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

INTRODUCTION TO BIOLOGICAL ENGINEERING

LECTURE 1.
INTRODUCTION TO BIOLOGICAL ENGINEERING: SCOPE, ROLE IN BIOTECHNOLOGY, AND COURSE STRUCTURE

PhD., Acting Associate
Professor Doktyrbay Gulina

Lecture Plan

The lecture is organized from foundational concepts to engineering interpretation and applied examples.

1. What biological engineering is
2. From biology to engineered systems
3. Core engineering principles
4. Relationship to biotechnology
5. Major application domains
6. Levels of biological organization
7. Design–Build–Test–Learn logic
8. Quantitative thinking and models
9. Ethics, safety and translation
10. Course map and student tasks

Learning Outcomes

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

LO1 Define biological engineering and distinguish it from adjacent disciplines.

LO2 Explain why quantitative engineering concepts are useful for biological systems.

LO3 Identify system inputs, transformations, outputs, constraints and performance metrics.

LO4 Relate biological engineering to biotechnology, bioprocessing, biomedical and environmental applications.

LO5 Describe the Design–Build–Test–Learn cycle and its role in modern engineering biology.

LO6 Recognize the importance of safety, ethics, regulation and sustainability in technology development.

Why engineer biology?

Biological systems can sense signals, process information, convert matter and energy, synthesize complex molecules and adapt to changing conditions. Biological engineering applies quantitative and engineering principles to understand these functions and redesign them for specific purposes.

Design and control. Biological components can be modified to perform defined functions, such as producing therapeutic proteins or detecting pollutants.

Quantitative performance. Engineered systems are evaluated by measurable parameters including productivity, yield, stability, specificity and robustness.

Scale-up and application. A successful design must operate reliably not only in the laboratory, but also in bioreactors, tissues or industrial systems.

Biological complexity. Unlike mechanical systems, living components are dynamic, adaptive and highly dependent on environmental and cellular context.

The central goal of biological engineering is to make biological systems more predictable, controllable and useful for medicine, biotechnology, agriculture and environmental applications.



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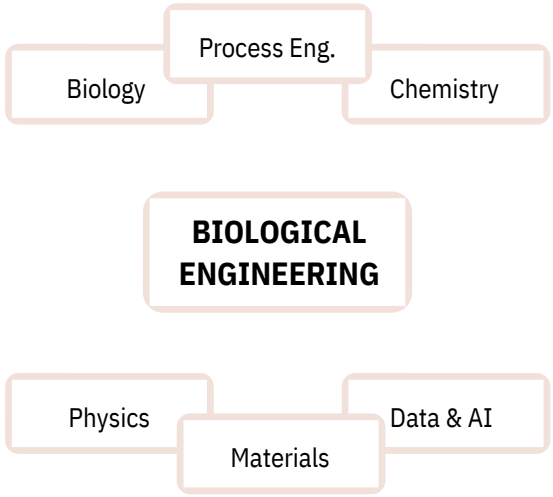
A working definition



Biological engineering applies engineering analysis, design and quantitative methods to biological systems and biologically derived materials.

- The object of engineering may be a molecule, cell, tissue, microbial community, bioreactor, medical device or environmental process.
- A useful definition must include both understanding and construction: engineers model existing systems and deliberately modify or design new ones.
- Success is judged by performance, robustness, safety, manufacturability, sustainability and fitness for the intended use.

Schematic for explanation; proportions are illustrative unless otherwise stated.

Biological engineering vs biotechnology

Biotechnology is an application domain that uses organisms, cells or biomolecules to make products and services.

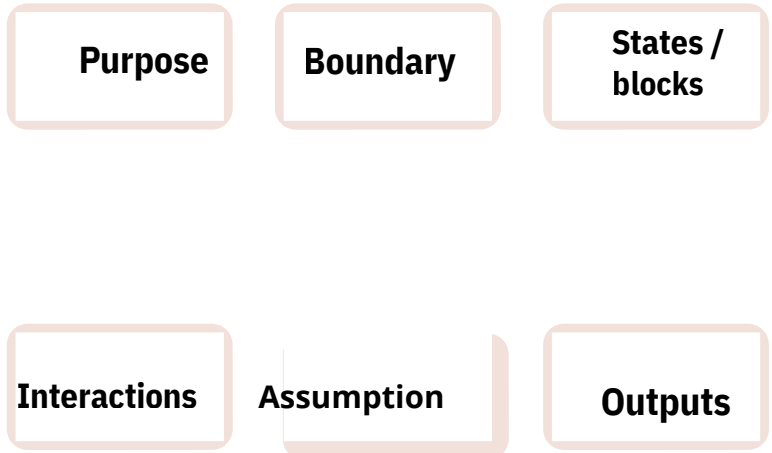
Biotechnology

- Focuses on the **application of biological systems**.
- Includes fermentation, vaccines, recombinant proteins and industrial enzymes.
- Main question: **What biological system can provide the desired function?**

Biological engineering

- Focuses on **design, modelling, optimization, control and scale-up**.
- Uses quantitative tools such as kinetics, mass balances and process modelling.
- Main question: **How can the system be engineered to achieve defined performance?**

The fields strongly overlap: modern biotechnology increasingly depe nds on engineering approaches to improve **yield, productivity, robustness and scalability**.



Interdisciplinary foundation

Interdisciplinary foundation

Biological engineering combines life sciences with engineering, quantitative and computational disciplines to understand, predict and control biological systems.

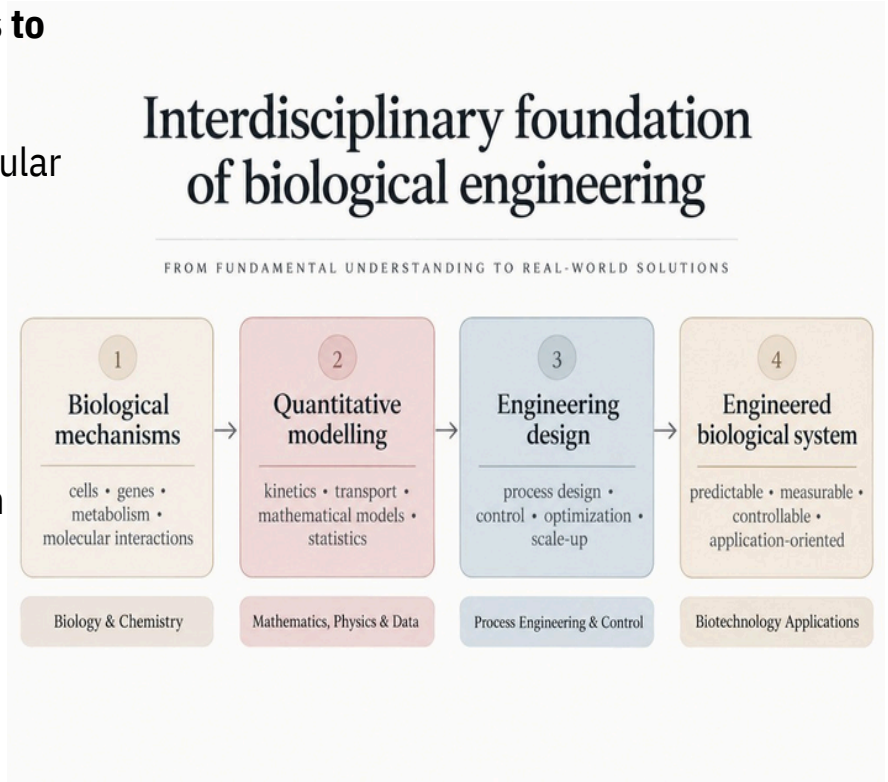
MECHANISTIC FOUNDATION
Biology and chemistry explain cellular mechanisms, molecular interactions and biochemical reactions.

ENGINEERING FOUNDATION
Physics and process engineering contribute transport, thermodynamics, reactor design, control and scale-up.

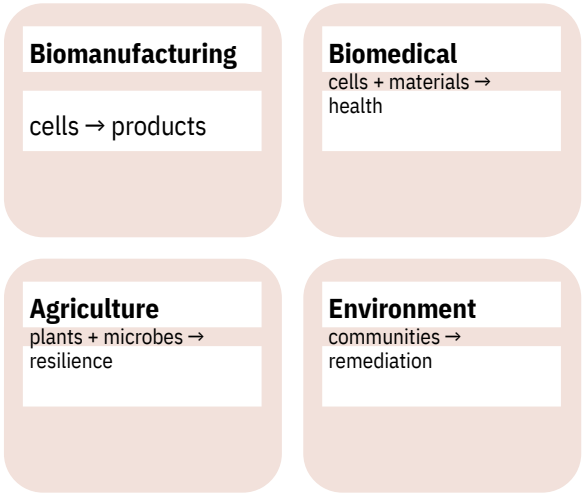
QUANTITATIVE FOUNDATION
Mathematics, statistics and computer science support modelling, simulation, data analysis and AI-based decision making.

ENGINEERING CONSEQUENCE
This integration transforms biological knowledge into **measurable, predictive and controllable systems**.

INTERDISCIPLINARY PERSPECTIVE
Effective biological engineering requires biological function, physical constraints and quantitative performance to be considered together.



From observation to specification



Schematic for explanation; proportions are illustrative unless otherwise stated.

Science explains how a biological system behaves; engineering defines how that system should perform.
A biological observation becomes an engineering problem when the desired function is translated into **measurable targets, operating conditions and acceptance criteria**.

- **Define the function:** what should the system produce, detect, remove or restore?
- **Specify performance:** use measurable parameters such as **titer, yield, productivity, sensitivity, stability or mechanical strength**.
- **Set operating conditions:** define relevant ranges of pH, temperature, nutrients, flow or stress.
- **Identify constraints:** consider biological variability, safety, cost, regulation and ethics.
- **Establish success criteria:** determine the minimum performance required for an acceptable design.

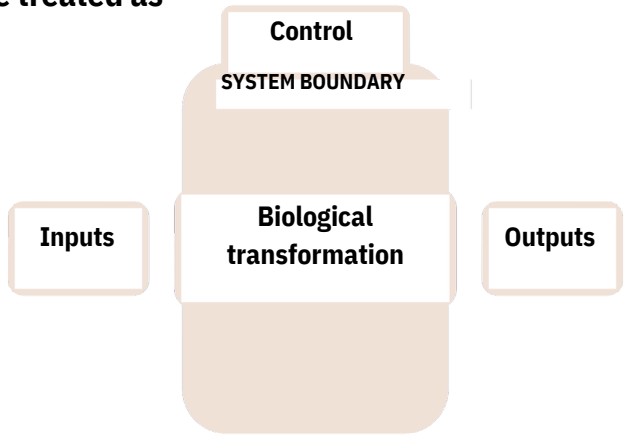
Clear specifications make biological systems testable, comparable and suitable for systematic optimization.

The engineered biological system

The engineered biological system

An engineered biological system is defined by its function, system boundary, material and information flows, internal transformations, disturbances and control mechanisms. The boundary determines which variables are treated as part of the system and which belong to its environment.

- **Inputs** may include substrates, nutrients, oxygen, energy, cells or regulatory signals.
- **Biological transformation** converts these inputs through cellular metabolism, enzymatic reactions or other biological processes.
- **Outputs** include the desired product together with biomass, heat, metabolites and waste streams.
- **Disturbances** such as changes in temperature, pH, nutrient supply or cell physiology can alter system performance.
- **Feedback and control** are used to maintain key variables within acceptable operating ranges.

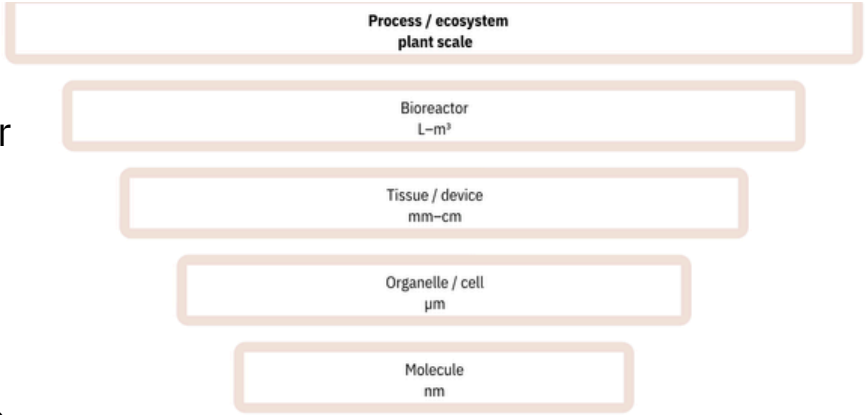


Conceptual figure — created for teaching from the cited literature.

Example — fermentation: glucose, oxygen and inoculum enter the system; microbial metabolism produces biomass and a target product, while pH, dissolved oxygen and temperature are monitored and controlled.

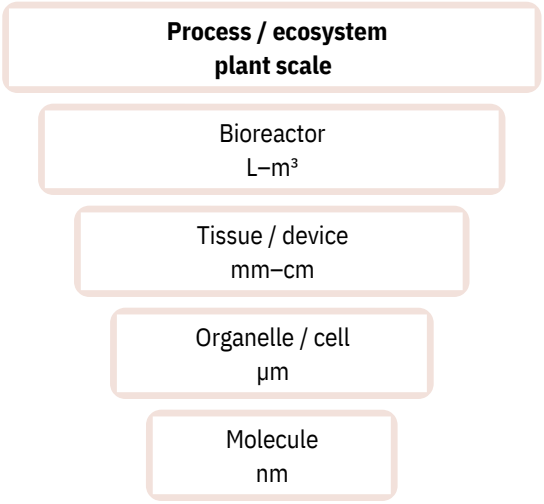
Levels of organization

Biological engineering operates across multiple levels of organization, from molecules and cells to tissues, bioreactors and ecosystems. At the molecular and cellular levels, DNA, RNA, proteins, metabolites and regulatory networks determine metabolism, growth, signalling and stress responses. At higher levels, interactions between cells, tissues and microbial communities generate more complex biological functions. These functions ultimately influence the performance of engineered systems such as bioreactors, biomedical devices and environmental processes. As scale increases, transport limitations, spatial gradients, mechanical forces and population interactions become increasingly important. Therefore, biological engineering must connect molecular mechanisms with system-level behaviour and select the appropriate scale for measurement, modelling and control.



Key principle: *System-level performance emerges from interactions across multiple biological scales.*

Abstraction and hierarchy



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Biological systems are inherently complex, so engineers use abstraction to represent only the features that are relevant to a specific question or design objective. Different levels of hierarchy require different variables, models and assumptions.

- At the **molecular level**, systems may be described by genes, proteins, binding interactions and reaction kinetics.
- At the **cellular level**, attention shifts to metabolism, regulatory networks, growth and phenotype.
- At the **tissue or device level**, transport, mechanics and cell–material interactions become important.
- At the **bioreactor and process level**, engineers focus on mass transfer, mixing, productivity, control and scale-up.

Abstraction reduces unnecessary complexity, but every simplification introduces assumptions that must be clearly stated and validated.

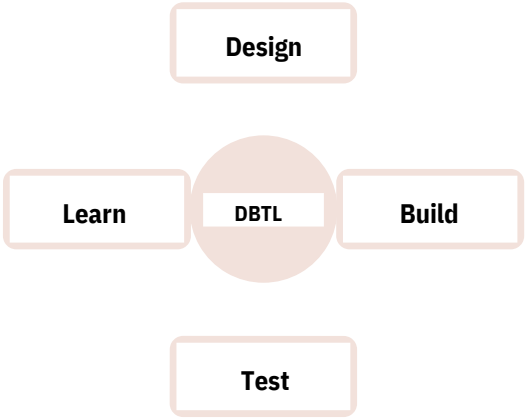
Design–Build–Test–Learn

The Design–Build–Test–Learn (DBTL) cycle is a core framework in biological engineering and synthetic biology. It organizes development as an iterative process in which each experimental round generates information for the next design.

- **Design** defines the desired function, performance criteria and biological or process components required to achieve them.
- **Build** implements the design in DNA constructs, cells, biomaterials or process hardware.
- **Test** measures system performance under controlled conditions using quantitative assays and defined metrics.
- **Learn** compares experimental results with predictions, identifies limitations and updates models or design assumptions.

The cycle is iterative: unsuccessful designs are not simply discarded; their data are used to refine the next round of engineering.

Automation, high-throughput screening and machine learning can accelerate DBTL by increasing experimental throughput and improving design selection.



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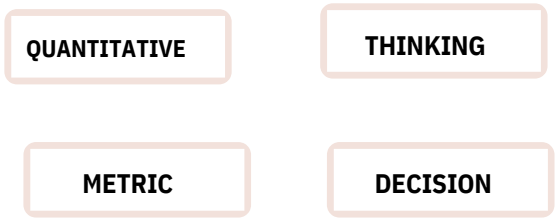
Quantitative thinking

Quantitative thinking converts biological observations into measurable variables, relationships and performance criteria. It allows engineers to compare alternatives, predict system behaviour and make evidence-based decisions.

- **Mass balances** track how matter enters, leaves and accumulates within a system.
- **Kinetics** describe the rates of biological and chemical transformations.
- **Transport and energy balances** explain the movement of heat, gases, nutrients and other resources.
- **Statistics and uncertainty analysis** are essential because biological measurements and populations are inherently variable.
- **Scaling and dimensionless relationships** help compare systems operating at different sizes and conditions.



Conceptual relation (schematic)

MECHANISTIC POINT

Dimensionless groups and scaling relations help compare systems of different sizes.

PRACTICAL POINT

Uncertainty analysis is essential because biological measurements and populations are inherently variable.

ENGINEERING CONSEQUENCE

Translate the biological description into an engineering question with a measurable outcome, explicit assumptions and a defined decision criterion.

Performance metrics

Performance metrics translate an engineering objective into measurable criteria that can be monitored, compared and optimized. No single metric usually captures the complete performance of a biological system; improvement in one parameter may reduce another.

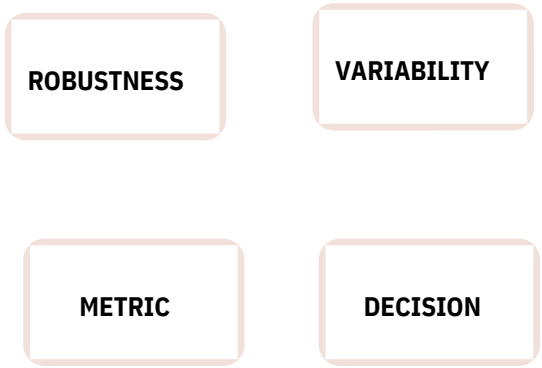
- Metrics should be selected according to the **intended function and operating context** of the system.
- Biological engineering often requires balancing **performance, cost, robustness, safety and sustainability**.
- Trade-offs can be analysed using **multi-objective optimization**, where several criteria are considered simultaneously.
- A useful metric must be **measurable, reproducible and directly relevant to the engineering decision**.

Performance metrics depend on the purpose of the engineered system. In **biomanufacturing**, performance is commonly assessed by **titer, yield, productivity and product quality**. Biomedical systems require metrics such as **sensitivity, specificity, efficacy, biocompatibility and reliability**. In agricultural and environmental applications, relevant indicators may include **stress tolerance, resource-use efficiency, removal efficiency, robustness and long- term stability**.

Robustness and variability

Biological systems are inherently variable. Differences between cells, batches, patients and environments produce distributions of outcomes rather than a single deterministic response. Robustness describes the ability of an engineered system to maintain acceptable performance despite this variability and external disturbances.

- Sources of variability include **genetic differences, stochastic gene expression, environmental fluctuations and measurement uncertainty**.
- Robust systems maintain key outputs within an acceptable range even when operating conditions change.
- **Feedback control, redundancy, buffering and appropriate operating windows** can reduce sensitivity to disturbances.
- Variability is not always harmful; in some biological systems, phenotypic diversity can improve adaptability and resilience.



Conceptual relation (schematic)

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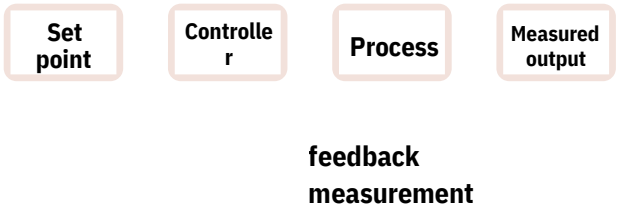
Control and feedback

Feedback control maintains a biological process near a desired operating state by continuously comparing measured output with a target value and adjusting system inputs. In biological engineering, control is essential because living systems are dynamic, variable and sensitive to environmental conditions.

- **Sensors** measure key variables such as pH, temperature, dissolved oxygen, biomass or metabolite concentration.
- **Controllers** compare the measured value with the set point and determine the required corrective action.
- **Actuators** modify inputs such as aeration, agitation, feed rate, heating or reagent addition.
- **Feedback** reduces the effect of disturbances and helps maintain stable, reproducible performance.
- Poorly tuned control can cause **oscillation, overshoot or instability**, especially when measurements are delayed or noisy.



ENGINEERING CONSEQUENCE

A control structure is only as useful as its measurement quality, response time and ability to manipulate the variable that truly limits performance.

Scale matters

A biological system that performs well at laboratory scale may behave very differently after scale-up. Increasing reactor size changes mixing, oxygen transfer, heat removal and concentration gradients, which directly affect cell physiology and process performance.

At larger scales, cells experience **heterogeneous microenvironments** caused by gradients in oxygen, substrate, pH and temperature.

Scale-up **I**therefore requires the preservation of relevant **transport and hydrodynamic conditions**, not simply geometric similarity.

Common scale-up criteria include **power input, mixing time, oxygen transfer capacity and shear conditions**.

Scale-down models reproduce large-scale stresses in smaller systems and help identify which gradients or limitations most strongly affect biological performance.

As system size increases, the characteristic times for **mixing, mass transfer and heat transfer** change. This can create local zones of nutrient limitation, oxygen depletion or pH variation. Cells moving through these zones may alter metabolism, growth rate and product formation. Therefore, successful scale-up requires linking **physical transport phenomena with biological response**.

Application landscape

Biological engineering applies quantitative design principles to living systems across industry, medicine, agriculture and environmental technologies. Although the biological platform differs between applications, the engineering objective remains similar: achieve a defined function with measurable, reproducible and scalable performance.

Biomanufacturing

Uses microorganisms, mammalian cells or cell-free systems to produce **enzymes, recombinant proteins, vaccines, chemicals, fuels and food ingredients**. Key priorities include yield, productivity, product quality and scale-up.

Biomedical engineering

Integrates cells, biomaterials and molecular technologies for **diagnostics, drug delivery, tissue engineering, implants and cell-based therapies**. Performance is evaluated through efficacy, safety, biocompatibility and reliability.

Agricultural biological engineering

Develops **improved crop traits, microbial inoculants, biosensors and biological control systems** to increase productivity, stress tolerance and resource-use efficiency.

Environmental biological engineering

Uses cells and microbial communities for **bioremediation, wastewater treatment, waste valorization, carbon management and resource recovery**, with emphasis on robustness and sustainability.

Case study: recombinant protein production

Goal: produce a recombinant therapeutic protein with defined **activity, purity, yield, reproducibility and manufacturing cost**. Successful production requires coordinated optimization of both the biological expression system and the manufacturing process.

Biological design

Select an appropriate host, expression vector and promoter system.
Optimize gene expression, protein folding and cellular stability.
Reduce metabolic burden, degradation and unwanted by-products.

Process engineering

Control **temperature, pH, dissolved oxygen, nutrient supply and induction conditions**.
Optimize biomass concentration, cultivation time and harvest strategy.
Design downstream processing for **recovery, purification and quality control**.

Key engineering variables: oxygen transfer • feed strategy • growth rate • expression level • recovery • purity

Engineering perspective: High expression alone does not define a successful process. Productivity must be balanced with **protein quality, cell viability, downstream recovery, reproducibility and scalability**.

Sustainability as a design criterion

Sustainability as a design criterion

Sustainability in biological engineering must be treated as a quantitative design criterion rather than an assumed benefit of using biological systems. A bio-based process may operate under mild conditions, yet still have a high environmental burden if it requires intensive aeration, cooling, water use, low-yield feedstocks or complex downstream purification.

Life-cycle assessment (LCA) evaluates impacts across the full process: raw materials, energy and water use, production, emissions, waste, transport and end-of-life.

Key sustainability indicators include **energy demand, water consumption, greenhouse-gas emissions, material efficiency and waste generation**.

Higher biological yield and selectivity can reduce downstream processing requirements and improve overall resource efficiency.

Sustainability must therefore be evaluated together with **performance, cost, scalability and product quality**.

Life-cycle perspective

Feedstock → Production → Separation & purification → Product use → End-of-life / recovery

At each stage, engineers quantify **material inputs, energy demand, emissions and waste generation**. The aim is not only to optimize the biological reaction itself, but to minimize the environmental burden of the complete system.

Safety, ethics and responsibility

Biological engineering can generate major benefits, but engineered organisms, cells and biological products may also create biosafety, biosecurity, ecological and societal risks. Safety and ethical considerations should therefore be integrated into the design process from the earliest stages, rather than treated only as regulatory requirements at the end.

- **Biosafety** focuses on preventing accidental exposure, release or unintended biological effects.
- **Biosecurity** addresses deliberate misuse, unauthorized access and dual-use concerns.
- **Risk assessment** evaluates the **hazard, probability of exposure and potential consequences**, followed by appropriate containment and control measures.
- **Ethical analysis** considers consent, equity, animal welfare, environmental impact, ownership and access to emerging technologies.

Responsible innovation combines **technical safeguards, transparent governance, stakeholder engagement and continuous risk review**.

Safety is not achieved by a single control measure. Effective risk management combines:

Hazard identification → Risk assessment → Risk reduction → Monitoring & review

Risk reduction may include **physical containment, biological containment, fail-safe mechanisms, restricted access, operating procedures and regulatory oversight**.

Data and digital tools

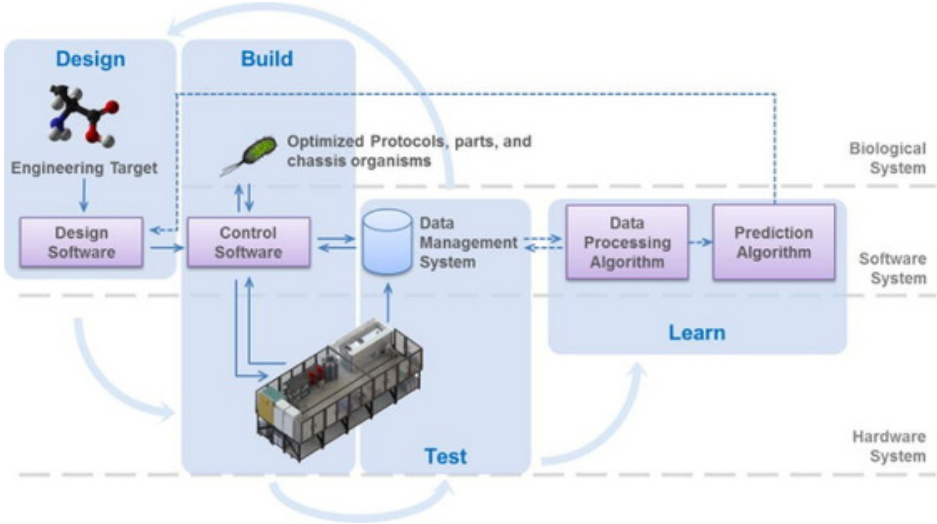
Modern biological engineering increasingly relies on digital tools to transform experimental data into models, predictions and design decisions. Multi-omics, high-throughput experimentation, laboratory automation and computational modelling allow biological systems to be analysed at a scale that would be impossible manually.

Databases and bioinformatics support sequence analysis, annotation, structure prediction and pathway reconstruction. **Omics technologies** generate genome-, transcriptome-, proteome- and metabolome-level data for system characterization.

Machine learning can identify patterns, prioritize designs and predict system behaviour from large datasets.

Automation and high-throughput platforms accelerate experimental testing and improve reproducibility.

Digital tools are most effective when combined with **mechanistic understanding and experimental validation**.



How this course is organized

The course progresses from fundamental concepts of biological engineering to the analysis and design of increasingly complex biological systems. Each stage introduces new engineering tools while building on concepts developed in previous lectures.

Module 1 — Foundations and engineering thinking

Introduces biological systems as engineering objects and develops the core principles of **systems thinking, process boundaries, conceptual modelling, bioreactors, process control and engineering analysis**.

Module 2 — Analysis, performance and design

Extends these concepts to **material and energy flows, metabolism, operating conditions, system performance, design principles, omics technologies and digital tools**.

Learning approach

Lectures establish theoretical concepts, while seminars and independent projects apply them through **case analysis, comparison, modelling and engineering reasoning**. Students progressively learn to move from biological description toward **quantitative analysis and justified design decisions**.

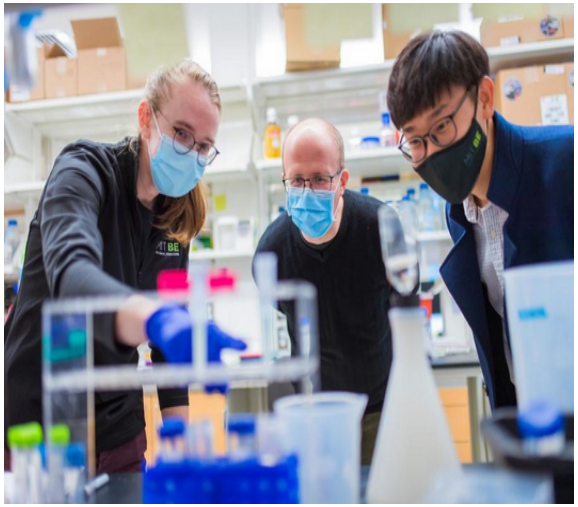
COURSE PROGRESSION

Foundations
Biological systems & engineering thinking
↓
Analysis
Models • flows • performance • constraints
↓
Design
Optimization • control • improvement
↓
Integration
Omics • data • digital tools • applications

What students should learn to ask

Engineering analysis begins by framing the biological system as a problem with a defined purpose, measurable performance and explicit constraints. Before selecting tools or proposing solutions, students should identify what the system is expected to achieve and how success will be evaluated.

- **What is the system purpose?** What function or outcome should be achieved?
- **Where is the system boundary?** Which components and interactions are included in the analysis?
- **What are the critical inputs and outputs?** Which material, energy or information flows determine performance?
- **Which variables can be measured or controlled?** What observations and interventions are technically possible?
- **What limits performance?** Consider biological variability, transport, resources, safety, cost and scale.
- **What assumptions are being made?** How would the conclusions change if those assumptions were incorrect?
- **How will success be judged?** Define quantitative performance criteria before comparing alternatives.



A compact engineering workflow

Biological engineering is an iterative process in which a biological problem is progressively translated into quantitative specifications, analysed using appropriate models, and refined through experimental evidence. The objective is not simply to obtain a working solution, but to develop a system whose performance can be measured, justified and reproduced.

1. Problem definition
Define the biological function, context of use and engineering objective.

2. System specification
Establish system boundaries, measurable performance criteria and relevant biological, physical and operational constraints.

3. Quantitative analysis
Identify critical variables, formulate appropriate models and evaluate parameter sensitivity and uncertainty.

4. Design development
Generate alternative biological or process configurations and compare them against predefined criteria.

5. Verification and validation
Test whether the proposed system satisfies the required performance under relevant operating conditions.

6. Iterative improvement
Use experimental and computational evidence to refine assumptions, update the design and improve robustness, efficiency and reproducibility.

Concept map: biological engineering

BIOLOGICAL SYSTEMS
Genes • proteins • cells • tissues • microbial communities
↓
ENGINEERING PRINCIPLES
System boundaries • mass and energy balances • kinetics • transport • feedback • scale-up
↓
DESIGN & ANALYTICAL TOOLS
Modelling • experimentation • optimization • automation • data analysis
↓
ENGINEERED OUTCOMES
Biomanufacturing • diagnostics • therapeutics • agriculture • environmental technologies

Biological engineering integrates biological knowledge with quantitative analysis and engineering design to create systems whose behaviour can be measured, predicted, controlled and improved. The field connects multiple levels of organization—from molecules and cells to bioprocesses and ecosystems—through a common engineering logic.

- **Biology provides the mechanisms and functional components**, while engineering defines specifications, constraints and performance criteria.
- Quantitative models connect molecular and cellular behaviour with **system-level performance**.
- Experimental data are used to test assumptions, identify limitations and guide iterative improvement.
- Successful biological engineering requires balancing **performance, robustness, safety, scalability and sustainability**.

Common misconceptions

Biological engineering is often misunderstood because biological origin is sometimes assumed to guarantee safety, sustainability or technical simplicity. In practice, these properties must be demonstrated quantitatively and under realistic operating conditions.

Misconception 1 — "Biological means inherently safe or sustainable."
Reality: Safety and sustainability depend on the complete system, including feedstocks, energy demand, containment, waste generation, downstream processing and end-of-life impacts.

Misconception 2 — "Engineering requires complete mechanistic understanding."
Reality: Useful designs can be developed with incomplete knowledge when experiments, quantitative models and iterative validation are combined appropriately.

Misconception 3 — "More data automatically lead to better decisions."
Reality: Data are valuable only when variables are well defined, uncertainty is considered and measurements are interpreted within the correct biological context.

Misconception 4 — "A successful laboratory prototype is ready for application."
Reality: Translation requires additional evidence of **robustness, scalability, manufacturability, safety, reproducibility and regulatory compliance**.

Common assumption	Engineering reality
Biological = safe	Safety must be demo
Bio-based = sustainable	Full life cycle must b assessed
More data = better design	Data quality and con matter
Lab success = scalable process	Scale-up introduces n constraints

Mini-case: choose the boundary

Mini-case: choose the boundary

The choice of system boundary determines which processes are included in the analysis and which are treated as external conditions. In biological engineering, the "correct" boundary is not universal; it must be selected according to the decision that needs to be made. For a **microbial biosensor**, a narrow boundary may include only the engineered cell, sensing mechanism and reporter response. This is sufficient for studying genetic circuit performance, sensitivity or response time.

A broader boundary may also include **sample collection and preparation, transport, signal detection, user interpretation, containment and waste disposal**. This wider perspective is required when evaluating real-world performance, safety and implementation.

Narrow boundary	Expanded boundary
Engineered cell	Sample preparation
Sensing circuit	Transport and storage
Reporter signal	Signal readout
Cellular response	User interpretation
Circuit performance	Containment and disposal

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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