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

INTRODUCTION TO BIOLOGICAL ENGINEERING

LECTURE 3.
ENGINEERING THINKING IN BIOLOGICAL SYSTEMS: INPUTS, PROCESSES, OUTPUTS, AND SYSTEM BOUNDARIES

PhD., Acting Associate
Professor Doktyrbay Gulina

Lecture Plan

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

1. Engineering problem formulation
2. System boundaries
3. Input–Process–Output models
4. State variables and parameters
5. Mass balances
6. Rates and kinetics
7. Transport and constraints
8. Feedback and disturbances
9. Uncertainty and sensitivity
10. Biotechnology case studies

Learning Outcomes

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

LO1 Formulate a biological problem using an engineering systems framework.

LO2 Define appropriate system boundaries for different questions.

LO3 Construct input–process–output representations of biotechnological processes.

LO4 Distinguish state variables, parameters and disturbances.

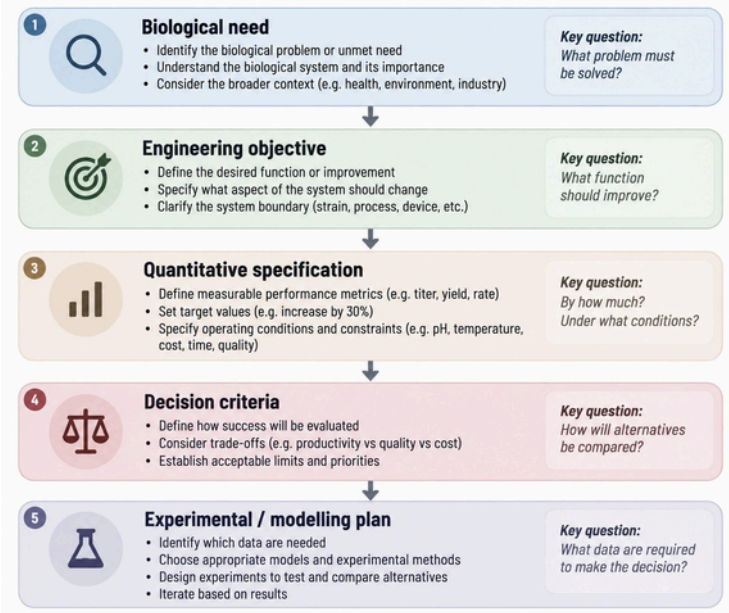
LO5 Apply basic conservation and rate concepts conceptually.

LO6 Use sensitivity and uncertainty thinking to prioritize measurements and design decisions.

Engineering thinking begins with the question

A biological problem becomes an engineering problem when the desired function, operating context, measurable performance and decision criteria are defined explicitly. Good problem formulation determines which variables should be measured, which models are appropriate and which experiments are actually informative.

- A broad goal such as **“increase production”** is insufficient because it does not define the magnitude of improvement, operating constraints or acceptable trade-offs.
- A stronger engineering specification might be: **“increase product titer by 30% while maintaining product quality and without increasing cycle time.”**
- The formulation should identify the **system boundary, controllable variables, constraints and quantitative performance metrics**.
- Poorly framed questions can lead to technically correct analyses that nevertheless address the wrong engineering objective.



Define the system boundary

A system boundary defines what is included in the analysis and what is treated as part of the external environment. Boundary selection determines which variables are considered inputs, outputs, internal states and disturbances, and therefore directly affects the conclusions that can be drawn from the model.

- Boundaries may be **spatial, temporal, organizational or conceptual**, depending on the engineering question.
- A **cell-level boundary** may focus on metabolism, gene regulation and intracellular transport while treating reactor conditions as external inputs.
- A **bioreactor-level boundary** includes cells, medium, gas transfer, mixing and operating conditions as part of the system.
- A **process-level boundary** may extend further to upstream preparation, downstream purification, utilities and waste streams.
- The boundary should be **as simple as possible, but sufficiently broad to include the mechanisms that materially influence the decision**.

Cell boundary
Metabolism • gene regulation • transport
↓ wider boundary
Bioreactor boundary
Cells • medium • mixing • O_2 transfer • pH ↓ wider boundary
Process boundary
Upstream • reactor • downstream • waste

Input–Process–Output model

The Input–Process–Output (IPO) model is a simple systems framework used to describe how a biological system receives resources or information, transforms them through internal processes, and generates measurable outputs. Although highly simplified, it is useful as an initial engineering representation because it makes the system structure and key assumptions explicit.

- **Inputs** may include substrates, gases, nutrients, inoculum, signals and operating conditions.
- **Processes** include transport, metabolism, growth, regulation and biochemical conversion.
- **Outputs** include biomass, target product, by-products, gases, heat and other measurable responses.
- The IPO model helps identify **missing variables, relevant system boundaries and candidate performance metrics** before more detailed mathematical modelling is introduced.
- Its main limitation is that it can hide internal feedback, accumulation and dynamic interactions if the system is represented too simply.

Engineering perspective

For a fermentation process, glucose, oxygen and inoculum may be treated as inputs; microbial growth and metabolism as the transformation; and product, biomass, CO_2 and heat as outputs. The usefulness of the model depends on whether the chosen level of detail is sufficient for the engineering decision.

Stocks, flows and state variables

Dynamic biological systems are described by variables that change with time and by flows that determine how rapidly those variables change. State variables represent the current condition of the system and provide the minimum information required to predict its future behaviour, given a defined model.

- **Stocks** are quantities that can accumulate within the system, such as biomass, substrate, product or intracellular metabolites.
- **Flows** increase or decrease these stocks through processes such as feeding, uptake, growth, secretion, oxygen transfer and harvest.
- **State variables** describe the instantaneous condition of the system, for example biomass concentration, substrate concentration or dissolved oxygen.
- **Parameters** are model properties or coefficients that are usually treated as constant over a defined experiment, such as maximum specific growth rate, yield coefficient or transport constant.
- Confusing states with parameters can lead to incorrect model structure, parameter estimation and interpretation of experimental data.

Substrate stock

↓ *uptake rate*

Biomass stock

↓ *growth / formation rate*

Product stock

Conservation of mass

Conservation of mass is one of the fundamental principles of bioprocess analysis. Matter may enter, leave, accumulate or be transformed within a system, but total mass is conserved. This provides the basis for material balances around cells, bioreactors and complete production processes.

The general balance for any conserved quantity is:

Accumulation = In – Out + Generation – Consumption

- For **total mass**, generation and consumption terms are zero because chemical and biological reactions redistribute matter rather than create or destroy it.
- For an individual **chemical species**, generation and consumption arise from reactions such as substrate uptake, biomass formation or product synthesis.
- At **steady state**, accumulation is zero, so inputs must balance outputs together with reaction terms.
- For dynamic systems, a non-zero accumulation term describes how the amount or concentration changes with time.
- Mass balances are useful even when detailed biological mechanisms are unknown because they provide a quantitative **consistency check on measurements and model assumptions**.

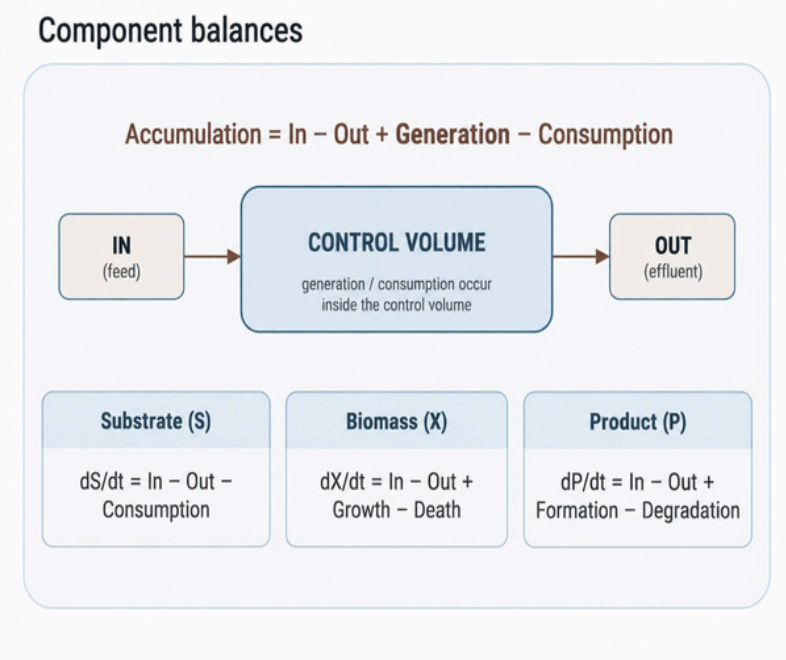
For substrate : **Accumulation of S = S in – S out – biological consumption**

For biomass : **Accumulation of X = X in – X out + biological growth**

Component balances

A component balance applies the general conservation equation to a specific chemical or biological species. It tracks how that component enters the system, leaves it, accumulates, and is generated or consumed by biological reactions.

- **Substrate balance:** substrate enters with the feed, may leave in the effluent, and is consumed by cells for growth, maintenance and product formation.
- **Biomass balance:** biomass changes through cell growth, inflow or harvest, and may decrease through death or lysis.
- **Product balance:** product may be formed intracellularly or extracellularly, accumulate in the system, leave with the outlet stream, or be lost through degradation.
- **Gas balances**, particularly for O_2 and CO_2, are useful for linking cellular metabolism with aeration, respiration and mass-transfer performance.
- The appropriate component balance depends on the **engineering question, system boundary and available measurements**.



Rates and kinetics

Rates quantify how rapidly biological or physicochemical processes occur, whereas kinetic models describe how these rates depend on the state of the system. In biological engineering, kinetics links measurable variables such as substrate concentration, biomass, temperature or oxygen availability to dynamic system behaviour.

- Important rates include **specific growth rate, substrate uptake rate, product formation rate and mass-transfer rate**.
- Kinetic expressions convert biological observations into quantitative relationships that can be incorporated into **mass balances and dynamic models**.
- For microbial growth, the **Monod model** is commonly used to describe the dependence of specific growth rate on a limiting substrate:

$$\mu = \mu_{max} \cdot S / (K_S + S)$$

where **μ** is the specific growth rate, **μmax** is the maximum specific growth rate, **S** is substrate concentration, and **KS** is the half-saturation constant.

- At low substrate concentration, growth is strongly substrate-limited; as **S increases, μ approaches μmax** and additional substrate produces progressively smaller increases in growth rate.
- Kinetic parameters are **condition-dependent** and should not be extrapolated outside the experimental range in which they were estimated.

Stoichiometry and yields

Stoichiometry describes the quantitative relationships between substrates, biomass, products and by-products in a biological conversion. Yield coefficients translate these relationships into measurable indicators of conversion efficiency and are therefore central to bioprocess analysis and design.

- A **stoichiometric equation** provides a mass-consistent representation of how substrates and other reactants are converted into biomass, products and metabolic by-products.
- **Biomass yield on substrate** describes how efficiently consumed substrate is converted into new cells:
- $\mathbf{Y/_{xs} = \Delta X / -\Delta S}$
- **Product yield on substrate** quantifies conversion of substrate into the desired product:
- $\mathbf{Y_p/_s = \Delta P / -\Delta S}$
- Observed yields are affected by **maintenance energy requirements, by-product formation, oxygen availability and physiological state**.
- Experimental yields should therefore be distinguished from the **theoretical maximum yield** predicted from stoichiometry or metabolic constraints.

BIOMASS YIELD

$\mathbf{Y/_{xs}}$ — biomass formed per substrate consumed

PRODUCT YIELD

$\mathbf{Y_p/_s}$ — product formed per substrate consumed

PROCESS INTERPRETATION

High rate does not necessarily mean high yield: a process may be **fast but inefficient**, or efficient but comparatively slow.

Time scales

Biological systems contain processes that operate over widely different characteristic time scales. Recognizing these differences is essential for model formulation, experimental design and process control because fast and slow dynamics often influence different aspects of system behaviour.

Fast molecular processes such as ligand binding, enzyme reactions and some signalling events may occur within milliseconds to seconds.

Regulatory processes, including transcriptional responses and metabolic adjustment, generally develop over seconds to minutes.

Cellular processes such as protein synthesis, growth and division occur over minutes to hours.

Population-level changes, including shifts in community composition and evolutionary adaptation, may require many generations.

A model should include only those dynamics that are relevant to the **observation window and engineering decision**.

Molecular interactions
enzyme binding • receptor activation → **Regulation**
signalling • metabolic response • gene expression
→ **Cellular dynamics**
protein synthesis • growth • division → **Population dynamics**
community shifts • adaptation • evolution

Transport versus reaction

Observed biological performance is determined by the interaction between transport processes and intrinsic reaction kinetics. A system may therefore be limited either by the rate at which substrates, oxygen, heat or products are transported, or by the biochemical capacity of the cells or catalyst itself.

Transport limitation occurs when substrate or oxygen delivery is slower than cellular consumption. In this regime, increasing enzyme concentration or cellular capacity may produce little improvement because the reactant cannot reach the reaction zone sufficiently fast.

Reaction limitation occurs when transport is sufficiently rapid but the biochemical conversion itself is slow. Under these conditions, increasing enzyme activity, biomass concentration or catalytic capacity can increase overall performance. Transport limitations may arise from **diffusion through membranes or matrices, external mass-transfer resistance, poor mixing or insufficient oxygen transfer**. Reaction limitations are associated with **enzyme kinetics, metabolic capacity, substrate affinity, regulation and available catalytic machinery**.

The dominant limitation can change with **scale, cell density, substrate concentration and operating conditions**, so laboratory behaviour may not predict large-scale performance directly.

Disturbances and noise

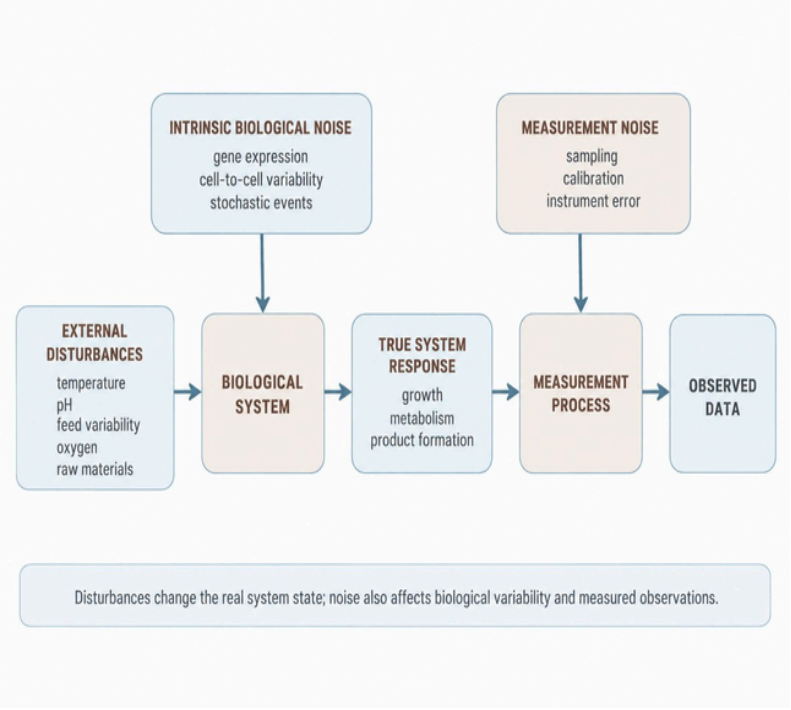
Engineered biological systems operate under unavoidable variability. Disturbances alter the true state of the system, whereas noise introduces variability into biological behaviour or into the way that behaviour is measured. Distinguishing these effects is essential for reliable modelling, control and experimental interpretation.

External disturbances include fluctuations in temperature, pH, feed composition, oxygen transfer, raw-material properties and environmental conditions.

Intrinsic biological noise arises from stochastic gene expression, molecular interactions, cell-cycle differences and population heterogeneity.

Measurement noise originates from sampling, instrument precision, calibration, background signal and analytical variability.

Disturbances can change the actual biological state, while measurement noise may change only the **observed signal**. Robust engineering therefore requires performance to remain acceptable across a realistic range of disturbances and biological variability.



Feedback and control variables

Feedback control maintains a biological process near a desired operating condition by continuously measuring system performance, comparing it with a target value and adjusting an appropriate manipulated variable. In bioprocesses, this is essential because biological systems respond dynamically to environmental and process disturbances.

- A **controlled variable** is the quantity that should remain near a desired set point, for example **pH, dissolved oxygen, temperature or biomass concentration**.
- A **manipulated variable** is deliberately adjusted to influence the controlled variable, such as **feed rate, agitation speed, gas flow, acid/base addition or heating/cooling duty**.
- A **sensor** measures the current process state, while the **controller** calculates the required correction and the **actuator** implements that action.
- Effective feedback depends on **measurement accuracy, response time, process dynamics and actuator capacity**.
- Delays, sensor noise or inappropriate controller tuning can produce **oscillation, overshoot or instability** rather than improved control.

Controlled variable: dissolved oxygen, DO
Sensor: DO probe
Set point: desired DO level
Controller: compares measured DO with set point
Manipulated variables: agitation speed / airflow / oxygen enrichment
Disturbance: increased cellular oxygen demand

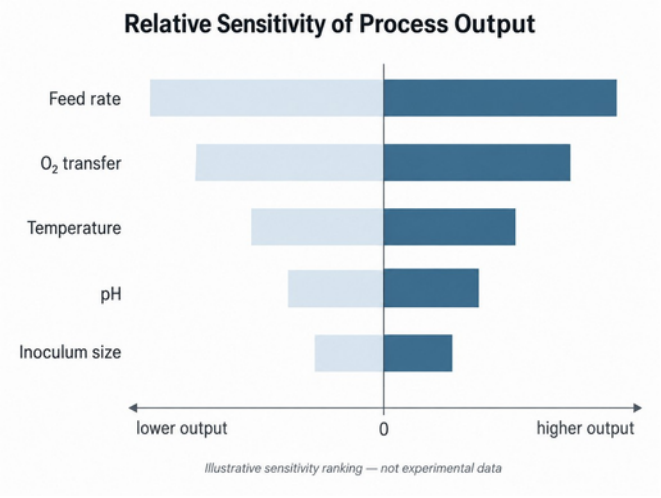
Engineering perspective

A feedback loop is effective only when the manipulated variable can influence the controlled variable rapidly enough relative to the process dynamics. The selected control strategy should therefore reflect both the biology of the system and the physical limitations of sensors and actuators.

Sensitivity analysis

Sensitivity analysis quantifies how variation in model inputs or parameters propagates to variation in system outputs. It is used to identify which factors most strongly influence performance, which parameters require accurate estimation, and where experimental or control effort should be concentrated.

- A **high-sensitivity parameter** produces a comparatively large change in the model output when it is perturbed; such parameters require accurate measurement, calibration and tighter control.
- A **low-sensitivity parameter** has limited influence within the studied range and may sometimes be fixed or simplified without substantially affecting model predictions.
- **Local sensitivity analysis** evaluates the response to small changes around a nominal operating point and is useful for linearized or well-characterized systems.
- **Global sensitivity analysis** explores variation across a wider parameter space and can reveal nonlinear effects, parameter interactions and context-dependent importance.
- Sensitivity rankings depend on the **selected output, operating region and parameter range**; a parameter that is unimportant for biomass may still be critical for product quality or process stability.



Uncertainty propagation

Uncertainty propagation evaluates how uncertainty in model inputs, parameters and measurements affects the uncertainty of predicted system behaviour. In biological engineering, this is essential because biological variability and imperfect parameter estimates can make a single deterministic prediction misleadingly precise.

Sources of uncertainty include **measurement error, parameter estimation, biological variability, uncertain initial conditions and model assumptions**.

When uncertain inputs are propagated through a nonlinear model, the resulting output may show a **broad or asymmetric distribution rather than a single value**.

Scenario analysis and confidence intervals provide simple representations of uncertainty, while **Monte Carlo simulation** propagates probability distributions through the model by repeated sampling.

Parameters with both **high uncertainty and high sensitivity** usually contribute most strongly to predictive uncertainty and therefore deserve additional measurement or experimental effort.

Engineering decisions should consider whether the **ranking of design alternatives remains unchanged across the plausible uncertainty range**.

Causal versus correlative thinking

Correlation describes an association between variables, whereas causation implies that changing one variable produces a change in another through a defined mechanism. In biological engineering, this distinction is critical because design and control decisions require interventions, not merely predictions.

- Two variables may correlate because they share a **common underlying cause**, respond to the same environmental condition, or change together over time.
- A predictive relationship does not necessarily identify a variable that can be successfully manipulated.
- **Causal hypotheses** should specify the direction of influence and the biological mechanism connecting intervention to response.
- Controlled perturbation experiments, mechanistic models and appropriate controls strengthen causal inference.
- Data-driven models can provide accurate prediction while still failing to identify the **true driver of system behaviour**.

CORRELATION

Variable A / Variable B

Observation:

A and B change together.

Limitation:

Direction and mechanism are unknown.

Possible explanation:

A ← **Hidden factor**

C → B

CAUSATION

Intervention on A

↓

Biological mechanism

↓

Change in B

Evidence:

Manipulating A reproducibly changes B under controlled conditions.

Failure-mode thinking

Failure-mode thinking asks not only how an engineered biological system is expected to function, but also how it may fail, why that failure may occur, and what consequences follow. This approach supports more robust design by identifying vulnerabilities before they become process, quality or safety problems.

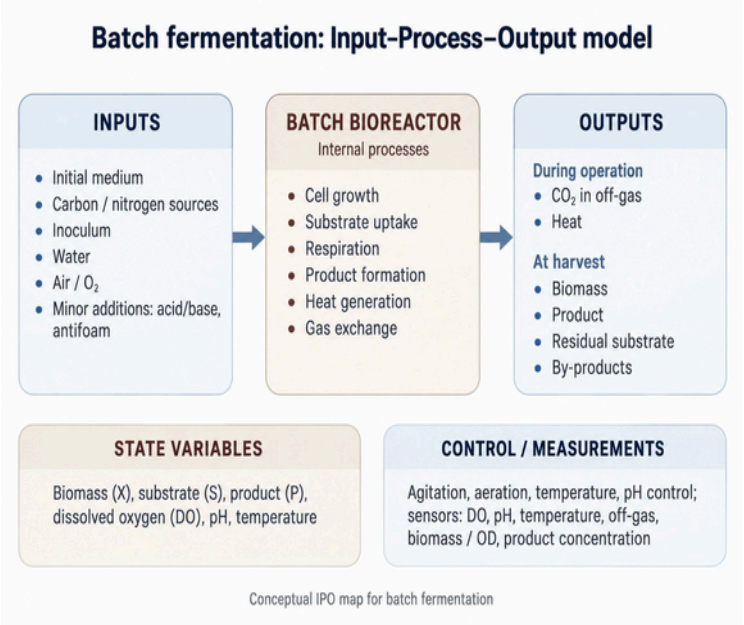
- Failure modes may arise from **biological, process, analytical or hardware causes**, including contamination, plasmid loss, oxygen limitation, sensor drift, foaming, overheating and product degradation.
- Each failure should be evaluated in terms of its **cause, observable effect and impact on system performance**.
- Risk assessment commonly considers **severity, likelihood of occurrence and detectability**, allowing failure modes to be prioritized.
- High-priority risks should be addressed through **preventive design, monitoring, control strategies, redundancy or predefined corrective actions**.
- Failure-mode analysis is especially important before **scale-up**, because larger systems introduce gradients, delays and operational complexity that may not appear at laboratory scale.

Failure mode	Possible cause	Effect	Mitigation
Oxygen limitation	insufficient kLa / high biomass	lower growth and productivity	aeration, agitation, scale-down testing
Plasmid loss	high metabolic burden	reduced expression	genomic integration, selection strategy
Sensor drift	calibration error	incorrect control action	calibration, redundancy

Case study: batch fermentation IPO

Batch fermentation is a closed liquid-phase cultivation mode in which the principal liquid nutrients are supplied before inoculation and no continuous liquid feed or harvest occurs during the main cultivation period. The system therefore evolves dynamically as substrate is consumed, biomass accumulates and product is formed.

- **Initial inputs** include culture medium, carbon and nitrogen sources, inoculum, water and process gases.
- During operation, **oxygen may be continuously supplied** and pH-control agents, antifoam or other minor additions may be introduced, even though the main liquid feed remains closed.
- Internal processes include **cell growth, substrate uptake, respiration, product formation, heat generation and gas exchange**.
- Dynamic state variables such as **biomass, substrate, dissolved oxygen and product concentration** change throughout the batch.
- Major outputs during cultivation include **CO_2-containing off-gas and heat**, while the final harvest contains biomass, product, residual substrate and soluble by-products.



Conceptual IPO map for batch fermentation

Case study: fed-batch boundary choice

In fed-batch cultivation, the definition of the system boundary determines which variables are treated as internal states, external inputs or disturbances. Because reactor volume and substrate availability change continuously during feeding, boundary choice directly affects the structure of the model and the engineering conclusions that can be drawn.

At the **reactor scale**, feed flow is an external input, while biomass, substrate, product concentration and liquid volume are internal state variables.

Unlike a simple batch process, fed-batch operation introduces a **time-dependent volume**, so dilution and accumulation terms must be included explicitly in material balances.

At the **cell scale**, extracellular substrate, dissolved oxygen and pH belong to the surrounding environment rather than to the intracellular state.

A model designed for **feed optimization** may require substrate concentration, reactor volume, biomass and specific uptake rate, whereas a model of intracellular regulation may exclude most reactor-scale variables.

The appropriate boundary is therefore determined by the **engineering question**, not by a fixed physical definition of the system.

Feed optimization model
Boundary includes: reactor volume, biomass, substrate, feed rate, oxygen transfer

Cell physiology model
Boundary includes: intracellular metabolites, enzymes, regulatory states

Process-scale model
Boundary may also include: feed preparation, off-gas, harvest and downstream interfaces

Engineering perspective

A boundary that is too narrow may omit the variable that actually limits performance, while an unnecessarily broad boundary adds complexity without improving the decision.

Case study: biosensor system

A biosensor converts a biological or chemical recognition event into a measurable signal. Its engineering performance depends not only on the sensing element itself, but on the entire chain from sample acquisition to signal interpretation.

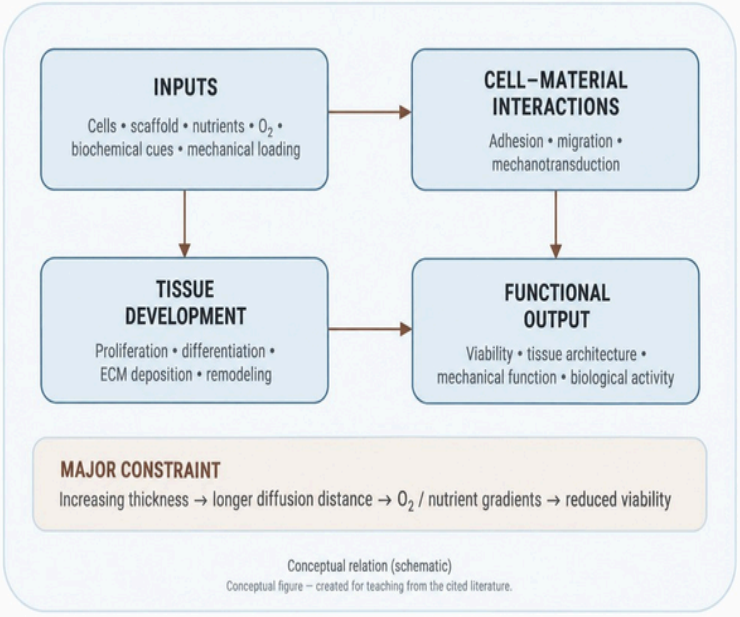
- A complete biosensor system includes **sample collection and preparation, analyte transport, molecular recognition, signal transduction, amplification, processing and readout**.
- The **recognition element** may be an enzyme, antibody, nucleic acid, receptor or engineered cell, while the **transducer** converts the biological interaction into an optical, electrical or mechanical signal.
- System performance is commonly evaluated using **sensitivity, specificity, limit of detection, response time, dynamic range, reproducibility and stability**.
- High performance of an isolated sensing component does not guarantee high performance of the complete device; losses may arise from **sample matrix effects, transport limitations, nonspecific binding, signal drift or user-dependent interpretation**.
- The appropriate system boundary therefore depends on whether the engineering question concerns the **molecular sensor, integrated device or complete diagnostic workflow**.

Analyte binding
↓
Optical / electrical signal
↓
Signal amplification & filtering
↓
Quantitative result / diagnostic decision

Case study: tissue-engineered construct

A tissue-engineered construct is a coupled biological–material system in which cells interact with a scaffold and their surrounding biochemical and mechanical environment to form functional tissue. Its performance therefore depends on both cellular behaviour and material design.

- **Inputs** include cells, scaffold material, nutrients, oxygen, growth factors and mechanical stimulation.
- Internal processes include **cell adhesion, proliferation, migration, differentiation, extracellular-matrix deposition and scaffold degradation**.
- Scaffold properties such as **stiffness, porosity, architecture and degradation rate** influence cell behaviour and tissue organization.
- As construct thickness increases, **oxygen and nutrient transport may become limiting**, leading to spatial gradients,
- reduced viability or heterogeneous tissue formation.
- Functional performance should therefore be evaluated not only by cell survival, but also by **tissue structure, mechanical properties, metabolic activity and integration potential**.



From qualitative map to model

Mathematical modelling should begin with a qualitative representation of the system rather than with equations. The first objective is to identify the relevant system boundary, state variables, dominant interactions and measurable outputs before introducing quantitative relationships.

- Begin with a **conceptual or block diagram** that identifies inputs, transformations, outputs and the system boundary.
- Define the **state variables** that describe the condition of the system, such as biomass, substrate, product concentration or dissolved oxygen.
- Add the dominant **flows and interactions**, then apply conservation relationships to determine how the states change over time.
- Introduce **kinetic expressions** only for mechanisms that materially influence the prediction or engineering decision.
- Estimate parameters from experimental data and evaluate whether the model can reproduce observations within acceptable uncertainty.
- Model complexity should increase only when the simpler representation is no longer sufficient for the intended purpose.

1. QUALITATIVE MAP
Components • inputs • outputs • interactions
↓
2. SYSTEM BOUNDARY & STATES
What is inside? What accumulates?
↓
3. BALANCE EQUATIONS
Mass / energy conservation
↓
4. KINETIC RELATIONS
Rates as functions of states and parameters
↓
5. PARAMETER ESTIMATION
Experimental data → model parameters
↓
6. VALIDATION & PREDICTION
Compare with data → refine → use for decision

Choosing model complexity

Model complexity should be determined by the engineering question, the available data and the level of predictive accuracy required. A more detailed model is not automatically a better model: each additional state, parameter or mechanism should provide measurable value for interpretation or decision-making.

- A **conceptual model** may be sufficient for defining system structure, communicating assumptions and generating hypotheses.
- **Steady-state or algebraic models** are useful when the objective is to estimate yields, capacities or average operating conditions.
- **Dynamic models** are required when transient behaviour, accumulation, feedback or time-dependent control is important.
- **Mechanistic models** improve interpretability by representing biological or physical processes explicitly, but usually require more parameters and experimental information.
- **Empirical or data-driven models** may predict accurately when sufficient data are available, even if the underlying mechanism is only partially known.

Excessive complexity can reduce parameter identifiability, increase uncertainty and make validation more difficult.

CONCEPTUAL MODEL
Components • interactions • hypotheses
↓ increasing detail
STEADY-STATE MODEL
Balances • yields • capacities
↓
DYNAMIC MODEL
State variables • rates • transients
↓
MECHANISTIC MODEL
Explicit biological / physical mechanisms
↓
HIGH-DIMENSIONAL MODEL
Networks • omics • multi-scale interactions

Documentation and reproducibility

Reproducibility requires that another researcher can understand how a result was obtained, repeat the analysis and trace every important assumption, parameter and transformation applied to the data. Documentation is therefore part of the engineering workflow rather than a final reporting step.

- Every analysis should clearly define the **system boundary, variables, units, assumptions, initial conditions and parameter sources**.
- Experimental records should distinguish **measured, calculated, estimated and assumed quantities**.
- Data-processing steps such as normalization, filtering, exclusion criteria and statistical transformations should be documented explicitly.
- Models and calculations should be **version-controlled**, with changes to equations, parameters and code traceable over time.
- Figures and tables should include **units, legends, sample size and sufficient methodological context** for independent interpretation.
- Reproducibility also depends on preserving the connection between **raw data, processed data, model inputs and reported conclusions**.

RAW DATA
Measurements • metadata • experimental conditions
↓
DOCUMENTATION
Units • protocols • assumptions • parameter sources
↓
PROCESSING & MODEL
Code • equations • filtering • calculations
↓
RESULTS
Figures • tables • predictions
↓
REPRODUCTION / VERIFICATION
Can another researcher obtain the same result?

What makes an analysis useful?

A useful engineering analysis does more than describe a biological system. It identifies the variables that control performance, quantifies relevant relationships, makes assumptions explicit and provides information that can support a real design or operating decision.

- The analysis should be **quantitatively consistent** with conservation laws, units and available measurements.
- Assumptions, system boundaries, parameter sources and model limitations should be **explicit and traceable**.
- It should identify the **dominant variables, constraints and failure modes** rather than include every known biological detail.
- Predictions should include **uncertainty and sensitivity**, especially when alternative designs give similar nominal performance.
- The level of model complexity should be appropriate to the decision: additional detail is useful only if it changes interpretation, prediction or confidence.
- Most importantly, the analysis should lead to an **actionable conclusion**—what should be measured, changed, controlled or tested next.

Take-home system template

Any biological engineering problem can be structured using the same systems framework. The purpose is to move from a descriptive biological picture to a quantitative representation that supports measurement, modelling and design decisions.

- **Purpose:** What function should the system perform, and how is success defined?
- **Boundary:** What is included in the system, and what is treated as the external environment? **Inputs:** Which materials, signals, energy sources or operating conditions enter the system?
- **State variables:** Which quantities describe the current condition of the system and may change with time?
- **Transformations:** Which biological, chemical or physical processes convert inputs into outputs?
- **Outputs:** Which products, signals, waste streams or performance measures leave or accumulate?
- **Disturbances and constraints:** What external variations or intrinsic limitations can change performance?
- **Metrics:** Which quantitative variables will be used to evaluate whether the system meets its objective?

PHYSICAL LAWS

Which relationships are governed by **mass or energy conservation**?

SYSTEM DYNAMICS

Which processes require **kinetics, transport or feedback** to describe their behaviour?

ENGINEERING ACTION

What can be **measured, manipulated, controlled or redesigned**?

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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