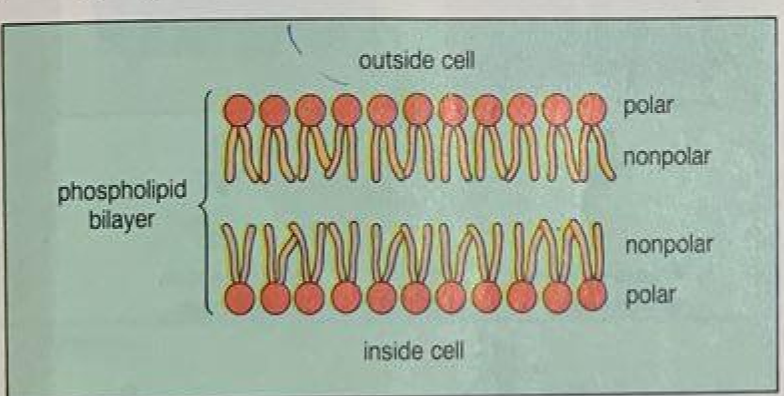
All cells have a plasma membrane that serves as an interface between the interior, which is alive, and the exterior, which is nonliving. An intact plasma membrane is absolutely essential to a cell, and if by chance the plasma membrane is disrupted, the cell loses its contents and dies. The plasma membrane was absolutely essential to the evolution of the first cell or cells. Only when a membrane is present can there be a cell at all.

The interior and exterior environments of a living cell are largely fluids, even if the cell is within a multicellular organism. Quite often the composition of intracellular fluid (i.e., cytosol) is not quite the same as that of the extracellular fluids. The plasma membrane functions to keep the intracellular fluid relatively constant. It regulates the entrance and exit of molecules into and out of the cell, and in this way the intracellular fluid remains compatible with the continued existence of the cell.

Studies of Membrane Structure

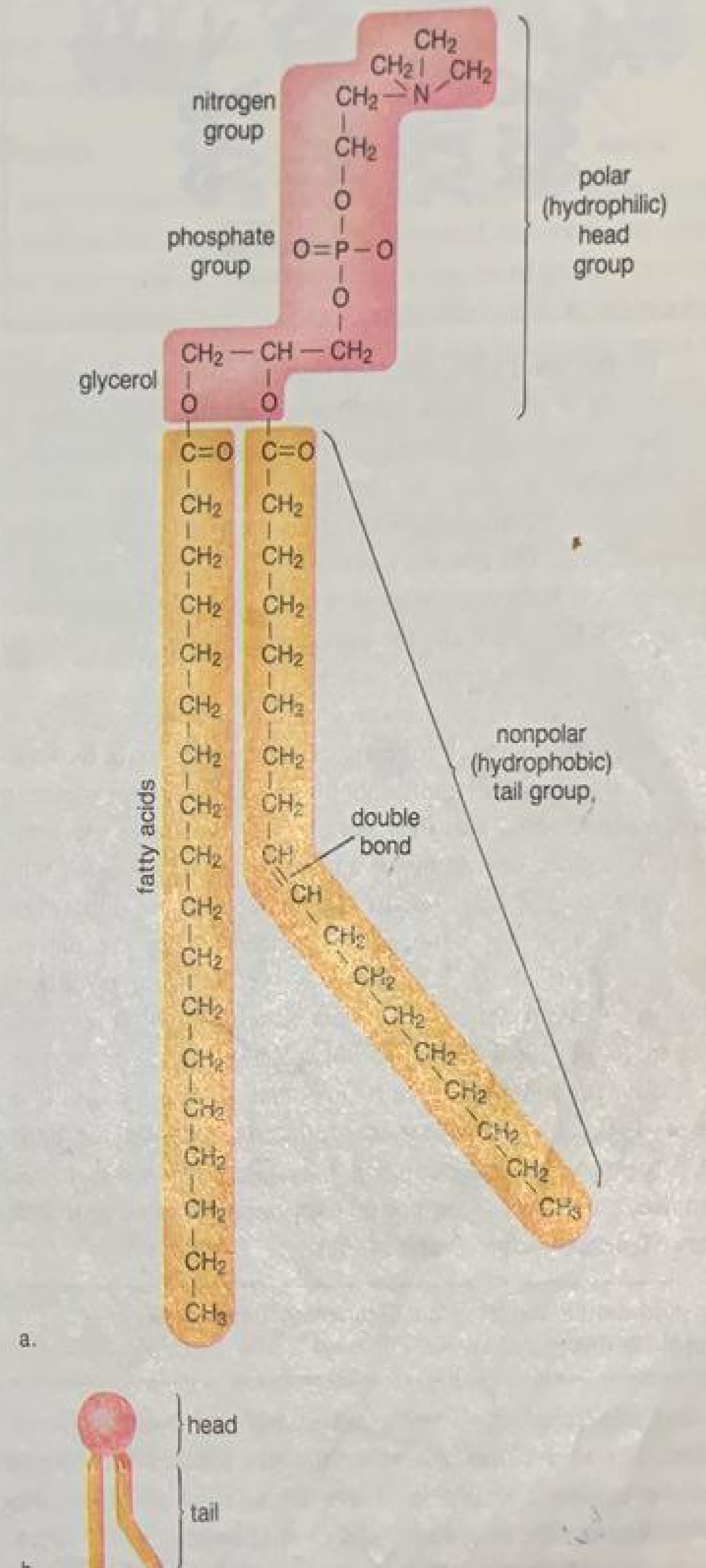
At the turn of the century, investigators noted that lipid-soluble molecules entered cells more rapidly than water-soluble molecules. This prompted them to suggest that lipids are a component of the plasma membrane. Later, chemical analysis disclosed that the plasma membrane contains phospholipids (fig. 6.1). In 1925, E. Gorter and G. Grendel measured the amount of phospholipid extracted from red blood cells and determined that there is just enough to form a bilayer around the cells.[1] They further suggested that the nonpolar (hydrophobic) tails are directed inward and the polar (hydrophilic) heads were directed outward:



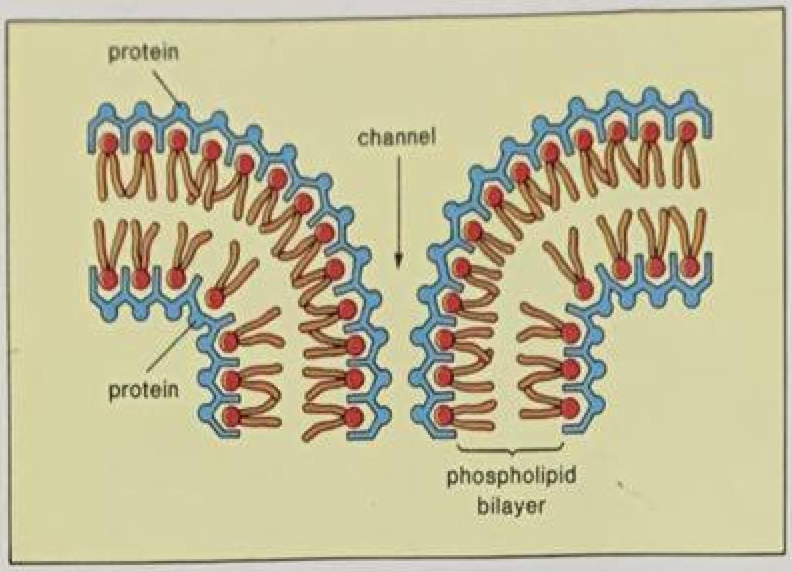
The presence of lipids cannot account for all the properties of the plasma membrane. For example, to account for the permeability of the membrane to certain nonlipid substances, J. Danielli and H. Davson suggested in the 1940s that globular proteins are also a part of the membrane. They proposed the "sandwich" model of membrane structure in which the phospholipid bilayer is a filling

[1]Later investigators found that Gorter and Grendel reported too low an amount of lipid and underestimated the surface area of red blood cells; however, since the 2 errors canceled each other, they still came to the correct conclusion.

Figure 6.1
The plasma membrane contains phospholipid molecules. ***a.*** Each phospholipid molecule is composed of glycerol bonded to 2 fatty acid chains and a chain that contains a phosphate group and a nitrogen group. ***b.*** The molecule arranges itself in such a way that the phosphate and nitrogen-containing chain forms a polar (hydrophilic) head, and the fatty acid chains form nonpolar (hydrophobic) tails. The presence of a double bond causes a "kink" in a fatty acid tail.



between 2 layers of proteins arranged to give channels through which polar substances may pass:



By the late 1950s, electron microscopy had advanced to allow viewing of the plasma membrane and other membranes in the cell. Since the membrane has a sandwichlike appearance (fig. 6.2), J. D. Robertson assumed that the outer dark layer (stained with heavy metals) contained protein plus the hydrophilic heads of the phospholipids. The interior was simply the hydrophobic tails of these molecules. Robertson went on to suggest that all membranes in various cells have basically the same composition. This proposal was called the "unit membrane" model.

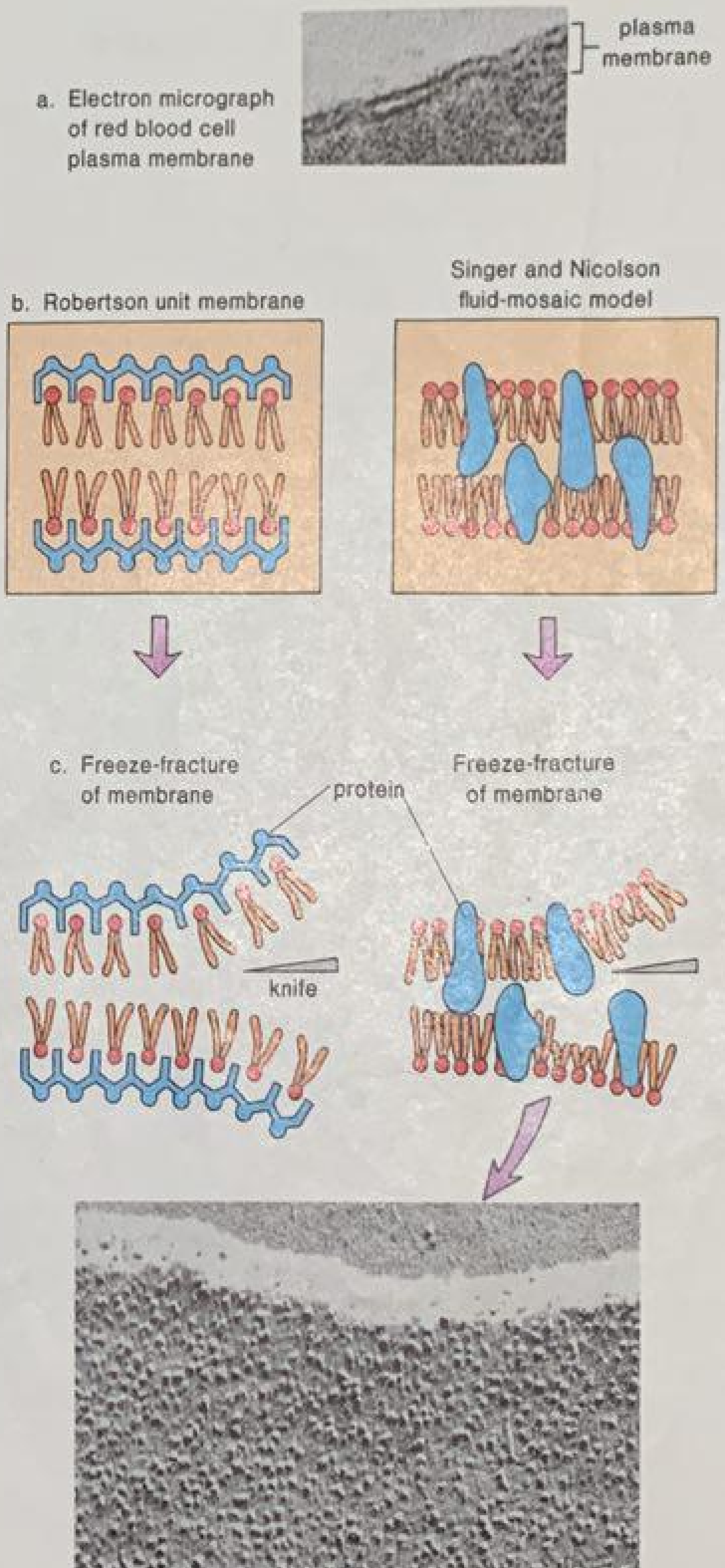
This model of membrane structure was accepted for at least 10 years, even though investigators began to doubt its accuracy. For example, not all membranes have the same appearance in electron micrographs, and they certainly do not have the same function. The inner membrane of a mitochondrion is coated with rows of particles and functions in cellular respiration; it therefore has a far different appearance and function from the plasma membrane. Finally, in 1972, S. Singer and G. Nicolson introduced the **fluid-mosaic model** of membrane structure, which proposes that the membrane is a bilayer of phospholipids with the consistency of olive oil, in which protein molecules are either partially or wholly embedded. The proteins are scattered throughout the membrane, forming a mosaic pattern (fig. 6.3). The fluid-mosaic model of membrane structure is supported especially by electron micrographs of freeze-fractured membranes.

The fluid-mosaic model of membrane structure is widely accepted at this time.

Our perception of the plasma membrane has changed over the years. There have been a series of models, each one developed to suit the evidence available at that time. This illustrates that scientific knowledge is always subject to change, and modifications are made whenever new data are presented. A model is useful because it pulls together the available data and suggests new avenues of research.

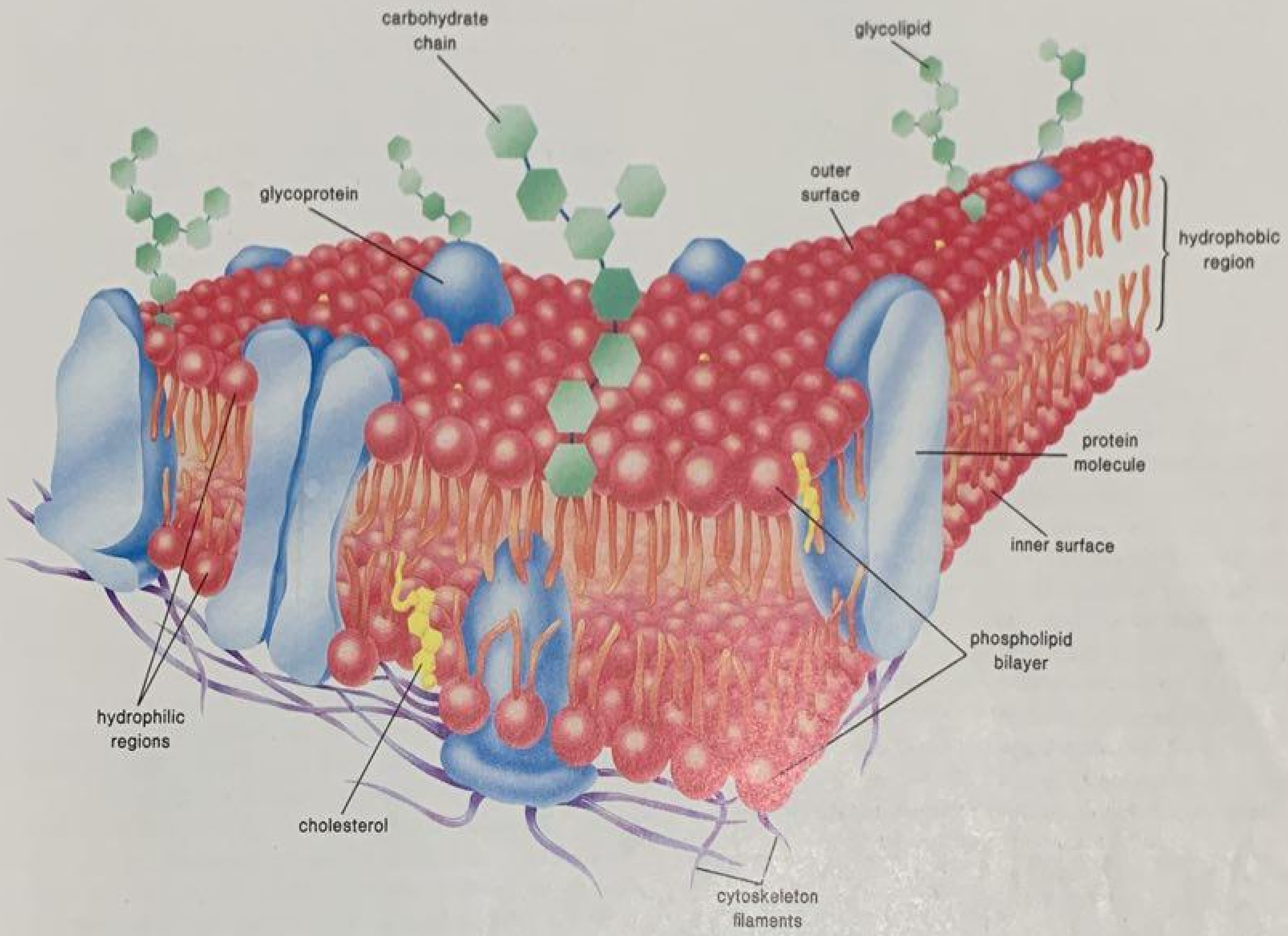
Figure 6.2

Membrane structure. ***a.*** The red blood cell plasma membrane typically has a 3-layered appearance in electron micrographs; there are 2 outer dark layers and a central light layer. Magnification, X415,000. ***b.*** In 1960, Robertson's unit membrane model was widely accepted. This model proposed that the outer dark layers in electron micrographs were made up of protein and polar heads of phospholipid molecules, while the inner light layer was composed of the nonpolar tails. The Robertson model was challenged, particularly by the Singer and Nicolson fluid-mosaic model, which puts protein molecules within the lipid bilayer. ***c.*** A technique, called freeze-fracture, allows an investigator to view the interior of the membrane. Cells are rapidly frozen in liquid nitrogen and then fractured with a knife. The fracture often splits the membrane in 2, just in the middle of the lipid bilayer. Platinum and carbon are applied to the fractured surface to produce a faithful replica that is observed by electron microscopy. ***d.*** The electron micrograph is not as smooth as it would be if the unit membrane model was correct. Instead, the micrograph shows the presence of particles as is expected by the fluid-mosaic model.



d. Electron micrograph of freeze-fractured membrane shows presence of particles

Figure 6.3
Fluid-mosaic model of the plasma membrane. The plasma membrane is composed of a phospholipid bilayer with embedded proteins. The hydrophilic heads of the phospholipids are at the surfaces of the membrane, and the hydrophobic tails make up the interior of the membrane. Note the asymmetry of the membrane; for example, carbohydrate chains project externally and cytoskeleton filaments attach to proteins on the cytoplasmic side of the plasma membrane.

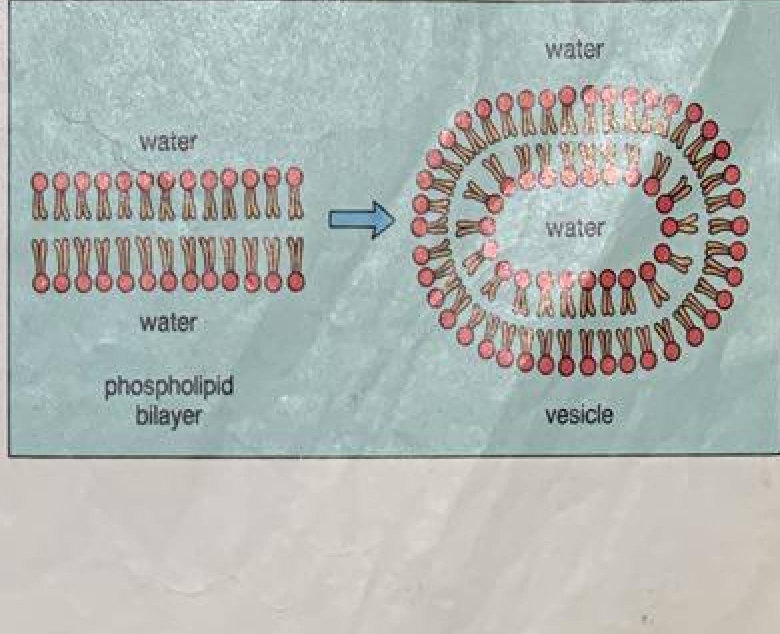


Fluid-Mosaic Model of the Plasma Membrane

The fluid-mosaic model of membrane structure has 2 components, lipids and proteins (fig. 6.3). The lipids form the matrix of the membrane, and the proteins carry out all of its functions.

Lipid Component

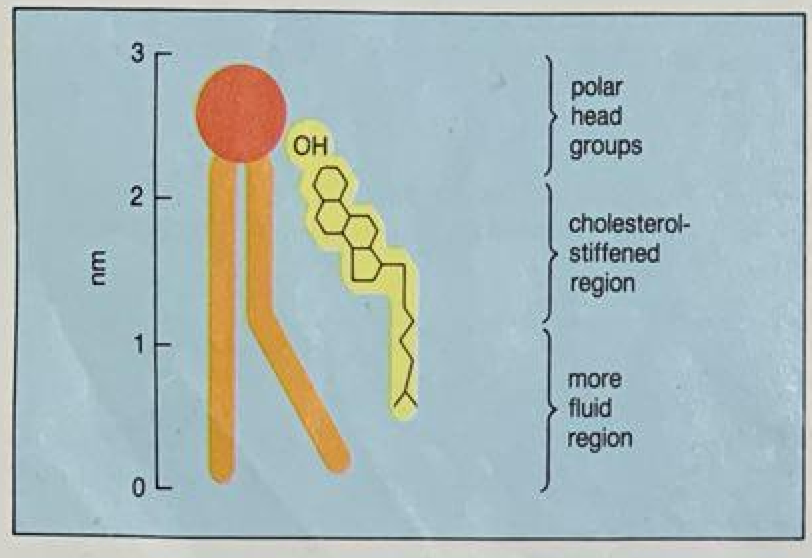
Most of the lipids in the plasma membrane are **phospholipids** (fig. 6.1). In a laboratory container, phospholipids spontaneously form a bilayer in which the hydrophilic (polar) heads face water on both sides and the hydrophobic tails avoid contact with water. The hydrophobic interior portions of the phospholipid bilayer are never exposed to water because it spontaneously forms a sphere—becoming a barrier just like the plasma membrane:



At body temperature, the phospholipid bilayer of the plasma membrane has the consistency of olive oil. The greater the concentration of unsaturated fatty acid residues, the more liquid the bilayer. In each monolayer, the hydrocarbon tails wiggle, and the entire phospholipid molecule can move sideways, even exchanging places with its neighbor. (Phospholipid molecules rarely flip-flop from one layer to the other, because this would require the hydrophilic head to move through the hydrophobic center of the membrane.) The fluidity of a phospholipid bilayer means that cells are pliable. Imagine if they were not—the nerve cells in your neck would crack whenever you nodded your head!

The plasma membrane is asymmetrical. For example, the types of phospholipids in each half of the lipid bilayer can be different. Phospholipids can vary especially by the kind of nitrogen group they have, and certain kinds are more likely to be found in the outer half of the membrane than in the inner half. *Glycolipids* are another type of lipid found in the plasma membrane. They are like phospholipids except that the hydrophilic head is made up of a variety of sugars joined to form a straight or branching carbohydrate chain. As figure 6.3 shows, glycolipids contribute to the asymmetry of the plasma membrane because the carbohydrate chain is always directed externally, an observation that offers a clue to their function. It is possible that glycolipids function as part of a receptor or help mark the cell as belonging to a particular individual. They might also regulate the action of plasma membrane proteins involved in the growth of the cell, and if so they might have a role in the occurrence of cancer.

In animal cells, **cholesterol** is a major membrane lipid, equal in amount to phospholipids. Cholesterol has both a hydrophilic and a hydrophobic end and arranges itself in this manner:

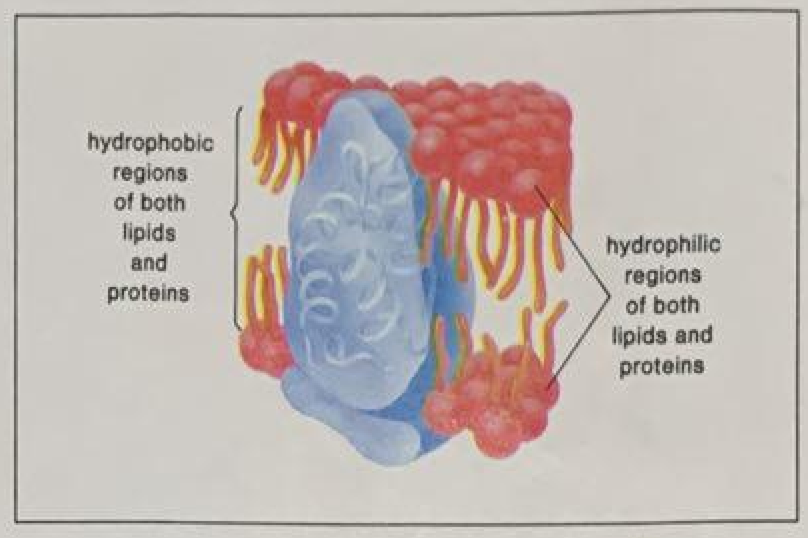


Cholesterol makes the membrane more impermeable to most biological molecules. Small molecules, like amino acids and sugars, do not pass through the membrane easily because they are polar, and the center of the membrane is nonpolar. Passage of molecules through the membrane is dependent upon the protein component.

> The phospholipid bilayer portion of the plasma membrane forms a hydrophobic impermeable barrier that prevents the movement of polar (most biological) molecules through the plasma membrane.

Protein Component

The proteins associated with the plasma membrane are either attached to its inner surface or embedded in the phospholipid bilayer. Proteins often have hydrophobic and hydrophilic regions; hydrophobic regions are within the membrane, while the hydrophilic regions project from both surfaces of the bilayer:



Although proteins are oriented so that a particular hydrophilic region always projects from either the outer or inner surface, they can move laterally in the fluid lipid bilayer. This has been demonstrated by the experiment explained in figure 6.4.

The protein composition of the plasma membrane varies among cells—red blood cell plasma membrane can have 20%–40% lipid and 60%–80% protein, for example. Also, the proteins on the outer and inner surfaces of the membrane can differ, and only those on the inner surface are attached to cytoskeletal filaments. This shows that the plasma membrane is asymmetrical, as does the placement of glycoproteins. *Glycoproteins*, like glycolipids, have an attached carbohydrate chain that only projects externally from the membrane.

Glycoproteins make cell-to-cell recognition possible and serve as the "fingerprints" of the cell. They enable the immune system to recognize its own organs and, unfortunately, are the cause of an immune system response to transplanted organs. As we will discuss in more detail, certain plasma membrane proteins are involved in the passage of molecules through the membrane. Some of these have a *channel* through which a substance simply can move across the membrane; others are *carriers* that combine with a substance and help it to move across the membrane. Still other proteins are *receptors;* each type of receptor has a specific shape that allows a specific molecule to bind to it. The binding of a molecule, such as a hormone, can influence the metabolism of the cell. Viruses often must attach to