

Chapter 7

Membrane Structure and Function

Lecture Outline

Overview: Life at the Edge

- The plasma membrane separates the living cell from its nonliving surroundings.
- This thin barrier, 8 nm thick, controls traffic into and out of the cell.
- Like all biological membranes, the plasma membrane is **selectively permeable**, allowing some substances to cross more easily than others.

Concept 7.1 Cellular membranes are fluid mosaics of lipids and proteins

- The main macromolecules in membranes are lipids and proteins, but carbohydrates are also important.
- The most abundant lipids are phospholipids.
- Phospholipids and most other membrane constituents are **amphipathic molecules**.
 - Amphipathic molecules have both hydrophobic regions and hydrophilic regions.
- The arrangement of phospholipids and proteins in biological membranes is described by the **fluid mosaic model**.

Membrane models have evolved to fit new data.

- Models of membranes were developed long before membranes were first seen with electron microscopes in the 1950s.
 - In 1915, membranes isolated from red blood cells were chemically analyzed and found to be composed of lipids and proteins.
 - In 1925, E. Gorter and F. Grendel reasoned that cell membranes must be a phospholipid bilayer two molecules thick.
 - The molecules in the bilayer are arranged such that the hydrophobic fatty acid tails are sheltered from water while the hydrophilic phosphate groups interact with water.
 - Actual membranes adhere more strongly to water than do artificial membranes composed only of phospholipids.
 - One suggestion was that proteins on the surface of the membrane increased adhesion.
 - In 1935, H. Davson and J. Danielli proposed a sandwich model in which the phospholipid bilayer lies between two layers of globular proteins.
 - Early images from electron microscopes seemed to support the Davson-Danielli model, and until the 1960s, it was widely accepted as the structure of the plasma membrane and internal membranes.
 - Further investigation revealed two problems.

- First, not all membranes were alike. Membranes differ in thickness, appearance when stained, and percentage of proteins.
 - * Membranes with different functions differ in chemical composition and structure.
 - Second, measurements showed that membrane proteins are not very soluble in water.
 - Membrane proteins are amphipathic, with hydrophobic and hydrophilic regions.
 - If membrane proteins were at the membrane surface, their hydrophobic regions would be in contact with water.
- In 1972, S. J. Singer and G. Nicolson presented a revised model that proposed that the membrane proteins are dispersed and individually inserted into the phospholipid bilayer.
 - In this fluid mosaic model, the hydrophilic regions of proteins and phospholipids are in maximum contact with water, and the hydrophobic regions are in a nonaqueous environment within the membrane.
- A specialized preparation technique, freeze-fracture, splits a membrane along the middle of the phospholipid bilayer.
- When a freeze-fracture preparation is viewed with an electron microscope, protein particles are interspersed in a smooth matrix, supporting the fluid mosaic model.

Membranes are fluid.

- Membrane molecules are held in place by relatively weak hydrophobic interactions.
- Most of the lipids and some proteins drift laterally in the plane of the membrane, but rarely flip-flop from one phospholipid layer to the other.
- The lateral movements of phospholipids are rapid, about 2 microns per second. A phospholipid can travel the length of a typical bacterial cell in 1 second.
- Many larger membrane proteins drift within the phospholipid bilayer, although they move more slowly than the phospholipids.
 - Some proteins move in a very directed manner, perhaps guided or driven by motor proteins attached to the cytoskeleton.
 - Other proteins never move and are anchored to the cytoskeleton.
- Membrane fluidity is influenced by temperature. As temperatures cool, membranes switch from a fluid state to a solid state as the phospholipids pack more closely.
- Membrane fluidity is also influenced by its components. Membranes rich in unsaturated fatty acids are more fluid than those dominated by saturated fatty acids because the kinks in the unsaturated fatty acid tails at the locations of the double bonds prevent tight packing.
- The steroid cholesterol is wedged between phospholipid molecules in the plasma membrane of animal cells.
- At warm temperatures (such as 37°C), cholesterol restrains the movement of phospholipids and reduces fluidity.
- At cool temperatures, it maintains fluidity by preventing tight packing.
- Thus, cholesterol acts as a “temperature buffer” for the membrane, resisting changes in membrane fluidity as temperature changes.
- To work properly with active enzymes and appropriate permeability, membranes must be about as fluid as salad oil.
- Cells can alter the lipid composition of membranes to compensate for changes in fluidity caused by changing temperatures.

- For example, cold-adapted organisms such as winter wheat increase the percentage of unsaturated phospholipids in their membranes in the autumn.
- This prevents membranes from solidifying during winter.

Membranes are mosaics of structure and function.

- A membrane is a collage of different proteins embedded in the fluid matrix of the lipid bilayer.
- Proteins determine most of the membrane's specific functions.
- The plasma membrane and the membranes of the various organelles each have unique collections of proteins.
- There are two major populations of membrane proteins.
 - **Peripheral proteins** are not embedded in the lipid bilayer at all.
 - Instead, they are loosely bound to the surface of the protein, often connected to integral proteins.
 - **Integral proteins** penetrate the hydrophobic core of the lipid bilayer, often completely spanning the membrane (as *transmembrane* proteins).
 - The hydrophobic regions embedded in the membrane's core consist of stretches of nonpolar amino acids, often coiled into alpha helices.
 - Where integral proteins are in contact with the aqueous environment, they have hydrophilic regions of amino acids.
 - On the cytoplasmic side of the membrane, some membrane proteins connect to the cytoskeleton.
 - On the exterior side of the membrane, some membrane proteins attach to the fibers of the extracellular matrix.
- The proteins of the plasma membrane have six major functions:
 1. Transport of specific solutes into or out of cells.
 2. Enzymatic activity, sometimes catalyzing one of a number of steps of a metabolic pathway.
 3. Signal transduction, relaying hormonal messages to the cell.
 4. Cell-cell recognition, allowing other proteins to attach two adjacent cells together.
 5. Intercellular joining of adjacent cells with gap or tight junctions.
 6. **Attachment to the cytoskeleton and extracellular matrix**, maintaining cell shape and stabilizing the location of certain membrane proteins.

Membrane carbohydrates are important for cell-cell recognition.

- The plasma membrane plays the key role in cell-cell recognition.
 - Cell-cell recognition, the ability of a cell to distinguish one type of neighboring cell from another, is crucial to the functioning of an organism.
 - This attribute is important in the sorting and organization of cells into tissues and organs during development.
 - It is also the basis for rejection of foreign cells by the immune system.
 - Cells recognize other cells by binding to surface molecules, often carbohydrates, on the plasma membrane.
- Membrane carbohydrates are usually branched oligosaccharides with fewer than 15 sugar units.

- They may be covalently bonded to lipids, forming glycolipids, or more commonly to proteins, forming glycoproteins.
- The oligosaccharides on the external side of the plasma membrane vary from species to species, from individual to individual, and even from cell type to cell type within the same individual.
 - This variation distinguishes each cell type.
 - The four human blood groups (A, B, AB, and O) differ in the external carbohydrates on red blood cells.

Membranes have distinctive inside and outside faces.

- Membranes have distinct inside and outside faces. The two layers may differ in lipid composition. Each protein in the membrane has a directional orientation in the membrane.
- The asymmetrical orientation of proteins, lipids and associated carbohydrates begins during the synthesis of membrane in the ER and Golgi apparatus.
- Membrane lipids and proteins are synthesized in the endoplasmic reticulum. Carbohydrates are added to proteins in the ER, and the resulting glycoproteins are further modified in the Golgi apparatus. Glycolipids are also produced in the Golgi apparatus.
- When a vesicle fuses with the plasma membrane, the outside layer of the vesicle becomes continuous with the inside layer of the plasma membrane. In that way, molecules that originate on the inside face of the ER end up on the outside face of the plasma membrane.

Concept 7.2 Membrane structure 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, such as 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.
- The plasma membrane allows the cell to take up many varieties of small molecules and ions and exclude others. Substances that move through the membrane do so at different rates.
- Movement of a molecule through a membrane depends on the interaction of the molecule with the hydrophobic core of the membrane.
 - Hydrophobic molecules, such as hydrocarbons, CO_2 , and O_2 , can dissolve in the lipid bilayer and cross easily.
 - The hydrophobic core of the membrane impedes the direct passage of ions and polar molecules, which cross the membrane with difficulty.
 - This includes small molecules, such as water, and larger molecules, such as glucose and other sugars.
 - An ion, whether a charged atom or molecule, and its surrounding shell of water also has difficulty penetrating the hydrophobic core.
- Proteins 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, called *channel proteins*, have a hydrophilic channel that certain molecules or ions can use as a tunnel through the membrane.
 - For example, the passage of water through the membrane can be greatly facilitated by channel proteins known as **aquaporins**.
 - Other transport proteins, called *carrier proteins*, bind to molecules and change shape to shuttle them across the membrane.
- Each transport protein is specific as to the substances that it will translocate.
 - For example, the glucose transport protein in the liver will carry glucose into the cell but will not transport fructose, its structural isomer.

Concept 7.3 Passive transport is diffusion of a substance across a membrane with no energy investment

- **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.
- Imagine a permeable membrane separating a solution with dye molecules from pure water. If the membrane has microscopic pores that are large enough, dye molecules will cross the barrier randomly.
- The net movement of dye molecules across the membrane will continue until both sides have equal concentrations of the dye.
- At this dynamic equilibrium, as many molecules cross one way as cross in the other direction.
- 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**.
- No work must be done to move substances down the concentration gradient.
- Diffusion is a spontaneous process that 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.
- 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 itself represents potential energy and drives diffusion.
- Because membranes are selectively permeable, the interactions of the molecules with the membrane play a role in the diffusion rate.
- Diffusion of molecules of limited permeability through the lipid bilayer may be assisted by transport proteins.

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** relative to the other solution.
- The solution with the lower concentration of solutes is **hypotonic** relative to the other solution.
- These are comparative terms.
 - Tap water is hypertonic compared to distilled water but hypotonic compared to seawater.
- 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. Net movement of water continues until the solutions are isotonic.
- The diffusion of water across a selectively permeable membrane is called **osmosis**.
- 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.
- The movement of water by osmosis is crucial to living organisms.

Cell survival depends on balancing water uptake and loss.

- An animal cell (or other cell without a cell wall) immersed in an isotonic environment experiences no net movement of water across its plasma membrane.
 - Water molecules move 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.
- For organisms living in an isotonic environment (for example, many marine invertebrates), osmosis is not a problem.
 - The cells of most land animals are bathed in 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**, the control of water balance, to maintain their internal environment.
- For example, *Paramecium*, a protist, is hypertonic 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* cells have a specialized organelle, the contractile vacuole, which 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.
- A plant cell in a hypotonic solution will swell until the elastic cell wall opposes further uptake.
 - At this point the cell is **turgid** (very firm), a healthy state for most plant cells.
- Turgid cells contribute to the mechanical support of the plant.
- If a plant cell and its surroundings are isotonic, there is no movement of water into the cell. The cell becomes **flaccid** (limp), and the plant may wilt.
- The cell wall provides no advantages when a plant cell is immersed in a hypertonic solution. As the plant cell loses water, its volume shrinks. Eventually, the plasma membrane pulls away from the wall. This **plasmolysis** is usually lethal.

Specific proteins facilitate passive transport of water and selected solutes.

- 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 their concentration gradient via transport proteins is called **facilitated diffusion**.
- Two types of transport proteins facilitate the movement of molecules or ions across membranes: channel proteins and carrier proteins.
- Some channel proteins simply provide hydrophilic corridors for the passage of specific molecules or ions.
 - For example, water channel proteins, **aquaporins**, greatly facilitate the diffusion of water.
- Many **ion channels** function as **gated channels**. These channels open or close depending on the presence or absence of a chemical or physical stimulus.
 - If chemical, the stimulus is a substance other than the one to be transported.
 - For example, stimulation of a receiving neuron by specific neurotransmitters opens gated channels to allow sodium ions into the 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 transport protein changes shape.
 - These shape changes may be triggered by the binding and release of the transported molecule.
- In certain inherited diseases, specific transport systems may be defective or absent.
 - Cystinuria is a human disease characterized by the absence of a protein that transports cysteine and other amino acids across the membranes of kidney cells.
 - An individual with cystinuria develops painful kidney stones as amino acids accumulate and crystallize in the kidneys.

Concept 7.4 Active transport uses energy to move solutes against their gradients

- Some transport proteins can move solutes across membranes 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 metabolic energy.

- Active transport enables 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.
 - ATP can power active transport by transferring a phosphate group from ATP (forming ADP) to the transport protein.
 - This may induce a conformational change in the transport protein, translocating the solute across the membrane.
- The **sodium-potassium pump** actively maintains the gradient of sodium ions (Na^+) and potassium ions (K^+) across the plasma membrane of animal cells.
 - Typically, K^+ concentration is low outside an animal cell and high inside the cell, while Na^+ concentration is high outside an animal cell and low inside the cell.
 - The sodium-potassium pump maintains these concentration gradients, using the energy of one ATP to pump three Na^+ out and two K^+ in.

Some ion pumps generate voltage across membranes.

- All cells maintain a voltage across their plasma membranes.
- Voltage is electrical potential energy due to the separation of opposite charges.
 - 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.
 - The voltage across a membrane is called a **membrane potential**, and ranges from -50 to -200 millivolts (mV). The inside of the cell is negative compared to the outside.
- 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.
 - One is a chemical force based on an ion's concentration gradient.
 - The other is an electrical force based on the effect of the membrane potential on the ion's movement.
- An ion does not simply diffuse down its concentration gradient but diffuses down its electrochemical gradient.
 - For example, there is a higher concentration of Na^+ outside a resting nerve cell than inside.
 - When the neuron is stimulated, a gated channel opens and Na^+ diffuse into the cell down their electrochemical gradient. The diffusion of Na^+ is driven by their concentration gradient and by the attraction of cations to the negative side of the membrane.
- Special transport proteins, **electrogenic pumps**, generate the voltage gradient across a membrane.
 - The sodium-potassium pump in animals restores the electrochemical gradient not only by the active transport of Na^+ and K^+ , setting up a concentration gradient, but because it pumps two K^+ inside for every three Na^+ that it moves out, setting up a voltage across the membrane.
- The sodium-potassium pump is the major electrogenic pump of animal cells.

- In plants, bacteria, and fungi, a **proton pump** is the major electrogenic pump, actively transporting H^+ out of the cell.
- Proton pumps in the cristae of mitochondria and the thylakoids of chloroplasts concentrate H^+ behind membranes.
- These electrogenic pumps store energy that can be accessed for cellular work.

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 in a mechanism called **cotransport**.
- 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 generated by proton pumps to drive the active transport of amino acids, sugars, and other nutrients into the cell.
- One specific transport protein couples the diffusion of protons out of the cell and the transport of sucrose into the cell. Plants use the mechanism of sucrose-proton cotransport to load sucrose into specialized cells in the veins of leaves for distribution to nonphotosynthetic organs such as roots.

Concept 7.5 Bulk transport across the plasma membrane occurs by exocytosis and endocytosis

- 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.
- Many secretory cells use exocytosis to export their products.
- During **endocytosis**, a cell brings in macromolecules and particulate matter by forming new vesicles from the plasma membrane.
- Endocytosis is a reversal of exocytosis, although different proteins are involved in the two processes.
 - A small area of the plasma membrane sinks inward to form a pocket.
 - As the pocket deepens, it pinches in to form a vesicle containing the material that had been outside the cell.
- There are three types of endocytosis: phagocytosis (“cellular eating”), pinocytosis (“cellular drinking”), and receptor-mediated endocytosis.
- 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**, a cell creates a vesicle around a droplet of extracellular fluid. All included solutes are taken into the cell in this nonspecific process.

- **Receptor-mediated endocytosis** allows greater specificity, transporting only certain substances.
- This process is triggered when extracellular substances, or **ligands**, bind to special receptors on the membrane surface. The receptor proteins are clustered in regions of the membrane called coated pits, which are lined on their cytoplasmic side by a layer of coat proteins.
- Binding of ligands to receptors triggers the formation of a vesicle by the coated pit, bringing the bound substances into the cell.
- 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 take in cholesterol for use in the synthesis of membranes and as a precursor for the synthesis of steroids.
 - Cholesterol travels in the blood in low-density lipoproteins (LDL), complexes of protein and lipid.
 - These lipoproteins act as ligands to bind to LDL receptors and enter the cell by endocytosis.
 - In an inherited disease called familial hypercholesterolemia, the LDL receptors are defective, leading to an accumulation of LDL and cholesterol in the blood.
 - This contributes to early atherosclerosis.