Membrane Transport

A. Permeability - ability of a substance to pass through a membrane
- cell membranes are selectively permeable
- permeability is determined by (1) the lipid bilayer
  (2) membrane transport proteins

1. Permeability through the Lipid Bilayer
   a. molecular size - smaller molecules are more permeable
   b. lipid solubility - non-polar molecules are lipid-soluble → more permeable
      - polar molecules and ions are less permeable or impermeable

2. Membrane Transport Proteins - enable certain ions and polar molecules to pass through
   channels - water-filled pores, for ions and H₂O
   carriers - protein “shuttles” for small polar molecules
   pumps - active transport, mostly ions

Permeability of the cell membrane to physiological molecules:

- highly permeable
- less permeable
- impermeable

O₂ & CO₂, Na⁺, K⁺, Cl⁻ (via channels)
H₂O (via aquaporins)

B. Transport Across Membranes

a) Passive transport
   - does not require energy
   - substances move down a gradient

1. simple diffusion
2. osmosis
3. diffusion through channels
4. facilitated diffusion

b) Active transport
   - requires energy
   - transport against a gradient

5. primary active transport
6. secondary active transport

1. Simple Diffusion
   - due to random molecular motion
   - net movement is from high concentration to low concentration

- Fick’s Law of Diffusion gives the rate of diffusion:
  \[ \text{Rate} = \frac{P \cdot A \cdot (C_{\text{out}} - C_{\text{in}})}{x} \]
  Rate is proportional to permeability (P), surface area (A), concentration gradient (C_{\text{out}} - C_{\text{in}});
  inversely proportional to membrane thickness (x)

2. Osmosis - passive movement of water across a membrane*
   in response to a solute concentration difference
   * selectively-permeable membrane: permeable to H₂O, impermeable to solutes
     - primary mechanism of H₂O movement across biological membranes
     - H₂O follows solutes, H₂O moves from dilute to concentrated solution (“solutes suck water”)

osmolarity = total concentration of all solutes in a solution;
  1 osmole/L (Osm) = 1 mole of solutes per liter
  a. non-ionic solutes: osmolarity = concentration e.g., 1 M glucose = 1 Osm = 1,000 mOsm
  b. salts: ionize in H₂O: 1M NaCl → 1 mole/L Na⁺ + 1 mole/L Cl⁻ ≈ 2 Osm

plasma osmolarity ≈ 290 mOsm (solutes: Na⁺, Cl⁻, other ions, proteins, glucose, etc.)

osmotic pressure - driving force for osmosis
  - depends on difference in total solute concentration (\(\pi = \text{CRT}\))
  - “negative pressure” pulls water from dilute to concentrated solution

tonicity - effect of an extracellular solution on cell volume, due to H₂O movement by osmosis
  hypotonic solution: H₂O moves in, cell expands
  hypertonic solution: H₂O moves out, cell shrinks
  isotonic solution: no net movement of H₂O, cell volume stays constant
  e.g., isotonic saline (0.9% = 0.9 g/dL NaCl) ≈ 290 mOsm
3. Diffusion through Channels

- **ion channels** are protein passageways for ions in the membrane
  - most channels are **selective** for certain ions (K⁺, Na⁺, etc.)
  - ions diffuse down **electrochemical gradients** (combined concentration and electrical forces)
  - channels may be **ungated** or **gated**
  - **aquaporins** are water channels, found in most cell membranes

- **carrier proteins** enable diffusion of certain polar molecules across the membrane
  - transport down a concentration gradient, no energy required
  - specificity - each carrier is specific to particular molecule(s)
  - saturation - rate limited by number of carrier proteins in the membrane → **transport maximum**

- **GLUT** proteins - family of glucose transporters, present in many cell membranes
  - most body cells take up glucose by facilitated diffusion using GLUT proteins
  - **GLUT4** is the **insulin-dependent** glucose carrier of skeletal muscle and adipose tissue; insulin promotes insertion of GLUT4 proteins into the membrane → enables glucose uptake into cells via facilitated diffusion

4. Facilitated Diffusion

- **Na⁺/K⁺ pump** (Na⁺/K⁺-ATPase) transports Na⁺ out, K⁺ in
  - maintains Na⁺ and K⁺ gradients between the ICF and ECF
  - Na⁺ gradient provides potential energy for transport of other molecules
  - Na⁺/K⁺ pump activity is stimulated by **thyroid hormones**
  - electrical properties of cells (**membrane potentials**) result from K⁺ and Na⁺ gradients

Other active transport proteins: Ca²⁺-ATPase in muscle, H⁺-ATPase in stomach

5. Primary Active Transport

- **pumps** are transport proteins that use energy from ATP directly (**ATPases**)
  - transport ions “uphill”, against **electrochemical gradients**

- **Na⁺/K⁺ pump** (Na⁺/K⁺-ATPase) transports Na⁺ out, K⁺ in
  - maintains Na⁺ and K⁺ gradients between the ICF and ECF
  - Na⁺ gradient provides potential energy for transport of other molecules
  - Na⁺/K⁺ pump activity is stimulated by **thyroid hormones**

Other active transport proteins: Ca²⁺-ATPase in muscle, H⁺-ATPase in stomach

6. Secondary Active Transport

- uses potential energy stored in **ionic gradients** to move other molecules
- transport protein couples downhill flow of an ion to uphill transport of another molecule

- **cotransport** - movement in the same direction (e.g., Na⁺-glucose transport)
- **countertransport** - movement in opposite directions (e.g., Na⁺/H⁺ exchanger)

- **SGLT** is a Na⁺-glucose cotransporter in small intestine and kidney epithelium
  - moves glucose against its gradient from the lumen into the epithelial cell
  - uses energy contained in the Na⁺ gradient (ultimately formed by the Na⁺/K⁺-ATPase)

7. Transport via Membrane-Bound Vesicles

- endocytosis - phagocytosis and pinocytosis
- exocytosis - secretion of products out of the cell (mucus, proteins, neurotransmitters, hormones)
  - also functions for inserting molecules into the cell membrane (lipids, proteins)

D. Epithelial Transport

1. Structure of Transport Epithelia

- **apical membrane** - faces lumen
  - **microvilli** increase surface area
- **basolateral membrane** - faces ECF, attached to basement membrane
  - contains Na⁺/K⁺ pumps
- **tight junctions** - join epithelial cells near apical surface, prevent fluid leakage between cells

2. Transepithelial Transport - NaCl, glucose and H₂O in the small intestine and kidneys

- NaCl - apical membrane: Na⁺ enters via **diffusion through channels** (apical Na⁺ channels)
  - basolateral membrane: primary **active transport** (Na⁺/K⁺ pump) moves Na⁺ to ECF
  - Cl⁻ follows Na⁺ passively by diffusion through channels
- glucose - apical membrane: **secondary active transport** - cotransport with Na⁺ (SGLT)
  - basolateral membrane: **facilitated diffusion** of glucose out to ECF (GLUT)
- water - **osmosis** across apical and basolateral membranes; follows solute movement
  - pumping of Na⁺ to ECF between cells promotes H₂O movement by osmosis