

Chapter 5: Membranes

Membrane Composition and Structure

- Cell membranes are bilayered, dynamic structures that perform vital physiological roles, form boundaries between cells and their molecular environments, and regulate movement of materials into and out of cells.
- Lipids, proteins, and carbohydrates in various combinations make these tasks possible.
- The lipid portion of a cellular membrane provides a barrier for water-soluble molecules and establishes the physical integrity of the membrane.
- Lipids are like the water of a lake in which proteins “float.” This general design is called the fluid mosaic model. (See Figure 5.1.)
- Membrane proteins are embedded in the lipid bilayer.
- Carbohydrates attach to lipid or protein molecules on the membrane, generally on the outer surface.
- (See Videos 5.1 and 5.2.)

Lipids constitute the bulk of a membrane

- Most of the lipid molecules found in biological membranes are phospholipids.
- Each has a hydrophilic (“water-loving”) side, where the phosphate groups are located, and a hydrophobic (“water-hating”) side, the fatty acid “tails.” (See Figure 5.2.)
- The phospholipids organize themselves into a bilayer with the hydrophilic regions facing either the outside of the cell or the interior cytoplasmic face. The hydrophobic, hydrocarbon-rich regions of each layer face each other and face away from the watery internal or external environment, an arrangement that stabilizes the entire membrane structure.
- Artificial membranes can be made in the laboratory. They naturally (spontaneously) form sheets of membranes that are lipid bilayers.
- The interior of the membrane is fluid, with the consistency of lightweight machine oil. This fluidity allows some molecules to move laterally along the plane of the membrane.
- Whereas phospholipid molecules can move laterally and do so rapidly, they seldom “flip-flop”—that is, they rarely move from the exterior layer to the cytoplasmic layer or vice versa.
 - *Flip-flop is rare without the aid of special proteins designed for the task.*
- Although all biological membranes are structurally similar, some have quite different compositions of lipids and proteins.
 - Some lipid membranes have 25 percent cholesterol, while others have no cholesterol at all.
 - Cholesterol is an important part of the lipid membranes that contain it. Under some conditions, cholesterol increases membrane fluidity; at other times it decreases fluidity.
 - The effect cholesterol has on fluidity depends on other factors, such as the fatty acid composition of the other lipids found in the membrane.
 - In general, shorter fatty acids make for a more fluid membrane, as do unsaturated fatty acids.
 - For any given membrane, fluidity decreases with declining temperature, and membrane function may decline in organisms that cannot maintain warm bodies. The membranes of cells that live at low temperatures tend to be high in unsaturated and short-chain fatty acids.

Membrane proteins are asymmetrically distributed

- All biological membranes contain proteins.
 - On average, there is one protein molecule for every 25 phospholipid molecules found in plasma membranes. This ratio varies, however, depending on membrane function.
 - The inner membranes of mitochondria have one protein for every 15 lipids.
 - Myelin, which coats nerve cells and acts as an insulator, has about one protein for every 70 lipids.
- Many proteins have both polar and nonpolar regions due to the presence of both hydrophilic and hydrophobic R groups in their amino acids.
- The association of many protein molecules with lipid molecules is not covalent; both are free to move around laterally, according to the fluid mosaic model.
- Integral membrane proteins are those that have hydrophobic regions of amino acids that penetrate or entirely cross the phospholipid bilayer.
 - These proteins have long hydrophobic amino acid areas and form an α -helical region, which tends to interact with only the hydrophobic membrane core. (See Figure 5.4.)
 - The hydrophilic R groups face the aqueous areas and interact with them.

- Peripheral membrane proteins lack hydrophobic regions and are not embedded in the bilayer. These proteins have polar or charged groups that interact with exposed portions of integral membrane proteins or phospholipid molecules. (See Figure 5.1.)
- Some membrane proteins are covalently attached to fatty acids or other lipid groups. The lipid portion inserts into the lipid bilayer and tethers the protein to the membrane.
- Transmembrane proteins have a specific orientation.
 - *The shape of one side may allow it to act as a receptor for a signaling molecule, with the other side changing shape in response to the signal binding.*
 - *Some cells are specialized to be anchored to the extracellular matrix. The externally exposed portion of the protein locks onto extracellular polymers, whereas the internal region may connect to the cytoskeleton.*
- Some of the proteins and lipids can move around in the membrane.
 - Experiments have demonstrated that when two cells are fused, a single continuous membrane forms around both cells and membrane proteins distribute themselves uniformly around this membrane.
 - Some proteins are restricted in movement because they are anchored to components of the cytoskeleton or are trapped within regions of lipid rafts.
 - This tethering causes an unequal distribution of proteins, allowing for specialization of certain regions of the cell membrane.

Membrane carbohydrates are recognition sites

- Some cells have carbohydrates associated with their external surfaces.
 - Carbohydrate-bound lipid is called glycolipid.
 - Most of the carbohydrate in the membrane is covalently bonded to proteins, forming glycoproteins.
- Plasma membrane glycoproteins enable cells to be recognized by other cells and proteins, utilizing an “alphabet” of single sugars to create a diversity of messages.

Cell Recognition and Adhesion

- The cells of multicellular organisms often exist in specialized blocks of cells with similar functions called tissues.
- There are about 60 trillion cells in the human body, arranged in different tissues such as muscle, nerve, and skin.
- Cells are able to arrange themselves into groups by two processes.
 - In cell recognition, one cell specifically binds to another cell of a certain type.
 - In cell adhesion, the relationship between the two cells is “cemented.”
- Experiments with sponges demonstrate these processes.
- If a sponge’s cells are made to disaggregate, what was a single animal is now thousands of individual cells.
 - If the cells are left together in a solution for a few hours, they reaggregate into a sponge. (See Figure 5.5.) This is an example of species-specific cell adhesion.
 - If two different species of sponges are disaggregated into individual cells and the two types of cells are placed together, the cells from one species will aggregate only with cells from its own species and two sponges will appear.
 - However, if the cells from two sponges of the same species are combined, one large sponge will form upon reaggregation.
- Tissue-specific and species-specific aggregation occur because of plasma membrane recognition proteins.

Cell recognition and adhesion involve proteins at the cell surface

- The membrane proteins responsible for the cell–cell recognition in sponges were the first ever to be identified and purified.
 - The recognition protein is a large glycoprotein composed of 80 percent sugar that is partially embedded in the plasma membrane.
 - The species-specific recognition portion faces outward and is exposed to the environment.
- There are two general ways that cell adhesion molecules work.
 - Homotypic (*homo* “same”, and *typic*, “type”) binding occurs when both cells possess the same type of cell surface receptor and their interaction causes them to stick together. In most cases, including that of the sponge cell adhesion proteins, cell binding involves homotypic cell–cell adhesion. (See Figure 5.5a.)
 - Heterotypic binding occurs between two different but complementary proteins and resembles a plug and socket. (See Figure 5.5b.) Mammalian sperm and egg binding is heterotypic.

Specialized cell junctions

- Complex multicellular organisms use special cell–cell recognition proteins to allow specific kinds of cells to adhere to each other and create tissues.
- These connections, called cell junctions, are particularly common in epithelial tissues, which line body cavities and cover body surfaces.
- There are three main categories of cell junctions in animals: tight junctions, desmosomes, and gap junctions. (See Figure 5.6.)
- Tight junctions are specialized structures at the plasma membrane that link adjacent epithelial cells; they have two primary functions:
 - They restrict the migration of membrane proteins and phospholipids from one region of the cell to another. (See Figure 5.6a.)
 - They prevent substances from moving through the intercellular space. Sealing the space between epithelial cells forces materials to pass through cells and provides the opportunity to regulate what passes from the lumen to the body.
- Desmosomes act like spot welds on adjacent cells, holding them together.
 - Desmosomes have dense plaques on the cytoplasmic surface of plasma membranes. (See Figure 5.6b.)
 - The plaques are attached both to cytoplasmic fibers and to membrane cell adhesion proteins.
 - Cytoplasmic fibers that connect to the plaques of desmosomes are intermediate filaments.
 - Made of a protein called keratin, intermediate filaments span the cell, connecting plaques to plaques via a network of fibers. (See Figure 4.20.)
 - Intermediate filaments are extremely strong and provide great mechanical stability to epithelial cells. Some epithelial cells, like those that form our skin, need this stability to resist wearing.
 - The desmosomes of one cell connect its fibrous network to the fibrous networks of other cells.
- Gap junctions are connections that facilitate communication between cells. (See Figure 5.6c.)
 - Gap junctions are made up of specialized protein channels called connexons.
 - *Connexons can open or close.*
 - *Connexons span the plasma membranes of two adjacent cells and protrude from them slightly.*
 - *Connexons are made of proteins called connexins, which snap together to generate a pore. Each connexon makes a pore.*
 - *The pores of a cell connect to the pores of another. Molecules the size of ions, amino acids, and nucleotides can get through, but large polymers are excluded.*

Passive Processes of Membrane Transport

- Biological membranes are selectively permeable. They allow some substances to pass, while other substances are restricted in their movement.
 - Some substances can move by simple diffusion through the phospholipid bilayer.
 - Some must travel through proteins to get in, but the driving force is still diffusion. This process is called facilitated diffusion.
 - There are two kinds of proteins involved in facilitated diffusion: channel and carrier proteins.

The physical nature of diffusion

- Molecules in solution vibrate, rotate, and move from place to place. The greater the temperature, the more quickly they move.
- The random movement of molecules results in their even distribution around an area.
- Once they are distributed evenly, they are said to be at equilibrium. (See Figure 5.7.) Diffusion is the process of random movement toward the state of equilibrium.
- Although individual particles move randomly, in diffusion the **net** movement is directional, from regions of greater concentrations to regions of lesser concentrations until equilibrium is reached.
- With all diffusion, it is the concentration and not the total number of molecules that determines the net direction of movement, because the probability of molecules moving from one point to another depends on how many molecules there are per unit area.
- *The following example describes the process of diffusion:*
 - *Imagine that the classroom has a glass pane separating one-half from the other.*
 - *Balls bouncing around on one side of the glass pane are prevented from reaching the other side.*
 - *Imagine that someone makes a hole in the glass pane large enough for a ball to escape.*

- *Eventually balls will escape through the hole until both halves of the room have approximately the same number of balls. At this point, the likelihood of a ball's leaving one side of the room is about the same as the likelihood of a ball's entering, although balls continue to pass back and forth.*
- *This state is equilibrium.*
- Diffusion over short distances is very fast. Small molecules and ions may move from one end of an organelle to another in a millisecond.
- Diffusion over larger distances is very slow. Diffusion across more than a centimeter may take an hour or more; diffusion across meters may take years.
- The process of diffusion cannot adequately distribute materials over the length of the human body. However, within our cells—across layers of membranes or from one cell to another—diffusion is rapid enough to distribute small molecules and ions almost instantaneously.
- In a solution, diffusion rates are determined by temperature, the physical size of the solute, the electrical charge of the diffusing material, and the concentration gradient.
- The insertion of a biological membrane affects the movement of chemicals in solution according to the membrane's properties.
 - It may be permeable to some molecules and impermeable to others.
 - If permeable, the concentration of the diffusing substance eventually reaches equilibrium on both sides of the membrane.

Simple diffusion takes place through the membrane bilayer

- Substances that can move freely through the lipid bilayer move by a passive process.
- Some substances can move by simple diffusion through the phospholipid bilayer.
- Membranes can influence diffusion rates.
 - How quickly molecules move across a lipid membrane depends on how permeable the membrane is to the solute.
 - *For example, ethanol moves much more rapidly than glycerol across the membrane, although both will eventually achieve equilibrium.*
- Substances to which the membrane is permeable move along the concentration gradient from the outside to the inside or from the inside to the outside.
- Molecules to which the membrane is impermeable necessarily remain on one side or the other.
 - Polar and charged molecules such as amino acids, sugars, and ions do not pass readily across the lipid bilayer.
 - The hydrophobic interior of the membrane tends to exclude hydrophilic substances.
 - One notable exception to this impermeability is water, which can pass through the lipid bilayer more readily than its lipid solubility would predict.
 - Consider two types of molecules, a small protein (a polar molecule) and a steroid of equivalent size. The polar nature of the protein will cause it to diffuse slowly through the membrane, while the nonpolar steroid will diffuse through it more readily.

Osmosis is the diffusion of water across membranes

- Water diffusion across membranes, or osmosis, is a special case.
- Osmosis is a completely passive process and requires no metabolic energy.
 - If a plant cell is placed in a solution with a high concentration of sucrose (table sugar), the plant cell membrane will shrink inside the cell wall. (See Figure 5.8.)
 - If the plant cell is placed in pure water, the cell membrane will expand (build turgor pressure) until it presses very firmly against the cell wall. Since the concentration of water is greater outside the cell, the net movement of molecules (in the absence of any obstruction) will be into the cell until equilibrium is reached.
- Three terms are used to compare the solute concentrations of solutions: isotonic, hypertonic, and hypotonic.
- Isotonic solutions have equal solute concentrations. When all the individual particles outside the cell are totaled and then adjusted for a certain volume (e.g., per ml), they will equal the total number of all particles inside the cell, per ml.
 - *Imagine the ball example, again.*
 - *A small area of the classroom is walled off by the glass panel in which a hole has been made.*
 - *Eventually, there will be fewer balls in the smaller area, although the balls per unit volume will be about equal.*
 - *This is the case because the probability of the balls moving from one area to another is influenced by the density of the balls, not the total number.*
- A hypertonic solution has a greater total solute concentration than the solution to which it is being compared.

- A hypotonic solution has a lower total solute concentration than the solution to which it is compared. Cells placed into solutions that are hypotonic (relative to the cell's cytoplasm) swell as water moves into the cell, down its concentration gradient.
- The integrity of cells such as red blood cells depends absolutely on the maintenance of constant solute concentrations in the plasma.
- Plants can be exposed to pure water because their rigid cell walls limit the amount of water that can enter. Animal cells, lacking cell walls, may continue to take on pure water and eventually burst. (See Figure 5.8.)

Diffusion may be aided by channel proteins

- Polar substances (such as amino acids and sugars) and charged substances (such as ions) do not diffuse across lipid bilayers.
- One way for these important raw materials to enter cells is through the process of facilitated diffusion.
- There are two kinds of facilitated diffusion across biological membranes, one that depends on carrier proteins and another that makes use of channel proteins.
- Channel proteins are integral membrane proteins that form channels lined with polar amino acids. Nonpolar (hydrophobic) amino acids face the outside of the channel, toward the fatty acid tails of the lipid molecules. (See Figure 5.9.)
- The best-studied protein channels are the ion channels, of which hundreds have been identified.
 - Ion channels can be open or closed (i.e., they are gated), with various mechanisms controlling their opening and closing.
 - Once the channel is opened, millions of ions can rush through per second. Just how fast and in which direction these ions move depends on the concentration gradient.
 - Ion channels are specific for one type of ion.
 - The mechanism for this specificity was discovered when the structure of a bacterial potassium channel was determined.
 - Specificity results from a tight fit between the ion and the funnel-shaped stem of the channel, where oxygen atoms are located.
 - Positive ions normally have a "shell" of water surrounding them in solution. If the fit between the ion and the funnel opening is exact, the ion will be more strongly attracted to the oxygen atoms in the funnel than those of water, and they will enter the channel.
 - If the ion is too small, it will retain its water "shell" and not enter the channel. (See Figure 5.10.)
 - One way that water crosses the plasma membrane is by hydrating ions as they pass through. Another way is through protein-lined membrane channels called aquaporins.

Carrier proteins aid diffusion by binding substances

- Facilitated diffusion using carrier proteins involves not just opening a channel but also binding the transported substance.
- Carrier proteins allow diffusion in both directions. This is one way sugars and amino acids are transported. (See Figure 5.11.)
 - The concentration gradient can be kept by metabolizing the transported substance once it enters the cell. For example, as soon as glucose enters the cell, it is metabolized; therefore, the cell's glucose concentration stays low, and the movement of glucose continues.
 - The rate of movement through carrier proteins is dependent on concentration, but only to a point, because the carrier must bind the substance it transports.
 - If the limited number of carrier protein molecules are loaded with solute molecules, the carrier proteins are said to be saturated. (See Animated Tutorial 5.1.)
 - Saturation can limit the number of molecules that can move into the cell per unit of time.

Active Transport

- In contrast to diffusion, active transport requires the expenditure of energy. (See Table 5.1.)
 - Ions or molecules are moved across the membrane from regions of lesser concentration to regions of greater concentration.
 - This is movement *against* the concentration gradient.
 - ATP is the energy currency used either directly or indirectly to achieve active transport.

Active transport is directional

- Three different protein-driven systems are involved in active transport: uniport, symport, and antiport. (See Figure 5.12.)
- Uniport transporters move a single type of solute, such as calcium ions, in one direction.
- Symport transporters move two solutes in the same direction.
 - For example, amino acid transport may be coupled to sodium ion transport.
 - *As sodium ions move from a greater concentration outside the cell, down the concentration gradient to the inside of the cell, an amino acid is moved up the concentration gradient and into the cell as well.*
- Antiport transporters move two solutes in opposite directions, one into the cell, and the other out of the cell.
 - An example is the sodium–potassium pump, which moves sodium out of the cell and potassium into it. (See Figure 5.13.)
 - For each molecule of ATP used, three sodium ions are pumped out and two potassium ions are pumped in.
- Symports and antiports are known as coupled transporters because they move two solutes at once.

Primary and secondary active transport rely on different energy sources

- If ATP is used directly for the pumping system, as in the sodium–potassium pump, the system is a primary active transport system.
 - Only cations, such as sodium, potassium, and calcium, are transported directly by pumps that use a primary active transport system.
- Secondary active transport systems use established gradients to move substances. (See Figure 5.14.)
 - This form of transport uses ATP indirectly. The ATP molecules are consumed to establish the ion gradient.
 - The gradient is then used to move a substance, as described for the symport and antiport systems.
 - Sodium and potassium ions are pumped by the primary active transport system, while glucose gains entry to the cell via a secondary active transport system. (See Animated Tutorial 5.2.)
 - An example is the symport system found in intestinal cells, which moves glucose up its concentration gradient, while moving sodium ions down its ion concentration gradient. Both sodium and glucose enter the cell. The sodium must be pumped out again, but the energy harvested from the glucose more than pays for this energy expense.

Endocytosis and Exocytosis

- There are a few systems designed to transport polymers, as opposed to simply monomers or ions.
- Macromolecules in general enter the cell via endocytosis and exit via exocytosis. (See Figure 5.15.)

Macromolecules and particles enter the cell by endocytosis

- Macromolecules such as proteins, polysaccharides, nucleic acids, and triglycerides are too large and too charged to enter through the membrane.
- The group of processes called endocytosis brings macromolecules, large particles, small molecules, and even other cells into the eukaryotic cell.
- There are three types of endocytosis: phagocytosis, pinocytosis, and receptor-mediated endocytosis.
 - In all three, the plasma membrane invaginates toward the cell interior while surrounding the materials on the outside.
 - The vesicle is formed when the pocket of membrane deepens, pinches off, and migrates with its contents to the cell's interior.
- During phagocytosis, which involves the largest vesicles, entire cells can be engulfed.
 - Phagocytosis is common among unicellular protists.
 - White blood cells in humans and other animals also use phagocytosis to defend the body against invading foreign cells.
- Pinocytosis, which means “cellular drinking,” involves vesicle formation as well, but the vesicles are far smaller.
 - Dissolved substances and fluids are brought into the cell.
 - There is little or no specificity as to what the cell brings in.
 - In humans, the single layer of cells separating blood capillaries from surrounding tissue uses pinocytotic vesicles to acquire fluids from the blood.
- (See Video 5.3.)

Receptor-mediated endocytosis is highly specific

- Receptor-mediated endocytosis is similar to pinocytosis, but it is highly specific. Animal cells use this type of endocytosis to transport specific macromolecules from the environment. (See Animated Tutorial 5.3.)

- Receptor proteins are exposed on the outside of the cell in regions called coated pits.
- Clathrin molecules form the coat of the pits. The forming vesicles are the pits. (See Figure 5.16.)
 - As the receptors bind specific macromolecules outside the cell, the receptors' cytoplasmic sides associate with clathrin molecules.
 - Coated vesicles form with the macromolecules trapped inside.
 - After the vesicles form and are embedded in the cell cytoplasm, they lose the clathrin coat. Depending on the particular substance retrieved, they might end up at specific locations within the cell or be digested in lysosomes.
- Receptor-mediated endocytosis is the method by which cholesterol is taken up by mammalian cells.
 - Cholesterol, which is water insoluble, is synthesized in the liver and transported throughout the body within low-density lipoproteins (LDL).
 - The LDL binds to the receptors found on the surface of the cell in coated pits.
 - Clathrin-coated pits cause an invagination of bound receptors.
 - Vesicles containing LDL are brought into the cell.
 - The LDL receptors are recycled back to the cell's surface. The LDL ends up in a lysosome and is digested, freeing the cholesterol for use by the cell.
 - Some humans inherit a condition in which their LDL receptors are deficient, resulting in dangerously high levels of cholesterol in their blood.

Exocytosis moves materials out of the cell

- Exocytosis is the process by which materials packaged in vesicles are secreted (cast out) from the cell.
- The vesicle membranes fuse with the plasma membrane and release vesicle contents (wastes, enzymes, hormones, etc.) into the environment.
- (See Video 5.4.)

Membranes Are Not Simply Barriers

- The plasma membrane is not simply a barrier. (See Figure 5.17a.)
- Plasma membranes are involved in information processing. The binding of specific substances in the environment can serve as a signal to initiate, modify, or turn off a cell function.
- Membranes are important in energy transformation.
 - The inner mitochondrial membrane helps convert the energy of fuel molecules to the energy in ATP.
 - The thylakoid membranes of chloroplasts are involved in the conversion of light energy into chemical bond energy. (See Figure 5.17b.)
- Membranes are involved in organizing chemical reactions into "assembly lines," allowing them to proceed rapidly and efficiently. (See Figure 5.17c.)

Membranes Are Dynamic

- Membranes actively participate in numerous cellular processes.
- Membranes continually form, move, and fuse.
- Eukaryotic cells form their membranes through a series of activities.
 - The smooth endoplasmic reticulum synthesizes and distributes the phospholipid molecules.
 - Ribosomes form the protein molecules, which are then inserted into rough endoplasmic reticulum.
 - Within cells, segments of membrane move about, change their structures, and fuse with other membranes.
 - Each organelle modifies its membranes to carry out specific functions.
- Despite the similar appearance and interconvertibility of membranes, they show major chemical differences depending on their location in the cell and the functions they serve.
- Dynamic in both structure and activity, membranes are central to life.