?

Platforms will change rapidly, but core engineering principles will remain: specification, conservation, transport, kinetics, control, uncertainty and iteration.

- Biology will continue to resist perfect standardization because living systems evolve and depend on context.
- Therefore future success will come from combining powerful digital tools with careful experimental and systems reasoning.
- The strongest innovations will connect molecular design to manufacturable, safe and socially useful systems.
- A useful engineering representation separates controllable variables from disturbances and constraints.



Take-home outlook

Biological engineering is becoming more automated, predictive and programmable.

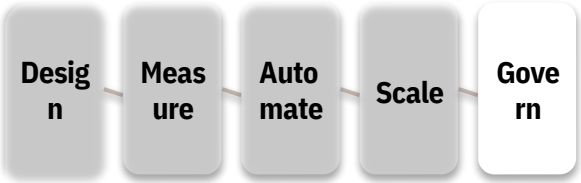
• A useful workflow makes the reasoning reproducible: define the objective and boundary, identify relevant variables, choose the simplest adequate representation, quantify…

• Emerging technologies expand design space from molecules to synthetic cells, living materials and communities.

• Translation increasingly demands sustainability, manufacturability, governance and real-world robustness from the beginning.

• The future field will be defined by integration across scales rather than by one single technology.

• Each step should generate information needed by the next.



Student Tasks and Discussion

1. Define one system boundary relevant to this lecture and explain what is deliberately excluded from the analysis.
2. Identify the three most important measurable variables for judging performance; state their units and why they matter.
3. Draw one conceptual diagram (process, causal loop, balance, or decision map) using the notation introduced in the lecture.
4. Describe one realistic failure mode or limitation and propose an engineering control, design change or monitoring strategy.
5. Locate one peer-reviewed article from the last five years that extends the lecture topic and summarize its engineering contribution, evidence and remaining limitation.

Selected References and Further Reading

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