Membrane Transport

Anatomy 36
Unit 1
Membrane Transport

• Cell membranes are selectively permeable
• Some solutes can freely diffuse across the membrane
• Some solutes have to be selectively moved across the membrane
  • Facilitated by a carrier or transport protein
    • Carrier mediated transport (passive transport)
    • Active transport
• **Passive transport:** Solutes move on their concentration gradient
  • Does not require energy input
• **Active transport:** Solutes move against their concentration gradient
  • Have to be pumped
  • Requires energy expenditure
Passive vs. Active Transport

• Passive transport
  • Diffusion
  • Osmosis
  • Filtration
  • Facilitated diffusion

• Active transport
  • Primary active transport
  • Secondary active transport
**Diffusion**

- Net movement of solutes from an area of high concentration to an area of low concentration by random molecular motion

- *Molecules move on their concentration gradient*
  - High to low concentration

*An Ink Drop Gradually Dissolves into a Glass of Water by DIFFUSION*
Diffusion Across a Cell Membrane

- **Easily diffuse**
  - $\text{H}_2\text{O}$ (small, polar covalent bonds)
  - Lipids
    - Various forms of fatty acids that do not carry a charge
    - 2-monoglyceride
    - Lipid soluble chemical messengers
  - Gases
    - $\text{O}_2$
    - $\text{CO}_2$
    - NO
- **Diffuse rapidly**
- **Movement driven by the concentration gradient of the molecule**

- **Do Not diffuse**
  - Movement across the membrane must be facilitated
  - Facilitated by a transporter
  - Solutes that carry a full charge and/or are too big
    - Ions
    - Large, polar molecules
      - Amino acids
      - Proteins
      - Free fatty acids (carry a negative charge)
      - Triglycerides
Rate of Diffusion

- **Flux** is the magnitude and direction of flow across a membrane due to a concentration gradient
  - **Influx** is diffusion into the cell
  - **Efflux** is diffusion out of the cell
  - **Net flux** is the overall direction of movement

- Influenced by
  - ✔ Magnitude of concentration difference
  - ✔ Mass of the molecule
  - ✔ Temperature
  - ✔ **Surface area of the membrane**
Osmosis
Diffusion of $\text{H}_2\text{O}$

- The movement of water from an area of high water concentration to an area of low water concentration across a semi-permeable membrane

- Water can freely move across cell membranes in both directions

- $\text{H}_2\text{O}$ will move to establish $\text{H}_2\text{O}$ equilibrium
Solutions and Solutes

• A solution is made up of
  • Solvent – \( \text{H}_2\text{O} \)
  • Solutes – everything else in the solution

• \( \text{H}_2\text{O} \) can freely move across cell membranes

• Solutes are non-penetrating \((\text{they can not move across the membrane})\)

• Water will move towards the higher solute concentration

• 2 ways we represent the concentration of the solutes
  • Osmolality – a measure of all solutes
  • Tonicity – a measure of \( \text{NaCl} \)

WATER CHASES THE SALT!
Osmolality

- **Molality** = # of moles of solute per kg of solvent

- **Osmolality** = ionic concentration of dissolved substances per kg of water (water is the solvent)
  - Osmolality of plasma = 300 mOsm = *isomotic*
  - Determined by the number of solute particles in 1 kg of water
    - 1 m of $C_6H_{12}O_6$ = 1 osmole (Osm)
    - 1 m of NaCl = 2 osmoles
    - 1 m of $CO_2$ + 1 m of KCl = 3 osmoles
Tonicity

- The relative concentration of NaCl dissolved in solution
- The concentration of NaCl outside of the cell compared to inside the cell
- The ability of a solution to cause a cell to gain or lose water
- Determines the direction and extent of water movement

WATER CHASES THE SALT!
Isotonic Solution

- The solute concentration is the same outside the cell and inside the cell
- Usually 0.9% NaCl
- The solute concentration is the same across the cell membrane
- Water moves in both directions across the plasma membranes
- **There is no net water gain/loss inside of the cell**
Hypertonic Solution

- The solute concentration is higher outside the cell than inside the cell
- Greater than 0.9% NaCl
- Water moves in both directions across the plasma membranes
- **There is a net loss of water inside of the cell**
- Causes crenation

**WATER CHASES THE SALT!**
Hypotonic Solution

• The solute concentration is lower outside the cell than inside the cell
• Less than 0.9% NaCl
• Water moves in both directions across the plasma membranes

• There is a net gain of water inside of the cell
• Causes lysis
Ion Channels

• Ions move through ion channels
  • *Ion channels can be considered transporters*
  • Ion channels formed by integral membrane proteins
  • Ions move on their concentration gradient through the ion channels
  • The electrical gradient also directs the movement of ions

• Ion channels are selective
  • Channel diameter
  • Charged and polar protein surfaces

• Ion channels are gated – they are **closed** until a “stimulus” causes them to open
  • Ligand gated (chemical messengers)
  • Voltage gated
  • Mechanically gated
Electrochemical Gradient

• Important consideration in ion diffusion
• Inner core of a cell is **negatively** charged
  • $\text{PO}_4^{3-}$ groups, proteins, amino acids
• Membrane separates electrical charges
  • Same charges repel
  • Opposite charges attract
Transporters

• Membrane transport proteins
• Integral membrane proteins span the plasma membrane
• Solute binds to the transporter
• Transporter changes shape
• Solute moves across the membrane
  • Small molecules
  • Macromolecules

• Movement of solutes on their the concentration gradient

• Examples
  • GLUT transporters (glucose)
  • Aquaporins (water)
  • Fatty acid transporters
Transporters

- GLUT transporters for glucose
- Aquaporins for H₂O
  - Usually transport solute-free water
  - About 10 different types of aquaporins
  - One will transport about 3 billion H₂O molecules per second

| Transporter | Tissue distribution | Special properties |
|-------------|---------------------|--------------------|
| GLUT 1      | Most cells.         | High capacity, relatively low Kᵥ (1-2mM). |
| GLUT 2      | Liver, beta cells, hypothalamus, basolateral membrane small intestine. | High capacity but low affinity (high Kᵥ, 15-20mM) part of "the glucose sensor" in β-cells. Carrier for glucose and fructose / liver and intestine. |
| GLUT 3      | Neurons, placenta, testes. | Low Kᵥ (1mM) and high capacity. |
| GLUT 4      | Skeletal and cardiac muscle, fat. | Activated by insulin. Kᵥ, 5mM. |
| GLUT 5      | Mucosal surface in small intestine, sperm. | Primarily fructose carrier in intestine. |

Adapted from King and Agre, 1998
Transporters

• Protein carriers transport molecules too large or polar across the plasma membrane
  • Facilitated diffusion
    • Transporters
    • Active transport

• Types of mediated transport
  • Uniport – one thing moves
  • Symport – two things move in the same direction
  • Antiport – two things move in opposite directions

• 4 characteristics of transporters
  • Chemical specificity
  • Competition
  • Affinity
  • Saturation

• These 4 characteristics apply to ALL ligand to protein binding
  • Ion Channels
  • Transporters
  • Enzymes
  • Receptors
Transporters
Chemical Specificity

- Only ligands with the requisite chemical structure will bind to the structural protein

- Ideally, functional protein specificity is absolute
  - ONLY one molecule can “fit”

- Realistically, specificity is not always absolute
  - More than one molecule can “fit”
  - This will result in
    - Affinity differences
    - Competition
Transporters

Competition

• Structurally related ligands may compete for binding to the functional protein
  • Some ligands may be inhibitory to the action of the functional protein

• Competition decreases the rate of action of the functional protein
Transporters

Affinity

• The attraction of the functional protein for the ligand
  • Ion channel to ion
  • Transporter to solute
  • Enzyme to substrate

• The action of the functional protein can be inhibited by ligands which alter the shape of the binding site.
Transporters

Saturation

• Transport system is saturated when all of the binding sites are occupied

• At that point, the rate of transport can not increase
Filtration

- Movement of a solution down a pressure gradient
  - High pressure to low pressure
  - Across a membrane
- What is filtered is determined by:
  - the blood pressure coming in to the nephron
  - the size of the pores (fenestrations) in the glomerulus and podocytes
- In the kidney
  - Protein and blood cells are not found in urine because of size and charge restrictions of the glomerulus
Solute Sizes

- **Crystalloid**
  - Diameter < 1\(\mu m\)
  - Solutes stay dissolved in solution
  - Solution is clear
  - Example: Ions

- **Colloid**
  - Diameter between 1\(\mu m\)-100\(\mu m\)
  - Solutes stay dissolved in solution
  - Solution is cloudy
  - Example: Proteins

- **Suspension Particle**
  - Diameter > 100\(\mu m\)
  - Solids settle out of solution
  - Solution is clear with visible sediment at the bottom
  - Not found in biological systems
Filtration Experiment

- Collect 250 mL of your mixed solution
  - FeCl₃
  - Starch
  - Charcoal

- Pour the mixture into the funnel lined with filter paper

- Observe how fast/slow the solution passes through the filter

- After 90 minutes, perform your indicator tests to determine what passed through the filter paper
Active Transport

• Movement against the concentration gradient
• Requires hydrolysis of ATP

• Transporters called pumps
• Two types
  • Primary active transport
  • Secondary active transport
Primary Active Transport

• Steps
  – Molecule or ion binds at recognition site
  – *Phosphorylation* of pump
  – Conformational change
  – Transported molecule flipped to other side of membrane
  – *Dephosphorylation* of pump releases the transported molecule
  – Returns to its original conformation
Na\(^+\)/K\(^+\)/ATPase Pump

• 1 cycle of the pump:
  • Requires 1 ATP
  • Pumps 3 Na\(^+\) out
  • Pumps 2 K\(^+\) in

• Establishes and maintains low intracellular [Na\(^+\)]
  • Commonly used for cotransport

• Establishes and maintains a negative membrane potential
  • Neurons
  • Muscle cells
Secondary Active Transport

• Movement of a substance B can be coupled to the movement of substance A.
  • Substance A is pumped out of the cell on the apical membrane – creating a concentration gradient
  • Substance A moves through an ion channel on the luminal side into the epithelial cell on its concentration gradient that was established by the pump
  • *The movement of Substance B is coupled to the movement of Substance A*
  • The energy expenditure comes from the pump for Substance A

• **Cotransport**
  • Same direction
  • SGLT’S (Na⁺ coupled)
    • Intestinal mucosa
    • PCT of nephron

• **Counter transport**
  • Opposite direction

\[ \text{Na}^+ \text{ is commonly coupled to the movement of something else across the same membrane} \]
Summary of Passive and Active Transport Mechanisms
Endocytosis and Exocytosis

- Requires ATP
- *Allows membrane impermeable molecules to pass*

- Endocytosis moves substance into the cell
  - May be receptor mediated
- Exocytosis moves substance out of the cell
  - Chylomicrons
    - Basolateral membrane transport
    - Absorption into blood
Enterocytes

Diffusion of 2 Monoglyceride fatty acids

Exocytosis of triglyceride
Epithelial Transport

- **ALL** tubes are lined with epithelial cells
- Movement of substances across the wall of the tube (absorption, filtration, secretion)
  - Apical/Basolateral membranes do not have same permeability or transport characteristics
  - Apical membrane faces the lumen of the tube
  - Basolateral membrane faces the blood vessels outside of the tube

- **Paracellular pathway**
  - Para = alongside, next to
  - Only H$_2$O can move in between some epithelial cells

- **Transcellular pathway**
  - Trans = across
  - Substance has to move across or through the cell