Table 3-1: Factors Influencing the Rate of Net Diffusion of a Substance Across a Cell Membrane (Fick’s Law of Diffusion)

<table>
<thead>
<tr>
<th>Factor</th>
<th>Effect on Rate of Net Diffusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ Concentration gradient of substance</td>
<td>Constant in homeostasis</td>
</tr>
<tr>
<td>↑ Surface area of membrane</td>
<td>Constant in homeostasis for neutral molecules only</td>
</tr>
<tr>
<td>↑ Lipid solubility</td>
<td>Constant in homeostasis for neutral molecules only</td>
</tr>
<tr>
<td>↑ Molecular weight of substance</td>
<td>Constant in homeostasis for neutral molecules only</td>
</tr>
<tr>
<td>↑ Distance (thickness)</td>
<td>Constant in homeostasis for neutral molecules only</td>
</tr>
</tbody>
</table>

The table indicates how changing the variable listed alone will alter diffusion rate.

Fick’s Law of Diffusion

\[
\text{Rate of Diffusion} = \frac{\text{Conc. Grad.} \times \text{SA} \times \text{Diffusion Coef.}}{\text{Membrane Thickness}}
\]

SA = Surface Area

\[
\text{Diffusion Coef.} = \frac{\text{Permeability}}{\sqrt{(\text{MW})}}
\]

\[K^+\] has a lower MW and is normally 30x more lipid soluble in most cell membranes than is \[Na^+\]

NEITHER HAS DIFFUSION COEFFICIENT OF “0”, SO DIFFUSION WILL OCCUR ACROSS THE MEMBRANE IF THERE IS A CONCENTRATION GRADIENT
Diffusion through Ion Channels

• Ions such as Na⁺, K⁺, Cl⁻, and Ca²⁺ all use specific protein channels to diffuse into and out of cells.

• Channels are integral membrane proteins that span the lipid bilayer.

• A single protein may have a conformation that looks like a doughnut, with the hole in the middle providing the channel for ion movement.

• More often, several proteins aggregate, each forming a subunit of the walls of a channel.

• Specificity is determined by pore size of the channel, charge, and binding sites.

Fig. 4-5
Regulation of “gated” ion channel

• Temporary change in shape of protein changes status of ion channel
  – Chemically regulated: a chemical messenger binds to a receptor that is a part of or associated with the ion channel
    • A form of allosteric modulation ➔ “gate opens/closes)
  – Mechanically regulated: physical force alters the shape of the protein ➔ gate opens/closes
  – Voltage regulated: distribution of charged particles in vicinity of gate alters shape of the protein ➔ opens/closes/locks(double gate)

Osmosis: Diffusion of water

• Movement of solute (water) from high water concentration to low water concentration through a membrane that is permeable to water but not the solute molecules in it
• If the membrane was permeable to solute, it would come into equilibrium
Nonpenetrating Solute

- A solute that cannot go through a membrane lowers the water concentration of the solution
  - Causes water to diffuse towards low water concentration

![Diagram showing water and solute concentrations](image-url)
Measurement of Osmolality of Human Plasma

1 mole of solute dissolved in 1 kg (1 liter) of H₂O forms a 1 \textit{molal} solution or 1000 \textit{millimolal} solution

-> ratio of solute particles (1 mole = 6.02 x 10^{23}) to solvent molecules the same in two different 1 molal solutions

- 18 grams H₂O = 1 mole
- 1 liter = 1 kg = 1000 grams = 55.56 moles = 3.345 x 10^{25} molecules H₂O

- 1 mole of glucose = 180 grams glucose + 1 liter H₂O = \textit{1 molal glucose solution}
- 1 mole of sodium = 23 grams sodium + 1 liter H₂O = \textit{1 molal sodium solution}

1 mole of any solute per 1 liter water depresses freezing point of water by \(-1.86°C\)

Measurement of Osmolality of Human Plasma

1 m glucose freezes at \(-1.86°C\)
1 m Na freezes at \(-1.86°C\)
1 m NaCl freezes at \(-3.72°C\) because NaCl ionizes to Na\(^+\)Cl\(^-\) (twice as many particles = twice as many moles = 2 moles per liter water = 2 molal solution)

0.5 NaCl freezes at \(-1.86°C\) because NaCl ionizes to Na\(^+\)Cl\(^-\) (twice as many particles = twice as many moles = 2x 0.5 moles per liter water = 1 molal solution)

___ m solution freezes at -0.93°C
___ m solution freezes at -0.62°C
___ m human plasma solution freezes at -0.56°C
human ECF, ICF = 300mOsm

- Cells maintain osmotic equilibrium
  - ECF, ICF have same osmotic pressure
  - cells exposed to ECF, ICF, or 300milliosmal (0.3 Osm) solutions are in osmotic equilibrium
  - when > 300milliosmolar, a solution is called hyperosmotic i.e. more osmotically active solute molecules than plasma
  - when < 300milliosmolar, a solution is called hypoosmotic i.e. few osmotically active solute molecules than plasma
  - when = 300milliosmolar, solution is isosmotic

- If exposure of a cell to a solution causes osmosis of water into or out from cell, regardless of the solution’s osmolality then different terms are employed to avoid confusion.
  - isotonic: does not influence osmosis
  - hypertonic: causes cell to lose water (dehydrate, crenate)
  - hypotonic: causes cell to gain water (swell, burst)
• Solutes “eaten” but not absorbed can become osmotically active particles and create a hypertonic fluid compartment in the lumen of the gastrointestinal tract
  – what happens to fluid volume of g.i. tract?

• Why is gargling salt water effect in treating a sore throat which is caused by pesky isotonic bacteria?

Tonicity

• Tonicity of a solution
  – Determines whether cell remains same size, swells, or shrinks when a solution surrounds the cell
    • Isotonic solution (Cell remain the same size)
    • Hypotonic solution (Cell swell)
    • Hypertonic solution (Cell shrinks)
Extracellular Osmolarity & Cell Volume

- **Intracellular fluid 300 mOsm nonpenetrating solutes**
  - Normal cell volume

- **300 mOsm nonpenetrating solutes**
  - No net movement of water; no change in cell volume.
  - (a) Isotonic conditions

- **200 mOsm nonpenetrating solutes**
  - Water diffuses into cells; cells swell.
  - (b) Hypotonic conditions

- **400 mOsm nonpenetrating solutes**
  - Water diffuses out of cells; cells shrink.
  - (c) Hypertonic conditions

- **Hypertonic solution**
  - Cell shrinks
  - 400 mOsm nonpenetrating solutes

- **Isotonic solution**
  - No change in cell volume
  - 300 mOsm nonpenetrating solutes

- **Hypotonic solution**
  - Cell swells
  - 200 mOsm nonpenetrating solutes
Assisted Membrane Transport

- **Outside energy source and/or protein assisted transport**
  - **ASSISTED CLASSIFIED BY Energy Source**
    - Random molecule motion coupled with protein carrier
      - facilitated diffusion
    - Random molecular motion coupled with regulated ion channel
      - Chemically regulated, mechanically regulated, voltage regulated ion channels
    - ATP expenditure coupled with protein carrier
      - Primary Active Transport (ATPase Pumps)
      - Secondary Active Transport
    - ATP expenditure coupled with vesicular activity
      - Endocytosis
      - Exocytosis
  - **ASSISTED CLASSIFIED BY (protein) Carrier-mediated transport**
    - Membrane carrier protein changes its shape
    - Membrane channel protein changes its status (closed or open)

**Primary (1°) active transport** involves the direct expenditure of energy in the form of adenosine triphosphate (ATP) hydrolysis and carrier phosphorylation to transport an ion against the gradient.

\[
\text{ATP} + \text{protein} \rightarrow \text{ADP} + \text{phosphorylated protein}
\]

1. Covalent phosphorylation by ATPase changes conformation of carrier protein (ATPase pump) until phosphate is removed by phosphatase activity;
2. two distinct conformations allow transported molecule(s) to bind as affinity with binding site(s) effected by presence/absence of phosphate group
3. Attracted molecule(s) are also transported through membrane as protein conformation changes
4. w/o ATP → ADP + P, for phosphorylation of carrier, no shape change or molecule binding so no transport occurs, which is bad for cell
1. Binding of ligand stimulates phosphorylation
2. Change in carrier's conformation
3. Expulsion of ligand on opposite side
4. Release phosphate by phosphatase
5. Restore original shape
6. Bind next ligand (back to 1)

1. Carrier protein's "ase" activity splits ATP into ADP plus phosphate. Phosphate group binds covalently to carrier, increasing affinity of its binding site for ion.
2. Ion to be transported binds non-covalently to carrier on low-concentration side.
3. In response to ion binding, carrier changes conformation and binding site faces opposite side of membrane. The change in conformation reduces affinity of site for ion.
4. Carrier releases ion to side of higher concentration. Phosphate group is also released (phosphatase activity).
5. Carrier reverts to its original conformation and affinity.

1. Binding of cytoplasmic Na⁺ to the protein stimulates phosphorylation by ATP.
2. Phosphorylation causes the protein to change its conformation.
3. The conformational change expels Na⁺ to the outside, and extracellular K⁺ binds.
4. K⁺ binding triggers release of a phosphate group.
5. Loss of phosphate restores original conformation.
6. K⁺ is released and Na⁺ sites are receptive again; the cycle repeats.
7. High Na
8. Low Na

High K
Low K
Active Transport (Primary Active Transport)
Secondary Active Transport

http://biomedicum.ut.ee/armpgb/1kursus/Ani_6.swf

On this site you can choose to view animations of either primary or secondary active transport.

Secondary Active Transport

- An active transport pump maintains an chemical gradient necessary for a different transporter or channel to function properly.

http://biomedicum.ut.ee/armpgb/1kursus/Ani_6.swf
Secondary Active Transport

Mechanism of the SGLT Transporter

Without a primary active transporter somewhere else in the membrane to move Na\(^+\) to lumen, concentration gradient for Na\(^+\) will be lost and SGLT can't operate.
Primary Active Transport maintains Na+ concentration gradient from lumen to cell, which drives Secondary Active Transport creating glucose concentration gradient from cell to blood used for Facilitated Diffusion.

1. Na+-K+ pump uses energy to drive Na+ uphill out of cell.
2. SGLT uses Na+ concentration gradient to simultaneously move Na+ downhill and glucose uphill from lumen into cell.
3. GLUT passively moves glucose downhill out of cell into blood.

1. Binding of Na+ on luminal side, where Na+ concentration is higher, increases affinity of SGLT for glucose. Therefore, glucose also binds to SGLT on luminal side, where glucose concentration is lower.
2. When both Na+ and glucose are bound, SGLT changes shape, opening to cell interior.
3. SGLT releases Na+ to cell interior, where Na+ concentration is lower. Because affinity of SGLT for glucose decreases on release of Na+, SGLT also releases glucose to cell interior, where glucose concentration is higher.
Vesicular Transport

- Material moves in/out of cell wrapped in membrane
- Active method of membrane transport
- Two types of vesicular transport
  - Endocytosis
  - Exocytosis
Vesicular Transport

- Two types of vesicular transport
  - **Endocytosis**
    - Process by which substances move into the cell
    - Pinocytosis – nonselective uptake of “stuff” in ECF to get it INTO INTRACELLULAR
    - Phagocytosis – selective uptake of multimolecular particle to get it INTO INTRACELLULAR
  - **Exocytosis**
    - Provides mechanism for secreting large polar molecules that “EXIT” the cell to EXTRACELLULAR ENVIRONMENT
    - Technically also enables cell to add specific components to cell membrane
END OF TEST MATERIAL