CHE 361
Bioprocess Engineering

Lecture 1: Introduction

Outline

- Course Structure
- Course Objectives
- Course Outline & Timetable

▪ **Introduction:**

➢ **The Central Dogma of Molecular Biology**

➢ **The Concept of Bioprocess**

Course Structure

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Schedule:

Lectures:	Tuesday,	01:30 – 03:20 PM,	E6 2024
	Thursday,	01:30 – 02:20 PM,	E6 2024
Tutorials:	Thursday,	02:30 – 03:20 PM,	E6 2024

Course Structure

Lecture Notes & Assignments:

UWaterloo LEARN (https://learn.uwaterloo.ca/)

Recommended Textbooks:

M.L. Shuler, F. Kargi, M. Delisa, Bioprocess Engineering. Basic Concepts, Prentice Hall, 2017; ISBN: 978-0-13-706270-6

H.W. Blanch, D.S. Clark, Biochemical Engineering, CRC Press, 1997; ISBN: 978-0-8247-0099-7

Grading Scheme:

Homework	**20%**
Midterm	**30%**
Final Exam	**50%**

Course Objectives

- This course reviews first basic aspects of biochemistry and molecular biology focusing on gene expression and metabolic regulation.
- Biological systems for the commercial production of pharmaceuticals, chemicals, fuels, biomaterials etc. are introduced. Biosafety and sustainability are discussed.
- After that the course introduces the concepts of ***enzyme catalysis*** and ***microbial growth*** and apply these concepts to the ***design of bioreactors***.

Course Objectives: Topics

Topics include ***enzyme kinetics, cell growth kinetics, and bioreactor design & analysis***.

- Biochemical reaction kinetics are derived and material balances are developed for bioreactors operated in different modes including batch, fed-batch, continuous stirred-tank reactor, recycle and perfusion.
- Transport (mass and heat) transfer considerations for bioreactors are introduced.
- Downstream processing associated with biological systems and recovery of biological products are discussed.

Learning Outcomes

At the end of the course, a student should be able to:

1. Demonstrate competence in the fundamental concepts of Biochemical Engineering
2. Demonstrate competence in the concepts of enzyme catalysis and microbial growth
3. Apply these concepts to design and analysis of bioreactors

Course Outline & Tentative Timetable

Week 1: Introduction & Basic Principles

Week 2: Gene Expression & Metabolic Regulation

Week 3: Enzyme Kinetics

Week 4: Enzymatic Reactor Design

Week 5: Microbial Growth

Week 6: Bioreactor Design: Stoichiometry & Mass Balances

Course Outline & Tentative Timetable

Week 7: Batch & CSTR

Week 8: Chemostat

Week 9: Fed-Batch & Perfusion

Week 10: Transport in Bioreactors

Week 11: Bioprocess Design

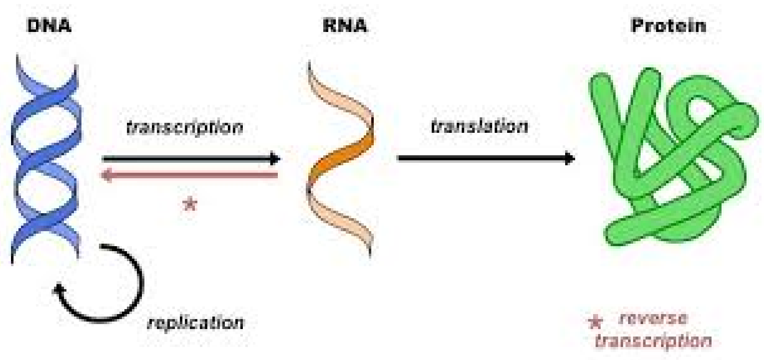
Week 12: Bioprocess Design

Basic Principles

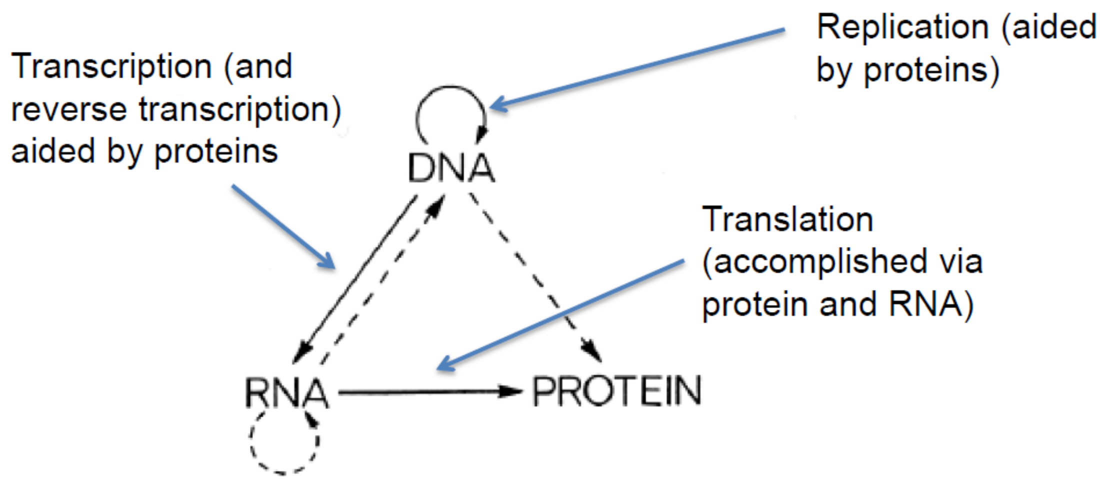
- Biochemical Engineering using the concepts from Biology, but focuses more on Engineering
- The focus is more on the development of equations and their analysis
- Biochemical Engineers heavily rely on Biology but use Biology more as a tool, less as a subject of investigation
- Biochemical Engineers want to describe biological processes using mathematical representation
- The ultimate goal is to perform a biological process in a confined, controllable environment (a bioreactor) and to produce the desirable product on a large scale

The Central Dogma of Molecular Biology

- The central dogma of molecular biology describes the two-step process, transcription and translation, by which the information in genes flows into proteins: DNA → RNA → protein.

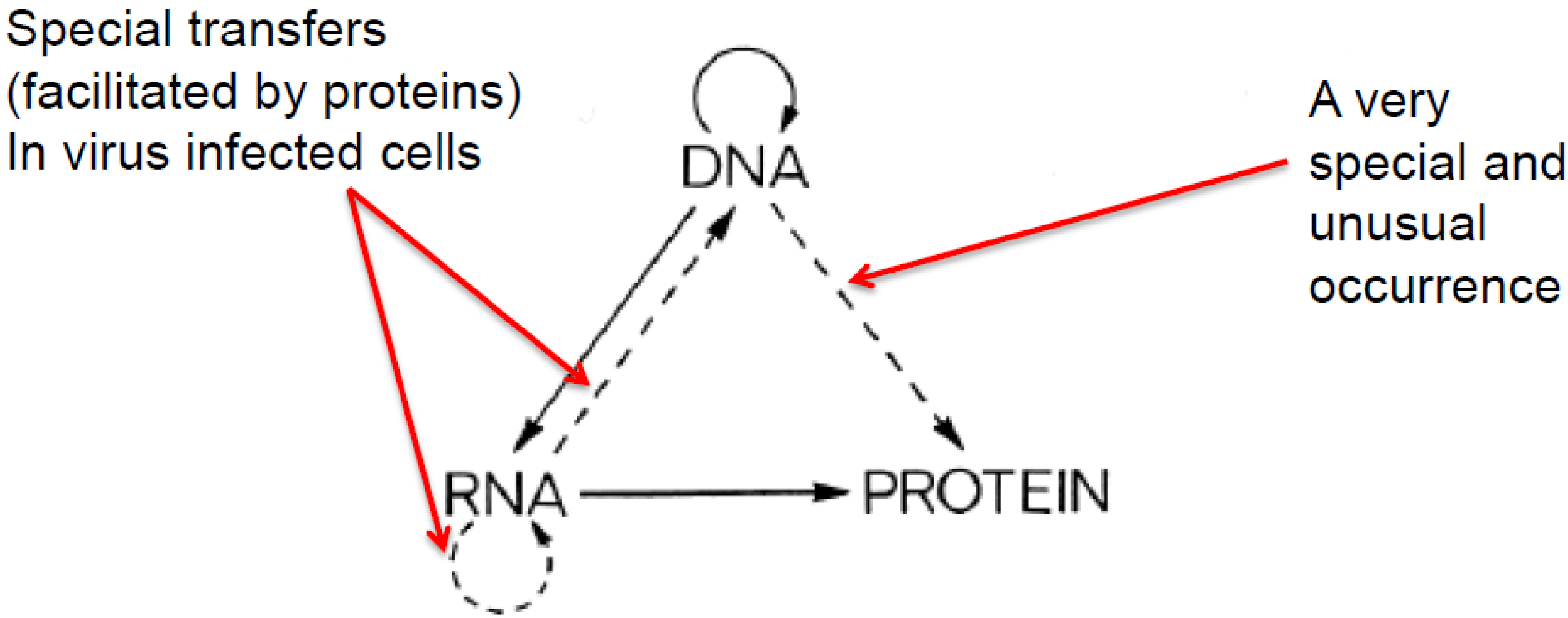


The Central Dogma (Cont'd)

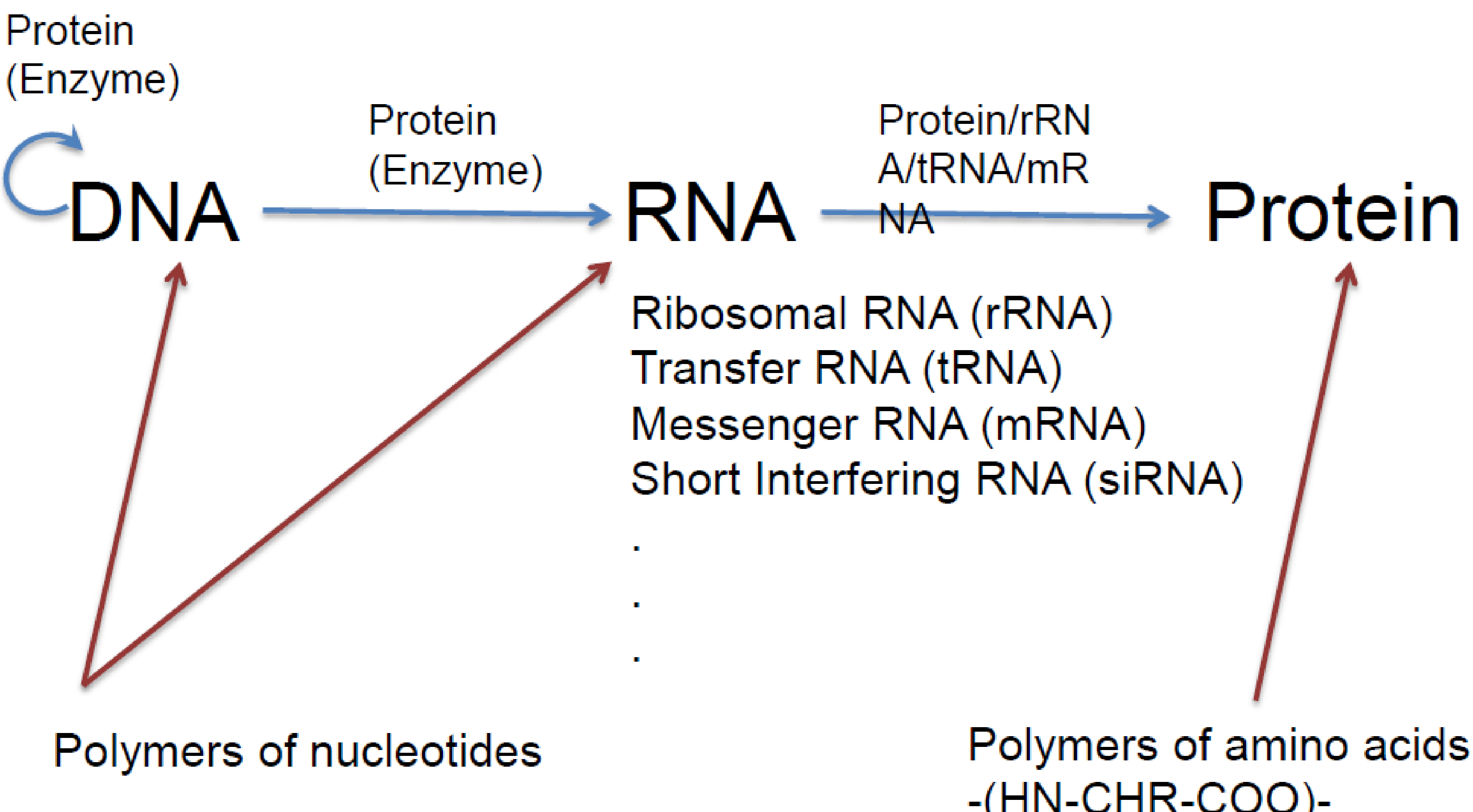


- Information is stored in the DNA molecule
- This information can be directly *replicated* to form an identical DNA molecule
- Segments of the DNA molecule is *transcribed* to yield RNAs
- The information decoded in RNAs is *translated* into proteins
- The proteins perform a <u>structural</u> or **<u>enzymatic</u>** role

Special Transfers



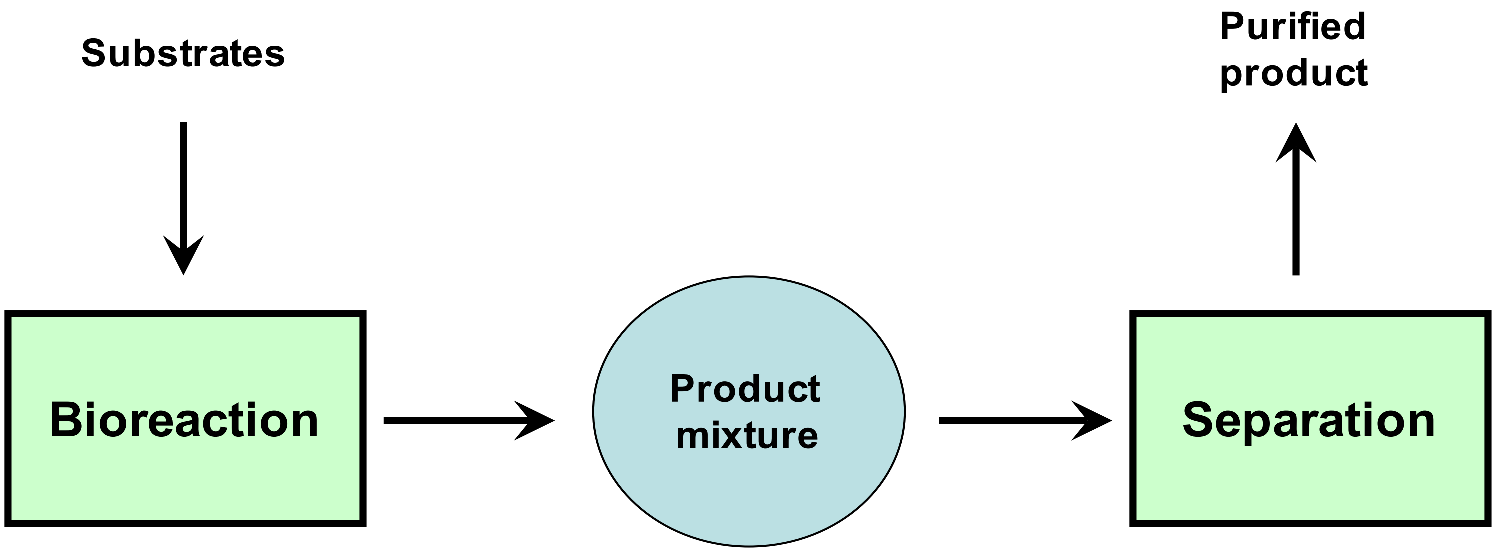
The Central Dogma: More details



The Concept of Bioprocess

- Purposes:
  - Biomanufacturing
  - Waste treatment
- Feedstocks (substrates):
  - Raw materials
  - Wastes
- Bioproducts (high value):
  - Ribosomal products (proteins & peptides)
  - Non-ribosomal products (metabolites)

General Bioprocess Flowsheet



Bioreaction

- Bioreaction (also known as biotransformation or bioconversion) is an essential part of any bioprocess
- Bioreactions are mediated/catalyzed by biocatalysts, either ***enzymes*** or ***living cells***
- Bioreactions are conducted in bioreactors, in a confined environment under well-controlled conditions

Types of Bioproducts

Products derived from bioprocess:

- Cells, Proteins, DNAs
- Metabolites (amino acids, organic acids, antibiotics, solvents, etc.)
- Can be ***intracellular*** or ***extracellular***
- Often diluted in a fermentation broth
- Can be structurally unstable (e.g., proteins)

Examples of Bioreactions/Bioproducts

- **Value-added:** 6-Aminopenicillanic acid (6-APA) production (*in vitro*, one-step)
- **Metabolites:** ethanol, butanol, amino acid production (*in vivo*, multi-step)
- **Recombinant proteins:** production of industrial enzymes and therapeutic proteins (*in vivo*, multi-step)

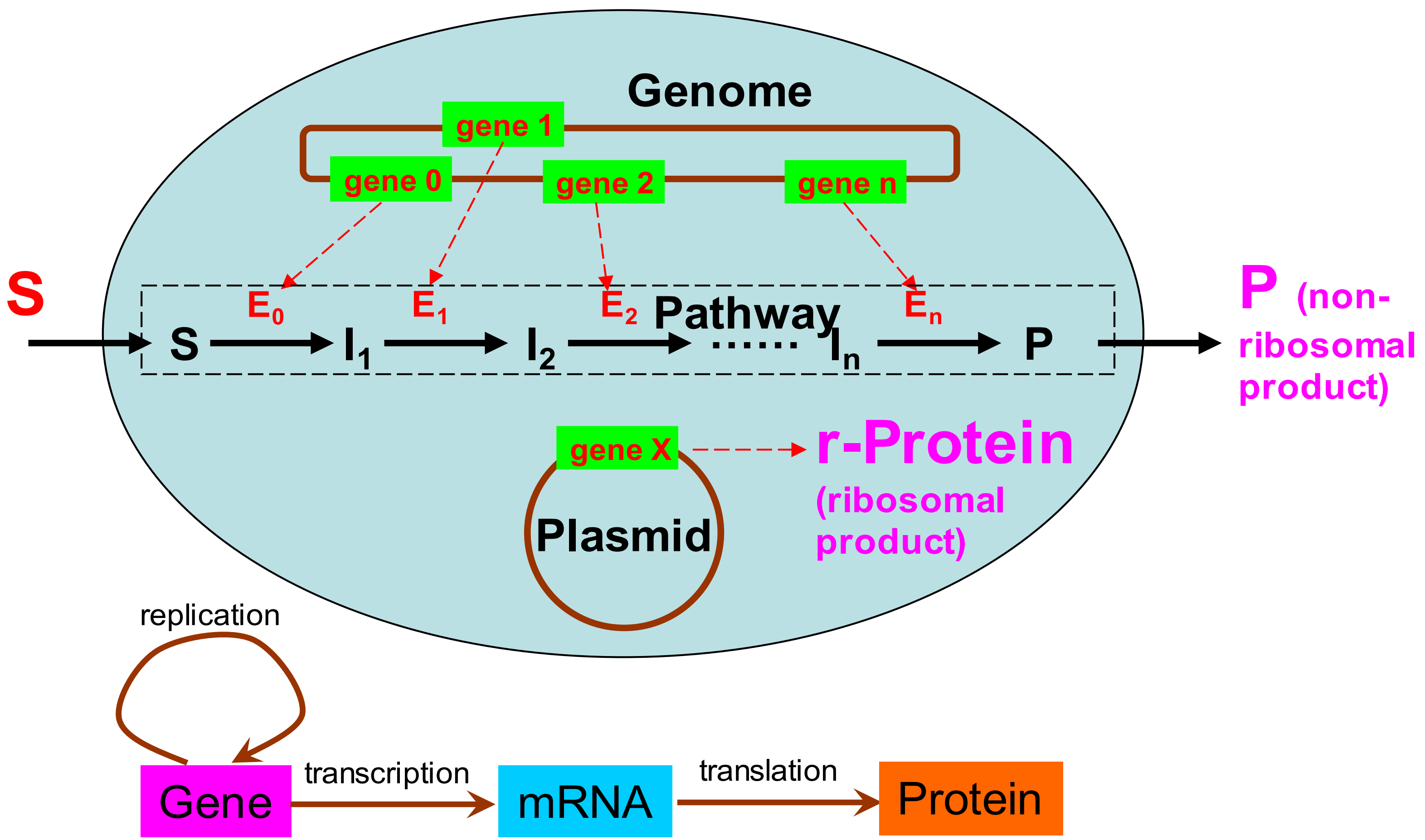
Biocatalysts

- Enzyme biocatalyst
  - ✓ Free enzymes
  - ✓ Immobilized enzymes
- Whole-cell biocatalyst
  - ✓ Cell suspensions
  - ✓ Immobilized cells

Enzymatic vs. Cell Catalysis

	Enzymatic	Cells
Specificity	single-step	multi-step
Byproducts	less (or none)	more
Transformation	only reaction	reaction + cell growth
Processing time	short	long

Cell Factory



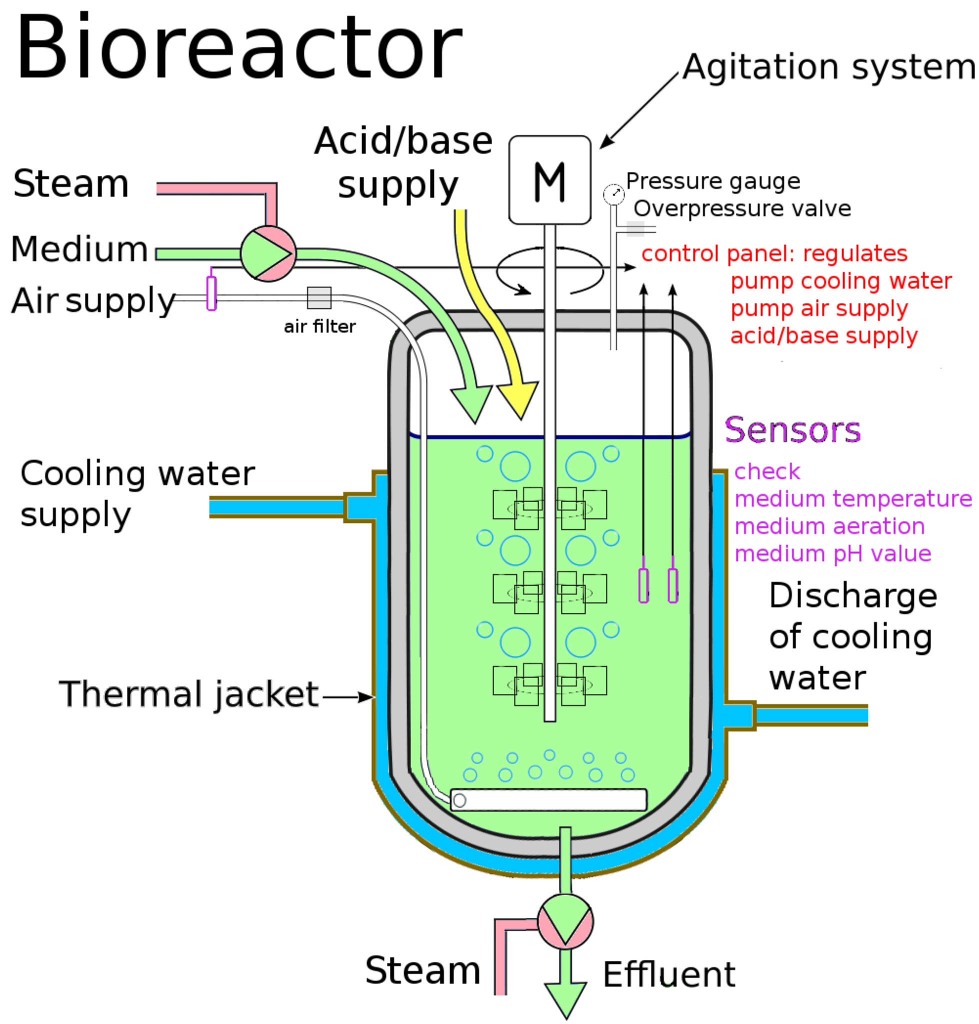
Examples of Cell Factories

- Prokaryotic cells: bacteria (e.g., *Escherichia coli*, *Bacillus*, *Clostridia*)
- Eukaryotic cells: yeast (e.g., *Saccharomyces cerevisiae*), fungi, (micro)algae, insects, animals (Chinese hamster ovary), plants

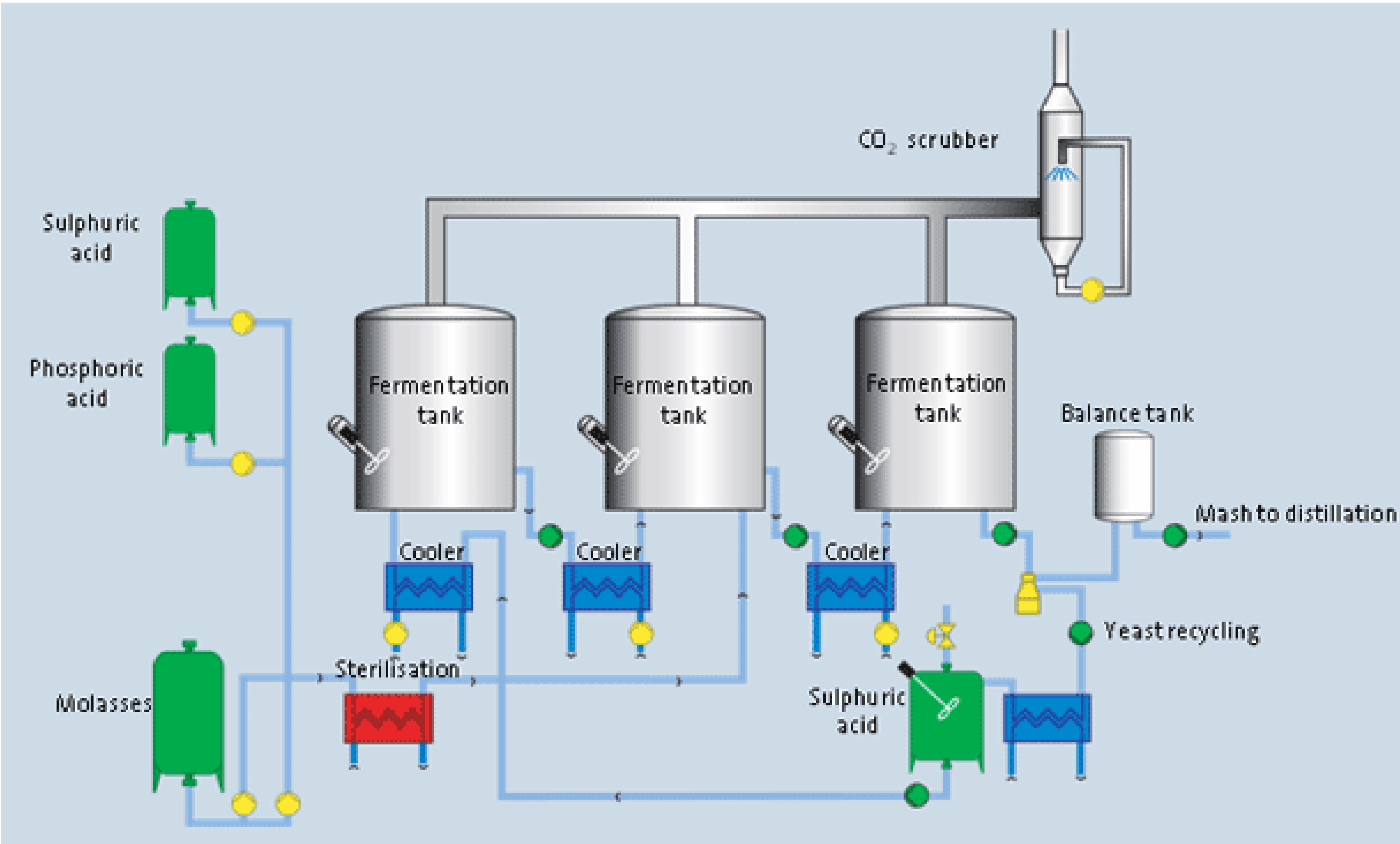
Cell Engineering

- Genetic manipulation of host cell to improve its practical applications
- Gene overexpression (plasmid); gene knockout (genome); gene knock-in (genome); gene knock-down (antisense RNA); gene editing (genome)
- Prerequisite for a new host cell system: gene transformation

Bioreactor (Stirred Tank)

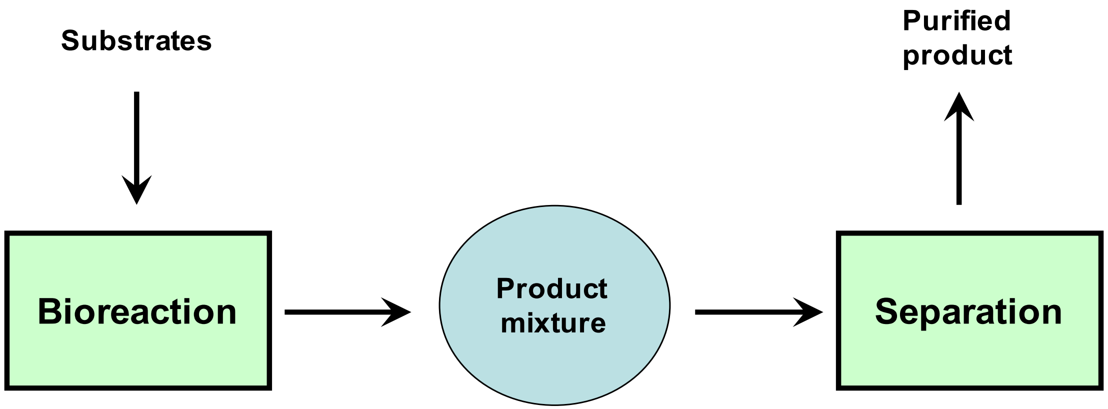


Bioprocess (Ethanol PFD)



Bioprocess Stages

- **Upstream:** construction of biological strains (molecular biological tools are required to derive host/vector systems)
- **Midstream:** cultivation and bioreaction
- **Downstream:** bioseparation and purification (representing the major cost, easily more than 50%, for the overall bioprocess)



Separations

- **Approach:** physical vs. chemical
- **Separation factors:** molecular/particle size, intermolecular force (e.g., ionic strength, hydrophobic interaction, affinity, etc.), physical/chemical properties (e.g., density, diffusivity, solubility, etc.)
- **Purpose:** analytical or preparative

Separation Methods

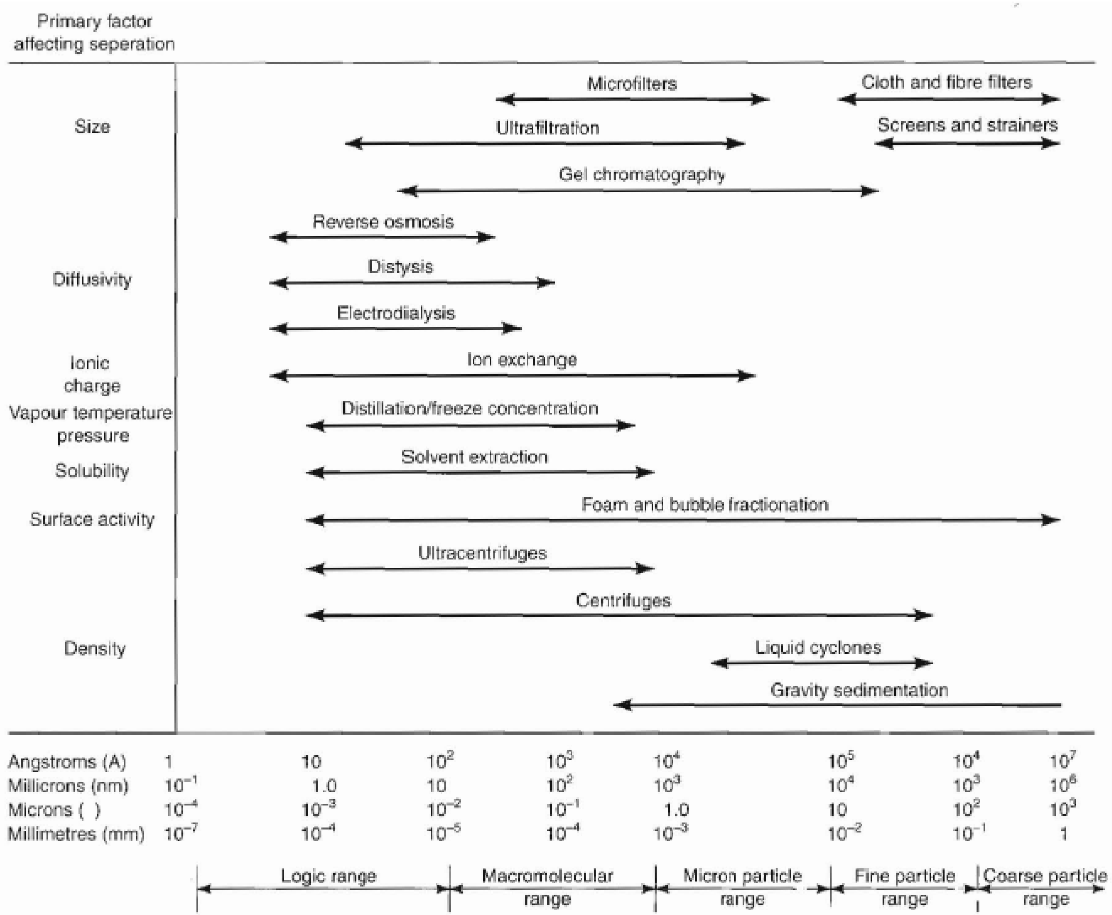
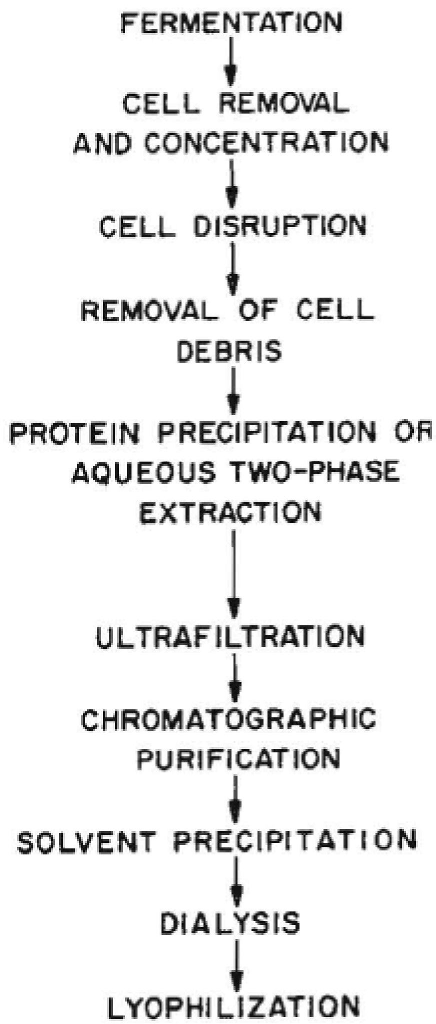


Figure 11.1. Ranges of applications of some standard unit operations. (With permission, from B. Atkinson and F. Mavituna, *Biochemical Engineering and Biotechnology Handbook*, Macmillan, Inc., New York, 1983.)

Bioseparations

- **Traditional unit operations for physical separation:** distillation, absorption, extraction, evaporation, crystallization, filtration, centrifugation
- **Preparative chromatography:** affinity, ion-exchange, hydrophobic interaction

Purification & Separation Example



(1) separation of insoluble products and other solids,

(2) primary isolation or concentration of product and removal of most of the water,

(3) purification or removal of contaminating chemicals,

(4) product preparation

Figure 11.2. Major steps involved in the separation and purification of intracellular enzymes.

Any questions so far?