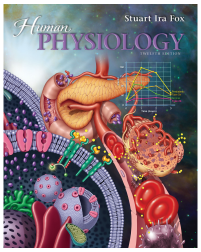
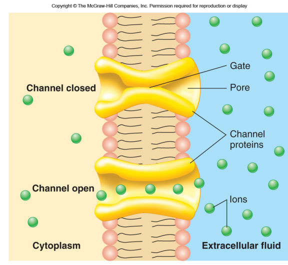


Chapter 6

Interactions Between Cells and the Extracellular Environment

Lecture PowerPoint

I. Extracellular Environment



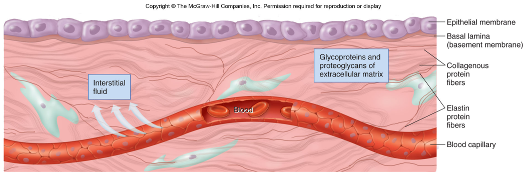
Extracellular Environment

- The extracellular environment includes everything located outside the cells.
- Cells receive nourishment from and release wastes into the extracellular environment.
- Cells communicate with each other by secreting chemical regulators into the extracellular environment.

Body Fluids

- 67% of our water is within cells in the intracellular compartment.
- 33% is in the extracellular compartment. Of this:
  - 20% is in blood plasma.
  - 80% makes up what is called tissue fluid, or interstitial fluid.

Extracellular Environment



Extracellular Matrix

- Contains protein fibers and a gel-like ground substance
  - Protein fibers provide structural support.
  - Gel is composed of glycoproteins (composed of proteins and sugars) and proteoglycans (composed of polysaccharides).
  - Integrins are glycoproteins that extend from the cell cytoskeleton and bind to the extracellular matrix.

Cell Transport

- The plasma membrane is selectively permeable, meaning that it allows some molecules to cross but not others.
  - Generally not permeable to proteins, nucleic acids, or other large molecules
  - Generally permeable to ions, nutrients, and wastes

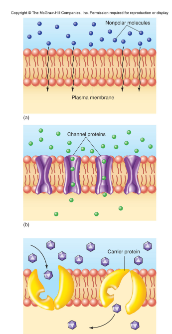
Categories of Membrane Transport

1. Carrier-mediated
   a. Facilitated diffusion
   b. Active transport
2. Noncarrier-mediated
   a. Simple diffusion of lipid-soluble molecules
   b. Simple diffusion of water = osmosis
   c. Simple diffusion of ions through nonspecific channels

Categories of Membrane Transport

- Passive transport: Molecules move from higher to lower concentration without using energy.
- Active transport: Molecules move from lower to higher concentration using ATP.

Categories of Membrane Transport

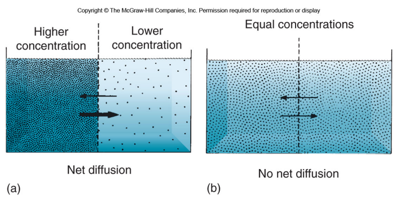


II. Diffusion and Osmosis

Diffusion

- Solution: consists of a solvent (water) and a solute (molecules dissolved in water)
  - Molecules in a solution are in a constant state of motion.
  - If there is a concentration difference between two regions, random motion will establish equilibrium via diffusion.

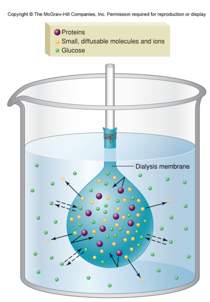
Diffusion



Diffusion

- Net diffusion: Due to random movement, the net direction of diffusion is from high to low solute concentration.
  - Will happen across a permeable membrane

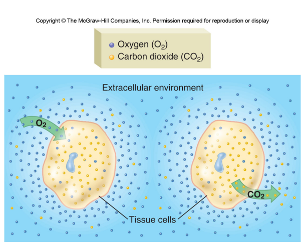
Diffusion



Diffusion Across the Plasma Membrane

- Nonpolar (or uncharged) lipid-soluble molecules pass easily.
  - Oxygen, carbon dioxide, and steroid hormones
- Gas exchange: net diffusion of O_2 into cells and CO_2 out of cells due to concentration
  - Opposite in lungs

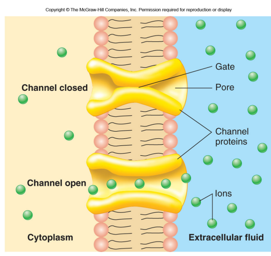
Diffusion Across the Plasma Membrane



Diffusion Across the Plasma Membrane

- Charged ions can pass through ion channels that cross the plasma membrane.
  - Channels may always be open or be gated.

Diffusion Across the Plasma Membrane



Rates of Diffusion

- Depend on:
  - Magnitude of concentration difference
  - Permeability of the membrane to the molecules
  - Temperature of the solution
  - Surface area of the membrane
    - Increased by microvilli

Osmosis

- Because water molecules do not carry a charge, they can pass through the plasma membrane slowly.

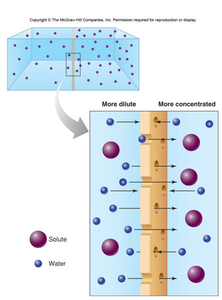
- Because this is the diffusion of solute instead of solvent, it is unique.
  - Aided by channels in membrane called aquaporins in some tissues

Requirements of Osmosis

1. There must be a solute concentration difference on either side of a membrane permeable to water.
2. The membrane must be impermeable to the solute, or the concentration difference will not be maintained.
   – Solutes that cannot cross and permit osmosis are called osmotically active.

Osmosis

- A model of osmosis

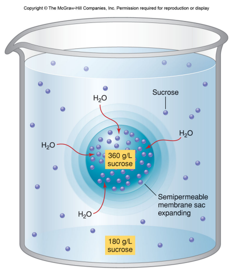


Osmosis

- The net movement of water is from the side with more water (more dilute) to the side with less water (less dilute).

- However, when osmosis is discussed, we say that water moves from an area of low solute concentration to an area of high solute concentration.

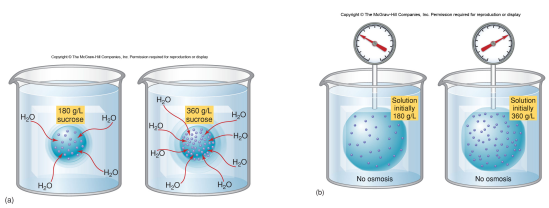
Osmosis



Osmotic Pressure

- Osmotic pressure is the force surrounding a cell required to stop osmosis.
- Can be used to describe the osmotic pull of a solution. A higher solute solution would require a higher osmotic pressure.

Osmotic Pressure



Moles

- A mole of a compound can be measured as its molecular weight in grams.
- The number of atoms in 1 mole is always the same no matter the compound:

  6.02×10^{23} molecules

- You can make molar solutions (1M) or molal solutions (1m).

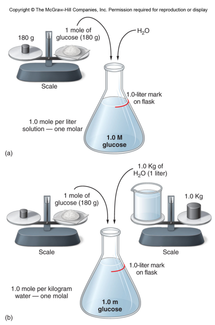
Molarity

- Glucose has a molecular weight of 180. To make a 1 molar solution of glucose, dissolve 180 g glucose in water to make 1 L solution.
- NaCl has a molecular weight of 58.5. To make a 1 molar solution of NaCl, dissolve 58.5 g NaCl in water to make 1 L solution.
- Not useful for a discussion of osmosis, since the solute concentration is different depending on the solute. More water is used to make the 1 molar solution of NaCl.

Molality

- 1 molal solutions take the molecular weight in grams dissolved in exactly 1 L water.
- The amount of water never changes, so you can compare solute concentrations to predict the direction of osmosis.

Molality

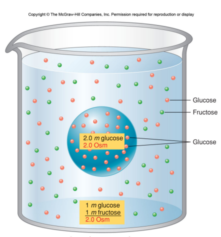


Osmolality

- Osmolality is the total molality of a solution when you combine all of the molecules within it.
- A 360 g (2m) glucose solution and a 180 g glucose (1m) + 180 g fructose (1m) solution would have the same osmolality.
- These are both 2 Osm solutions.

Osmolality

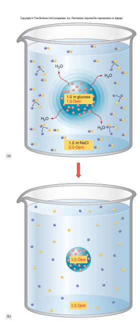
- Osmolality of sugar solutions



Osmolality

- Electrolytes that dissociate in water have to be assessed differently.
  - NaCl dissociates into Na^+ and Cl^- in water and must be counted as separate molecules.
  - A 1m NaCl solution would actually be a 2 Osm solution.

Osmolality



Tonicity

- Plasma has the same osmolality as a 0.3m glucose or a 0.15m NaCl solution.
  - These solutions are considered isosmotic to plasma.
- Tonicity is the effect of a solute concentration on the osmosis of water.
  - If a membrane separates a 0.3m glucose solution and a 0.15m NaCl solution, there will be no net movement of water = isotonic.

Tonicity

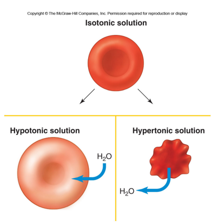
- Tonicity takes into account the permeability of the membrane to the solutes. If the solutes can cross the membrane, the tonicity will change.
  - If you place RBCs in a 0.3m solution of urea, the tonicity will not be isotonic. Urea can cross into the RBCs and draw water with it.
  - These cells will eventually burst.

Tonicity

- Solutions with a lower solute concentration than the cell are hypoosmotic and hypotonic.
  - Will pull water into the cell = lysis
- Solutions with a higher solute concentration than the cell are hyper-osmotic and hypertonic.
  - Will pull water out of the cell = crenation

Tonicity

- The fate of red blood cells in isotonic, hypotonic, and hypertonic solutions

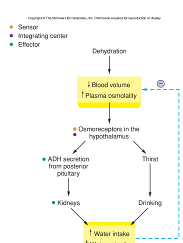


Regulation of Blood Osmolality

- Constant osmolality must be maintained, or neurons will be damaged.
- Osmoreceptors in the hypothalamus detect increases in osmolality (due to dehydration). This triggers:
  - Thirst
  - Decreased excretion of water in urine

Regulation of Blood Osmolality

- With a lower plasma osmolality, osmoreceptors are not stimulated, so more water is excreted in urine.



III. Carrier-Mediated Transport

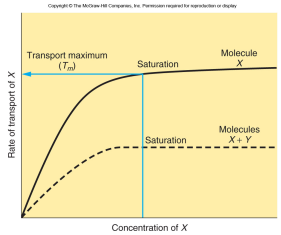
Carrier-Mediated Transport

- Molecules that are large or polar cannot diffuse across the membrane.
- Carrier proteins within the plasma membrane move these molecules across.
- These proteins are specific to a given molecule.

Carrier-Mediated Transport

- Some proteins can transport more than one molecule, but then there is a competition effect.
- Transport rates increase with increased molecule concentration until saturation is met = transport maximum (T_m).

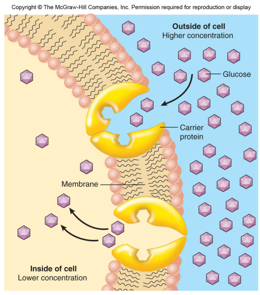
Carrier-Mediated Transport



Facilitated Diffusion

- Powered by the random movement of molecules--no ATP used
- Net movement from high to low concentration
- Requires specific carrier-mediated proteins

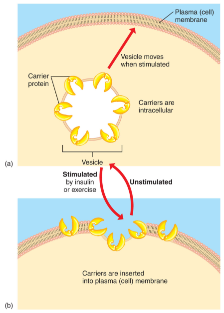
Facilitated Diffusion



Facilitated Diffusion

- Transport proteins may always exist in the plasma membrane or be inserted when needed.
  - Muscle cells do this during exercise to transport glucose.

Facilitated Diffusion



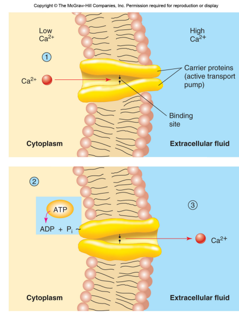
Active Transport

- Sometimes molecules must be moved from an area of low concentration to an area of high concentration.
- This requires the expenditure of ATP.
- Often, these carrier-mediated proteins are called *pumps.*

Primary Active Transport

- Occurs when the hydrolysis of ATP is directly responsible for the protein function. The transport protein is also an ATPase enzyme.
- Pump is activated by phosphorylation using a P_i from ATP.

Primary Active Transport



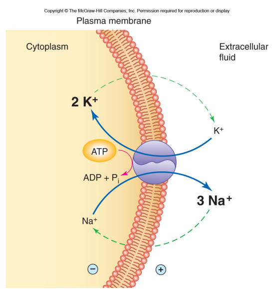
The Ca^{2+} Pump

- Located on all cells and in the endoplasmic reticulum of muscle cells
- Removes Ca^{2+} from the cytoplasm by pumping it into the extracellular space
- Creates a strong concentration gradient for rapid movement of Ca^{2+} back into the cell
- Aids in release of neurotransmitter in neurons and in muscle contraction

Na^+/K^+ Pump

- Found in all body cells
- ATPase enzyme that pumps 3 Na^+ out of the cell and 2 K^+ into the cell
- Serves three functions:
  - Provides energy for coupled transport of other molecules
  - Produces electrochemical impulses in neuron and muscle cells
  - Maintains osmolality

Na⁺/K⁺ Pump



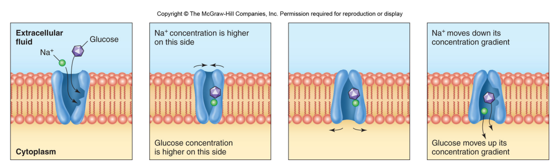
Secondary Active Transport

- Also called coupled transport
- The energy needed to move molecules across their concentration gradient is acquired by moving sodium back into the cell.
- Since the sodium was originally pumped out of the cell using ATP, this is considered active transport.

Secondary Active Transport

- Cotransport: The other molecule is moved with sodium.
  - Common way to transport glucose
- Countertransport: The other molecule is moved in the opposite direction from sodium.

Secondary Active Transport



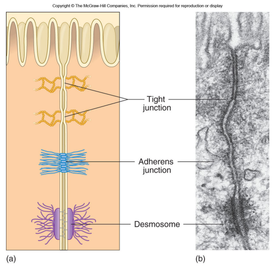
Transport Across Epithelial Membranes

- Involves transcellular transport: movement of molecules through the cytoplasm of the epithelial cells
- May also involve paracellular transport: movement across the tiny gaps between cells

Transport Across Epithelial Membranes

- Paracellular transport is limited by junctional complexes:
  - Tight junctions: do not allow easy diffusion
  - Adherens junctions
  - Desmosomes

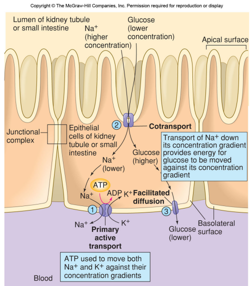
Transport Across Epithelial Membranes



Transport Across Epithelial Membranes

- Involves many different types of carrier-mediated proteins at both ends of the epithelial cells
  - Example: movement of glucose across the intestinal wall

Transport Across Epithelial Membranes



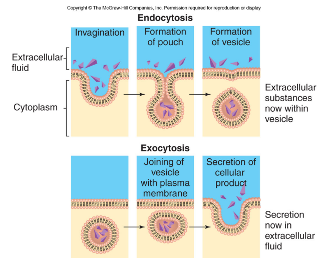
Bulk Transport

- Large molecules such as proteins, hormones, and neurotransmitters are secreted via exocytosis.
  - Involves fusion of a vesicle with the plasma membrane
  - Requires ATP

Bulk Transport

- Movement of large molecules such as cholesterol into the cell requires endocytosis.
  - Usually a transport protein interacts with plasma membrane proteins to trigger endocytosis.

Bulk Transport



IV. The Membrane Potential

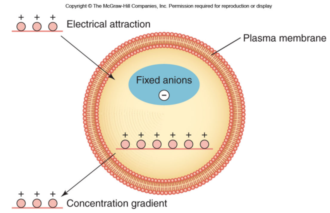
Membrane Potential

- There is a difference in charge on each side of the plasma membrane due to:
  - Permeability of the membrane
  - Action of Na^+/K^+ pumps
  - Negatively charged molecules inside the cell
- The inside of the cell is negative compared to the outside.

Membrane Potential: K^+

- K^+ accumulates at high concentrations in the cell because:
  - The Na^+/K^+ pumps actively bring in K^+.
  - The membrane is very permeable to K^+.
  - Negative anions inside the cell attract cations outside the cell.
  - Limited by strong concentration gradient.

Membrane Potential: K^+



Potential Difference

- Even with all the K^+ inside the cell, the negative molecules inside and all of the sodium outside make the cell more negative inside compared to outside.
  - This difference can be measured as a voltage.
  - Because the membrane is so permeable to K^+, this difference is often maintained by K^+.

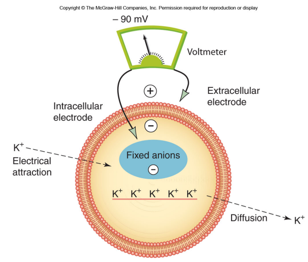
K^+ Equilibrium

- Addressing just K^+, the electrical attraction would pull K^+ into the cell until it reaches a point where the concentration gradient drawing K^+ out matches this pull.
  - K^+ would reach an equilibrium, with more K^+ inside than outside.
  - Normal cells have 150mM K^+ inside and 5mN K^+ outside.

K⁺ Equilibrium

- The resulting potential difference measured in voltage would be the equilibrium potential for K^+; measured at −90mV.
  - This means the inside has a voltage 90mV lower than the outside.
  - This is the voltage needed to maintain 150 mM K^+ inside and 5mM K^+ outside.

K⁺ Equilibrium



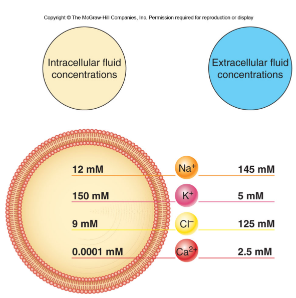
Na⁺ Equilibrium

- Sodium is also an important ion for establishing membrane potential.
  - The concentration of sodium in a normal cell is 12mM inside and 145mM outside.
  - To keep so much sodium out, the inside would have to be positive to repel the sodium ions.

Na+ Equilibrium

- The equilibrium potential for sodium is +66mV.
- The membrane is less permeable to Na^+, so the actual membrane potential is closer to that of the more permeable K^+.

Na+ Equilibrium



Nernst Equation

- Used to calculate equilibrium potentials
- Based on ion concentrations:

$$E_x = \frac{61}{z} \log \frac{[X_o]}{[X_t]}$$

E_x = equilibrium potential in mV for ion X
X_o = concentration of ion outside the cell
X_t = concentration of ion inside the cell
z = valence of ion (+1 for sodium or potassium)

Nernst Equation for K^+ and Na^+

$$E_{potassium} = \frac{61}{1} \log \frac{5}{150} = -90mV$$

$$E_{sodium} = \frac{61}{1} \log \frac{145}{12} = +66mV$$

Resting Membrane Potential

- Membrane potential of a cell not producing any impulses. Depends on:
  - Ratio of the concentrations of each ion on either side of the membrane
  - Specific permeability to each ion
- K^+, Na^+, Ca^{2+} and Cl^- contribute to the resting potential.

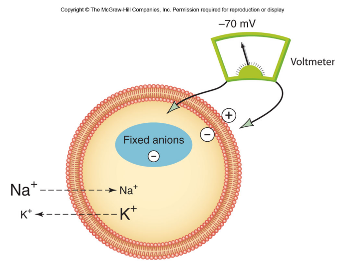
Resting Membrane Potential

- Membrane potential of a cell not producing any impulses
  - Because the membrane is most permeable to K^+, it has the greatest influence.
  - A change in the permeability of the membrane for any ion will change the resting potential.
  - A change in the concentration of any ion inside or outside the cell will change the resting potential.
  - Key to how neurons work

Resting Membrane Potential

- In most cells, the resting potential is between -65mV and -85mV.
  - Neurons are usually at −70mV.
  - Close to K^+ equilibrium potential
- When a neuron sends an impulse, it changes the permeability of Na^+, driving the membrane potential closer to the equilibrium potential for Na^+.

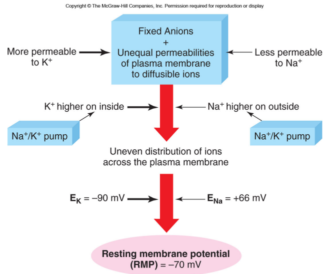
Resting Membrane Potential



Role of Na^+/K^+ Pump

- Acts to counter K^+ leaking out
- Because it transports 2 K^+ in for every 3 Na^+ out, it maintains voltage difference.
- Keeps both the resting potential and the concentration differences stable

Role of Na^+/K^+ Pump



V. Cell Signaling

Cell Signaling

- Cells communicate using chemical signals.
- Types:
  1. Gap junctions: allow adjacent cells to pass ions and regulatory molecules through a channel between the cells
  2. Paracrine signaling: Cells within an organ secrete molecules that diffuse across the extracellular space to nearby cells.
     - Often called local signaling

Cell Signaling

- Cells communicate using chemical signals.
- Types:
  3. Synaptic signaling: involves neurons secreting neurotransmitters across a synapse to target cells
  4. Endocrine signaling: involves glands that secrete hormones into the bloodstream; these can reach multiple target cells

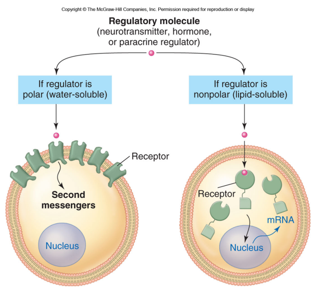
Receptor Proteins

- A target cell receives a signal because it has receptor proteins specific to it on the plasma membrane or inside the cell.
  – Nonpolar signal molecules such as steroid hormones can penetrate the plasma membrane and interact with receptors inside the cell.

Second Messengers

- Polar or large signal molecules bind to receptors on the cell surface.
- Other proteins pass the information to the inside of the cell to effect change.

Second Messengers



Second Messengers--cAMP

- Cyclic adenosine monophosphate (cyclic AMP or cAMP) is a common second messenger.
  - A signaling molecule binds to a receptor.
  - This activates an enzyme that produces cAMP from ATP.
  - cAMP activates other enzymes.
  - Cell activities change in response.

G-Proteins

- Receptor proteins that bind to a signal and enzyme proteins that produce a second messenger are rarely together. They require something to shuttle between them.
  - G-proteins are made up of 3 subunits.
  - One subunit dissociates when a signal molecule binds to the receptor and travels to the enzyme.

G-Proteins