

Chapter 5: Cellular Membranes

I Membrane Composition and Structure

- The lipid portion provides a permeability barrier for water-soluble molecules and continuity to the membrane.
- Lipids are like the water of a lake in which the protein “boats” float.
- This is called the fluid-mosaic model. (*See Figure 5.1*)
- The carbohydrate portions of the lipid membrane are carbohydrates, attached to lipid or protein molecules.
- The carbohydrates are generally found on the outer surface membrane.

A. 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 is located, and a hydrophobic (water hating) side, the fatty acid tails. (*See Figure 5.2*)
 - The lipids 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 away from the water.
 - Artificial membranes can be made in the laboratory. They naturally (spontaneously) form sheets of membranes that are lipid bilayers.
 - The bilayer is fluid and allows molecules to move laterally along the plain of the membrane.
 - Whereas lipid molecules can move laterally and do so rapidly, they seldomly move from one layer such as the exterior layer to the other cytoplasmic layer or vice versa.
 - Such a change in position would be referred to as flip-flop.
 - Flip-flop is rare without the aid of special proteins designed for the task.
- Although biological membranes are structurally similar, some have quite different compositions of lipids and proteins.
 - Some lipid membranes have 25% cholesterol, while others have no cholesterol at all.
 - Cholesterol is an important part of lipid membranes. Under some conditions, cholesterol increases membrane fluidity and 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 does unsaturated fatty acids.
 - For any given membrane, fluidity decreases with declining temperature. It is important to have fluidity in membranes that are exposed to cold

temperatures. Therefore, the membranes of cells that live at low temperature tend to be high in unsaturated fatty acids and short chain fatty acids.

B. Membranes proteins are asymmetrically distributed

- Membrane proteins are found inserted in the lipid bilayer. All biological membranes contain proteins.
 - On average, there is one protein molecule for every 25 phospholipid molecules found in biological membranes.
 - The ratio varies. The inner membrane of mitochondria has one protein for every 15 lipids. Myelin sheath, which coat nerve cells and acts as an insulator, has about 1 protein for every 70 lipids.
 - Because of the peptide bonds, all proteins are hydrophilic. However, some have R groups (or side chains) which are hydrophobic.
 - See Figure 5.1 for a better understanding of membrane proteins and their association with the lipid bilayer.
 - The association of the protein molecules with lipid molecules is non-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 the phospholipid bilayer.
 - These have long hydrophobic amino acid regions and their peptide backbone form an alpha helix region, which tends to keep the peptide bonds away from the lipid molecules. (*See Figure 5.4*)
 - The hydrophobic R groups face outward.
 - Peripheral membrane proteins lack hydrophobic regions and are not imbedded in the bilayer. These have polar or charged groups that interact with exposed portions of integral membrane proteins or phospholipid molecules.
 - 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.
 - The some of the proteins and lipids can move around in the membrane; others are tethered to the cytoskeleton, or otherwise restricted in movement, depending on the cell type.
 - Experiments demonstrated that when two cells are fused to form a continuous membrane, membrane proteins distributed rapidly and uniformly around this new cell.
 - Two cells were stained in such a way that each cell's proteins were a different color.
 - The two cells were fused.
 - Within minutes, the mixing of membrane proteins could be seen using light microscopy.

- Although many proteins are mobile in the membrane, some are restricted in movement, because of anchoring to components of the cytoskeleton.
 - This restricts their movement.
 - This tethering causes an unequal distribution of these proteins so that certain regions of the cell membrane can be specialized.
- Transmembrane proteins have a specific orientation.
 - One side might be shaped such that it can act as a receptor for a signaling molecule, and the other side changes shape in response to the signal binding.
 - Some cells are specialized to be anchored to the extra cellular matrix. The externally exposed portion of the protein locks onto extracellular polymers, while the internal region might tie to the cytoskeleton.

C. Membrane carbohydrates are recognition sites

- Some eukaryotic cells have carbohydrate associated with their external surfaces.
 - Carbohydrate-bound lipid is called glycolipid.
 - Most of the carbohydrate in the membrane is covalently bound to proteins called glycoproteins.
 - The endoplasmic reticulum is where the carbohydrate is added and modifications occur in the golgi apparatus.
- Plasma membrane glycoproteins enable cells to be recognized by other cells' proteins.

II Cell Adhesion

A. Glycoproteins are involved with some types of cell to cell adhesion

- An example is the cell to cell adhesion found in sponges.
 - A sponge is a multicellular marine animal.
 - If the sponge is treated in such a way as to cause its cells to disassociate, what was a single animal now are thousands of individual cells. If the cells are left together in a solution for a few hours, they re-aggregate back into a sponge. (*See Figure 5.5*)
 - Even more interestingly, if two different species are dissociated into individual cells and the two types of cells are placed together, the cells will reaggregate back the way they were; two sponges will appear. The cells from one species will aggregate only with cells from its own species. If the cells from two sponges of the same species are combined together, just one large sponge will form upon re-aggregation.
 - This is because there are species specific cell adhesion molecules that fit together in order to create the tissues of the sponge.
 - The adhesion involves plasma membrane recognition proteins.

B. Cell adhesion involves recognition proteins

- The membrane proteins responsible for the cell to cell recognition in sponges were the first ever to be identified and purified.
 - It is a large glycoprotein, composed of 80 % sugar. It is partially imbedded into 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.
 - One is called homotypic (homo means same; typic, type) and is when both cells possess the same type of cell surface receptor and their interaction causes them to stick together. This is how the sponge cell adhesion proteins work.
 - The other is called heterotypic and is like a plug and socket.
 - It has been found that most cases involve the homotypic style of cell to cell adhesion.
 - The heterotypic binding has been found to be the case for mammalian sperm and egg binding. Interesting, since the sperm and egg are conceptually complementary cell types.

III Specialized Cell Junctions

- Complex multicellular organisms use special cell adhesion proteins to allow specific kinds of cells to adhere together and create tissues. These connections are called cell junctions. They are particularly predominant in epithelial tissues.
- The three main major categories of cell junctions in animals are tight junctions, desmosomes, and gap junctions. (*See Figure 5.6*)

A. Tight junctions seal tissues and prevent leaks

- The purpose of tight junctions is to prevent solutes from moving between adjacent cells.
 - Tight junctions also restrict the migration of membrane proteins and phospholipids and therefore can help polarize the cell.
 - Sealing between cells force materials that must pass through to do so by entering cells. This provides the opportunity to regulate what passes through.

B. Desmosomes hold cells together

- Desmosomes hold cells together. Whereas tight junctions have little structural integrity, desmosomes are connected to other protein components inside the cell forming what is called a plaque. The plaque connects to the cytoskeleton of the cell.
- Desmosomes are like spot welds on adjacent cells.

- Cytoplasmic fibers that connect to the plaques of desmosomes are intermediate filaments. The intermediate filaments span throughout the cell connecting plaques to plaques via a network of fibers.
- The desmosomes of one cell connect its fibrous network to the fibrous networks of other cells.
- Intermediate filaments are extremely strong and provide great mechanical stability to epithelial cells. Some epithelial cells, like those that form our skin, need the strength to resist wearing.

C. Gap junctions are a means of communication

- Gap junctions are connections that provide a means of communication.
 - Gap junctions are made up of specialized protein channels called connexons.
 - Each connexon makes a pore.
 - Connexons are made of connexins, which snap together to generate the pore.
 - These proteins span the membrane and protrude from them slightly.
 - The pores of a cell connect to the pores of another. Molecules the sizes of ions, amino acids and nucleotides can get through, but polymers are too large.
 - Connexons can open or close.

IV 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.

A. 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 the molecules distributing equally around an area. When they are, 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 until equilibrium is reached.

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concentrations to regions of lesser concentrations.

- Imagine that the classroom has a glass pane that separates one half from the other. Imagine that balls are bouncing around in one half of the room.
- The balls are kept in one half of the room because there is no way for balls to leave that area and enter the other.
- Imagine that someone makes a hole in the glass pane just large enough for a ball to escape and enter the other side.
- Eventually balls will escape through the hole until the likelihood of a ball leaving the side that had all the balls equals the likelihood of a ball entering. This would be equilibrium. At this point the number of balls per area would be the same or close to it.

- 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, across meters takes years.
- Diffusion is not adequate to 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 and the concentration gradient.

B. 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 pass through until equilibrium is achieved.
 - Substances that are permeable to the membrane move across from the outside to the inside and from the inside to the outside.
 - If the concentration is greater outside, more molecules will move from the outside to the inside, because there are more molecules to move in that direction.
 - Impermeable substances cannot move across the membrane. Molecules that are impermeable to membranes stay on one side or the other of the membrane.
 - 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 is the small molecule water, which can pass through the lipid bilayer.

C. Osmosis is the diffusion of water across membranes

- Water diffusion across membranes is a special case and is referred to as osmosis.
 - It is a completely passive process and requires no metabolic energy.
 - If you take a plant cell and place it 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 you put the plant cell in pure water, the cell membrane will expand until it presses very firmly against the cell wall.
 - Remembering the rules of diffusion, molecules move from areas of greater to lesser concentration. When pure water is outside the cell, the concentration of water is greater there and so the net movement is into the cell.
 - Water will continue to move until the concentration is the same on both sides of the membrane, unless something prevents this from occurring.
 - In plants, the cell wall prevents additional water from moving in because no more space is accommodated due to the size and rigidity of the cell wall.
 - The effect of the solute concentration on the movement of water is interesting: the greater the solute concentration, the lesser the water concentration.
 - The net movement of water molecules will be down its concentration gradient towards the region with greater osmolarity (greater solute concentrations), which has a lower (free) water concentration.
 - It is thought that the water molecules that associate with solute molecules are unable to move freely.
 - The three terms we use to describe the osmolarity of a solution are isotonic, hypertonic and hypotonic.
 - Isotonic solutions have equal solute concentrations. In other words, when all the individual particles outside the cell are totaled and then adjusted for a certain volume, for example per μl , they will equal the total number of all particles inside the cell, per μl .
 - With all diffusion, it is the *concentration* and not the total number of molecules that determine the net direction of movement, because the probability of molecules moving from one point to another depends on how many there are per unit area.
- Imagine the ball example, again. If a small area of the classroom was walled off by the glass panel, after the hole in the glass is made and the balls had time to distribute, there would be fewer balls in the smaller

area, but the balls per unit area would be about equal.

- This, 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 other solution to which it is being compared. The solution's concentration is greater than the cytosol of the cell.
- A hypotonic solution has a lesser total solute concentration. Cells placed into hypotonic solutions 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, on the other hand, can be exposed to pure water but their cell walls prevent more than a certain amount of water from entering.

How do cells take up needed substances that are impermeable to the lipid membrane?

- Polar substances such as amino acids and sugars, and charged substances such as ions, do not diffuse across lipid bilayers.
- So how do these substances, which are important to cells, enter cells?
- One way they enter is through a process referred to as facilitated diffusion. Facilitated diffusion involves proteins that are imbedded in the plasma membrane.
- The two kinds of facilitated diffusion across biological membranes depend on two kinds of proteins: channel and carrier proteins.

D. Diffusion may be aided by channel proteins

- Channel proteins are integral membrane proteins that form polar amino acid-lined channels. Nonpolar amino acids face outward toward the fatty acid tails of the lipid molecules. (*See Figure 5.9*)
 - Best studied of these are the ion channels. Hundreds of different ion channels have been identified.
 - Ion channels are gated. The gates can either be open or closed. There are various mechanisms for controlling the open or closed state of ion channels.
 - Once the channel is opened millions of ions can rush through it per second. Just how fast these ions move and in which direction depends on the concentration gradient. (Water can move through ion channels as well. Another way water enters a cell rapidly is through water channels called aquaporins.)

E. Carrier proteins aid diffusion by binding substances

- Carrier proteins, the other mechanism for facilitated diffusion, involves not just opening a channel but actually binding the transported substance.

- They allow diffusion in both directions. This is one of the ways sugars and amino acids are transported.
- The concentration gradient can be kept by metabolizing the transported substance once it enters the cell. For example, as soon as the glucose enters the cell, it is metabolized and therefore the cell's glucose concentration stays low, and the movement of glucose continues.
- The rate of movement through carrier proteins again is dependent upon concentration, but only to a point, because the carrier must bind the substance it transports.
 - All the binding sites can be occupied.
 - This is called saturation.
 - Saturation can limit the number of molecules that can move into the cell per unit time.

V Active Transport

In contrast to diffusion, active transport requires energy.

- 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.
- Three characteristically different protein driven systems that are involved in active transport are uniport, symport and antiport. (*See Figure 5.11*)

A. Active transport is directional

- 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 might be coupled to the sodium ion transport.
 - Sodium ions move from greater concentration outside the cell, down the concentration gradient to the inside of the cell, and as that occurs, an amino acid is moved *up* the concentration gradient into the cell.
- Antiport transporters couple the movement of different solutes in opposite directions, one into the cell, the other out of the cell.
 - An example is the sodium-potassium pump, which moves sodium out of the cell and potassium into it.
 - Be sure to study the sodium-potassium pump. (*See Figure 5.12*)
 - For every 3 sodium ions pumped out, 2 potassium ions are pumped in.
 - Notice that ATP is used for the required energy.

B. Primary and secondary active transport rely on different energy sources

- If energy is used directly for the pumping system, such as in the sodium-potassium pump, and if ATP is used, the system is a *primary active transport system*.
- Only cations, like sodium, potassium and calcium, are transported directly by pumps that use a primary active transport system.
- Secondary active transport systems are systems that use established gradients to move substances. (See Figure 5.13)
 - 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 was described for the symport transport system.
 - Sodium and potassium ions are pumped by the primary active transport system, while glucose gains entry to the cell via a secondary act of transport system.
 - 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 glucose more than pays for this energy expense.

VI Endocytosis and Exocytosis

Although there are a few systems designed to transport polymers as opposed to simply monomers or ions. Macromolecules in general enter the cell via endocytosis. (See Figure 5.14)

A. 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.
- Endocytosis is a general term for the process of bringing into cells macromolecules, large particles, small molecules and even other cells.
- There are three types of endocytosis: phagocytosis, pinocytosis and receptor mediated endocytosis. In all three cases 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 floats away from the interior surface of the membrane.
 - During phagocytosis, which involves the largest vesicles, entire cells can be engulfed. This is a common method used by unicellular protists.
 - Pinocytosis, which means cellular drinking, involves vesicle formation as well but the vesicles are far smaller. (See Figure 5.15)
 - Dissolved substances and fluids are brought into the cell.
 - There is no specificity as to what the cell brings in.

- Receptor mediated endocytosis is like pinocytosis except it is highly specific. Animal cells use this type of endocytosis to transport specific macromolecules from the environment.

B. Receptor-mediated endocytosis is highly specific

- Receptor proteins are exposed on the outside of the cell and collected in regions called coated pits.
- A molecule called clathrin forms on the internal face of the plasma membrane, and is largely responsible for the creation of the vesicles. (*See Figure 5.16*)
 - Clathrin molecules are what form the “coat” of the pits.
 - The forming vesicles are the “pits”.
 - As the receptors bind specific macromolecules outside, the receptors’ cytoplasmic sides associate with clathrin molecules.
 - Coated vesicles form with the macromolecules trapped inside.
 - After the vesicles form they lose the clathrin coat. Depending on the particular substance retrieved, it 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.
 - Low-density lipoproteins are called LDL.
 - The LDL bind to the receptors found on the surface of the cell.
 - Clathrin coated pits cause an invagination of bound receptors.
 - Vesicles containing cholesterol and 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.

C. Exocytosis moves materials out of the cell.

- Exocytosis is the process by which materials packaged in vesicles are removed or released from the cell. This happens when the vesicle membranes fuse with the plasma membrane.
 - If only endocytosis occurred and no reverse process, exocytosis, eventually the plasma membrane would disappear.
 - In fact, exocytosis balances with endocytosis in such a manner so that there is no net gain or loss of plasma membrane.

VII The Plasma Membrane: Not Simply a Barrier

Plasma membrane is not simply a barrier. (*See Figure 5.17a*)

- Plasma membranes are involved in information processing.
- Membranes are important in energy transformation.

- The inner mitochondrial membrane helps convert the energy of fuel molecules into 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. (*See Figure 5.17c*)

VIII Membranes are Dynamic

Membranes are dynamic. (*See Figure 5.18*)

- Phospholipids and eukaryotes are synthesized on the surface of the smooth endoplasmic reticulum.
- These are distributed throughout the cell as vesicles (the endomembrane system) or are carried to locations by special carrier proteins (mitochondria and peroxisomes). (Chloroplasts make most of their own lipids.)
- Integral plasma membrane, ER and golgi proteins are inserted into the membrane during translation on the rough ER.