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

INTRODUCTION TO BIOLOGICAL ENGINEERING

LECTURE 10.
MATERIAL AND ENERGY FLOWS IN BIOLOGICAL ENGINEERING

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Lecture Plan

1. Why flows matter
2. Material balances
3. Stoichiometry and yields
4. Biomass and substrate balances
5. Gas balances
6. Energy balances
7. Heat generation and removal
8. Flow diagrams
9. Resource efficiency
10. Fermentation case study

Learning Outcomes

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

LO1 Explain material and energy flow concepts in biological engineering.

LO2 Apply the general material-balance equation conceptually to bioprocesses.

LO3 Interpret stoichiometry, yields and conversion efficiency.

LO4 Describe oxygen, carbon dioxide and heat flows in aerobic cultivation.

LO5 Construct a simplified flow diagram for a fermentation process.

LO6 Use flow analysis to identify resource losses and engineering constraints.

Why track flows?

Biological systems transform matter and energy; engineering analysis requires knowing where resources enter, accumulate, transform and leave. Flow analysis provides a **physical consistency check** for biological processes by accounting for material and energy entering and leaving the system.

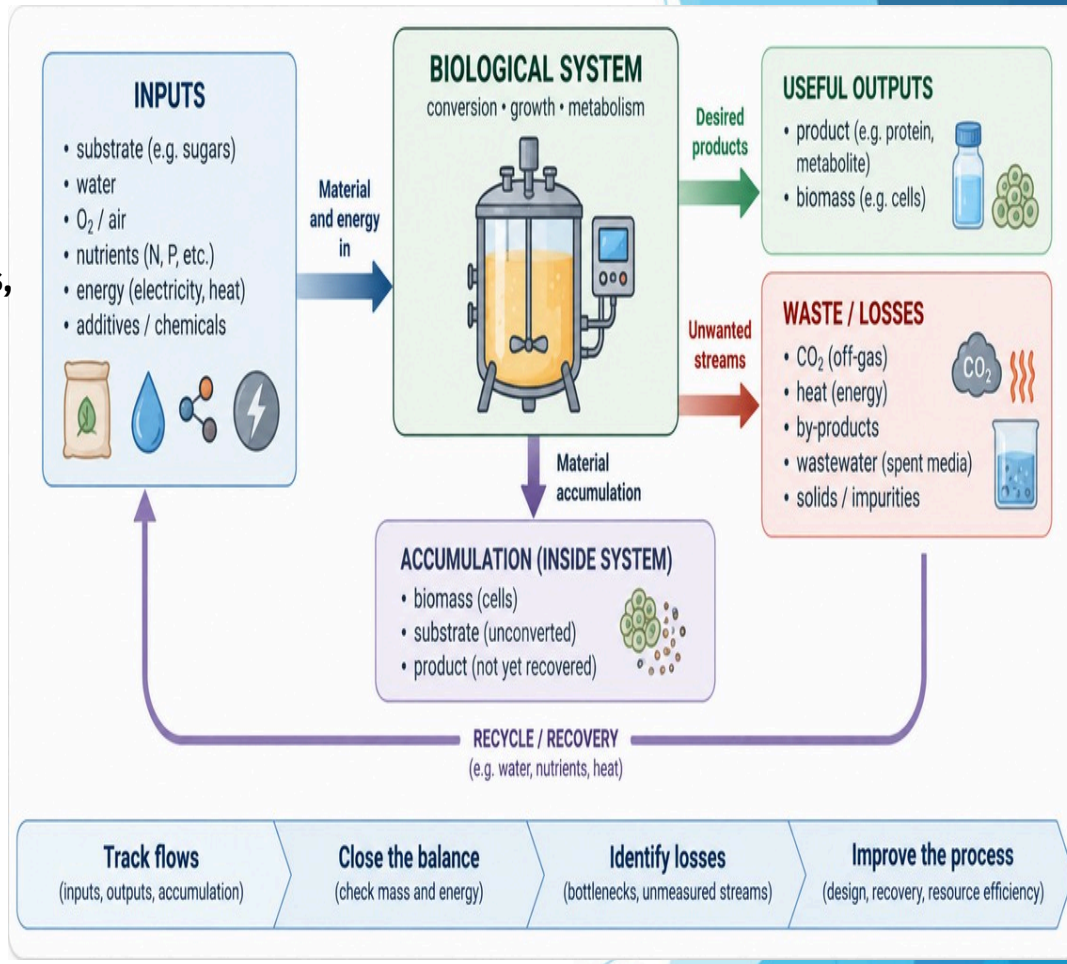
It helps identify **hidden losses, unmeasured streams, accumulation and process bottlenecks** before detailed kinetic modelling is available.

Quantifying flows supports decisions about **feed rate, reactor capacity, oxygen demand, utility use and downstream processing**.

Comparing useful output with waste streams helps evaluate **yield, recovery, resource efficiency and environmental burden**.

If the balance does not close, the discrepancy may indicate an **incorrect assumption, missing stream, measurement error or unexpected accumulation**.

Even a simple flow map therefore provides a foundation for later **mass balances, energy balances and process optimization**.



The general material balance

Accumulation = In - Out + Generation - Consumption Balances enforce conservation and expose missing information.

In and **Out** describe material crossing the system boundary.

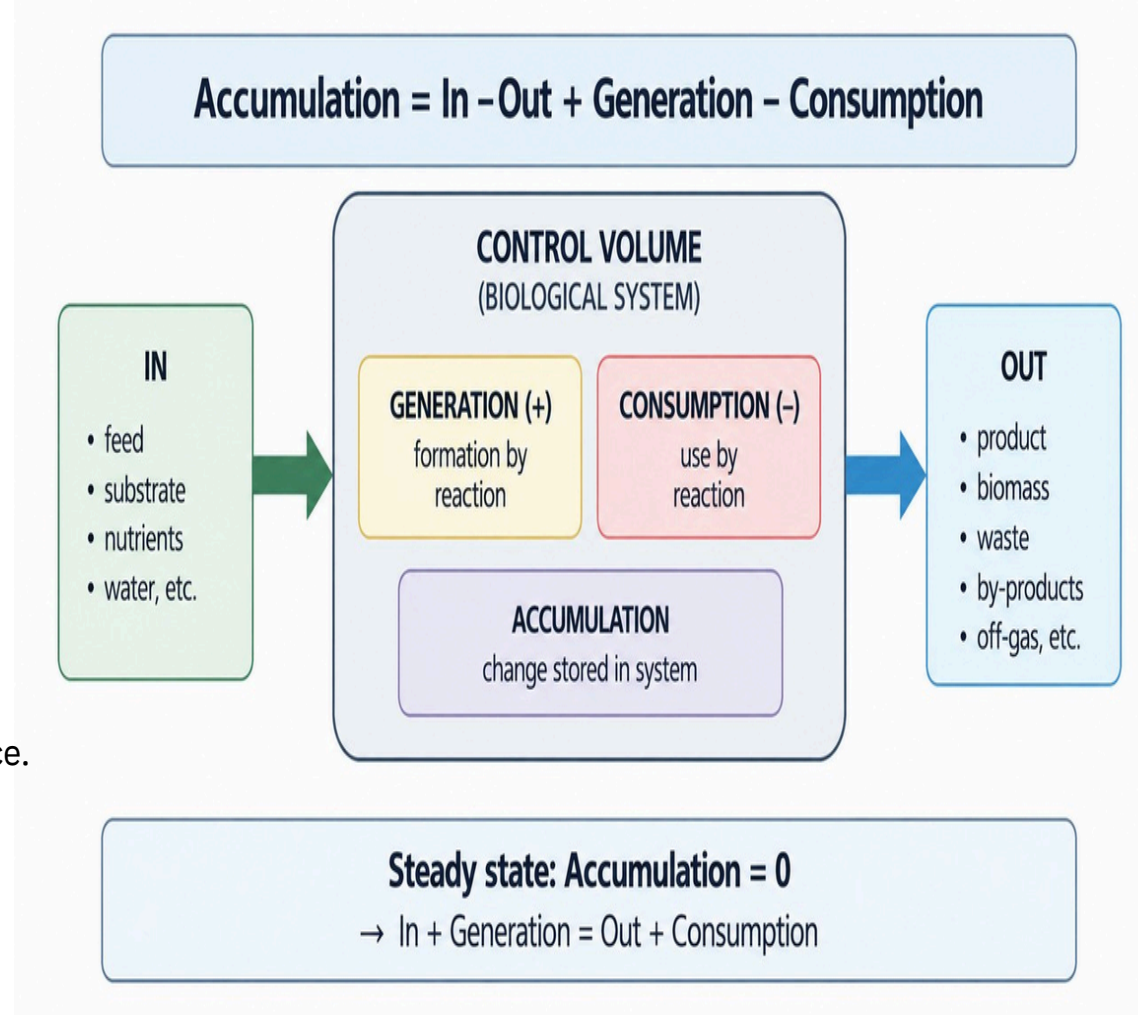
Generation and **consumption** occur inside the control volume because of chemical or biological transformations.

Accumulation represents the change in the amount of the component stored inside the system over time.

The balance must be written for a clearly defined **component, system boundary and time interval**.

At **steady state**, accumulation is zero, so input, output and reaction terms must balance.

For **total mass**, matter is conserved; individual components may be generated or consumed, but total mass is not created or destroyed.



Choosing the basis

Balances can be expressed per batch, per hour, per liter reactor or per kilogram product.

A material balance may be expressed **per batch, per unit time, per reactor volume, per kilogram of substrate or per kilogram of final product**.

The selected basis should match the **engineering question and process mode**.

Batch basis is convenient for recipes, total material requirements and batch yields.

Time basis is appropriate for continuous processes, flow rates and utility demand.

Mass- or volume-normalized bases are useful for comparing yield, productivity and resource efficiency between processes of different scales.

Once the basis is selected, **all inputs, outputs, inventories and calculated quantities must be converted to the same reference basis**.

Aspect	Engineering meaning
Per batch	Useful for recipes and batch totals.
Per hour	Useful for continuous rates and utilities.
Per kg substrate	Useful for yield and efficiency comparisons.
Per L reactor	Useful for scale and equipment utilization.

Stoichiometry

Stoichiometric coefficients specify how reactants and products are related in a balanced reaction representation.

Stoichiometric coefficients show **how much of each reactant is consumed and how much product is formed** in a balanced reaction.

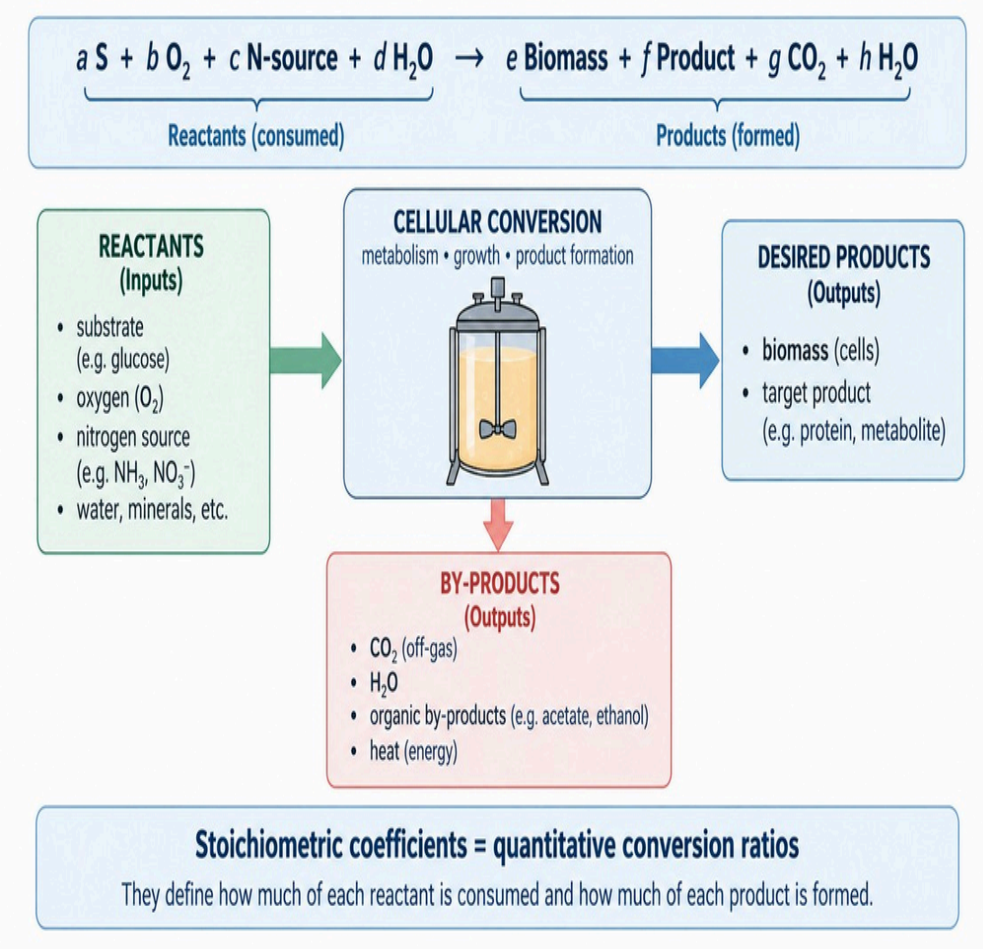
In biological systems, reactants may include **substrate, oxygen, nitrogen source and water**, while products may include **biomass, target product, CO_2 and by-products**.

A simplified overall reaction can represent the **net cellular conversion** without describing every intracellular metabolic step.

Stoichiometry provides a conservation framework for checking whether proposed conversions are **physically and chemically feasible**.

It also provides the basis for calculating **theoretical yields, substrate requirements and product formation**.

Stoichiometric relationships describe what is possible; actual process performance is then characterized using **yield, conversion and selectivity**.



Yield coefficients

Yield relates the amount of one quantity produced or consumed to another, such as g biomass per g substrate.

A yield coefficient is defined as the **amount of one component formed or consumed relative to another component**.

The most common examples are **biomass yield on substrate** and **product yield on substrate**.

Biomass yield shows how much cell mass is formed from a given amount of substrate consumed.

Product yield shows how efficiently substrate is converted into the desired product.

Observed yield may be lower than the theoretical value because substrate is also used for **maintenance, respiration and by-product formation**.

Yield values should always be reported with **units and operating conditions**, because they may change with temperature, oxygen availability, growth phase and cell physiology.

Aspect	Engineering meaning
Biomass yield	Biomass formed per substrate consumed.
Product yield	Target product formed per substrate consumed.
Oxygen yield	O2 demand relative to biomass or product.
Observed yield	Includes maintenance and by-product effects.

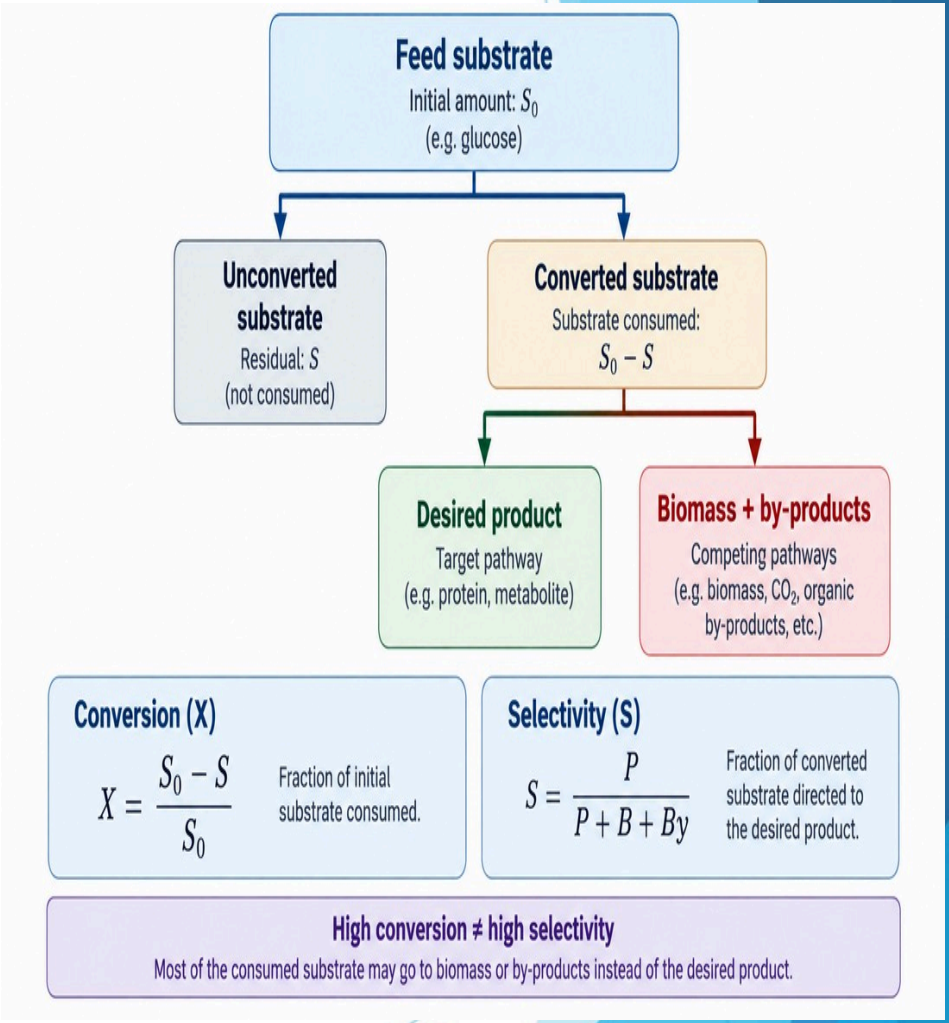
Conversion and selectivity

Conversion describes how much of a reactant is consumed; selectivity describes how much of the consumed material reaches the desired product.

Conversion measures the fraction of the initial substrate that is consumed during the process. **Selectivity** describes how preferentially the converted substrate forms the desired product instead of biomass or by-products.

High conversion does **not necessarily mean high product formation** if much of the consumed substrate is diverted to competing pathways.

A process can therefore have **high conversion but low selectivity**, or lower conversion but high selectivity toward the target product. Carbon or material balances help determine where the consumed substrate is distributed. Conversion and selectivity should be considered together with **yield and productivity** when evaluating overall process performance.



Biomass balance

Biomass increases by growth and decreases through harvest, dilution, death or lysis.
Biomass accumulation follows the general balance:

Accumulation = In – Out + Growth – Death/Lysis

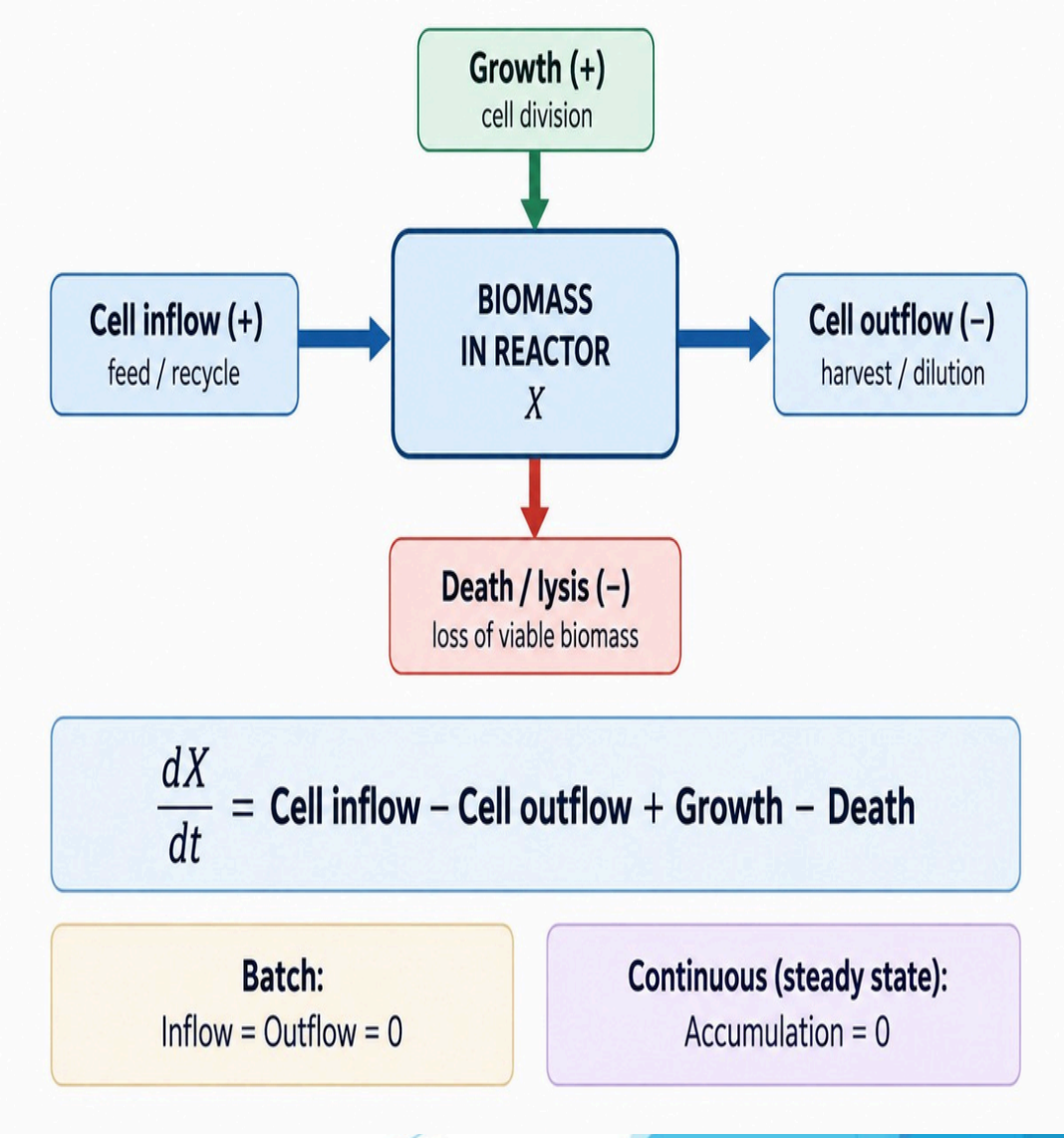
Growth generates new biomass inside the reactor as cells consume substrate and nutrients.

Death and lysis reduce viable biomass and may release intracellular material into the medium.

In a **batch culture**, there is usually no biomass inflow or outflow during cultivation, so biomass changes mainly because of growth and death.

In a **continuous culture**, biomass leaves with the outlet stream, and at steady state biomass growth must balance biomass removal and losses.

Biomass is especially important because it is both a **process output and the biological catalyst** responsible for substrate conversion and product formation.



Substrate balance

Accumulation = In - Out + Generation - Consumption
Balances enforce conservation and expose missing information.
Substrate enters the system through the **initial charge or feed stream**.
Cells consume substrate for **growth, maintenance and product formation**.
The substrate balance can be written as:
Accumulation = In – Out – Cellular consumption
In a **batch process**, there is no continuous substrate inflow or outflow after the initial charge, so substrate mainly decreases because of cellular uptake.
In a **fed-batch process**, the feed rate can be adjusted to match cellular demand and avoid excessive substrate accumulation.
High residual substrate may indicate that **feeding exceeds metabolic capacity**, while very low substrate may limit growth or product formation.

SUBSTRATE FEED (+)
glucose / nutrient feed
→
SUBSTRATE IN REACTOR – S
→
CELLULAR UPTAKE (–)
growth • maintenance • product formation

Product balance

Product can be formed, degraded, retained inside cells, secreted or removed.

Product may be **formed inside cells, secreted into the medium, degraded or removed during harvest**.

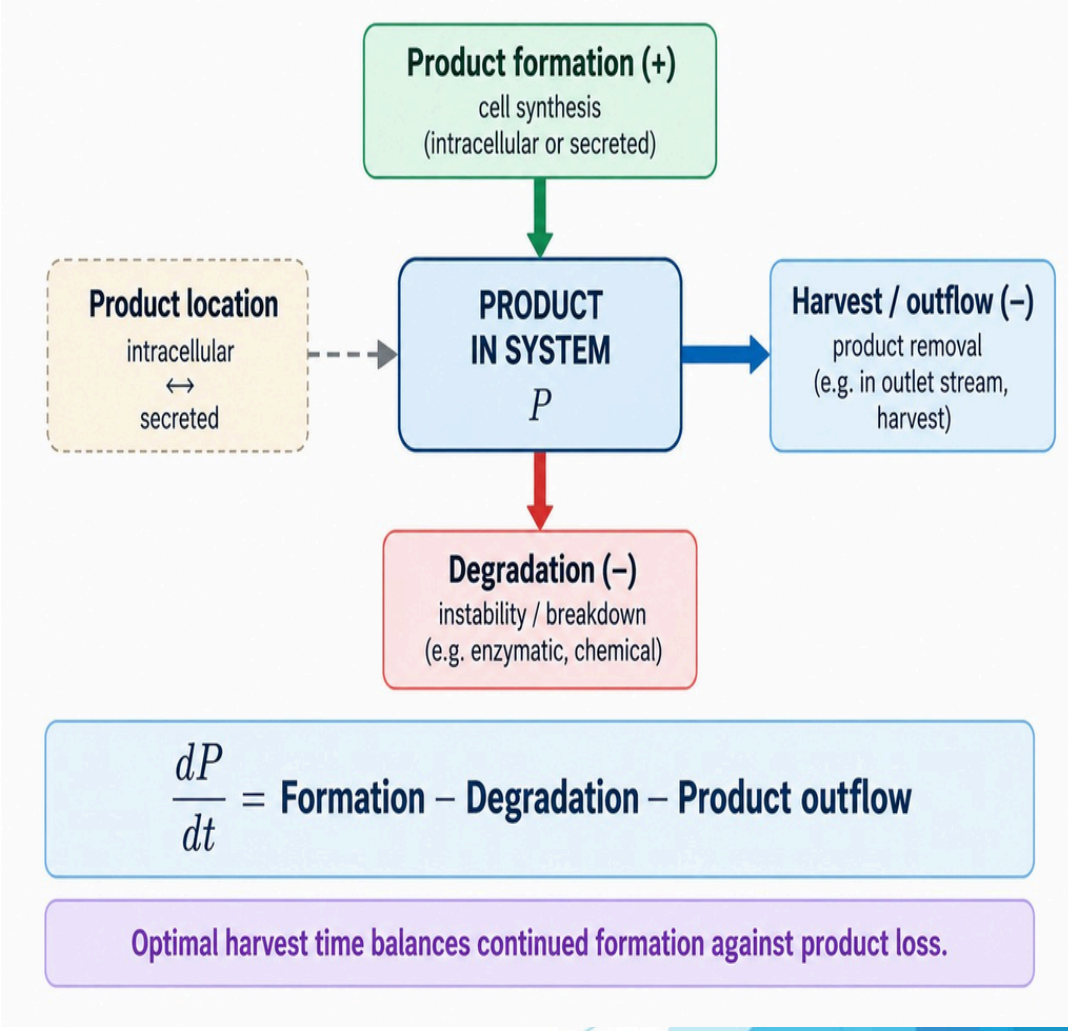
The general product balance can be written as: **Accumulation = In – Out + Formation – Degradation**

In many bioprocesses, product inflow is zero, so accumulation mainly depends on the balance between **formation, degradation and removal**.

If the product is unstable, prolonged cultivation may reduce final recovery even when synthesis continues.

Product localization is important: **intracellular products require cell disruption**, while secreted products may simplify downstream recovery.

Product balance therefore links biological production with **harvest timing, recovery and downstream processing**.



Oxygen balance

Oxygen enters with gas, transfers into liquid and is consumed by cells.

Oxygen enters the bioreactor through the **gas phase** and must first transfer into the liquid before cells can use it.

The oxygen transfer rate is commonly described by:

$OTR = kLa\ (C^* - C_l)$

where **kLa** is the volumetric mass-transfer coefficient, **C^*** is the saturation concentration and **C_l** is the actual dissolved oxygen concentration.

Cells consume dissolved oxygen at the **oxygen uptake rate (OUR)**, which depends on biomass concentration and metabolic activity.

The dissolved-oxygen balance can therefore be simplified as:

Accumulation of O_2 = OTR – OUR

If **OTR > OUR**, dissolved oxygen increases or remains sufficient.

If **OUR approaches or exceeds OTR**, dissolved oxygen falls and oxygen may become the limiting factor for growth or product formation.

GAS PHASE O_2

↓

OXYGEN TRANSFER — OTR

$kLa(C^* - C_l)$

↓

DISSOLVED O_2 IN LIQUID C_l

↓

CELLULAR UPTAKE — OUR

biomass + metabolism

$dO_2/dt = OTR - OUR$

OTR > OUR → sufficient O_2
OTR < OUR → O_2 limitation

Carbon dioxide balance

Accumulation = In - Out + Generation - Consumption Transport sets how rapidly resources and signals reach the biological system.

CO_2 is generated inside cells during **respiration and metabolic conversion**.

Part of the produced CO_2 remains **dissolved in the liquid phase**, while the rest transfers into gas bubbles and leaves the reactor.

A simplified balance can be written as:

CO_2 accumulation = metabolic CO_2 generation – CO_2 removal

CO_2 removal depends on **gas–liquid mass transfer, aeration and gas flow rate**.

At high cell density, CO_2 generation may exceed removal capacity, causing **dissolved CO_2 accumulation**.

Measuring CO_2 in the exhaust gas provides a useful **non-invasive indicator of cellular metabolic activity**.

METABOLIC CO_2 FORMATION (+)

cell respiration

↓

DISSOLVED CO_2 IN LIQUID

↓

GAS–LIQUID TRANSFER

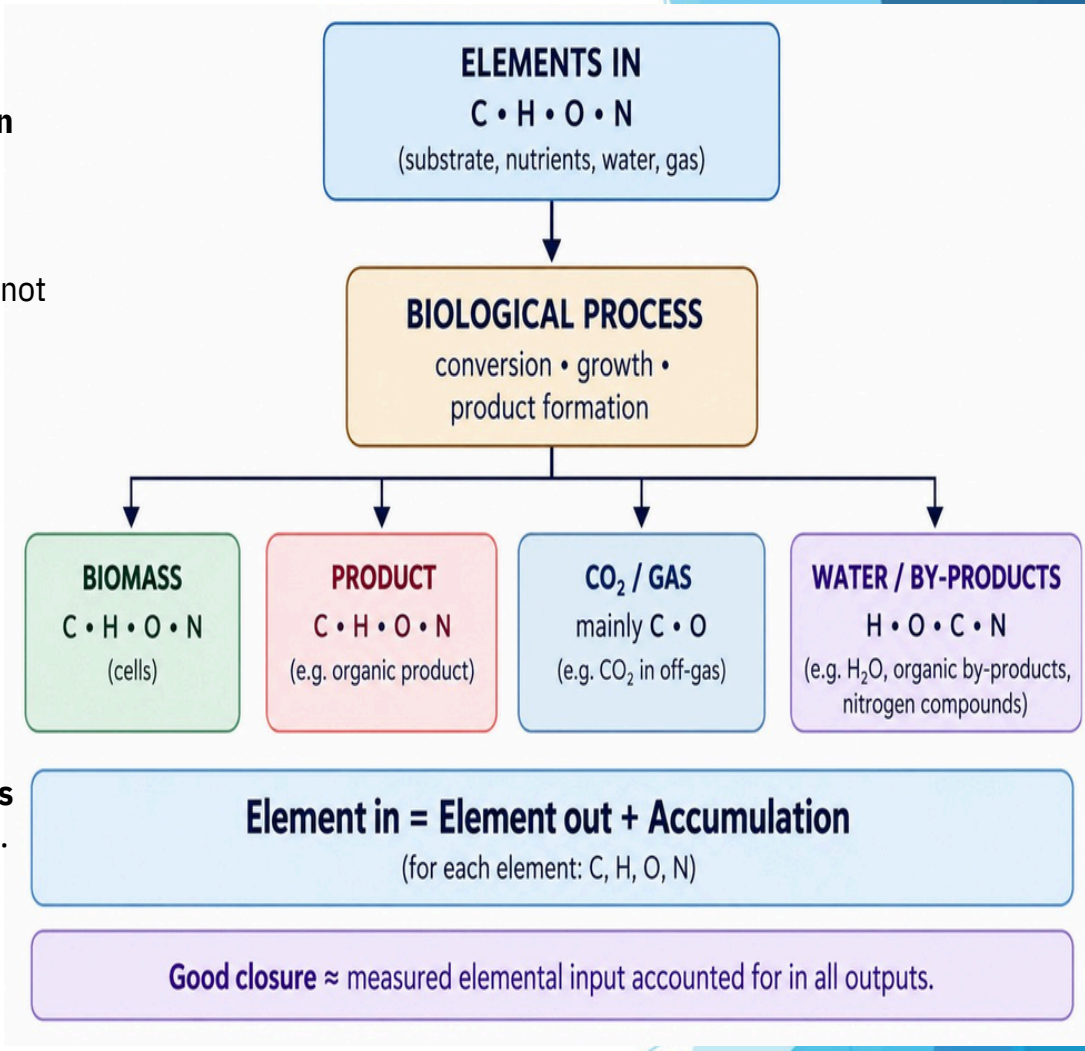
↓

OFF-GAS CO_2 (–)

CO_2 accumulation = generation – removal

Elemental balances

Carbon, nitrogen, oxygen and other elements can be balanced independently across the system.
Elemental balances are based on **conservation of atoms**: chemical and biological reactions redistribute elements between compounds but do not create or destroy them.
For each element, the balance can be written as:
Accumulation = Element in – Element out
Carbon balance tracks carbon from substrate into biomass, product, CO_2 and organic by-products.
Nitrogen balance follows nitrogen from ammonia, nitrate or amino acids into biomass, proteins and nitrogen-containing products.
Oxygen and hydrogen balances help verify water, gas and reaction stoichiometry.
If the elemental balance does not close, this may indicate **unmeasured products, incorrect biomass composition, analytical error or missing streams**.
Elemental closure is therefore an important **consistency check for experimental data and stoichiometric models**.



Energy enters biological systems

Chemical energy enters with substrates; electrical energy drives agitation, pumps, aeration and cooling.

Chemical energy enters mainly with substrates such as glucose and is converted by cells into biomass, products, maintenance energy and heat.

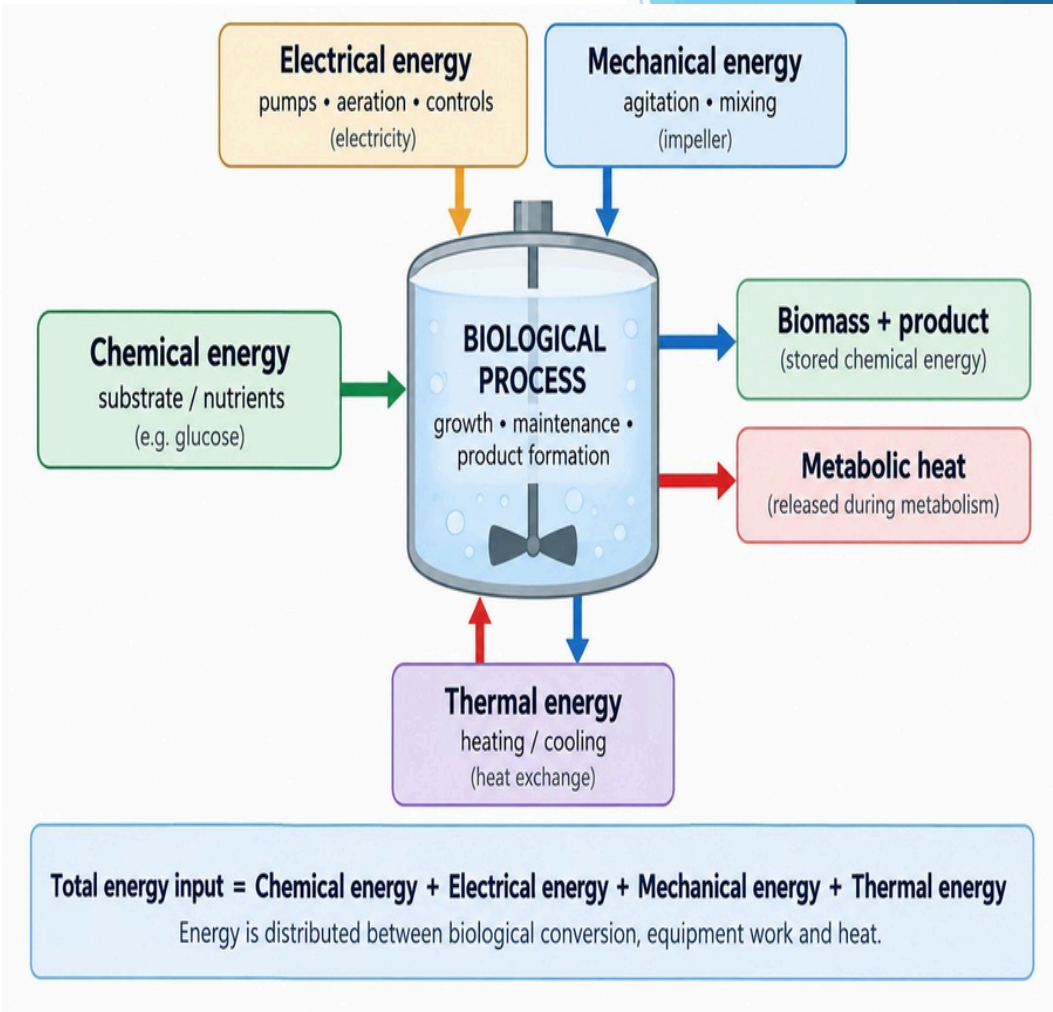
Electrical energy is supplied to equipment such as pumps, compressors, sensors and control systems.

Mechanical energy is delivered through agitation and mixing to improve mass transfer and maintain a homogeneous culture.

Thermal energy is exchanged through heating and cooling systems to maintain the required process temperature.

Aeration and agitation can become major energy demands at large scale because oxygen transfer becomes more difficult as reactor volume increases.

Energy analysis therefore connects **cell metabolism, reactor operation, scale-up and manufacturing cost**.



Energy balance concept

Bioreactor Energy analysis links metabolism to utilities and scale-up.

Energy enters a bioreactor through **feed streams, electrical power, agitation, aeration and heating**.

Cells transform chemical energy from substrates into **biomass, products and metabolic heat**.

Mechanical work from mixing and gas compression is also converted partly into heat.

A general energy balance can be written as:

Energy accumulation = Energy in – Energy out + Heat added – Work done

In many bioreactors, the practical objective is to maintain a stable **temperature set point** by removing metabolic and mechanical heat.

At steady temperature, heat generation must be balanced by **heat removal through cooling and outgoing streams**.

ENERGY INPUTS

feed • electricity • agitation • aeration

↓

BIOREACTOR

conversion + energy storage

HEAT GENERATION

metabolism + mixing

ENERGY IN PRODUCTS / BIOMASS

↓

HEAT REMOVAL / ENERGY OUT

cooling • exhaust • outlet streams

Metabolic heat generation

Aerobic metabolism releases substantial heat as chemical energy is dissipated. Aerobic metabolism releases part of substrate chemical energy as **metabolic heat**.

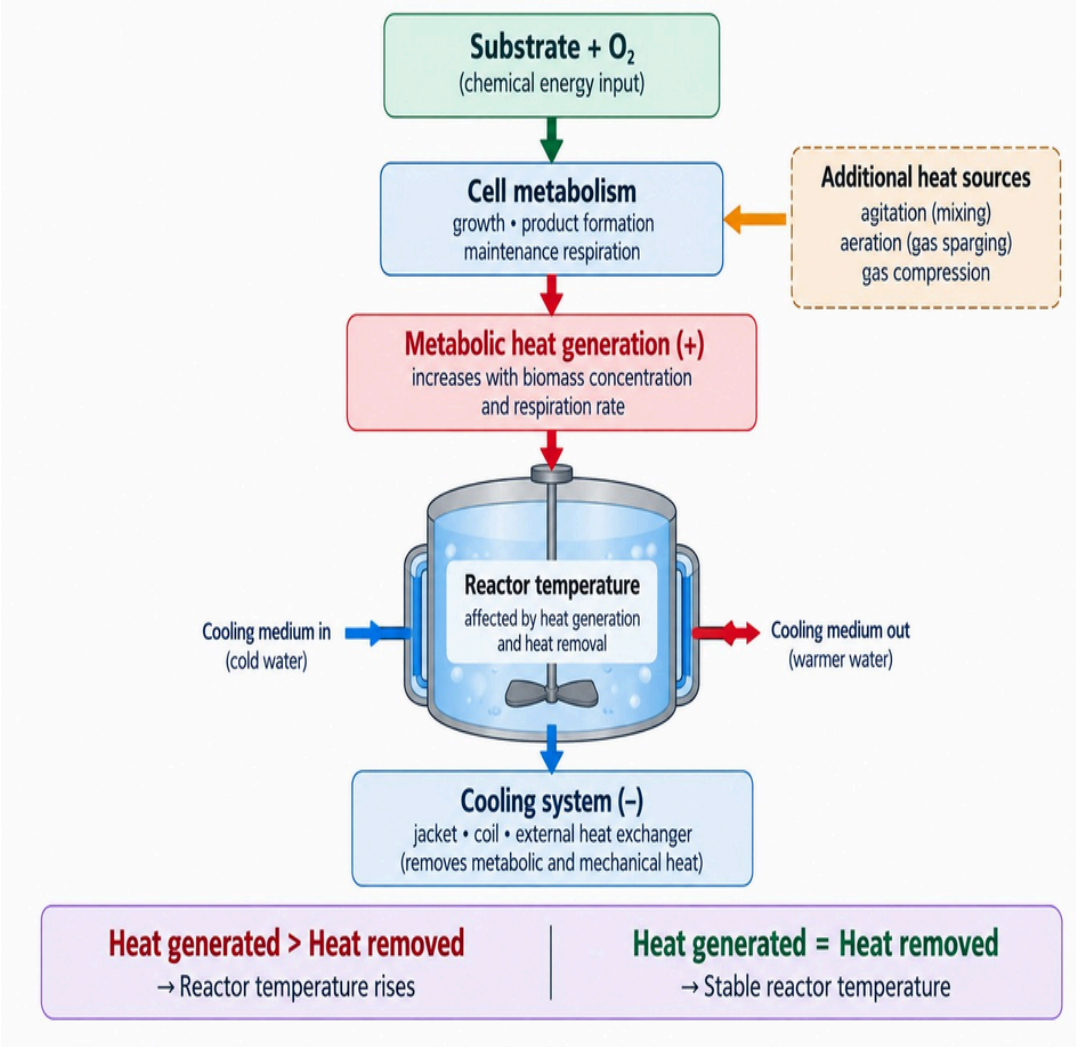
Heat generation generally increases with **biomass concentration and metabolic activity**.

Agitation, aeration and gas compression can add additional heat to the bioreactor.

If heat generation exceeds heat-removal capacity, the **reactor temperature rises**, which can affect growth, product quality and cell viability.

During scale-up, heat removal becomes more difficult because reactor **volume increases faster than available heat- transfer area**.

Cooling capacity must therefore be evaluated together with biomass concentration, oxygen demand and expected metabolic rate.



Mechanical energy input

Agitators supply power to mix liquid and disperse gas; compressors and pumps move fluids.

Mechanical energy enters the bioreactor mainly through **agitators, pumps and gas compression**.

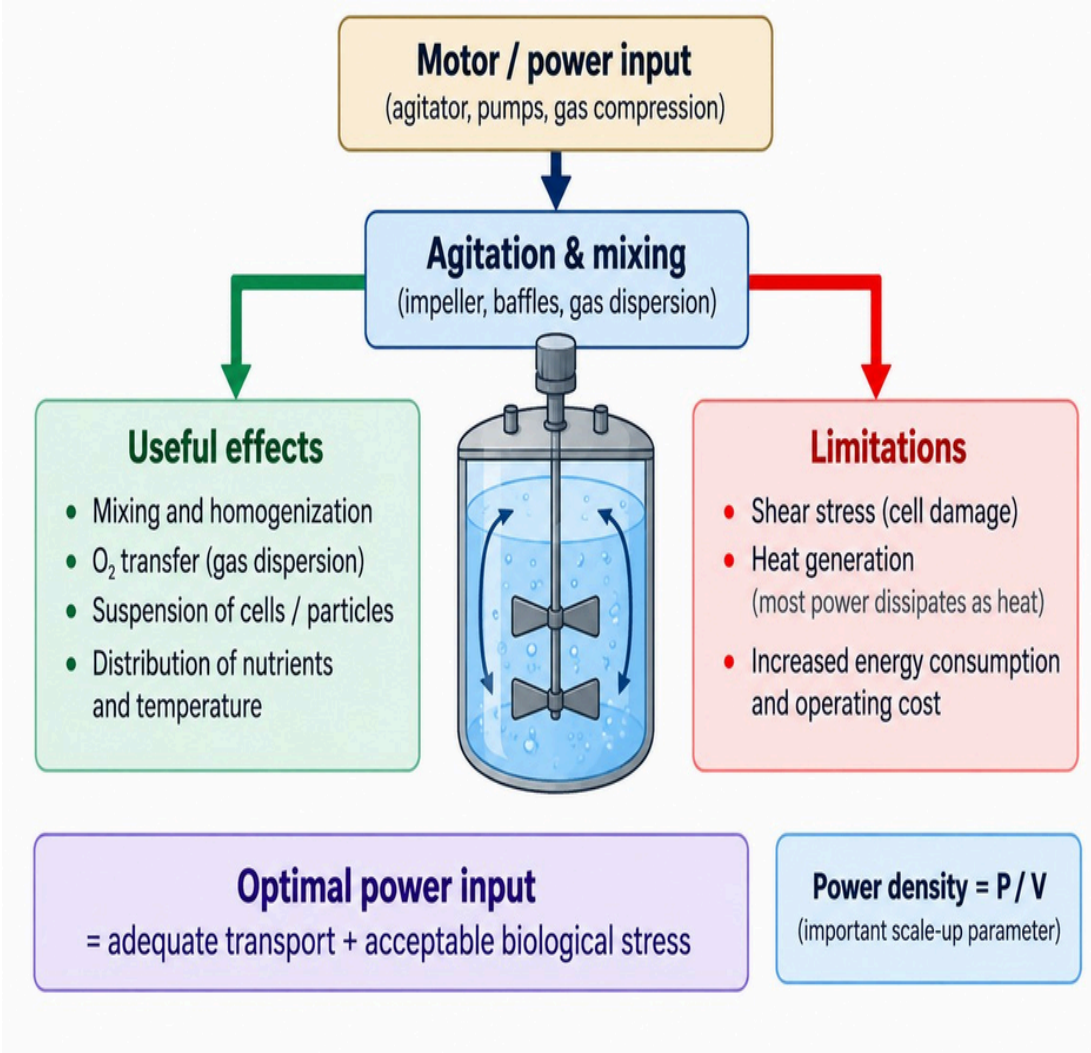
Agitation improves **mixing, suspension of cells or particles, and distribution of nutrients and temperature**.

Increased impeller power can enhance **oxygen transfer** by improving gas dispersion and increasing interfacial mass transfer.

However, stronger agitation also increases **shear stress**, which may damage shear-sensitive cells or biological structures.

Most mechanical energy is ultimately dissipated as **heat**, increasing the cooling requirement of the reactor.

The engineering objective is therefore not maximum agitation, but sufficient **mixing and mass transfer with acceptable shear, energy use and cost**.



Flow diagrams

A process flow diagram represents unit operations and major material streams.

A flow diagram represents the main **unit operations, material streams and system boundaries** of a process.

For a bioprocess, typical stages include **media preparation, sterilization, cultivation, harvest, separation and purification**.

Each stream should be labelled with relevant information such as **flow rate, composition, concentration or phase**.

Side streams such as **air, utilities, waste, recycle and off-gas** should be included when they affect the balance.

Flow diagrams help identify **where material is transformed, lost, recycled or accumulated**.

A quantitative flow diagram should be based on a **closed mass balance**, not used as a substitute for one.

RAW MATERIALS / MEDIA
→ **PREPARATION & STERILIZATION**
→ **BIOREACTOR**
→ **HARVEST / SEPARATION**
→ **PURIFICATION**
→ **FINAL PRODUCT**

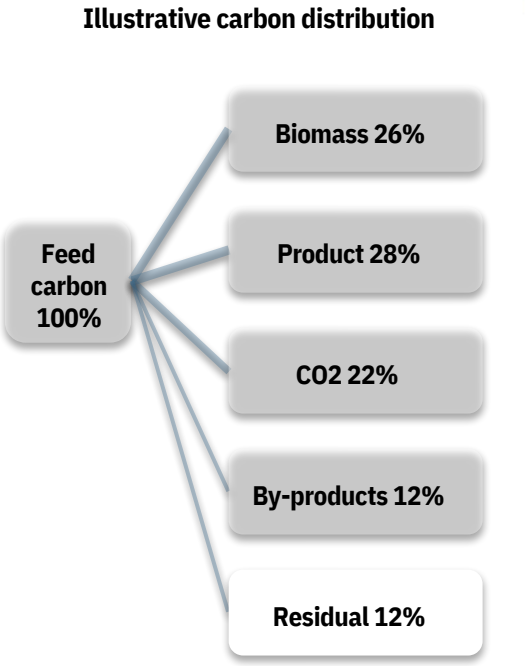
AIR / O_2 → Bioreactor
Bioreactor → **OFF-GAS / CO_2**
Harvest / Purification → **WASTE**
Purification → **RECYCLE**

Sankey diagrams

Sankey diagrams show flows with widths proportional to quantity, making losses and dominant pathways visually obvious.

- Flow visualization becomes informative when stream magnitudes are tied to a defined basis.
- They are useful for carbon, product, energy or water accounting.
- A Sankey diagram does not replace a balance- it visualizes a balanced dataset.
- It is especially valuable for communicating system-level inefficiency.
- PRACTICAL INTERPRETATION

Sankey and process-flow diagrams help reveal dominant pathways and losses, but they should be constructed from a closed balance rather than used as...



Illustrative values - actual distribution depends on organism and process conditions.

Resource efficiency

Key resource metrics include substrate yield, water use, energy intensity and waste generation per unit product.

Important resource-efficiency metrics include **substrate yield, carbon efficiency, water use, energy intensity and waste generation per unit product**.

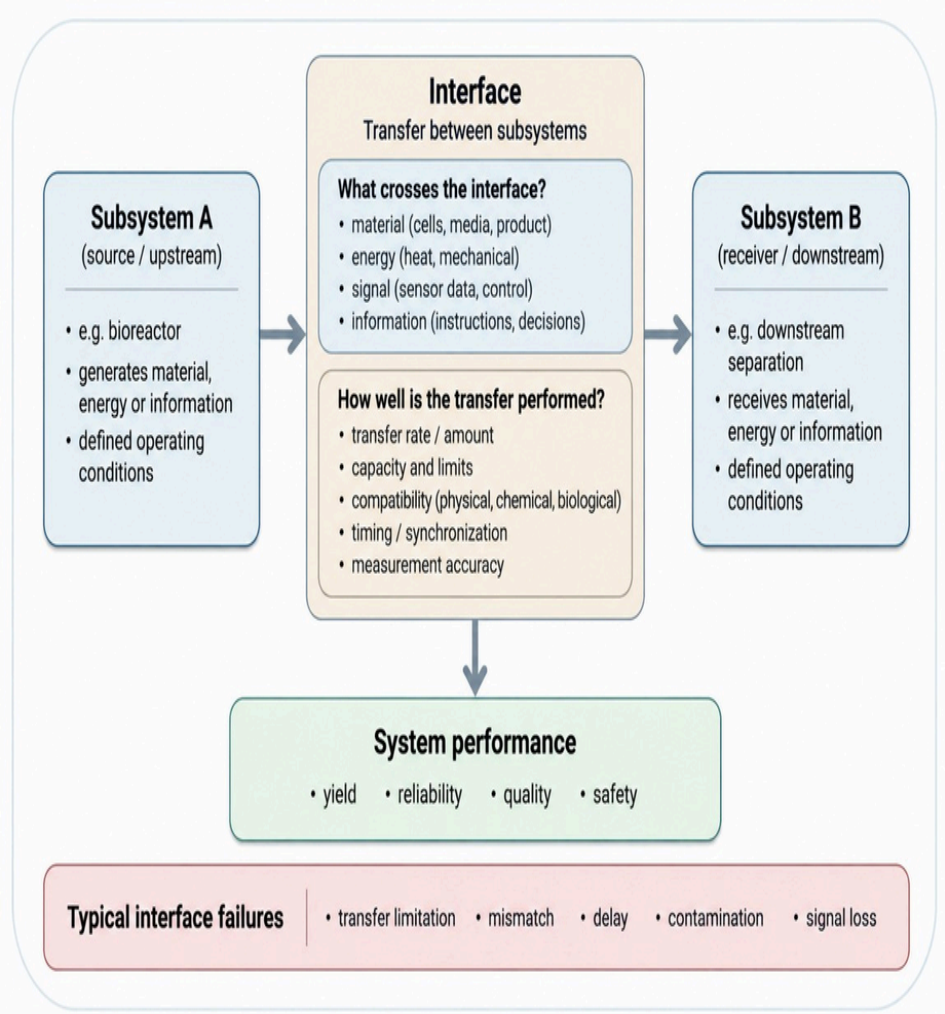
Higher substrate and carbon efficiency means a larger fraction of the feed is converted into **desired biomass or product rather than CO_2 and by-products**.

Water demand includes not only process water, but also **cleaning, cooling, media preparation and downstream operations**.

Energy intensity depends on **agitation, aeration, heating, cooling, separation and purification**.

Product concentration and recovery strongly affect resource demand because dilute or unstable products may require **energy- and material-intensive downstream processing**.

Resource efficiency should therefore be evaluated across the **whole process**, not from a single metric such as yield alone.



Waste and by-product flows

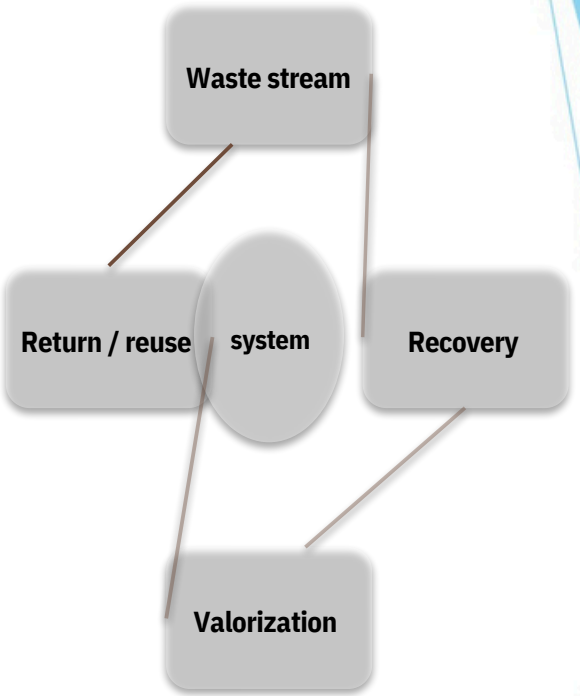
By-products can reduce yield, inhibit cells and increase purification burden.

By-products and waste streams may contain **residual substrate, salts, biomass, solvents, cleaning chemicals and process water**.

Excess by-product formation can reduce **product yield** and may inhibit cell growth or complicate downstream purification.

Waste streams should be quantified using a defined basis, such as **kg waste per kg product** or **L wastewater per batch**.

Some side streams can be **recovered, recycled or reused** within the process. Others may be **valorized** as secondary products, raw materials or energy sources. Reuse or valorization is beneficial only when the added **energy, separation effort and cost** do not exceed the recovered value.



Case setup: aerobic fermentation

Assume a fed-batch reactor producing a metabolite

The system is a **fed-batch bioreactor** supplied with concentrated glucose and air as the oxygen source.

Main material inputs are **glucose feed, nitrogen source, water, base/acid and air**.

Cells consume **glucose and O_2** for growth, maintenance and target-product formation.

Major outputs include **target product, biomass, CO_2, water vapor, heat and residual substrate**.

Because the process is fed-batch, reactor **volume, biomass and product concentration change with time**.

The first engineering task is to define the system boundary and construct **carbon, oxygen and energy balances** around the reactor.

GLUCOSE FEED
N-SOURCE + WATER
AIR / O_2
↓
FED-BATCH BIOREACTOR
growth • respiration • product formation
→ **TARGET PRODUCT + BIOMASS**
→ **CO_2 / OFF-GAS**
→ **METABOLIC HEAT**

Residual glucose + dissolved O

Inputs → Biological conversion → Outputs

Carbon-flow interpretation

Glucose carbon is partitioned among target product, biomass, CO2 and organic by-products.

Glucose provides the main **carbon input** to the fermentation system.

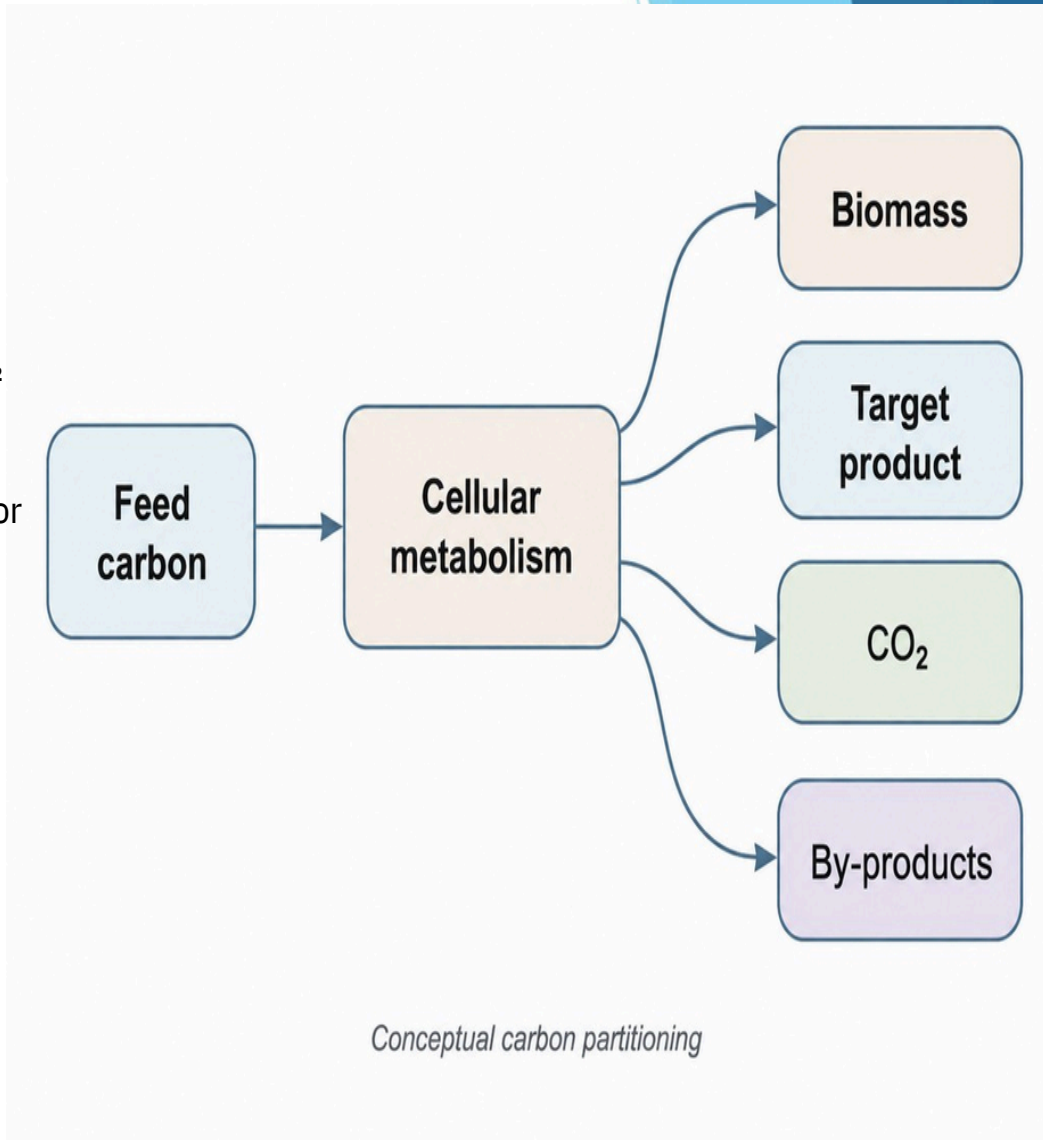
During metabolism, substrate carbon is distributed among **biomass, target product, CO_2 and organic by-products**.

A carbon balance quantifies this partitioning and checks whether the measured outputs account for the carbon supplied.

High CO_2 formation may indicate that a larger fraction of substrate carbon is being directed toward **respiration rather than product formation**.

Unexpected carbon loss can indicate **unmeasured metabolites, sampling errors or incorrect biomass-composition assumptions**.

Carbon-flow diagrams are most useful when stream magnitudes are expressed on a common basis, such as **C-mol or % of carbon input**.



Conceptual carbon partitioning

Oxygen-feed coupling

Increasing feed raises potential growth and production but also increases oxygen demand.

Increasing the substrate feed can increase **cell growth and product formation**, but it also raises the cellular oxygen uptake rate.

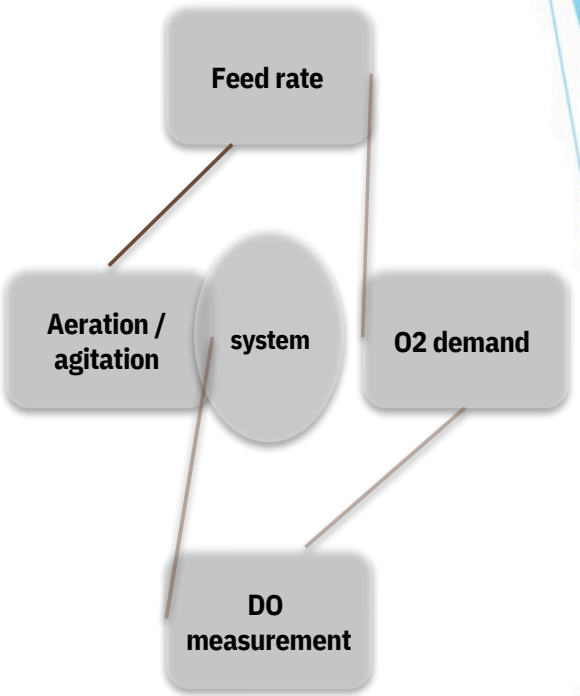
Oxygen supply is limited by the reactor's **oxygen-transfer capacity (OTR)**, which depends on aeration, agitation and mass transfer.

When **OUR approaches OTR**, dissolved oxygen begins to decrease.

If feed continues to increase beyond oxygen-transfer capacity, substrate may accumulate and metabolism may shift toward **undesired by-products**.

In fed-batch operation, **DO measurement** can therefore be used as an indicator of whether feed matches the metabolic capacity of the culture.

Feed rate, aeration and agitation should be coordinated rather than optimized independently.



Heat-removal constraint

Higher biomass and agitation increase heat generation at the same time that large scale reduces surface-area-to-volume ratio.
Heat is generated by **cell metabolism, agitation, aeration and other mechanical inputs**.
As biomass concentration and metabolic activity increase, the total **heat-generation rate also increases**.
During scale-up, reactor volume grows faster than available **heat-transfer surface area**, reducing heat-removal capacity per unit volume.
Cooling systems therefore have a finite maximum duty determined by **heat-transfer area, temperature driving force and overall heat-transfer coefficient**.
If heat generation exceeds cooling capacity, reactor temperature rises even when **substrate and oxygen are still available**.
Heat removal can therefore set the practical limit for **feed rate, biomass concentration and reactor productivity**.

Take-home balance workflow

Choose boundary and basis -> list all streams -> write component balances -> add stoichiometry/yields -> check closure.

Start by defining the **system boundary** and the engineering question.

Select a consistent **calculation basis** such as per batch, per hour or per kilogram of product.

Identify all relevant **input, output and accumulation streams**, including gases, waste and recycle streams.

Write the appropriate **total, component, elemental and energy balances**.

Add **stoichiometry and yield coefficients** to relate substrate consumption, biomass growth and product formation.

Check **mass, elemental and energy closure** before interpreting the results.

Finally, connect the balances to **kinetics, oxygen transfer, heat removal and operating constraints**.

1. DEFINE BOUNDARY

What is inside the system?

→

2. CHOOSE BASIS

batch • time • mass • volume

→

3. MAP STREAMS

inputs • outputs • recycle • waste

→

4. WRITE BALANCES

mass • components • C/N/O • energy

→

5. ADD STOICHIOMETRY / YIELDS

conversion relationships

→

6. CHECK CLOSURE

Does input ≈ output + accumulation?

→

7. INTERPRET LIMITS

kinetics • O_2 transfer • heat • constraints

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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