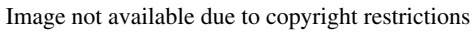
5

Biological Membranes



KEY CONCEPTS

Biological membranes are selectively permeable membranes that help maintain homeostasis in the cell.

According to the fluid mosaic model, cell membranes consist of a fluid bilayer composed of phospholipids in which a variety of proteins are embedded.

Membrane proteins, and thus membranes, have many functions, including transport of materials, enzymatic activity, transmission of information, and recognition of other cells.

Diffusion is a passive process that does not require the cell to expend metabolic energy, whereas active transport requires a direct expenditure of energy.

Cells in close contact form specialized junctions between one another.

The evolution of biological membranes that separate the cell from its external environment was an essential step in the origin of life. Later, membranes made the evolution of complex cells possible. The extensive internal membranes of eukaryotic cells form multiple compartments with unique environments for highly specialized activities.

An exciting area of cell membrane research focuses on membrane proteins. Some proteins associated with the plasma membrane transport materials, whereas others transmit information or serve as enzymes. Still others, known as *cell adhesion molecules,* are important in connecting cells to one another to form tissues.

The principal cell adhesion molecules in vertebrates and in many invertebrates are **cadherins.** These molecules are responsible for calcium-dependent adhesion between cells that form multicellular sheets. For example, cadherins form cell junctions important in maintaining the structure of the epithelium that makes up human skin (see photograph). An absence of these membrane proteins is associated with the invasiveness of some malignant tumors. Certain cadherins mediate the way cells adhere in the early embryo, and thus they are important in development.

In Chapter 4, we discussed a variety of cell organelles. In this chapter, we will focus on the structure and functions of the biological membranes that surround many organelles as well as the plasma membrane that surrounds the cell. We first consider

what is known about the composition and structure of biological membranes. Then we discuss how cells transport various materials, from ions to complex molecules and even bacteria, across membranes. Finally, we examine specialized structures that allow membranes of different cells to interact. Although much of our discussion centers on the structure and functions of plasma membranes, many of the concepts apply to other cell membranes. ■

THE STRUCTURE OF BIOLOGICAL MEMBRANES

Learning Objectives

1 Evaluate the importance of membranes to the homeostasis of the cell, emphasizing their various functions.
2 Describe the fluid mosaic model of cell membrane structure.
3 Relate properties of the lipid bilayer to properties and functions of cell membranes.
4 Describe the ways that membrane proteins associate with the lipid bilayer, and discuss the functions of membrane proteins.

To carry out the many chemical reactions necessary to sustain life, the cell must maintain an appropriate internal environment. Every cell is surrounded by a **plasma membrane** that physically separates it from the outside world and defines it as a distinct entity. By regulating passage of materials into and out of the cell, the plasma membrane helps maintain a life-supporting internal environment. As we discussed in Chapter 4, eukaryotic cells are characterized by numerous organelles that are surrounded by membranes. Some of these organelles—including the nuclear envelope, endoplasmic reticulum, Golgi complex, lysosomes, vesicles, and vacuoles—form the endomembrane system, which extends throughout the cell.

Biological membranes are complex, dynamic structures made of lipid and protein molecules that are in constant motion. The properties of membranes allow them to perform vital functions in the cell. They regulate the passage of materials, divide the cell into compartments, serve as surfaces for chemical reactions, adhere to and communicate with other cells, and transmit signals between the environment and the interior of the cell. Membranes are also an essential part of energy transfer and storage systems. How do the properties of cell membranes enable the cell to carry on such varied functions?

Long before the development of the electron microscope, scientists knew that membranes consist of both lipids and proteins. Work by researchers in the 1920s and 1930s had provided clues that the core of cell membranes consists of lipids, mostly phospholipids (see Chapter 3).

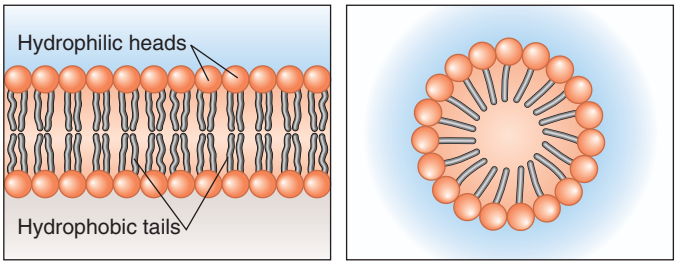
Phospholipids form bilayers in water

Phospholipids are primarily responsible for the physical properties of biological membranes, because certain phospholipids have unique attributes, including features that allow them to form bilayered structures. A phospholipid contains two fatty acid chains linked to two of the three carbons of a glycerol molecule (see Fig. 3-13). The fatty acid chains make up the nonpolar, *hydrophobic* ("water-fearing") portion of the phospholipid. Bonded to the third carbon of the glycerol is a negatively charged, *hydrophilic* ("water-loving") phosphate group, which in turn is linked to a polar, hydrophilic organic group. Molecules of this type, which have distinct hydrophobic and hydrophilic regions, are called **amphipathic molecules.** All lipids that make up the core of biological membranes have amphipathic characteristics.

Because one end of each phospholipid associates freely with water and the opposite end does not, the most stable orientation for them to assume in water results in the formation of a bilayer structure (Fig. 5-1a). This arrangement allows the hydrophilic heads of the phospholipids to be in contact with the aqueous medium while their oily tails, the hydrophobic fatty acid chains, are buried in the interior of the structure away from the water molecules.

Amphipathic properties alone do not predict the ability of lipids to associate as a bilayer. Shape is also important. Phospholipids tend to have uniform widths; their roughly cylindrical shapes, together with their amphipathic properties, are responsible for bilayer formation. In summary, phospholipids form bilayers because the molecules have (1) two distinct regions, one strongly hydrophobic and the other strongly hydrophilic (making them strongly amphipathic); and (2) cylindrical shapes that allow them to associate with water most easily as a bilayer.

Do you know why detergents remove grease from your hands or from dirty dishes? Many common detergents are amphipathic molecules, each containing a single hydrocarbon chain (like a fatty acid) at one end and a hydrophilic region at the other. These



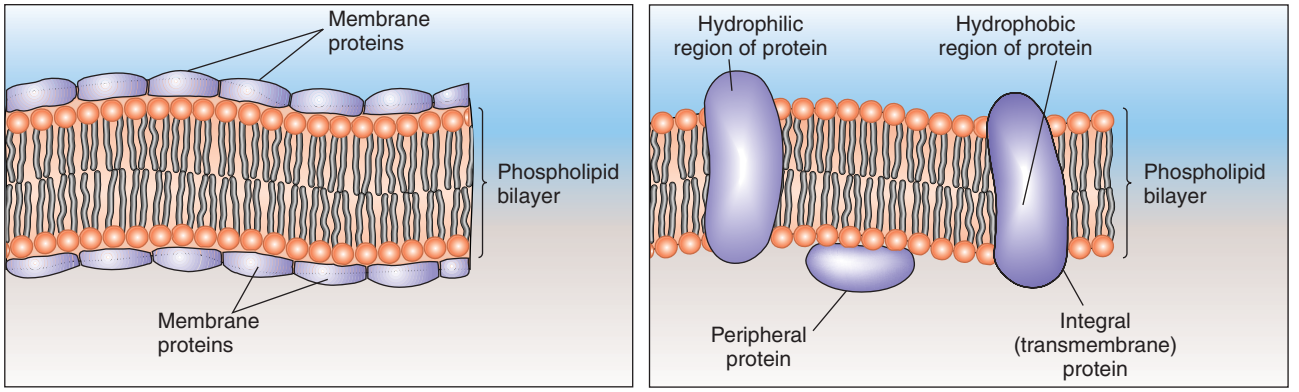
(a) Phospholipids in water. Phospholipids associate as bilayers in water because they are roughly cylindrical amphipathic molecules. The hydrophobic fatty acid chains are not exposed to water, whereas the hydrophilic phospholipid heads are in contact with water.

(b) Detergent in water. Detergent molecules are roughly cone-shaped amphipathic molecules that associate in water as spherical structures.

Figure 5-1 ***Animated*** Properties of lipids in water

Key Point

The Davson–Danielli model was the accepted view until about 1970 when advances in biology and chemistry led to new findings about biological membranes that were incompatible with this model. The fluid mosaic model fits the new data.



(a) The Davson–Danielli model. According to this model, the membrane is a sandwich of phospholipids spread between two layers of protein. Although accepted for many years, this model was shown to be incorrect.

(b) Fluid mosaic model. According to this model, a cell membrane is a fluid lipid bilayer with a constantly changing "mosaic pattern" of associated proteins.

Figure 5-2 Two models of membrane structure

molecules are roughly cone shaped, with the hydrophilic end forming the broad base and the hydrocarbon tail leading to the point. Because of their shapes, these molecules do not associate as bilayers but instead tend to form spherical structures in water (Fig. 5-1b). Detergents can "solubilize" oil because the oil molecules associate with the hydrophobic interiors of the spheres.

Current data support a fluid mosaic model of membrane structure

By examining the plasma membrane of the mammalian red blood cell and comparing its surface area with the total number of lipid molecules per cell, early investigators calculated that the membrane is no more than two phospholipid molecules thick. In 1935, these findings, together with other data, led Hugh Davson and James Danielli, working at London's University College, to propose a model in which they envisioned a membrane as a kind of "sandwich" consisting of a *lipid bilayer* (a double layer of lipid) between two protein layers (Fig. 5-2a). This useful model had a great influence on the direction of membrane research for more than 20 years. Models are important in the scientific process; good ones not only explain the available data but are testable. Scientists use models to help them develop hypotheses that can be tested experimentally (see Chapter 1).

With the development of the electron microscope in the 1950s, cell biologists were able to see the plasma membrane for the first time. One of their most striking observations was how uniform and thin the membranes are. The plasma membrane is no more than 10 nm thick. The electron microscope revealed a three-layered structure, something like a railroad track, with two dark layers separated by a lighter layer (Fig. 5-3). Their findings seemed to support the protein–lipid–protein sandwich model.

During the 1960s, a paradox emerged regarding the arrangement of the proteins. Biologists assumed membrane proteins were uniform and had shapes that would allow them to lie like

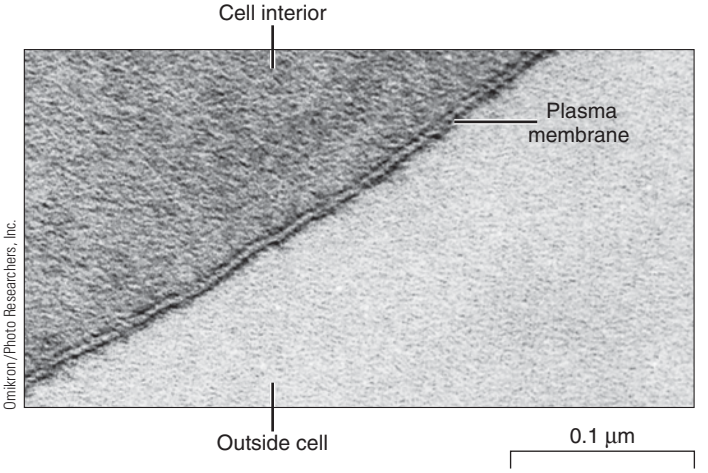


Figure 5-3 TEM of the plasma membrane of a mammalian red blood cell

The plasma membrane separates the cytosol (*darker region*) from the external environment (*lighter region*). The hydrophilic heads of the phospholipids are the parallel dark lines, and the hydrophobic tails are the light zone between them.

thin sheets on the membrane surface. But when purified by cell fractionation, the proteins were far from uniform; in fact, they varied widely in composition and size. Some proteins are quite large. How could they fit within a surface layer of a membrane less than 10 nm thick? At first, some researchers tried to answer this question by modifying the model with the hypothesis that the proteins on the membrane surfaces were a flattened, extended form, perhaps a β-pleated sheet (see Figure 3-20b).

Other cell biologists found that instead of having sheetlike structures, many membrane proteins are rounded, or globular. Studies of many membrane proteins showed that one region (or domain) of the molecule could always be found on one side of the bilayer, whereas another part of the protein might be located on the opposite side. Rather than form a thin surface layer, many membrane proteins extended completely through the lipid bilayer. Thus, the evidence suggested that membranes contain different types of proteins of different shapes and sizes that are associated with the bilayer in a mosaic pattern.

In 1972, S. Jonathan Singer and Garth Nicolson of the University of California at San Diego proposed a model of membrane structure that represented a synthesis of the known properties of biological membranes. According to their **fluid mosaic model,** a cell membrane consists of a fluid bilayer of phospholipid molecules in which the proteins are embedded or otherwise associated, much like the tiles in a mosaic picture. This mosaic pattern is not static, however, because the positions of the proteins are constantly changing as they move about like icebergs in a fluid sea of phospholipids. This model has provided great impetus to research; it has been repeatedly tested and has been shown to accurately predict the properties of many kinds of cell membranes. Figure 5-2b depicts the plasma membrane of a eukaryotic cell according to the fluid mosaic model; prokaryotic plasma membranes are discussed in Chapter 24.

Biological membranes are two-dimensional fluids

An important physical property of phospholipid bilayers is that they behave like *liquid crystals.* The bilayers are crystal-like in that the lipid molecules form an ordered array with the heads on the outside and fatty acid chains on the inside; they are liquidlike in that despite the orderly arrangement of the molecules, their hydrocarbon chains are in constant motion. Thus, molecules are free to rotate and can move laterally within their single layer (Fig. 5-4). Such movement gives the bilayer the property of a *two-dimensional fluid.* This means that under normal conditions a single phospholipid molecule can travel laterally across the surface of a eukaryotic cell in seconds.

The fluid qualities of lipid bilayers also allow molecules embedded in them to move along the plane of the membrane (as long as they are not anchored in some way). David Frye and Michael Edidin elegantly demonstrated this in 1970. They conducted experiments in which they followed the movement of membrane proteins on the surface of two cells that had been joined (Fig. 5-5).When the plasma membranes of a mouse cell and a human cell are fused, within minutes at least some of the membrane proteins from each cell migrate and become randomly distributed over the single, continuous plasma membrane that surrounds the joined cells. Frye and Edidin showed that the fluidity of the lipids in the membrane allows many of the proteins to move, producing an ever-changing configuration. Occasionally, with the help of enzymes in the cell membrane, phospholipid molecules flip-flop from one layer to the other.

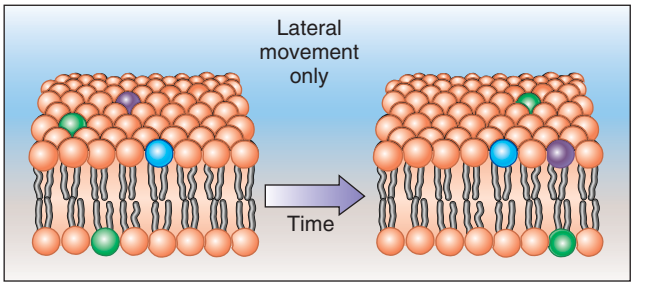


Figure 5-4 Membrane fluidity

The ordered arrangement of phospholipid molecules makes the cell membrane a liquid crystal. The hydrocarbon chains are in constant motion, allowing each molecule to move laterally on the same side of the bilayer.

For a membrane to function properly, its lipids must be in a state of optimal fluidity. The membrane's structure is weakened if its lipids are too fluid. However, many membrane functions, such as the transport of certain substances, are inhibited or cease if the lipid bilayer is too rigid. At normal temperatures, cell membranes are fluid, but at low temperatures the motion of the fatty acid chains is slowed. If the temperature decreases to a critical point, the membrane is converted to a more solid gel state.

Certain properties of membrane lipids have significant effects on the fluidity of the bilayer. Recall from Chapter 3 that molecules are free to rotate around single carbon-to-carbon covalent bonds. Because most of the bonds in hydrocarbon chains are single bonds, the chains themselves twist more and more rapidly as the temperature rises.

The fluid state of the membrane depends on its component lipids. You have probably noticed that when melted butter is left at room temperature, it solidifies. Vegetable oils, however, remain liquid at room temperature. Recall from our discussion of fats in Chapter 3 that animal fats such as butter are high in saturated fatty acids that lack double bonds. In contrast, a vegetable oil may be polyunsaturated, with most of its fatty acid chains having two or more double bonds. At each double bond there is a bend in the molecule that prevents the hydrocarbon chains from coming close together and interacting through van der Waals interactions. In this way, unsaturated fats lower the temperature at which oil or membrane lipids solidify.

Many organisms have regulatory mechanisms for maintaining cell membranes in an optimally fluid state. Some organisms compensate for temperature changes by altering the fatty acid content of their membrane lipids. When the outside temperature