**MOVEMENT ACROSS MEMBRANES**

(a) Ion concentration inside a single animal cell

(b) Ion concentration across gill epithelium of a freshwater fish

(c) Glucose transport across intestinal epithelium into the blood system

**MEMBRANE STRUCTURE**

How do phospholipids build a membrane?
**Phospholipid structure**

- Polar head: Choline$^+$, Phosphate$^-$, Glycerol
- Non-polar fatty acid chains
- Nonpolar tails

Many positively charged groups can occupy this position.

Bends symbolize double bonds - less densely packed lipids.

**Phospholipid “behavior” in water**

- Micelle: Water, Hydrophilic heads, Hydrophobic tails
- Phospholipid bilayer

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Fluidity of membranes

(a) Lateral Movement (frequent) Flip-flops (rare)

Frequent lateral movement of lipids; infrequent flip-flops across membrane leaflets.

(b) Fluid Viscous

Unsaturated fatty acid tails with kinks Saturated fatty acid tails

Degree of unsaturated/saturated fatty acid tails (hydrocarbon) determines membrane fluidity.

Phospholipid composition and habitat temperature

Fatty acid chains vary in chemical unsaturation = double bonds that produce a bend in the chain. Unsaturated phospholipids are less densely packed and increase membrane fluidity. To maintain membrane fluidity at low temperatures, cold adapted species incorporate more unsaturated lipids into their membrane.

after Logue et al. (2000), J Exp Biol 203, 2105-2115
Membrane proteins

TABLE 2.1 The five functional types of membrane proteins and the functions they perform

<table>
<thead>
<tr>
<th>Functional type</th>
<th>Function performed (defining property)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Channel</td>
<td>Permits simple or quasi-simple diffusion of solutes in aqueous solution (page 70)— or osmosis of water (page 87)—through a membrane; a simplified view of a channel is that it creates a direct water path from one side to the other of a membrane (i.e., an aqueous pore) through which solutes in aqueous solution may diffuse or water may undergo osmosis</td>
</tr>
<tr>
<td>Transporter (carrier)</td>
<td>Binds noncovalently and reversibly with specific molecules or ions to move them intact across a membrane; that transport through the membrane is active transport (page 74) if it employs metabolic energy; it is facilitated diffusion (page 74) if metabolic energy is not employed</td>
</tr>
<tr>
<td>Enzyme</td>
<td>Catalyzes a chemical reaction in which covalent bonds are made or broken (page 41)</td>
</tr>
<tr>
<td>Receptor</td>
<td>Binds noncovalently with specific molecules and as a consequence of this binding, initiates a change in membrane permeability or cell metabolism; receptor proteins mediate the responses of a cell to chemical messages (signals) arriving at the outside face of the cell membrane (page 56)</td>
</tr>
<tr>
<td>Structural protein</td>
<td>Attaches to other molecules (e.g., other proteins) to anchor intracellular elements (e.g., cytoskeleton filaments) to the cell membrane, creates junctions between adjacent cells (Figure 2.7), or establishes other structural relations</td>
</tr>
</tbody>
</table>

PASSIVE AND ACTIVE TRANSPORT

What are equilibrium conditions?

A system moves towards its "equilibrium" when there is no further input of energy or matter - has minimal potential for more work.

Passive transport mechanisms work only in the direction of equilibrium.

Active transport mechanisms are capable of working in a direction against the equilibrium.
PASSIVE: Diffusion as passive solute transport

Due to molecular movement glucose passes through the membrane passively. Because there is more glucose on the left side, on average and by chance more molecules pass from left to right. This leads to equal concentrations on both sides - the equilibrium for this system.

PASSIVE: Solute diffusion

\[ J = D \cdot \frac{A \cdot (C_1 - C_2)}{X} \]

Fick's diffusion equation (Adolf Fick, 1829-1901)

- \( J \sim C_1 - C_2 \): Diffusion rate is proportional to concentration gradient
- \( J \sim (C_{solute Y}) \): Diffusion rate for solute \( Y \) depends on concentration gradient of the solute \( Y \)
- \( J \sim 1/X \): Diffusion rate is greater when diffusion distance is shorter
- \( J \sim A \): Diffusion rate is greater when diffusion area (surface) is greater
- \( J \sim D \): Diffusion rate is proportional to the diffusion coefficient

\( D \) is a measure of the ease with which a solute moves through a medium separating the two concentrations; temperature dependent; defines permeability.

How do membranes affect diffusion?
Outward diffusion from the animal or cell increases the concentration in the environmental solution next to the outer surface. The boundary layer thus created may be very thin yet still have a substantial impact on the rate of diffusion.

**TABLE 3.1** The time required for diffusion through water to halve a concentration difference. Values are calculated for small solutes such as O$_2$ or Na$^+$. For each distance between solutions, the time listed is the time that will be required for diffusion to transport half the solute molecules that must move to reach concentration equilibrium. It is assumed that no electrical effects exist, and thus only diffusion based on concentration effects is occurring.

<table>
<thead>
<tr>
<th>Time required to halve a concentration difference by diffusion</th>
<th>Distance between solutions</th>
<th>A biological dimension that exemplifies the distance specified</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 nanoseconds</td>
<td>10 nanometers</td>
<td>Thickness of a cell membrane</td>
</tr>
<tr>
<td>100 milliseconds</td>
<td>10 micrometers</td>
<td>Radius of a small mammalian cell</td>
</tr>
<tr>
<td>17 minutes</td>
<td>1 millimeter</td>
<td>Half-thickness of a frog sartorius muscle</td>
</tr>
<tr>
<td>1.1 hours</td>
<td>2 millimeters</td>
<td>Half-thickness of a human eye lens</td>
</tr>
<tr>
<td>4.6 days</td>
<td>2 centimeters</td>
<td>Thickness of the human heart muscle</td>
</tr>
<tr>
<td>32 years</td>
<td>1 meter</td>
<td>Length of a long human nerve cell</td>
</tr>
</tbody>
</table>

Source: After Weiss 1996.
PASSIVE: Permeability of a membrane for a solute

The permeability of a membrane to a solute is the ease with which it can move through the membrane by simple diffusion.

Membrane permeability is based on:

- $D_m$, the diffusion coefficient:
  rate of diffusion of a substance through a membrane

- $K$, the partition coefficient:
  an indicator for the ratio between dissolved and undissolved solute in the membrane

$$J = P \, A \, \frac{C_1 - C_2}{X} \quad P = D_m \, K$$

PASSIVE: Membranes and the diffusion of solutes

- The diffusion of a solute across membranes depends on the hydrophobic or hydrophilic nature of the solute.

1. **Lipid solutes** (steroids and fatty acids): enter the interior of the cell membrane because of their hydrophobic nature.

2. **Molecular oxygen** ($O_2$): enter interior of membrane because of their small and nonpolar nature.

3. **Inorganic ions**: low permeability across membrane, but can diffuse passively through cell membranes at rapid rates due to ion channels.

**Ion channels** allow only passive transport across membranes. They do not bind the ions that pass through them. They are selective in determining which ion can pass. Types include: voltage-gated, stretch-gated, phosphorylation-gated and ligand-gated channels.
Types of gated ion channels

(a) Voltage-gated channel

Extracellular
Closed
Change membrane potential
Open
Cytoplasm

(b) Stretch- or tension-gated channel

Stretch
Cytoskeleton

Types of gated ion channels

(c) Phosphorylation-gated channel

Phosphorylate

(d) Ligand-gated channel

Ligand
Receptor site
Bind ligand
$PO_4^-$
PASSIVE: Selectively permeable membranes can create electrical gradients

Passive: Selectively permeable membranes can create electrical gradients: Nernst equation

\[ E_x = \frac{RT \ln \frac{C_{\text{out}}}{C_{\text{in}}}}{zF} \]

Consequences:

Unequal concentrations of ions across a membrane can create a membrane potential = resting potential.

A membrane potential can affect the concentration gradient across a membrane.
PASSIVE: Diffusion of ions is affected by a chemical and an electrical gradient

Electrical gradient moves ions in the same direction as the concentration gradient = fast diffusion.

Electrical gradient opposes the concentration gradient = slowing diffusion or reversing direction.

High Na+ concentration: Diffusion (fast)

Low Na+ concentration: Diffusion (slow)

PASSIVE: An electrochemical view of a single cell

Cl⁻ is near electrochemical equilibrium because the concentration gradient and electrical effect oppose each other.

K⁺: The conc. effect is greater than the electrical effect, but not as much as for Na⁺.

Na⁺ is far from electrochemical equilibrium, because the conc. gradient and electrical effect move it into the cell.
**PASSIVE: Facilitated diffusion**

Polar organic solutes (glucose, amino acids) are hydrophilic: diffuse through membrane with the help of carrier proteins:
- In direction of electrochemical gradient
- Facilitated because faster than simple diffusion
- Reversible and non-covalent binding

**PASSIVE SOLUTE TRANSPORT - SUMMARY**

- Passive transport moves towards the **electrochemical equilibrium**.

- The **permeability** of a membrane for a lipid solute depends on how readily the solute enters into and moves across the membrane lipid bilayer – **simple diffusion**.

  For inorganic ions, the permeability depends on the number of **ion channels**.

- **Polar organic solutes** (glucose, amino acids) move across membranes with the help of **transporter** proteins in the direction of the electrochemical equilibrium (facilitated diffusion).

- Simple diffusion depends on the **concentration gradient** for an uncharged solute. In case of a charged solute, conc. gradients and **electrical effects** contribute to diffusion.
Primary and secondary ACTIVE TRANSPORT

- Na\(^+\)-K\(^+\)-ATPase is an example of a primary active transport mechanism: it draws energy directly from ATP. An ATPase is a transporter and an enzyme.

- Other important ATPases:
  - Ca\(^{2+}\)-ATPase in the sarcoplasmic reticulum of muscle cells.
  - H\(^+\)-K\(^+\)-ATPase is the proton-pump that acidifies stomach content.
  - Vesicular or v-type H\(^+\)-ATPase in gills and kidneys.

- Secondary active transport draws energy from an electrochemical gradient of a solute, and therefore indirectly from ATP.
ACTIVE: Primary active transport mechanisms

Cl⁻ is close to electrochemical equilibrium.

Electrochemical gradients favor steady diffusion of Na⁺ and K⁺ through resting channels in the cell membranes.

The Na⁺-K⁺ pump maintains Na⁺ and K⁺ ions out of equilibrium by using ATP-bond energy.

(a) Ion concentration inside a single animal cell

Anionic proteins are trapped inside the cell.

ACTIVE: Secondary active transport mechanisms

A transporter carries Na⁺ towards its EC equilibrium, and thereby forces the cotransport of glucose across the membrane.

The Na⁺-K⁺-ATPase in the basolateral membrane pumps Na⁺ outside the cell, and thereby maintains the Na⁺ gradient across the apical membrane.

(c) Glucose transport across intestinal epithelium into the blood system
ACTIVE: Ion movements in fresh water fish gills

(b) Ion concentration across gill epithelium of a freshwater fish

**ACTIVE SOLUTE TRANSPORT - SUMMARY**

- Solute transport is **active** if it can move solutes away from **electrochemical equilibrium**.

- Active transport is **primary** if the transporter is an ATPase (energy comes directly from ATP), **secondary** if the energy comes from a solute electrochemical gradient. **Organic solutes** are pumped by secondary-active transport mechanism.

- The transport of ions can create voltage differences (**electrogenic**) or not (**electroneutral**).
MEMBRANE TRANSPORT - SUMMARY

- **Equilibrium** is the state of a system without input of energy or matter from outside.
- **Passive** transport moves towards, **active transport** can move against the electrochemical equilibrium of a system.
- **Uncharged** molecules equalize concentrations by **simple diffusion**, charged molecules are also moved by **electrical forces**.
- The **permeability** of a membrane for a solute depends on how readily it dissolves into the membrane and the number of channels (inorganic ions).
- Active transport uses **metabolic energy (ATP)** to transport a solute against the electrochemical gradient.
- Organic solutes can be moved across membranes by transporters, but only towards the electrochemical equilibrium (**facilitated diffusion**).
- Active transport is **primary** when it directly uses ATP (ATPases), **secondary** if the energy for transport comes from a concentration gradient.

OSMOSIS - The transport of water

- Osmotic pressure is measured in **osmolarity**: 1 Osm is equivalent to a solvent with 1 Mole of dissolved solutes per liter.
**OSMOSIS - An example**

Isotonic solution: empirical evaluation if cell loses or gains water

**Transport across membranes - summary II**

- The transport of water depends on the **colligative properties** of a solvent.
- Water moves from **solution of lower osmotic pressure** (more abundant water) to the solution of **higher osmotic pressure** (less abundant water).
- If two solutions have the same osmotic pressure they are called **iso-osmotic**. A solution with higher osmotic pressure is **hyper-osmotic** relative to one with lower pressure (**hypo-osmotic**).