

Figure 11.1 Structure and properties of biological membranes.

(A) A major constituent of many membranes is a lipid molecule, shown here diagrammatically as having a hydrophilic (water loving) head group and a hydrophobic (water fearing) tail. One spontaneous arrangement of these molecules consists of a bilayer, two molecules thick, where all the head groups are arranged on the two surfaces and the tails span the space in between. Membrane bilayers of this kind can be extremely large. In order to avoid edge effects, it is common for bilayers to form closed structures such as the sphere shown here. (B) Within the lipid bilayer, individual molecules can move in several ways. Lipid molecules may spontaneously diffuse laterally within each of the two leaflets within the bilayer. Protein molecules embedded in the bilayer may also diffuse laterally, and in addition, some interesting membrane proteins may undergo conformational changes that open selective channels, for example, to allow the passage of charged ions across the hydrophobic barrier. At a very slow spontaneous rate, individual lipids may flip over from one leaflet to the other. This process of flipping may be sped up by certain membrane proteins called flippases. (C) Membrane shape changes associated with biological function. All membranes undergo spontaneous shape changes and fluctuations due to thermal energy. Application of external forces, for example by molecular motor proteins, can further deform equilibrium membrane shapes. A common geometry is the extrusion of a tube. Membranes may also undergo fusion and fission (or budding) to change their topology.

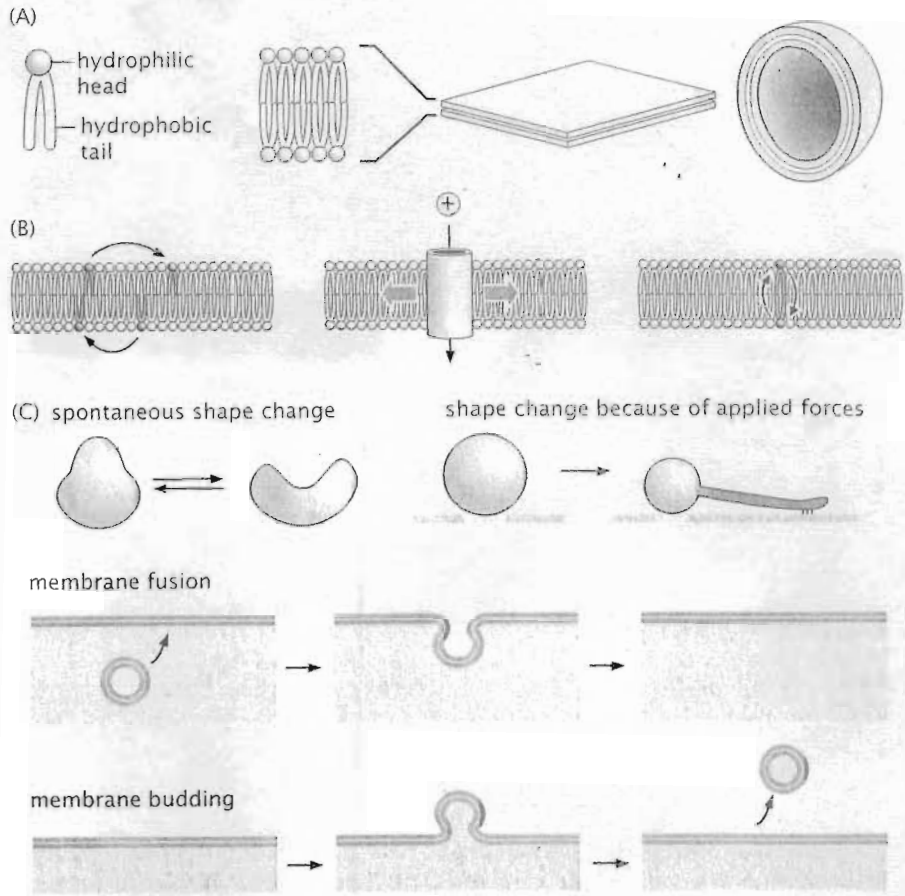


Figure 11.2 Key examples of membranes in biological systems. Eukaryotic cells, such as this fibroblast, are rife with many specialized membranes. The plasma membrane is a single phospholipid bilayer riddled with membrane proteins. The rough endoplasmic reticulum, also a single bilayer, is the site of synthesis of membrane-bound and secreted proteins. The ribosomes synthesizing these proteins are intimately associated with a transport apparatus in the endoplasmic reticulum membrane. The nuclear envelope consists of two phospholipid bilayers with a thin space between them. This nuclear envelope is perforated by nuclear pores that permit transport of materials from the cytoplasm to the nucleus and back. Bacterial cells rarely have internal membranous organelles, but may have very complex external membranes. For *E. coli*, the cell envelope consists of two bilayers, an inner membrane and an outer membrane, separated by a rigid cell wall. The outer leaflet of the outer membrane is largely composed of an unusual molecule called lipopolysaccharide, rather than of phospholipids.

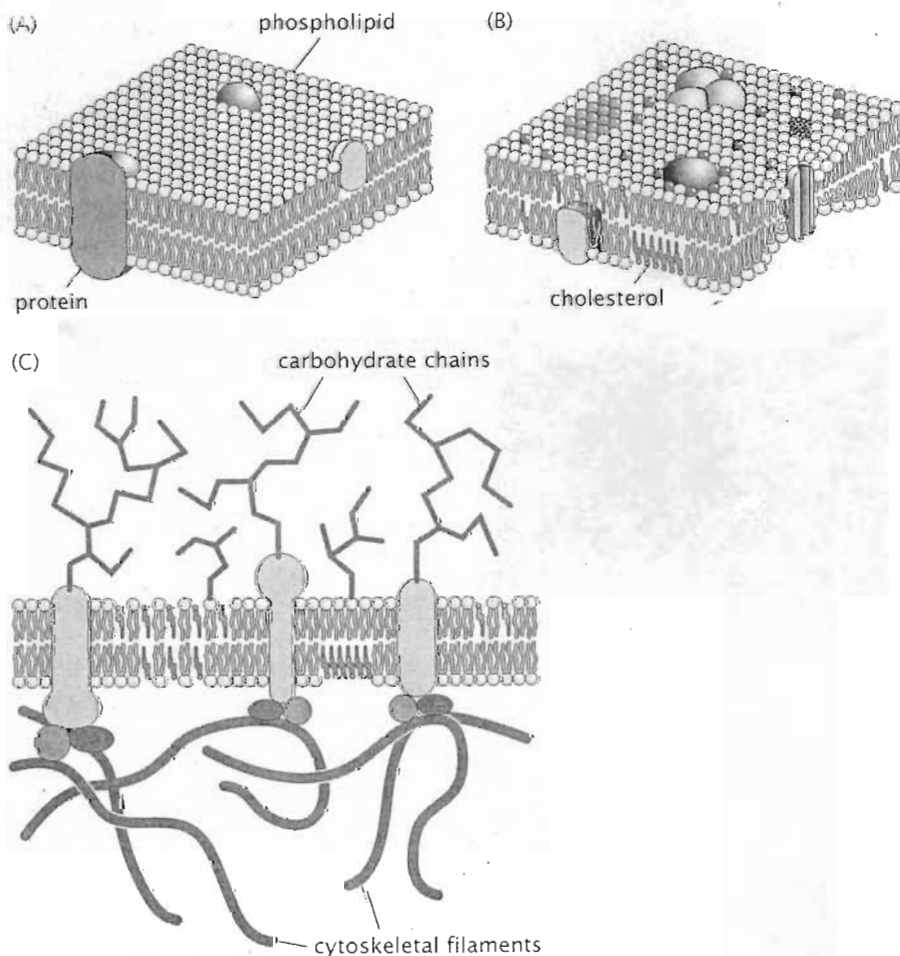
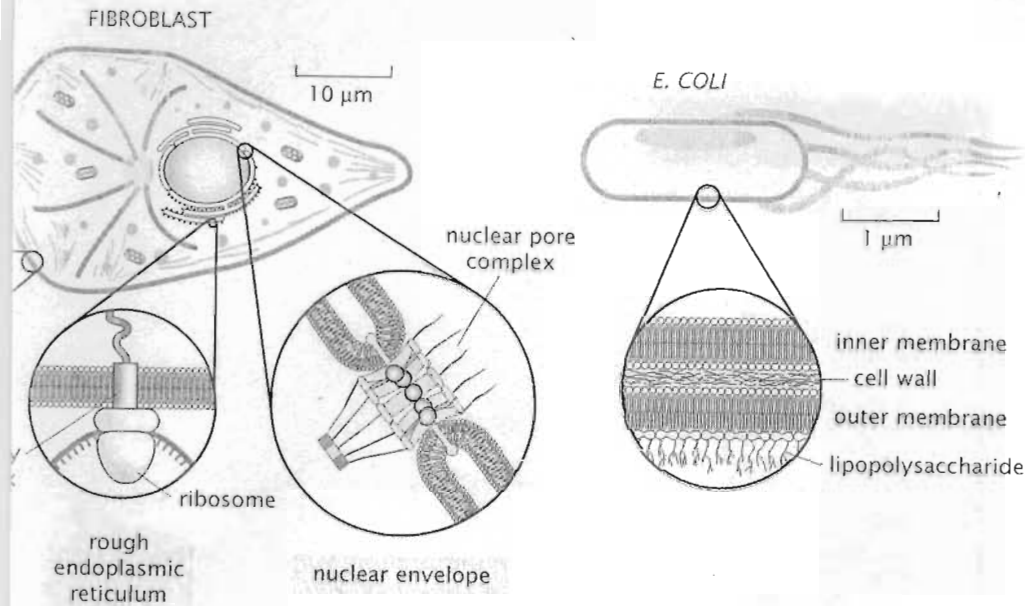


Figure 11.4 Schematic models of our understanding of cell membranes. (A) In the early fluid-mosaic hypothesis, the membrane was envisioned as a two-dimensional fluid of phospholipids studded with occasional proteins. (B) Further refinements of this model have acknowledged multiple kinds of heterogeneity. Phospholipids with different chemical character and cholesterol can self-associate to form subdomains. Proteins also may tend to self-associate within the plane of the membrane and, furthermore, can distort the membrane by locally altering its thickness or composition. (C) Beyond the plane of the phospholipid bilayer, complex carbohydrate chains attached to both lipids and proteins extend outward and many proteins and lipids are attached to structural elements within the cell, further restricting their movement. (Adapted from O. G. Mouritsen, *Life – As a Matter of Fat*, Berlin, Springer, 2005.)

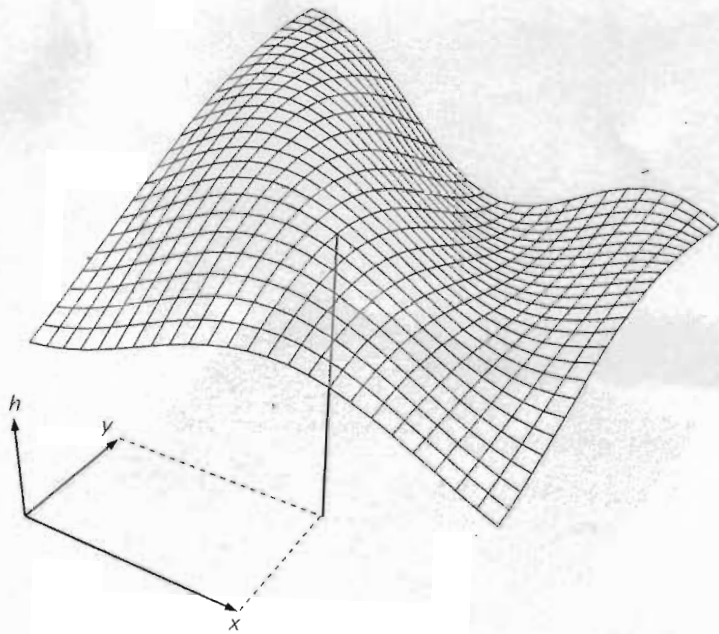
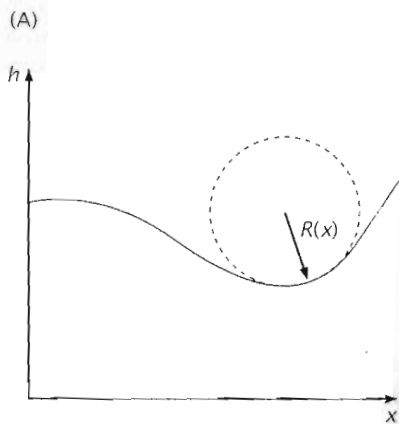


Figure 11.14 The height function, $h(x, y)$. The surface of the membrane is characterized by a height at each point (x, y) . This height function tells us how the membrane is disturbed locally from its preferred flat reference state.



(B)

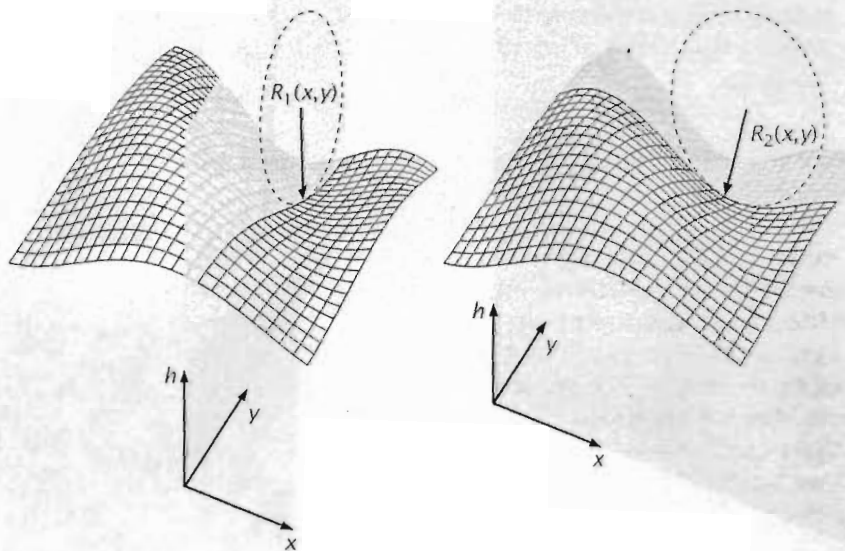
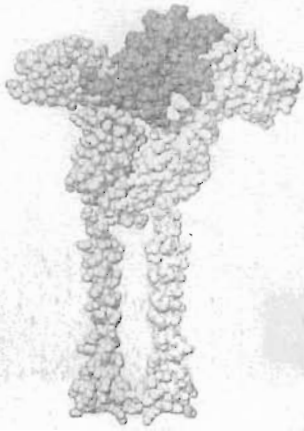


Figure 11.15 The curvature of space curves and surfaces. (A) The curvature of a curve is found by making the best fit of a circle to the point at which we are computing the curvature. (B) The curvature of a surface is obtained by finding the best circle along two orthogonal directions on the surface. This figure shows the intersection between a surface and a plane parallel to the y -axis and a second intersection between the surface and a plane parallel to the x -axis.

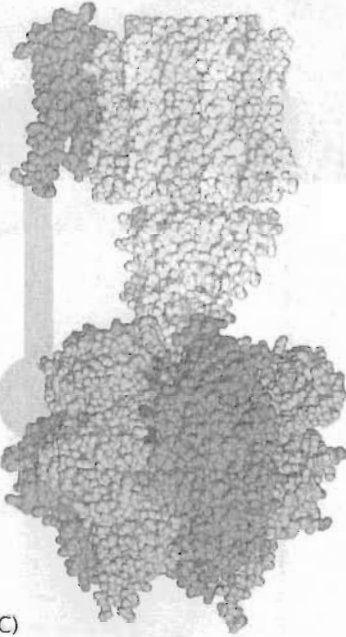
Figure 11.9 Examples of various membrane proteins which are responsible for the flow of information and material across membranes. (A) Potassium channel, (B) growth hormone receptor, and (C) ATP synthase. (Courtesy of D. Goodsell.)



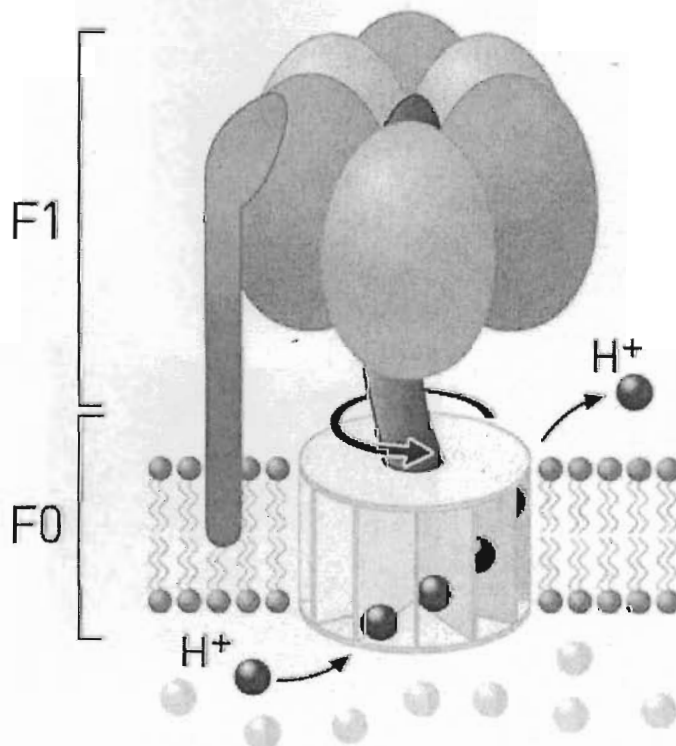
(A)



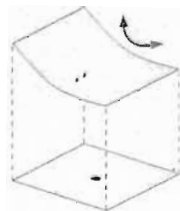
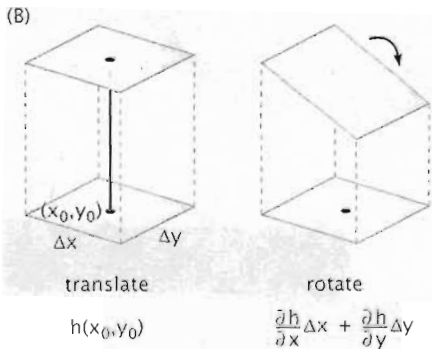
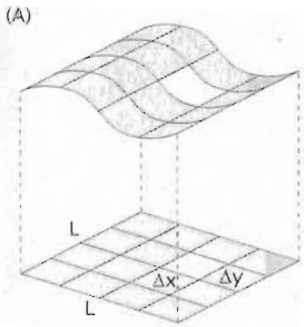
(B)



(C)



by M. Dittrich, S. Hayashi & K. Schulten,
"ATP hydrolysis in the β TP and β DP catalytic sites of F1-ATPase,"
Biophysical Journal, 87, 2954-2967 (2004).



bend

$$\frac{1}{2} \frac{\partial^2 h}{\partial x^2} \Delta x^2 + \frac{\partial^2 h}{\partial x \partial y} \Delta x \Delta y + \frac{1}{2} \frac{\partial^2 h}{\partial y^2} \Delta y^2$$

Figure 11.17 Geometrical interpretation of the Taylor expansion of the height function. (A) Representation of membrane as a series of small patches. (B) The terms in the Taylor expansion of the height function take a flat patch of the reference plane and map it onto a patch of the deformed membrane.

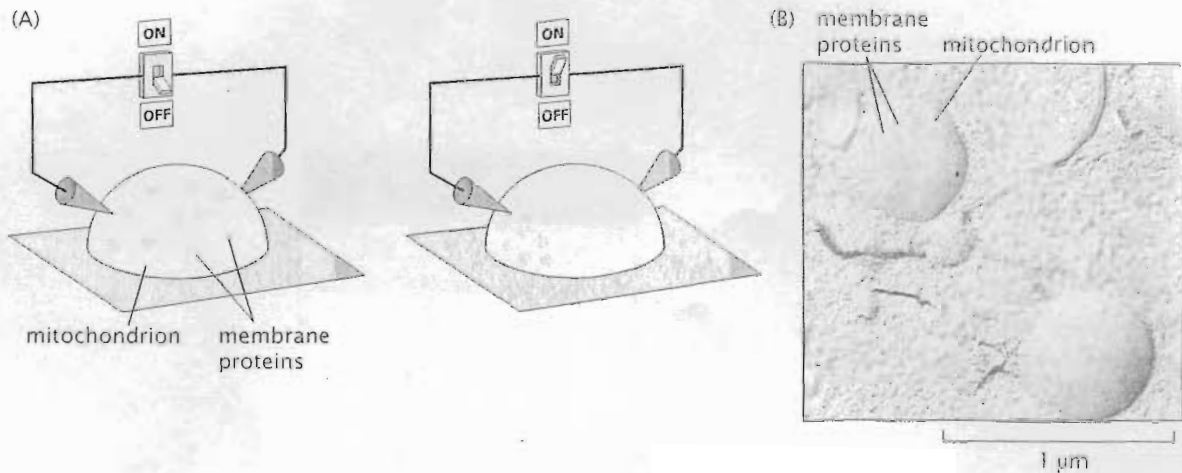


Figure 11.10 An experiment demonstrating the mobility of proteins in the mitochondrial membrane. (A) Isolated mitochondrial membranes were exposed to an electric field. When the field is off, the proteins are uniformly distributed on the mitochondrial surface. When the field is turned on, the membrane proteins migrate preferentially to one pole. If the field is turned off again, they return to their uniformly distributed state in several seconds. (B) Freeze fracture electron microscopy shows the membrane proteins as small bumps collected on the left half of the two membrane regions shown here. (Adapted from A. E. Sowers and C. R. Hackenbrock, *Proc. Natl Acad. Sci.* 78:6246, 1981.)

Figure 11.7 Geometrical shape of lipids. This figure shows a coarse-grained representation of lipid geometries that is useful in developing intuition for the spontaneous curvature induced by different lipid types. The small insets show the kinds of three-dimensional geometries adopted by these lipids.

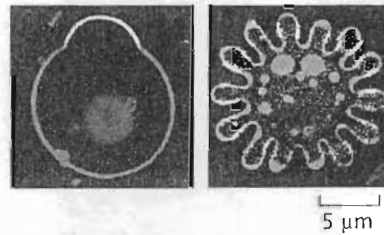
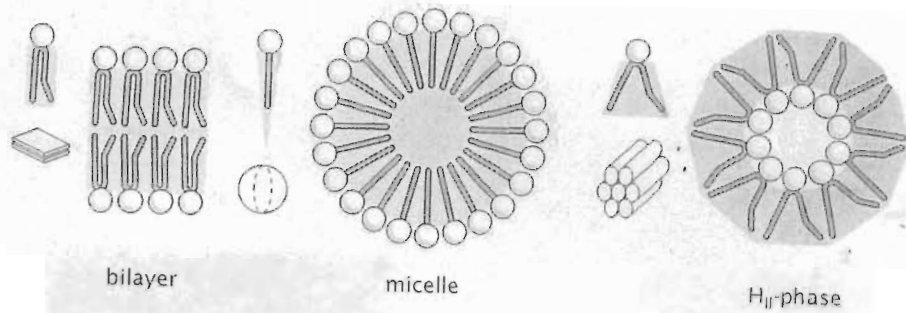


Figure 11.8 Structures of multicomponent vesicles. Vesicles made of more than one species of lipid can give rise to structures with complex geometries. Different lipid species are labeled with different fluorescent dyes, shown here in different shades of gray. The lipids with distinct physical properties tend to spontaneously segregate into domains. On the left, a vesicle at low temperature (25 °C) exhibits two large domains. The line tension caused by the mismatch at the boundary between the two domains (discussed later in the chapter) causes a deformation of the vesicle, such that one domain (light) adopts a higher curvature than the other (dark). On the right, a similar vesicle held at a higher temperature (50 °C) adopts a much more complicated shape. The individual domains are smaller, and the overall shape again separates regions with high curvature (dark) from regions with low curvature (light). (Adapted from T. Baumgart et al., *Nature* 425:821, 2003).

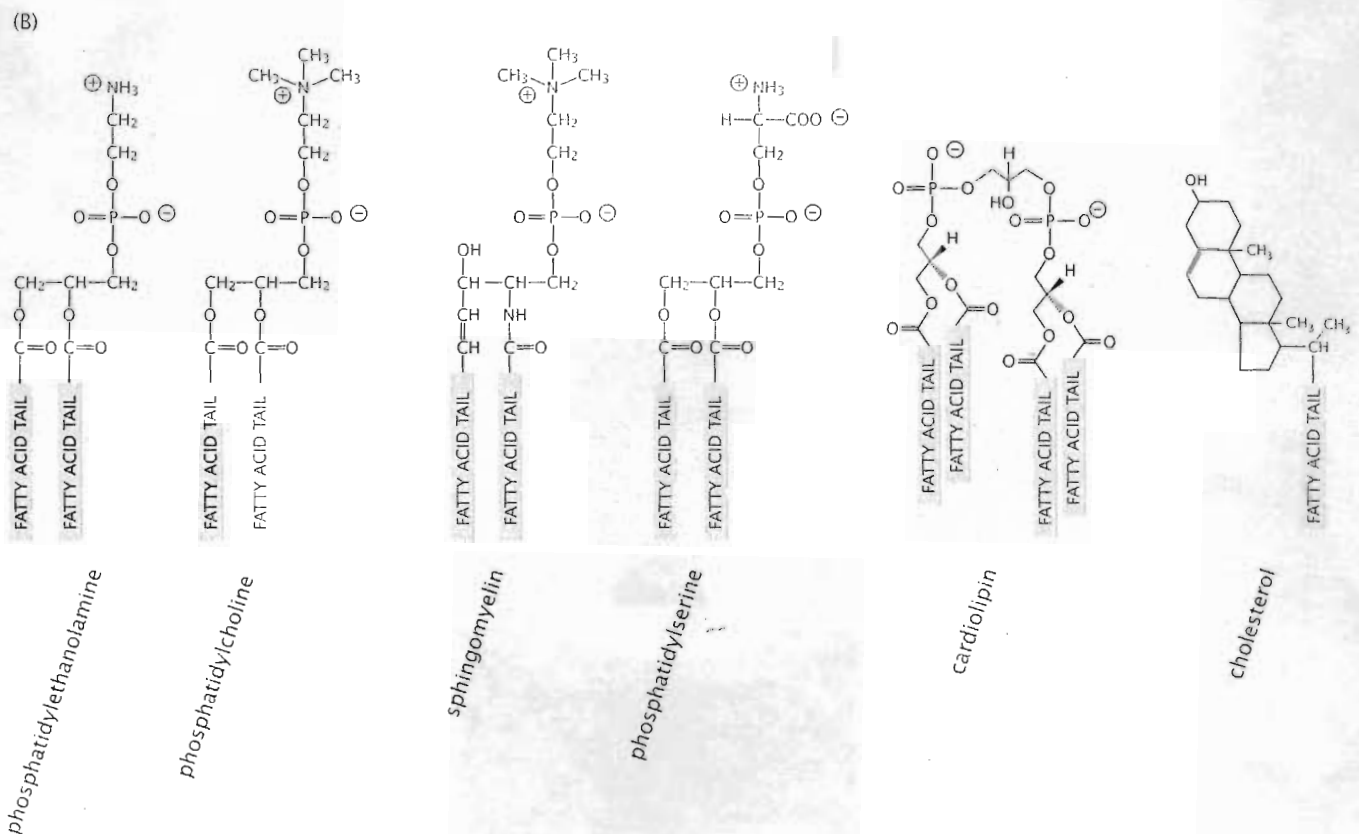
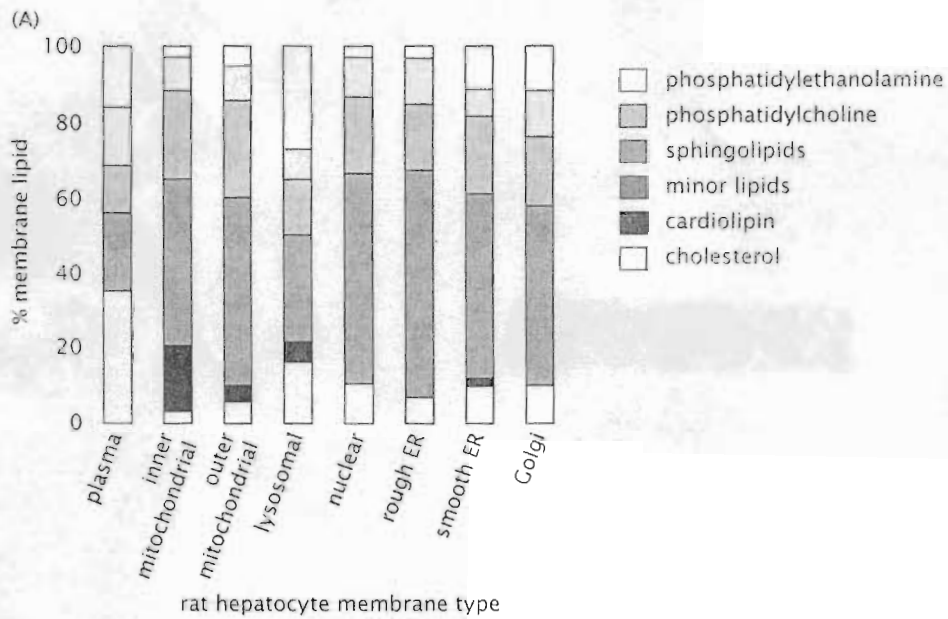


Figure 11.6 Lipid diversity in cells. (A) Relative concentrations of different lipid types in a rat hepatocyte (ER = endoplasmic reticulum). (B) Chemical structure of the different lipids considered in (A). (A, adapted from D. L. Nelson and M. M. Cox, *Lehninger's Principles of Biochemistry*, New York, Worth Publishers, 2000.)