

Membrane Structure and Functions

2.2

Thanks to a complex system of membrane-bound cells with organelles, we can live healthy lives. When part of this system malfunctions or becomes damaged, however, diseases can result.

Cystic fibrosis (CF) is a genetic disorder that impairs the lungs and gastrointestinal tract. It is caused by mutations to a single gene that codes for a protein called the cystic fibrosis transmembrane conductance regulator, or CFTR. In properly functioning cells, CFTR acts as a membrane transport protein. It helps to move negatively charged chloride ions, Cl^- , out of the cells that line the lungs and intestinal tract and into the surrounding mucus lining (Figure 1). This results in an electrical gradient across the membrane and leads to the movement of positively charged sodium ions, Na^+ , in the same direction as the chloride. The high Na^+ and Cl^- concentrations cause water, moving by osmosis, to move into the mucus lining.

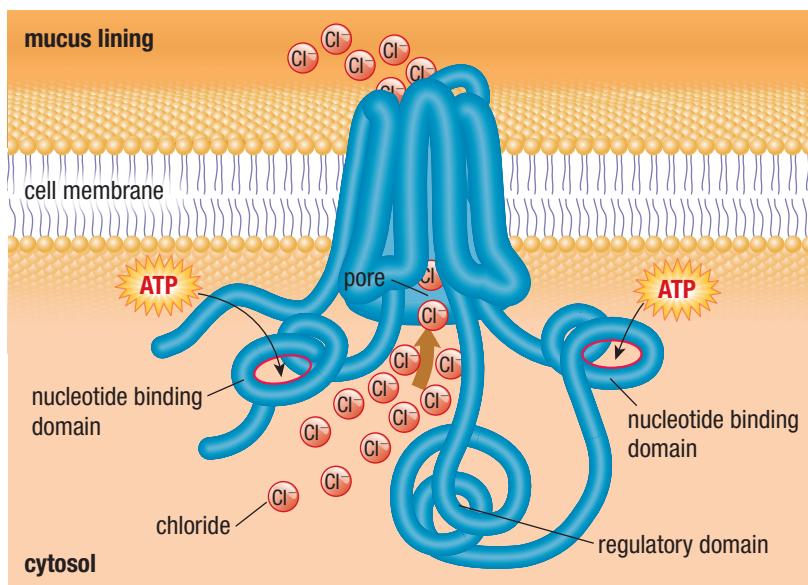
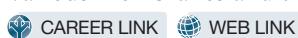


Figure 1 A cystic fibrosis transmembrane conductance regulator (CFTR) is a membrane transport protein that removes chloride from a cell. Cystic fibrosis is caused by a defect in this mechanism.

Keeping the lining of the lungs and intestinal tract hydrated is critical to its proper functioning. In individuals with CF, the Cl^- channel of CFTR malfunctions and water is retained within the cells. A lack of moisture in the mucus lining makes the mucus very thick. When this happens in the lungs, breathing becomes difficult because mucus blocks the airways. The buildup of mucus in the lungs also makes CF patients very susceptible to bacterial infections. In the gastrointestinal system, thick mucus can clog pancreatic ducts, blocking enzymes that would normally enter the small intestine. This can destroy the pancreas and, with it, the ability to produce necessary digestive enzymes. CF patients need to take dietary supplements to survive.

Approximately one in 3900 Canadian children are born with CF. Although the treatment of CF patients is slowly improving, their average lifespan remains under 40 years. Patients may have lung transplants as the disease progresses, but there is no cure. Since CF is caused by a defect to a single gene, the greatest hope is in gene therapy to correct the CFTR gene mutation in the affected cells. However, there are many technical hurdles to overcome before gene therapy becomes a viable treatment option. Understanding the complex structure and function of cell membranes is critical to understanding the causes of diseases such as CF and to finding possible treatments and cures. In this section, you will learn about various membranes and their structures, as well as how they function to protect cells.



The Fluid Mosaic Model

One of the key factors in the evolution of the cell was the development of the cell membrane. By filtering what went into and out of the cell, the semipermeable plasma membrane allowed for the uptake of key nutrients and the elimination of waste products, while maintaining a protected environment in which metabolic processes could occur. The subsequent development of internal membranes allowed for the compartmentalization of processes. This, in turn, allowed for more complex processes and cell functions. A good example of an internal membrane is the nuclear envelope, which encloses the nucleus and is a characteristic of eukaryotic cells.

fluid mosaic model the idea that a biological membrane consists of a fluid phospholipid bilayer, in which proteins are embedded and float freely

Our current view of membrane structure is based on the **fluid mosaic model** (Figure 2). This model proposes that membranes are not rigid, with molecules locked into place. Instead, membranes consist of lipid molecules in which proteins are embedded and float freely. Membranes are described as a fluid because the lipid and protein molecules are generally free to move laterally within the two layers.

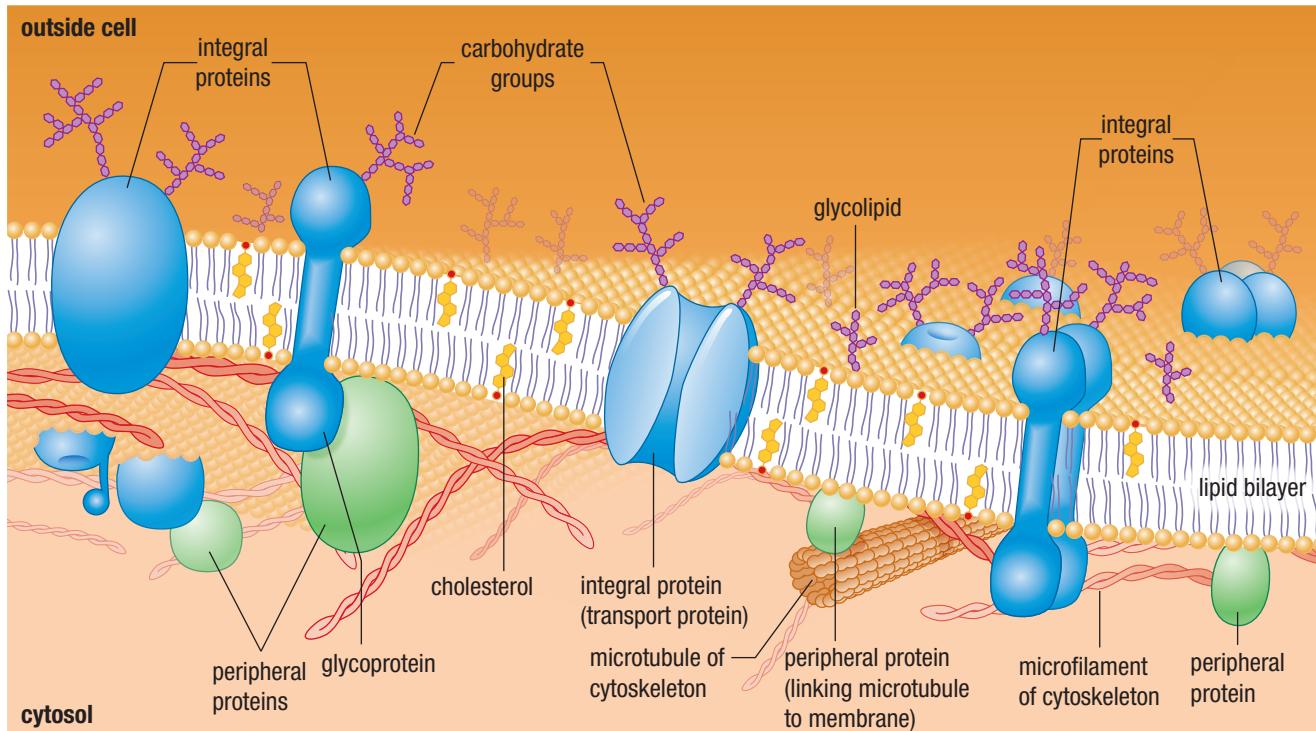


Figure 2 The membrane structure according to the fluid mosaic model, in which integral membrane proteins are suspended individually in a dynamic lipid bilayer

The lipid molecules in all biological membranes are highly dynamic or fluid, which is critical for membrane function. The lipid molecules exist in a double layer, called a bilayer, that is less than 10 nm (nanometres) thick. (By comparison, this page is approximately 100 000 nm thick.) Millions of times a second, the lipid molecules may vibrate, flex back and forth, spin around their long axis, move sideways, and exchange places within the same half of the bilayer.

Membranes contain a mosaic, or wide assortment, of proteins. Some proteins are involved in transport and attachment. Others are enzymes that are used in a variety of biochemical pathways. Because the proteins are larger than the lipid molecules, they move more slowly in the fluid environment of the membrane. A small number of membrane proteins anchor cytoskeleton filaments to the membrane, and thus do not move (Figure 2). Several of the lipid and protein components of some membranes have carbohydrate groups linked to them, forming **glycolipids** and **glycoproteins** that face the exterior of the cell. These molecules often play a role in cell recognition and cell–cell interactions.

The plasma membrane is the outer cell membrane and is responsible for regulating the substances moving into and out of the cell. Myelin, a membrane that functions to insulate nerve fibres, is composed mostly of lipids (18 % protein and 82 % lipid).

glycolipid any membrane lipid that is bound to a carbohydrate

glycoprotein a membrane component that contains a sugar, or carbohydrate, bound to an amino acid

An important characteristic of membranes is membrane asymmetry: the proteins and other components of one half of the lipid bilayer differ from those that make up the other half of the bilayer. This reflects the differences in the functions performed by each half of the membrane. For example, a range of glycolipids and carbohydrate groups attach to proteins on the external half of the membrane, whereas components of the cytoskeleton bind to proteins on the internal half of the membrane. In addition, hormones and growth factors bind to receptor proteins that are found only on the external surface of the plasma membrane. Their binding triggers changes to distinctly different protein components found on the inner surface of the membrane, spurring a cascade of reactions that send a signal within the cell. For example, serotonin is a hormone and neurotransmitter that provides communication between nerve cells. If serotonin is not available in sufficient amounts or does not bind properly, people often experience depression. Doctors treat the symptoms of depression by recommending prescription drugs that help to regulate the level of serotonin.

The Role of Phospholipids

The dominant lipids that are found in membranes are phospholipids. A phospholipid contains two fatty acid tails, which are usually linked to glycerol, a phosphate group, and a compound such as choline (Figure 3(a)). This composition is important for membrane function. The fatty acid tails of a phospholipid are very hydrophobic (non-polar), whereas the phosphate-containing head group is charged and hydrophilic (polar). When added to an aqueous solution, large numbers of phospholipids form a bilayer, or a structure that is two lipid molecules thick (Figure 3(b) and (c)).

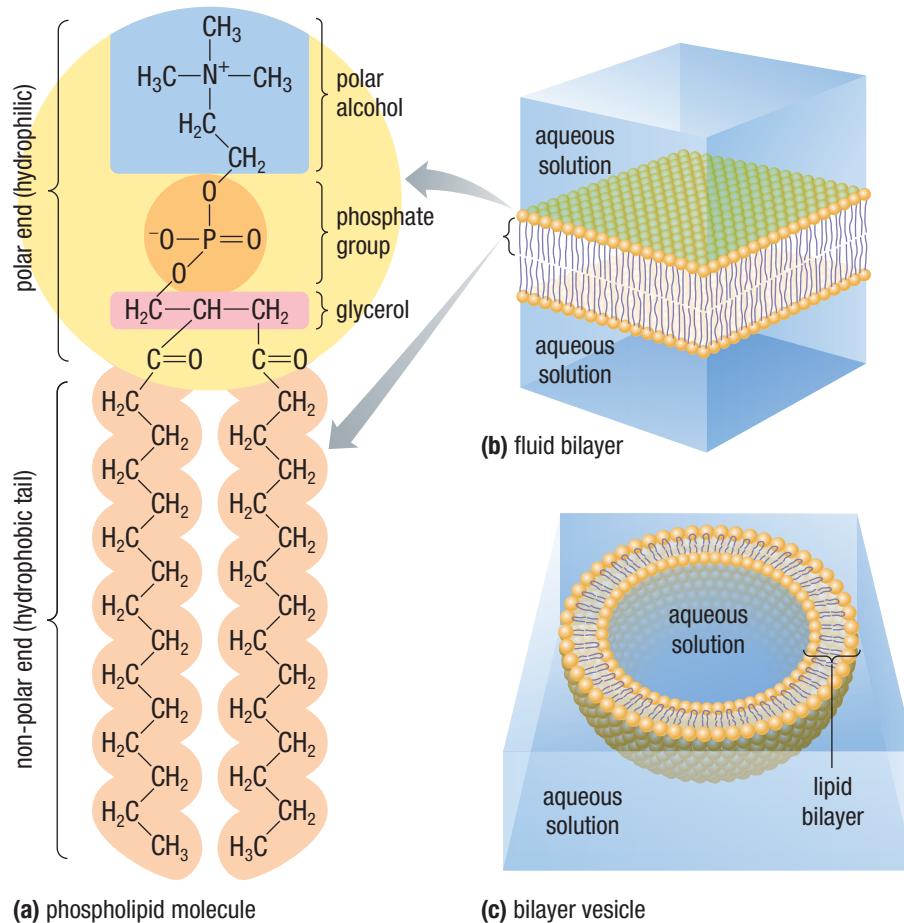


Figure 3 (a) In a phospholipid molecule (phosphatidyl choline), the head has a polar alcohol (choline, shown in blue), a phosphate group (orange), and a glycerol unit (pink). (b) Individual molecules are free to flex, rotate, and exchange places in a phospholipid bilayer in the fluid state. (c) This phospholipid bilayer is forming a vesicle.

A bilayer forms spontaneously in an aqueous environment because of the tendency of the non-polar hydrophobic fatty acids to aggregate together while the polar heads associate with water. These arrangements are favoured because they represent the lowest energy state, and therefore are more likely than any other arrangement to occur.

Fluidity

The dynamic nature of the lipid bilayer is dependent on how densely the individual lipid molecules can pack together. This is influenced by two major factors: the composition of the lipid molecules that make up the membrane and the temperature. Fatty acids composed of saturated hydrocarbons (in which each carbon is bound to the maximum number of hydrogen atoms) tend to have a straight shape, which allows the lipids to pack together more tightly. In comparison, the double bonds in an unsaturated fatty acid bend its structure, so the lipid molecules are less straight and more loosely packed (Section 1.4).

Membranes remain in a fluid state over a relatively wide range of temperatures. However, if the temperature drops low enough, the lipid molecules in a membrane become closely packed, and the membrane forms a highly viscous semisolid gel. At any given temperature, the fluidity of a membrane is related to the degree to which the membrane lipids are unsaturated. The more unsaturated a membrane is, the lower its gelling temperature.

Besides lipids, a group of compounds called **sterols** also influence membrane fluidity. The best example of a sterol is cholesterol, which is found in the membranes of animal cells, but not in the membranes of plants or prokaryotes (Figure 4). Sterols act as membrane stabilizers. At high temperatures, they help to restrain the movement of the lipid molecules in a membrane, thus reducing the fluidity of the membrane. At lower temperatures, however, sterols occupy the spaces between the lipid molecules, thus preventing fatty acids from associating and forming a non-fluid gel.

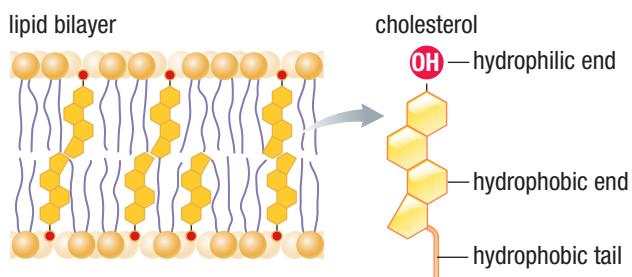


Figure 4 The hydrophilic OH group at one end of the molecule extends into the polar regions of the bilayer. The ring structure extends into the non-polar interior of the membrane.

The Role of Membrane Proteins

Although lipid molecules constitute the backbone of a membrane, the set of proteins associated with the membrane determines its function and makes it unique. Membrane proteins can be separated into the following four functional categories (Figure 5, next page):

- *Transport*: Many substances cannot freely diffuse through membranes. Instead, a specific compound may be able to cross a membrane by way of a hydrophilic protein channel. Alternatively, shape shifting may allow some membrane proteins to shuttle molecules from one side of a membrane to the other.
- *Enzymatic activity*: Some membrane proteins, such as those associated with respiration and photosynthesis, are enzymes.
- *Triggering signals*: Membrane proteins may bind to specific chemicals, such as hormones. Binding to these chemicals triggers changes on the inner surface of the membrane, starting a cascade of events within the cell.

- **Attachment and recognition:** Proteins that are exposed to both the internal and external membrane surfaces act as attachment points for a range of cytoskeleton elements, as well as components involved in cell–cell recognition, and bond to the extracellular matrix. For example, surface proteins can recognize elements of disease-causing microbes that may try to invade cells, triggering an immune response.

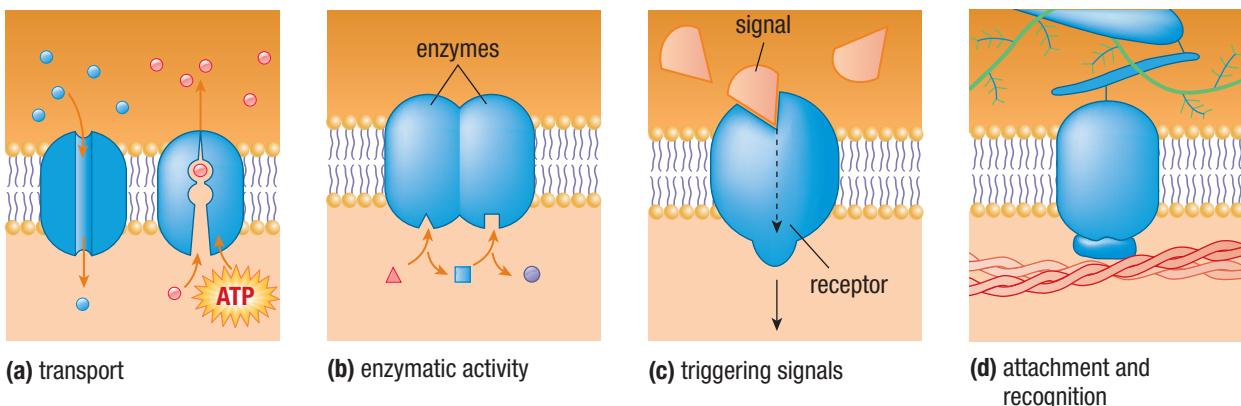


Figure 5 The major functions of membrane proteins are (a) transport, (b) enzymatic activity, (c) triggering signals, and (d) attachment and recognition.

All of these functions may exist in a single membrane, and one protein or protein complex may serve more than one of these functions. Beyond function, all membrane proteins can be separated into two additional categories: integral and peripheral membrane proteins (Figure 2). Membrane proteins that are embedded in the lipid bilayer are called **integral membrane proteins**. All integral membrane proteins have at least one region that interacts with the hydrophobic core of the membrane. However, most integral proteins are transmembrane proteins. This means that they span the entire membrane bilayer and have regions that are exposed to the aqueous environment on both sides of the membrane (Figure 6).

integral membrane protein a protein that is embedded in the lipid bilayer

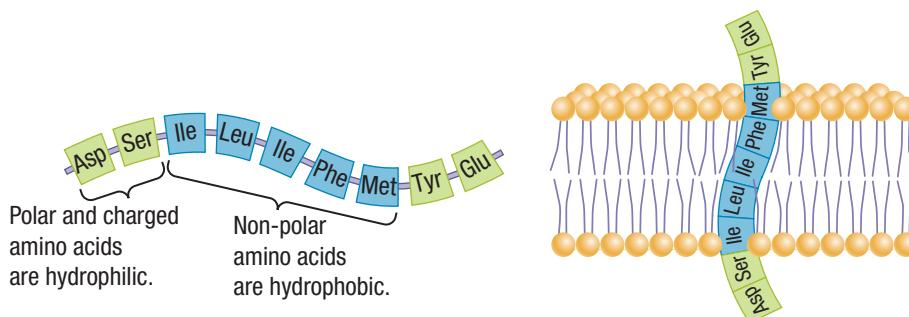


Figure 6 Transmembrane proteins are easy to identify because they have a segment of non-polar amino acids that are hydrophobic and stay within the membrane, as well as polar hydrophilic regions that are exposed to the environment.

The second major group of proteins are **peripheral membrane proteins**. They are positioned on the surface of a membrane and do not interact with the hydrophobic core of the membrane. Peripheral proteins are held to membrane surfaces by non-covalent bonds (hydrogen bonds and ionic bonds), usually by interacting with the exposed portions of integral proteins as well as directly with membrane lipid molecules. Most peripheral proteins are on the cytosol side of the membrane, and some are part of the cytoskeleton. Examples of peripheral proteins that are part of the cytoskeleton are microtubules, microfilaments, intermediate filaments, and proteins that link the cytoskeleton together. These proteins hold some integral membrane proteins in place.

peripheral membrane protein a protein on the surface of the membrane

2.2 Review

Summary

- A biological membrane consists of a bilayer of phospholipids and proteins that move around freely within the layer. This is described as the fluid mosaic model.
- The fluidity of a plasma membrane depends on the composition of the lipid molecules that make up the membrane, as well as the temperature.
- Membranes contain sterols, which help to maintain their fluidity.
- Membrane proteins have four functions: transport, enzymatic activity, triggering signals, and attachment and recognition of molecules.
- Membrane proteins may be embedded in the lipid bilayer (integral membrane proteins) or positioned on top of the phospholipid bilayer (peripheral membrane proteins).

Questions

1. Our current view of membrane structure is based on the fluid mosaic model. What does the word “mosaic” refer to in the expression “fluid mosaic model”? **K/U**
2. When referring to membrane glycolipids and glycoproteins, what does the prefix “glyco” indicate? **K/U**
3. When comparing the outside and inside halves of a cell membrane’s phospholipid bilayer, the composition of lipids on the two surfaces is asymmetrical. **K/U**
 - (a) Describe how membranes are asymmetric.
 - (b) Why is membrane asymmetry an important characteristic in cell membranes?
4. How does the structure of the plasma membrane facilitate its function? **K/U**
5. (a) What is meant by membrane fluidity?
(b) Explain how the chemical makeup of a membrane gives it fluidity.
(c) Which components affect the fluidity of a membrane?
(d) How is their movement related to this fluidity?
K/U T/I
6. (a) What is the function of sterols?
(b) Identify a sterol that is found in membranes of animal cells but not in plants or prokaryotes. **K/U**
7. Cholesterol molecules are aligned with the lipid molecules on both sides of the bilayer. Is cholesterol polar or non-polar? Explain your answer. **K/U**
8. The basic components of a cell membrane are phospholipids, proteins, and carbohydrates. What are the functions of each component? **K/U**
9. Explain the four functional categories of membrane proteins. **K/U**
10. How are protein receptors and enzymes similar? **K/U**
11. If proteins were rigid, how would this affect their ability to act as receptors? **K/U**
12. Describe what is meant by integral and peripheral membrane proteins. How do they differ in their chemical makeup and their arrangement of amino acids? **K/U**
13. Do all organelles have identical membranes? Give some examples of similarities and differences. **K/U**
14. Serotonin is a hormone and neurotransmitter that provides communication between nerve cells. If it is not available in sufficient amounts or does not bind properly, people can experience depression. Using the Internet and other sources, find out how SSRIs (selective serotonin reuptake inhibitors), a newer class of antidepressants often prescribed by doctors to alleviate depression, work.  **T/I**



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