Department of Biochemistry /Second Stage

Lecture-3: Membrane Transport Mechanisms

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1. Concept of Membrane Transport

Biological membranes are **selectively permeable structures** that preserve the distinct internal composition of the cell while permitting controlled exchange of substances with the extracellular environment. This selective permeability is a fundamental requirement for life, as it allows cells to maintain homeostasis while remaining metabolically active.

Although membranes exhibit **fluidity**, the lipid bilayer possesses a **hydrophobic core** formed by fatty acid chains. This core creates a formidable energetic barrier to:

- Ions
- Polar molecules
- Large solutes

As a result, spontaneous diffusion across membranes is limited to small nonpolar molecules, and **most biologically relevant substances require specialized transport systems**.

Thus, membrane transport is not a passive phenomenon but a **highly regulated biological process** governed by membrane proteins.

2. Functional Importance of Membrane Transport

Membrane transport underlies nearly all cellular functions:

2.1 Nutrient Uptake

Cells rely on transport proteins to import:

- Glucose
- Amino acids
- Ions
- Vitamins

Because intracellular concentrations are often higher than extracellular levels, active and facilitated transport mechanisms are essential for sustaining metabolism.

2.2 Waste Removal

Metabolic by-products such as:

- CO_2
- Urea
- Lactate
  must be efficiently removed to prevent toxicity and maintain intracellular pH and osmotic balance.

2.3 Maintenance of Ion Gradients

Cells actively establish and preserve gradients of:

- Na^+
- K^+
- Ca^{2+}
- Cl^-

These gradients are essential for:

- Osmoregulation
- Secondary active transport
- Membrane potential generation

2.4 Electrical Signaling

In excitable cells (neurons and muscle cells), ion transport generates:

- Resting membrane potential
- Action potentials
- Synaptic transmission

Precise regulation of ion channels and pumps is critical for nervous system function

2.5 Energy Metabolism

Ion gradients represent stored energy. Cells exploit these gradients to:

- Drive ATP synthesis (mitochondria, chloroplasts)
- Power secondary active transport
- Regulate metabolic flux

Without membrane transport, cellular energy metabolism would collapse.

2. Driving Forces for Membrane Transport

Transport across membranes is governed by the **laws of thermodynamics**, particularly the concept of free energy change (ΔG).

The direction and rate of transport depend on the **net driving force**, which arises from differences in concentration and electrical potential across the membrane.

2.1 Concentration Gradient (Chemical Gradient)

A concentration gradient exists when a substance is unevenly distributed across a membrane.

Principles

- Molecules tend to move from regions of **high concentration to low concentration**
- This movement increases entropy and is thermodynamically favorable
- Transport down a concentration gradient is considered **passive**

The magnitude of the gradient directly affects the rate of diffusion

2.2 Electrical Gradient

The electrical gradient results from differences in charge distribution across the membrane.

Membrane Potential

- Most cells maintain a **negative internal membrane potential**
- Charged molecules respond to electrical forces

For example:

- Cations (Na^+, Ca^{2+}) are attracted to negative intracellular environments
- Anions (Cl^-) may be repelled depending on membrane potential

Electrical gradients are especially important for ion transport.

2.3 Electrochemical Gradient

For ions, transport is influenced simultaneously by:

- Concentration gradient
- Electrical gradient

The combined effect is known as the **electrochemical gradient**.

Thermodynamic Description

The free energy change for ion movement depends on:

- Ion concentration difference
- Membrane potential
- Ion charge

Transport occurs spontaneously only if the overall ΔG is negative

3. Biological Utilization of Electrochemical Gradients

Cells do not merely tolerate gradients—they **actively create and exploit them**.

Key Applications

- Secondary active transport (e.g., Na^+/glucose symport)
- Electrical excitability
- Regulation of intracellular Ca^{2+}
- ATP synthesis via chemiosmosis

Electrochemical gradients thus serve as a universal form of stored biological energy.

3. Passive Transport Mechanisms

Passive transport does **not require direct metabolic energy**. Instead, it depends on pre-existing gradients.

3.1 Simple Diffusion

Simple diffusion occurs directly through the lipid bilayer.

characteristics:

- No protein involvement
- No saturation
- Rate depends on lipid solubility and membrane thickness

Examples:

- O_2 and CO_2 exchange
- Steroid hormones

Despite its simplicity, simple diffusion is limited to a small group of molecules.

3.2 Facilitated Diffusion

Facilitated diffusion uses specific membrane proteins to transport molecules down their gradient.

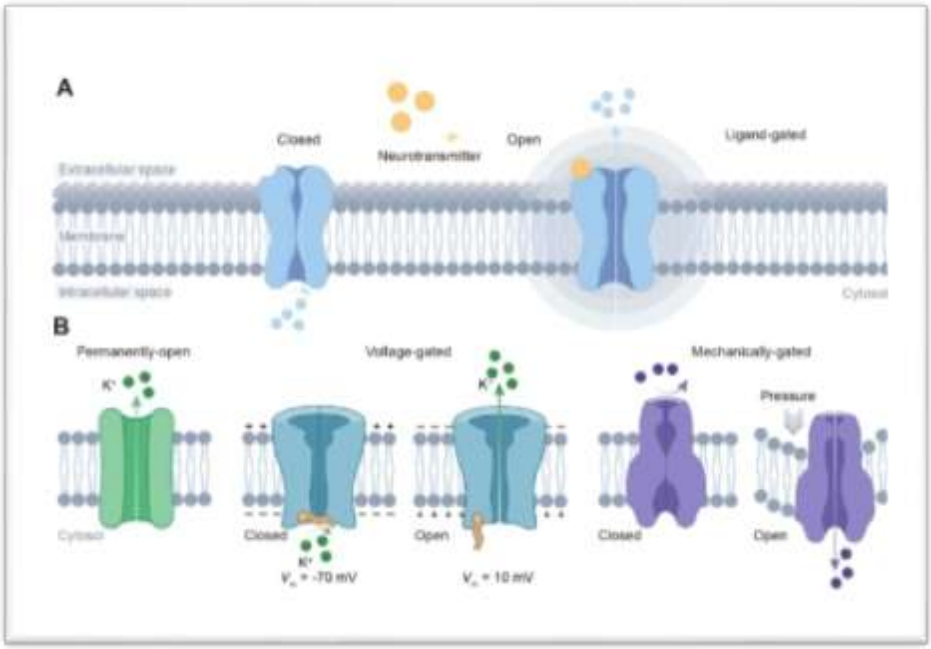
Important features:

- Highly selective
- Saturable (transport maximum)
- Subject to competitive inhibition

Examples:

- Glucose transporters (GLUT family)
- Amino acid transporters

Facilitated diffusion combines efficiency with specificity, resembling enzyme-catalyzed reactions.



Facilitated diffusion involves the use of a protein to facilitate the movement of molecules across the membrane. In some cases, molecules pass through channels within the protein. In other cases, the protein changes shape, allowing molecules to pass through.

4. Channel Proteins

Channel proteins form hydrophilic pores that allow rapid passage of ions or small molecules.

Distinctive properties:

- Extremely high transport rates
- Minimal conformational change
- Selective ion permeability

Gated Channels : Channels can switch between open and closed states.

Types of gating:

- **Voltage-gated** (neuronal signaling)
- **Ligand-gated** (neurotransmitter binding)
- **Mechanically gated** (stretch or pressure)

Channel dysfunction often leads to severe neurological and muscular disorders.

5. Carrier Proteins (Transporters)

Carrier proteins bind their substrate and undergo a conformational change to move it across the membrane.

Characteristics:

- Lower transport rates than channels
- High specificity
- Show Michaelis–Menten-like kinetics

Carriers play a central role in nutrient uptake and metabolite exchange.

6. Active Transport Mechanisms

Active transport moves substances **against their electrochemical gradients**, requiring energy input.

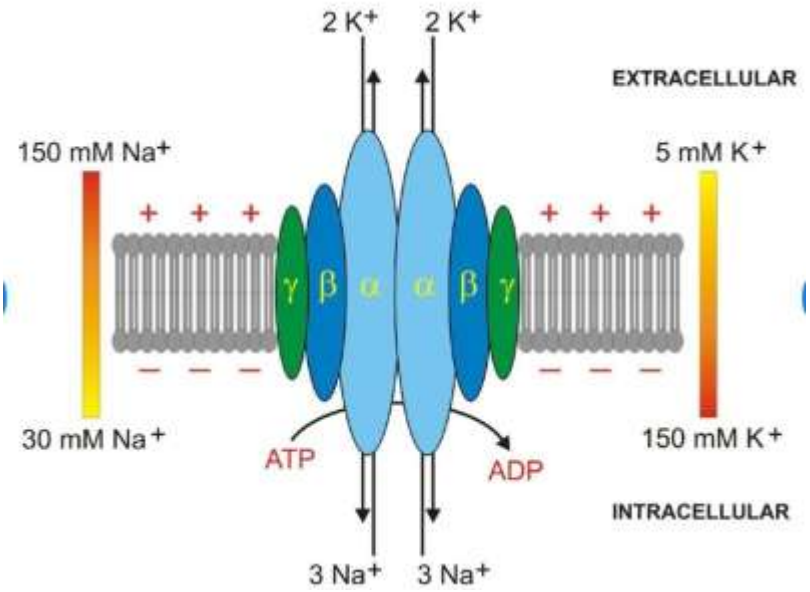
6.1 Primary Active Transport

Energy is derived directly from **ATP hydrolysis**.

Na^+/K^+-ATPase

- Pumps 3 Na^+ out and 2 K^+ in
- Maintains membrane potential
- Accounts for a large fraction of cellular ATP consumption

This pump is essential for nerve impulse transmission and osmotic balance.



Na^+/K^+ ATPase subunit assembly in plasma membrane. Na^+/K^+ ATPase is a heterodimer of 1 alpha (α, light blue) and 1 beta (β, dark blue) subunit. A regulatory gamma (γ, dark green) subunit sometimes oligomerizes in some tissues. 3 Na^+ and 2 K^+ ions are translocated across the plasma membrane by hydrolysis of 1 ATP to 1 ADP molecule. Extracellular to intracellular ionic gradients for Na^+ (150–30 mM) and K^+ (5–150 mM) are shown. Positive and negative signs depict membrane potential created by Na^+ and K^+ ion translocation.

6.2 Secondary Active Transport (Detailed Explanation)

Secondary active transport is a membrane transport mechanism in which the movement of one molecule **against its concentration or electrochemical gradient** is driven indirectly by the energy stored in the gradient of another ion, typically **Na^+ in animal cells** or **H^+ in bacteria and plant cells**.

Unlike primary active transport, secondary active transport **does not use ATP directly**. Instead, it depends on ion gradients previously established by ATP-driven pumps such as the Na^+/K^+-ATPase.

Energy Source for Secondary Active Transport

The true energy source is the **electrochemical gradient** of the driving ion.

This gradient has two components:

1. **Chemical gradient** (difference in concentration)
2. **Electrical gradient** (membrane potential)

The free energy released when the driving ion moves down its gradient is harnessed to transport another molecule uphill.

Thus, ATP hydrolysis is required **indirectly**, linking secondary transport tightly to cellular energy metabolism.

Molecular Mechanism

Secondary active transporters are **carrier proteins** that undergo conformational changes.

General mechanism:

1. Binding of the driving ion (e.g., Na^+) increases affinity for the transported substrate.
2. Both substrates bind simultaneously to the transporter.
3. A conformational change translocates both molecules across the membrane.
4. Release occurs on the opposite side of the membrane.

Transport is therefore **coupled**: one molecule cannot be transported without the other.

References

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3. Watson JD et al. *Molecular Biology of the Gene*.
4. Harper's Illustrated Biochemistry.