Section B: Traffic Across Membranes

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1. A membrane’s molecular organization results in selective permeability

• A steady traffic of small molecules and ions moves across the plasma membrane in both directions.
  • For example, sugars, amino acids, and other nutrients enter a muscle cell and metabolic waste products leave.
  • The cell absorbs oxygen and expels carbon dioxide.
  • It also regulates concentrations of inorganic ions, like Na\(^+\), K\(^+\), Ca\(^{2+}\), and Cl\(^-\), by shuttling them across the membrane.
• However, substances do not move across the barrier indiscriminately; membranes are selectively permeable.
• Permeability of a molecule through a membrane depends on the interaction of that molecule with the hydrophobic core of the membrane.

• Hydrophobic molecules, like hydrocarbons, CO₂, and O₂, can dissolve in the lipid bilayer and cross easily.

• Ions and polar molecules pass through with difficulty.

  • This includes small molecules, like water, and larger critical molecules, like glucose and other sugars.

  • Ions, whether atoms or molecules, and their surrounding shell of water also have difficulties penetrating the hydrophobic core.

• Proteins can assist and regulate the transport of ions and polar molecules.
Specific ions and polar molecules can cross the lipid bilayer by passing through transport proteins that span the membrane.

- Some transport proteins have a hydrophilic channel that certain molecules or ions can use as a tunnel through the membrane.
- Others bind to these molecules and carry their passengers across the membrane physically.

Each transport protein is specific as to the substances that it will translocate (move).
- For example, the glucose transport protein in the liver will carry glucose from the blood to the cytoplasm, but not fructose, its structural isomer.
2. Passive transport is diffusion across a membrane

- **Diffusion** is the tendency of molecules of any substance to spread out in the available space
  - Diffusion is driven by the intrinsic kinetic energy (thermal motion or heat) of molecules.

- Movements of individual molecules are random.

- However, movement of a population of molecules may be directional.
• For example, if we start with a permeable membrane separating a solution with dye molecules from pure water, dye molecules will cross the barrier randomly.

• The dye will cross the membrane until both solutions have equal concentrations of the dye.

• At this dynamic equilibrium as many molecules pass one way as cross the other direction.

Fig. 8.10a  (a) Diffusion of one solute

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• In the absence of other forces, a substance will diffuse from where it is more concentrated to where it is less concentrated, down its concentration gradient.

• This spontaneous process decreases free energy and increases entropy by creating a randomized mixture.

• Each substance diffuses down its own concentration gradient, independent of the concentration gradients of other substances.

Fig. 8.10b  (b) Diffusion of two solutes

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• The diffusion of a substance across a biological membrane is **passive transport** because it requires no energy from the cell to make it happen.

  • The concentration gradient represents potential energy and drives diffusion.

• However, because membranes are selectively permeable, the interactions of the molecules with the membrane play a role in the diffusion rate.

• Diffusion of molecules with limited permeability through the lipid bilayer may be assisted by transport proteins.
3. Osmosis is the passive transport of water

• Differences in the relative concentration of dissolved materials in two solutions can lead to the movement of ions from one to the other.
  
  • The solution with the higher concentration of solutes is **hypertonic**.
  
  • The solution with the lower concentration of solutes is **hypotonic**.
  
  • These are comparative terms.
    
    • Tap water is hypertonic compared to distilled water but hypotonic when compared to sea water.
  
  • Solutions with equal solute concentrations are **isotonic**.
• Imagine that two sugar solutions differing in concentration are separated by a membrane that will allow water through, but not sugar.

• The hypertonic solution has a lower water concentration than the hypotonic solution.
  • More of the water molecules in the hypertonic solution are bound up in hydration shells around the sugar molecules, leaving fewer unbound water molecules.
• Unbound water molecules will move from the hypotonic solution where they are abundant to the hypertonic solution where they are rarer.

• This diffusion of water across a selectively permeable membrane is a special case of passive transport called **osmosis**.

• Osmosis continues until the solutions are isotonic.
• The direction of osmosis is determined only by a difference in total solute concentration.
  • The kinds of solutes in the solutions do not matter.
  • This makes sense because the total solute concentration is an indicator of the abundance of bound water molecules (and therefore of free water molecules).
• When two solutions are isotonic, water molecules move at equal rates from one to the other, with no net osmosis.
4. Cell survival depends on balancing water uptake and loss

- An animal cell immersed in an isotonic environment experiences no net movement of water across its plasma membrane.
  - Water flows across the membrane, but at the same rate in both directions.
  - The volume of the cell is stable.
• The same cell in a hypertonic environment will lose water, shrivel, and probably die.

• A cell in a hypotonic solution will gain water, swell, and burst.

Fig. 8.12

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• For a cell living in an isotonic environment (for example, many marine invertebrates) osmosis is not a problem.
  • Similarly, the cells of most land animals are bathed in an extracellular fluid that is isotonic to the cells.

• Organisms without rigid walls have osmotic problems in either a hypertonic or hypotonic environment and must have adaptations for osmoregulation to maintain their internal environment.
• For example, *Paramecium*, a protist, is hypertonic when compared to the pond water in which it lives.

• In spite of a cell membrane that is less permeable to water than other cells, water still continually enters the *Paramecium* cell.

• To solve this problem, *Paramecium* have a specialized organelle, the contractile vacuole, that functions as a bilge pump to force water out of the cell.
• The cells of plants, prokaryotes, fungi, and some protists have walls that contribute to the cell’s water balance.

• An animal cell in a hypotonic solution will swell until the elastic wall opposes further uptake.

• At this point the cell is **turgid**, a healthy state for most plant cells.

![Fig. 8.12](image-url)
• Turgid cells contribute to the mechanical support of the plant.

• If a cell and its surroundings are isotonic, there is no movement of water into the cell and the cell is **flaccid** and the plant may wilt.
• In a hypertonic solution, a cell wall has no advantages.

• As the plant cell looses water, its volume shrinks.

• Eventually, the plasma membrane pulls away from the wall.

• This **plasmolysis** is usually lethal.
5. Specific proteins facilitate passive transport of water and selected solutes: a closer look

- Many polar molecules and ions that are normally impeded by the lipid bilayer of the membrane diffuse passively with the help of transport proteins that span the membrane.

- The passive movement of molecules down its concentration gradient via a transport protein is called facilitated diffusion.
• Transport proteins have much in common with enzymes.
  • They may have specific binding sites for the solute.
  • Transport proteins can become saturated when they are translocating passengers as fast as they can.
  • Transport proteins can be inhibited by molecules that resemble the normal “substrate.”
    • When these bind to the transport proteins, they outcompete the normal substrate for transport.
  • While transport proteins do not usually catalyze chemical reactions, they do catalyze a physical process, transporting a molecule across a membrane that would otherwise be relatively impermeable to the substrate.
• Many transport proteins simply provide corridors allowing a specific molecule or ion to cross the membrane.

• These channel proteins allow fast transport.

• For example, water channel proteins, aquaporins, facilitate massive amounts of diffusion.
• Some channel proteins, **gated channels**, open or close depending on the presence or absence of a physical or chemical stimulus.

• The chemical stimulus is usually different from the transported molecule.

• For example, when neurotransmitters bind to specific gated channels on the receiving neuron, these channels open.

  • This allows sodium ions into a nerve cell.

  • When the neurotransmitters are not present, the channels are closed.
• Some transport proteins do not provide channels but appear to actually translocate the solute-binding site and solute across the membrane as the protein changes shape.

• These shape changes could be triggered by the binding and release of the transported molecule.
6. Active transport is the pumping of solutes against their gradients

- Some facilitated transport proteins can move solutes against their concentration gradient, from the side where they are less concentrated to the side where they are more concentrated.

- This **active transport** requires the cell to expend its own metabolic energy.

- Active transport is critical for a cell to maintain its internal concentrations of small molecules that would otherwise diffuse across the membrane.
• Active transport is performed by specific proteins embedded in the membranes.

• ATP supplies the energy for most active transport.
  
  • Often, ATP powers active transport by shifting a phosphate group from ATP (forming ADP) to the transport protein.
  
  • This may induce a conformational change in the transport protein that translocates the solute across the membrane.
• The sodium-potassium pump actively maintains the gradient of sodium (Na\(^+\)) and potassium ions (K\(^+\)) across the membrane.

• Typically, an animal cell has higher concentrations of K\(^+\) and lower concentrations of Na\(^+\) inside the cell.

• The sodium-potassium pump uses the energy of one ATP to pump three Na\(^+\) ions out and two K\(^+\) ions in.
Fig. 8.15

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 sites; the cycle repeats.
Fig. 8.16 Both diffusion and facilitated diffusion are forms of passive transport of molecules down their concentration gradient, while active transport requires an investment of energy to move molecules against their concentration gradient.
7. Some ion pumps generate voltage across membranes

- All cells maintain a voltage across their plasma membranes.
  - The cytoplasm of a cell is negative in charge compared to the extracellular fluid because of an unequal distribution of cations and anions on opposite sides of the membrane.
  - This voltage, the **membrane potential**, ranges from -50 to -200 millivolts.
• The membrane potential acts like a battery.

• The membrane potential favors the passive transport of cations into the cell and anions out of the cell.

• Two combined forces, collectively called the electrochemical gradient, drive the diffusion of ions across a membrane:
  • a chemical force based in an ion’s concentration gradient
  • an electrical force based on the effect of the membrane potential on the ion’s movement.
• Ions diffuse not simply down its concentration gradient, but diffuses down its electrochemical gradient.
  • For example, before stimulation there is a higher concentration of Na\(^+\) outside a resting nerve cell.
  • When stimulated, a gated channel opens and Na\(^+\) diffuse into the cell down the electrochemical gradient.

• Special transport proteins, **electrogenic pumps**, generate the voltage gradients across a membrane
  • The sodium-potassium pump in animals restores the electrochemical gradient not only by the active transport of Na\(^+\) and K\(^+\), but because it pumps two K\(^+\) ions inside for every three Na\(^+\) ions that it moves out.
• In plants, bacteria, and fungi, a **proton pump** is the major electrogenic pump, actively transporting \( H^+ \) out of the cell.

• Protons pumps in the cristae of mitochondria and the thylaloids of chloroplasts, concentrate \( H^+ \) behind membranes.

• These electrogenic pumps store energy that can be accessed for cellular work.
8. In cotransport, a membrane protein couples the transport of two solutes

- A single ATP-powered pump that transports one solute can indirectly drive the active transport of several other solutes through cotransport via a different protein.

- As the solute that has been actively transported diffuses back passively through a transport protein, its movement can be coupled with the active transport of another substance against its concentration gradient.
• Plants commonly use the gradient of hydrogen ions that is generated by proton pumps to drive the active transport of amino acids, sugars, and other nutrients into the cell.

• The high concentration of $\text{H}^+$ on one side of the membrane, created by the proton pump, leads to the facilitated diffusion of protons back, but only if another molecule, like sucrose, travels with the hydrogen ion.

Fig. 8.18
9. Exocytosis and endocytosis transport large molecules

- Small molecules and water enter or leave the cell through the lipid bilayer or by transport proteins.
- Large molecules, such as polysaccharides and proteins, cross the membrane via vesicles.
- During **exocytosis**, a transport vesicle budded from the Golgi apparatus is moved by the cytoskeleton to the plasma membrane.
- When the two membranes come in contact, the bilayers fuse and spill the contents to the outside.
• During **endocytosis**, a cell brings in macromolecules and particulate matter by forming new vesicles from the plasma membrane.

• **Endocytosis** is a reversal of exocytosis.
  
  • A small area of the plasma membrane sinks inward to form a pocket
  
  • As the pocket into the plasma membrane deepens, it pinches in, forming a vesicle containing the material that had been outside the cell
• One type of endocytosis is **phagocytosis**, “cellular eating”.

• In phagocytosis, the cell engulfs a particle by extending pseudopodia around it and packaging it in a large vacuole.

• The contents of the vacuole are digested when the vacuole fuses with a lysosome.
• In **pinocytosis**, “cellular drinking”, a cell creates a vesicle around a droplet of extracellular fluid.

• This is a non-specific process.
• **Receptor-mediated endocytosis** is very specific in what substances are being transported.

• This process is triggered when extracellular substances bind to special receptors, **ligands**, on the membrane surface, especially near coated pits.

• This triggers the formation of a vesicle
• Receptor-mediated endocytosis enables a cell to acquire bulk quantities of specific materials that may be in low concentrations in the environment.

• Human cells use this process to absorb cholesterol.

• Cholesterol travels in the blood in low-density lipoproteins (LDL), complexes of protein and lipid.

• These lipoproteins bind to LDL receptors and enter the cell by endocytosis.

• In familial hypercholesterolemia, an inherited disease, the LDL receptors are defective, leading to an accumulation of LDL and cholesterol in the blood.

• This contributes to early atherosclerosis.