

Chapter 12

Objectives:

Properties of fatty acids

Phospholipids and glycolipids

Membrane proteins

Properties of phospholipid membrane

Biological membrane:

Provide physical boundaries to cells and to organelles

Energy storage

Information transduction

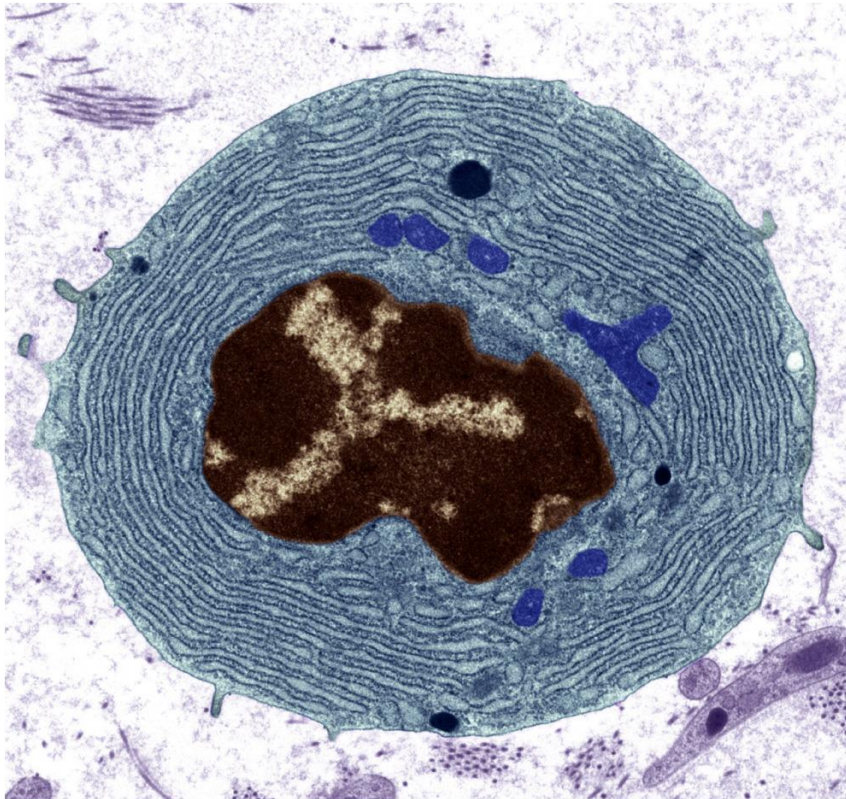


Figure 12.1
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Steve Gschmeissner/Photo Researchers

Membrane are formed by self-assembled lipid molecules and membrane proteins

Electron micrograph of plasma cell

1. Membranes are sheet-like structures, two molecules thick, that form closed boundaries.
2. Membranes are composed of lipids and proteins, either of which can be decorated with carbohydrates.
3. Membrane lipids are small amphipathic molecules that form closed bimolecular sheets that prevent the movement of polar or charged molecules.
4. Proteins serve to mitigate the impermeability of membranes and allow movement of molecules and information across the cell membrane.
5. Membranes are noncovalent assemblies.
6. Membranes are asymmetric in that the outer surface is always different from the inner surface.
7. Membranes are fluid structures.
8. Most cell membranes are electrically polarized.

Fatty acids

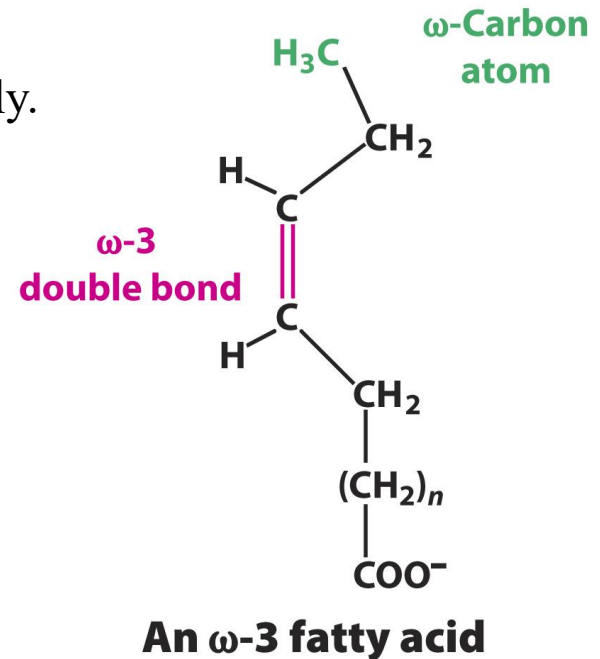
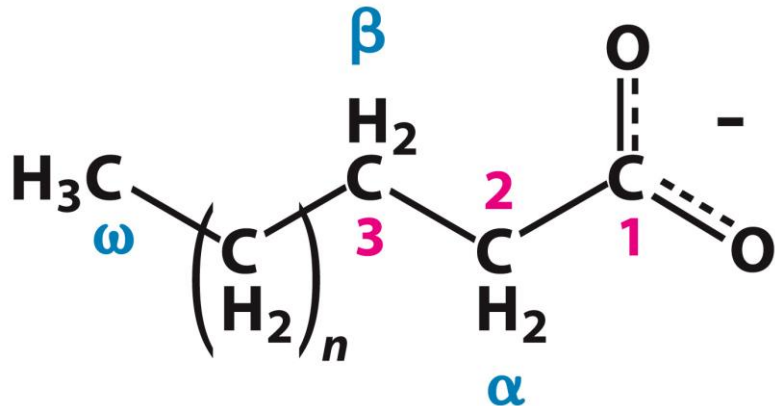
Fatty acids are chains of hydrogen-bearing carbon atoms that have a carboxylic acid at one end and a methyl group at the other end.

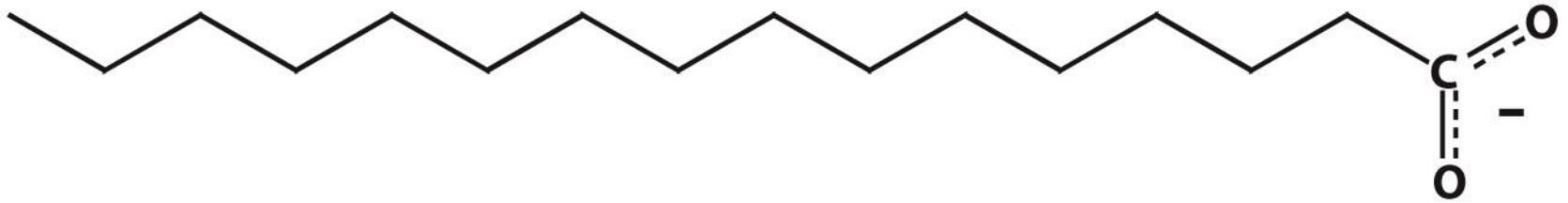
Fatty acids may be saturated or unsaturated.

Fatty acid carbon atoms are usually numbered beginning with the carboxyl terminal carbon atom.

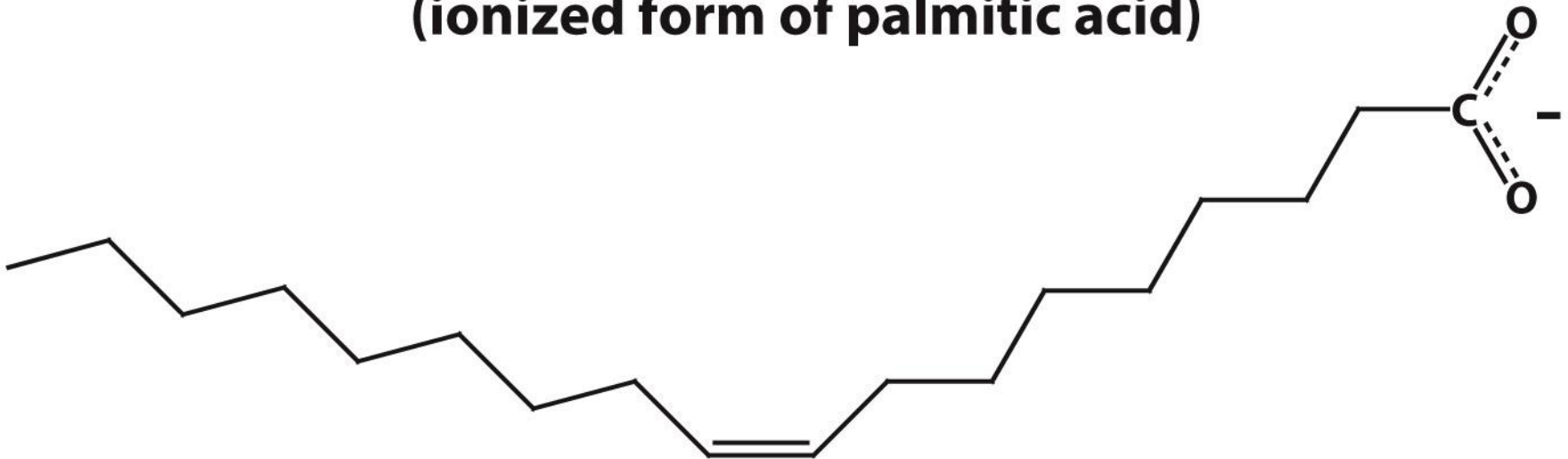
Carbon atoms 2 and 3 are also referred to as α and β , respectively.

Fatty acids can also be numbered from the methyl carbon atom which is called the omega (ω) carbon.





Palmitate
(ionized form of palmitic acid)



Oleate
(ionized form of oleic acid)

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Structures of two fatty acids. Palmitate is a 16-carbon, saturated fatty acid, and oleate is an 18-carbon fatty acid with a single cis double bond.

Fatty acids in biological systems usually contain an even number of carbon atoms, with the 16- and 18-carbon atom chains the most common.

When double bonds are present, they are commonly in the cis configuration.

In polyunsaturated fatty acids, the double bonds are separated by at least one methylene group.

The properties of fatty acids are dependent on chain length and degree of unsaturation.

Short chain length and the presence of cis double bonds enhances the fluidity of fatty acids.

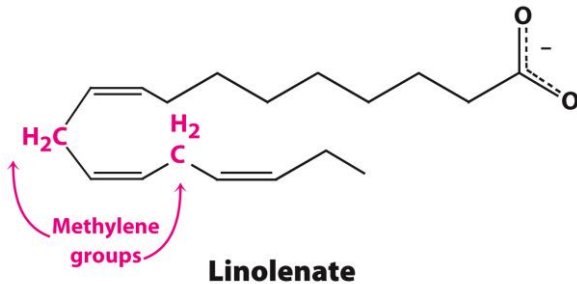


TABLE 12.1 Some naturally occurring fatty acids in animals

Number of carbons	Number of double bonds	Common name	Systematic name	Formula
12	0	Laurate	<i>n</i> -Dodecanoate	$\text{CH}_3(\text{CH}_2)_{10}\text{COO}^-$
14	0	Myristate	<i>n</i> -Tetradecanoate	$\text{CH}_3(\text{CH}_2)_{12}\text{COO}^-$
16	0	Palmitate	<i>n</i> -Hexadecanoate	$\text{CH}_3(\text{CH}_2)_{14}\text{COO}^-$
18	0	Stearate	<i>n</i> -Octadecanoate	$\text{CH}_3(\text{CH}_2)_{16}\text{COO}^-$
20	0	Arachidate	<i>n</i> -Eicosanoate	$\text{CH}_3(\text{CH}_2)_{18}\text{COO}^-$
22	0	Behenate	<i>n</i> -Docosanoate	$\text{CH}_3(\text{CH}_2)_{20}\text{COO}^-$
24	0	Lignocerate	<i>n</i> -Tetracosanoate	$\text{CH}_3(\text{CH}_2)_{22}\text{COO}^-$
16	1	Palmitoleate	<i>cis</i> - Δ^9 -Hexadecenoate	$\text{CH}_3(\text{CH}_2)_5\text{CH}=\text{CH}(\text{CH}_2)_7\text{COO}^-$
18	1	Oleate	<i>cis</i> - Δ^9 -Octadecenoate	$\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{COO}^-$
18	2	Linoleate	<i>cis,cis</i> - Δ^9, Δ^{12} -Octadecadienoate	$\text{CH}_3(\text{CH}_2)_4(\text{CH}=\text{CHCH}_2)_2(\text{CH})_6\text{COO}^-$
18	3	Linolenate	<i>all-cis</i> - $\Delta^9, \Delta^{12}, \Delta^{15}$ -Octadecatrienoate	$\text{CH}_3\text{CH}_2(\text{CH}=\text{CHCH}_2)_3(\text{CH}_2)_6\text{COO}^-$
20	4	Arachidonate	<i>all-cis</i> $\Delta^5, \Delta^8, \Delta^{11}, \Delta^{14}$ -Eicosatetraenoate	$\text{CH}_3(\text{CH}_2)_4(\text{CH}=\text{CHCH}_2)_4(\text{CH}_2)_2\text{COO}^-$

Table 12.1

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The common types of membrane lipids are:

1. Phospholipids
2. Glycolipids
3. Cholesterol

Phospholipids are composed of four components: fatty acids (1 or more), a platform, a phosphate, and an alcohol.

Two common platforms are glycerol and sphingosine.

Phospholipids with a glycerol platform are called phosphoglycerides or phosphoglycerols.

The major phospholipids are derived from phosphatidate (diacylglycerol 3-phosphate).

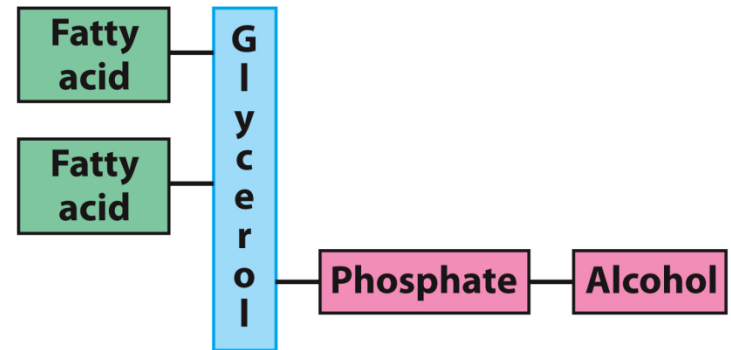
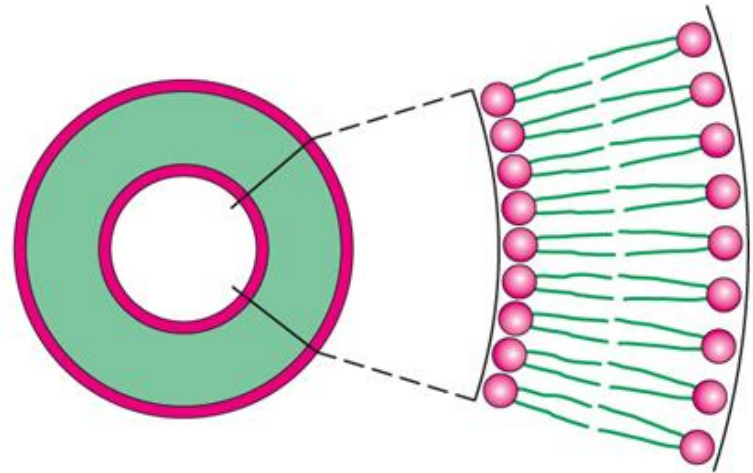


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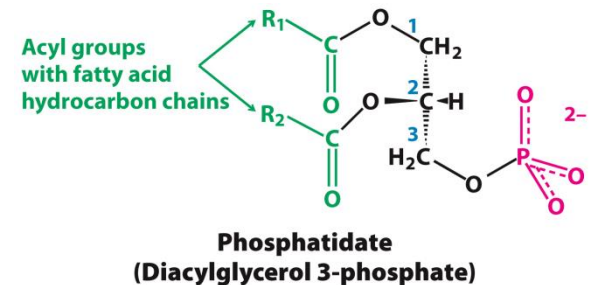
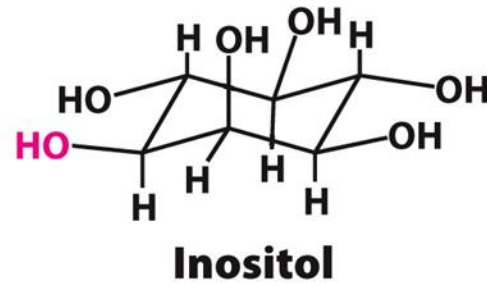
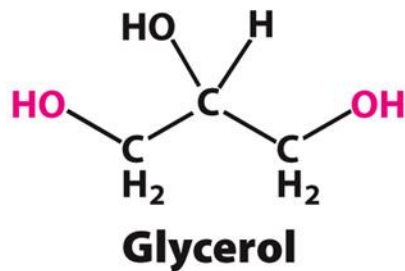
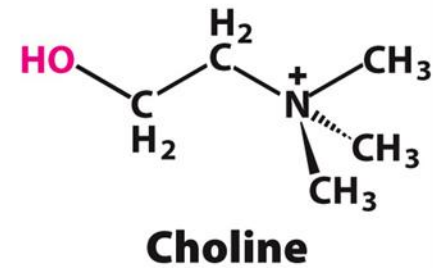
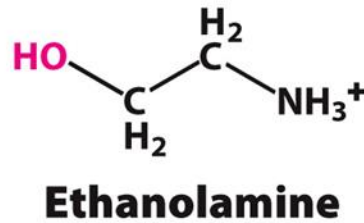
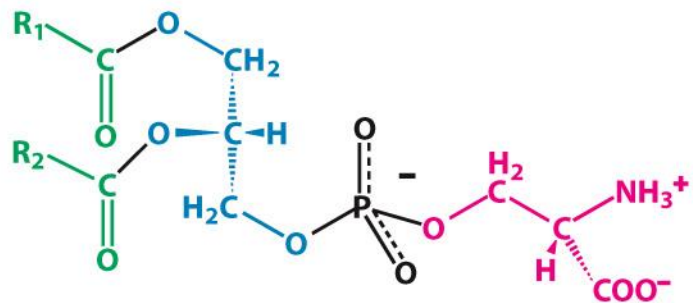


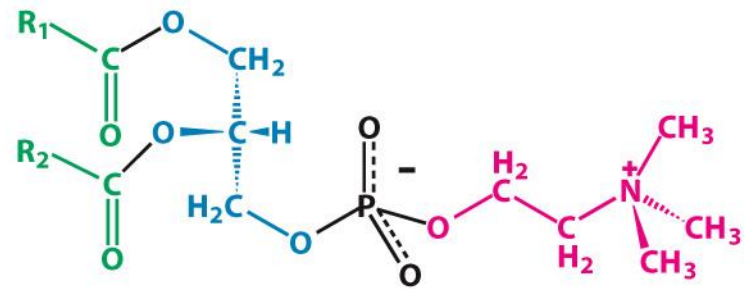
Figure 12.4
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Phosphoglycerides are derived from phosphatidate by the formation of an ester bond between the phosphate and an alcohol.

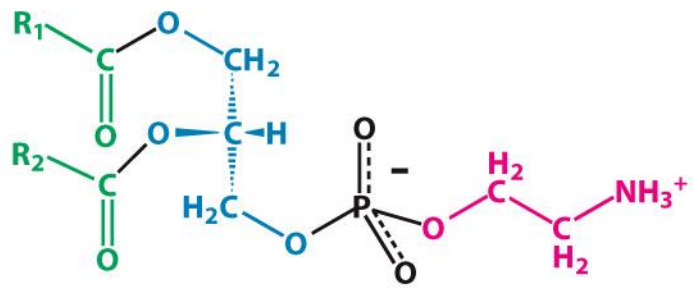




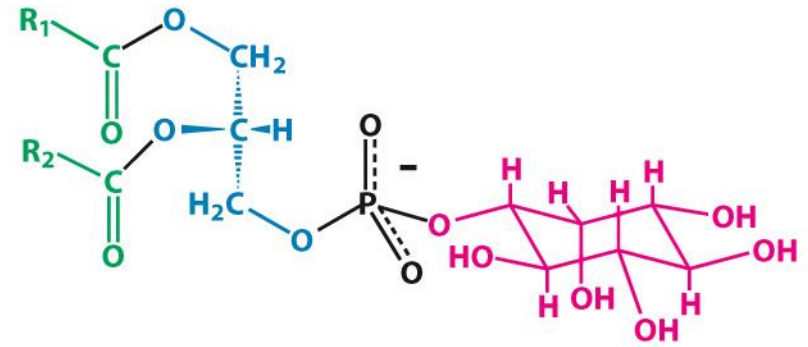
Phosphatidylserine



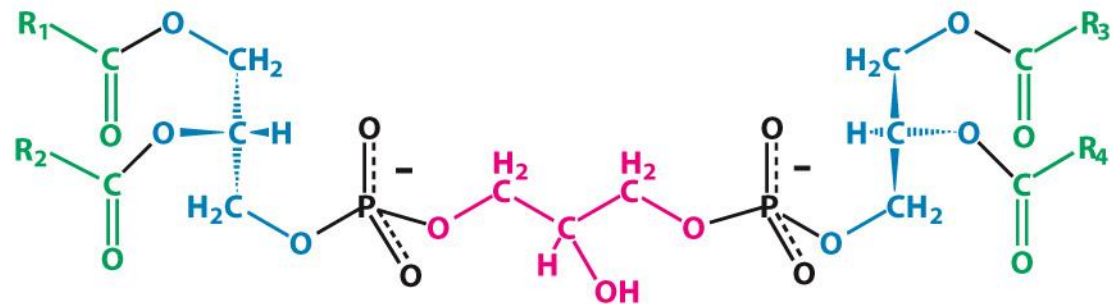
Phosphatidylcholine



Phosphatidylethanolamine



Phosphatidylinositol



Diphosphatidylglycerol (cardiolipin)

Figure 12.5

Phospholipids may also be built on a sphingosine platform.

Sphingomyelin is a common membrane lipid in which the primary hydroxyl group of sphingosine is esterified to phosphorylcholine.

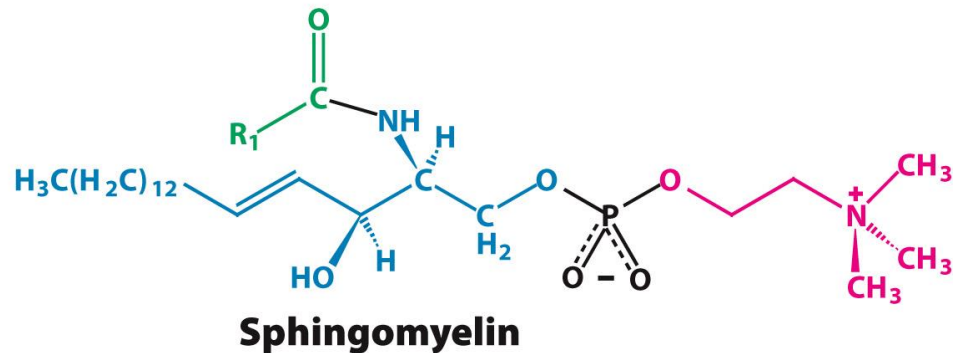


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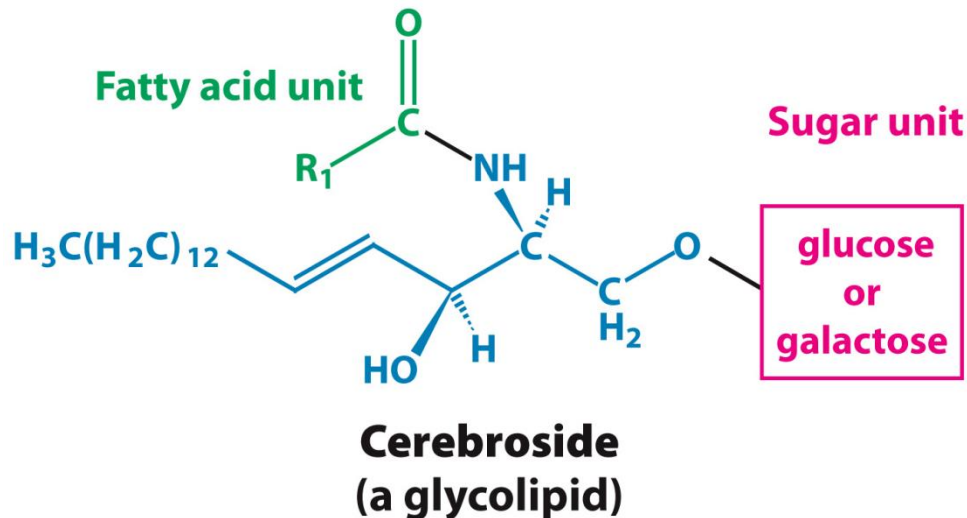
Glycolipids are carbohydrate-containing lipids derived from sphingosine.

The carbohydrate is linked to the primary alcohol of sphingosine.

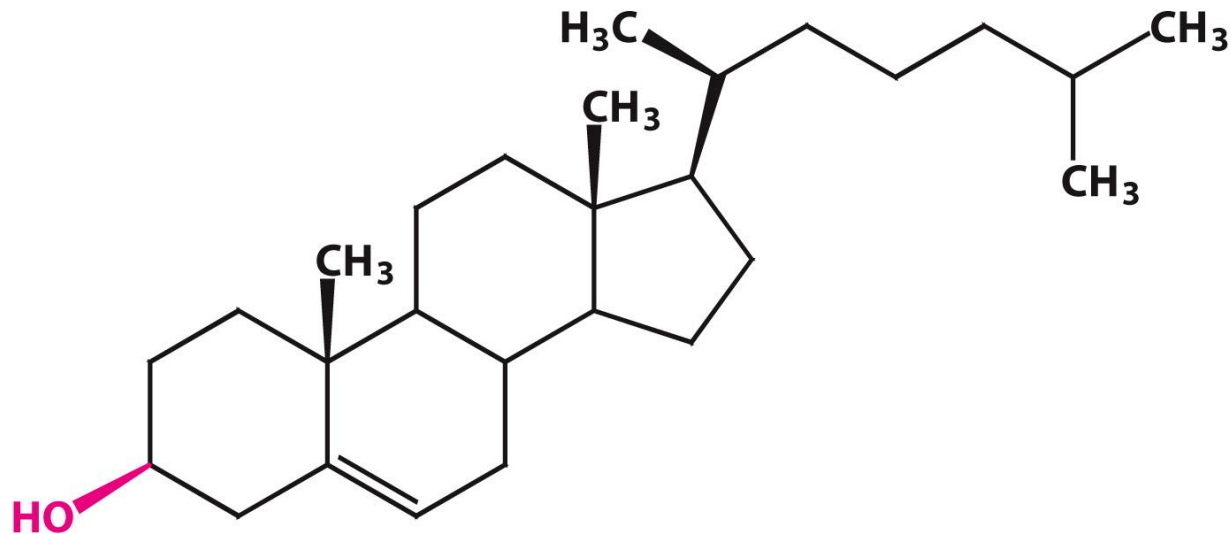
Cerebrosides are the simplest glycolipids, containing only a single sugar.

Gangliosides contain a branched chain of as many as seven sugar molecules.

The carbohydrate components of glycolipids are on the extracellular surface of the cell membrane, where they play a role in cell-cell recognition.

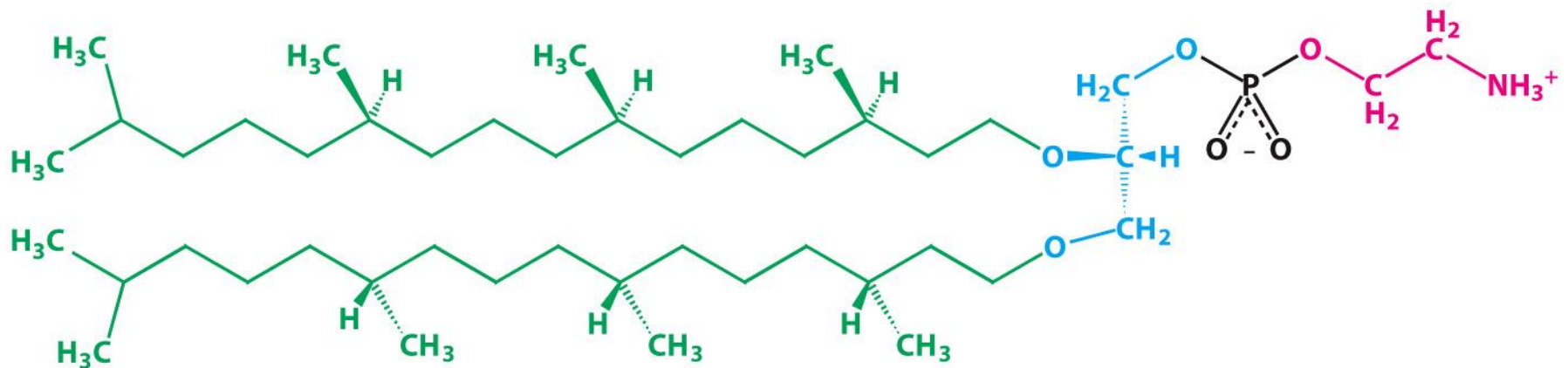


Cholesterol is a steroid that is modified on one end by the attachment of a fatty acid chain and at the other end by a hydroxyl group. In membranes, the hydroxyl group interacts with phospholipid head groups.



Cholesterol

The ether linkages and branching structure of membrane lipids of extremophiles prevent hydrolysis and oxidation of membranes in harsh environments.



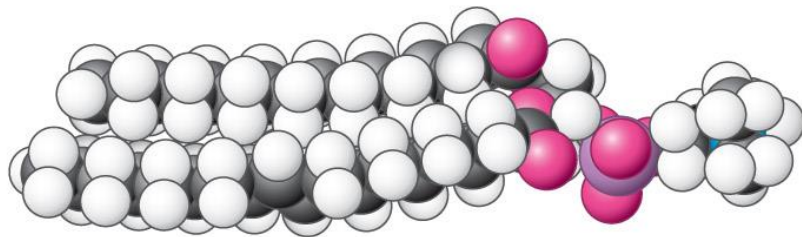
Membrane lipid from the archaeon *Methanococcus jannaschii*

Unnumbered 12 p347

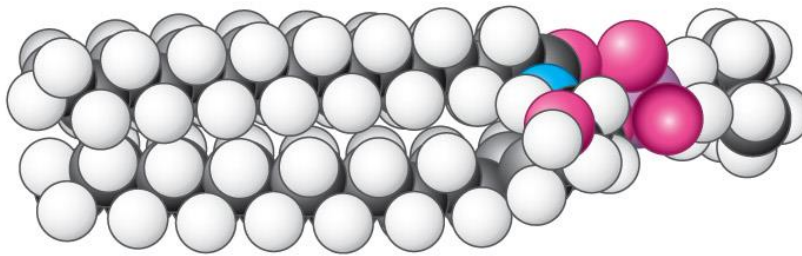
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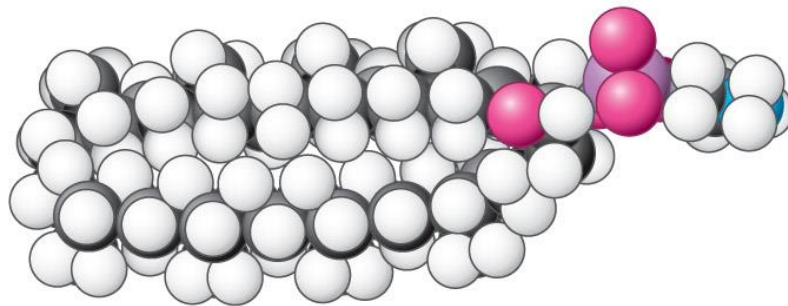
(A)



Phosphoglyceride



Sphingomyelin

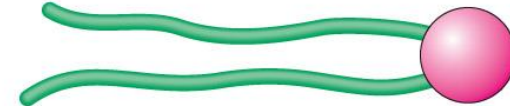


Archaeal lipid

Membrane lipids are amphipathic molecules, containing hydrophobic and hydrophilic properties.

The fatty acid components provide the hydrophobic properties, whereas the alcohol and phosphate components, called the polar head group, provide the hydrophilic properties.

(B)



Shorthand depiction

Figure 12.8

Membrane formation is a consequence of the amphipathic nature of the constituent lipid molecules.

Phospholipids are too large to form micelles.

Phospholipids and glycolipids spontaneously form lipid bilayers in aqueous solutions.

The hydrophobic effect powers membrane formation, and van der Waals interactions between the hydrophobic tails stabilize membranes.

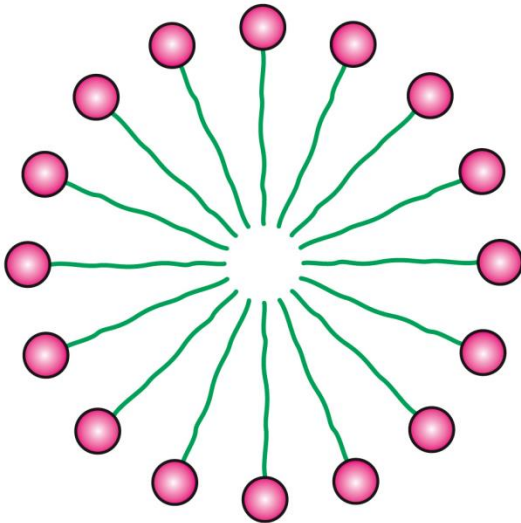


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micelle

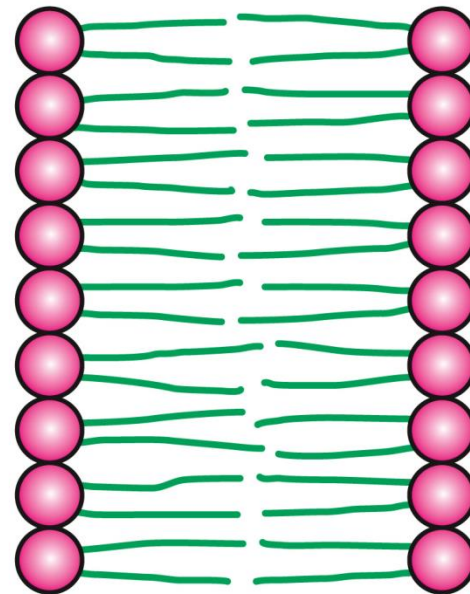


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Bilayer membrane

Liposomes, or lipid vesicles, are aqueous compartments enclosed by a lipid membrane.

Protein-liposome complexes can be used to investigate membrane protein functions.

Liposomes, formed by sonicating a mixture of phospholipids in aqueous solution, may be useful as drug-delivery systems.

Planar bilayer membranes are also useful for examining membrane properties such as ion permeability in the presence of a voltage difference across the membrane.

The ability of small molecules to cross a membrane is a function of their hydrophobicity.

Membranes have a low permeability for ions and polar molecules.

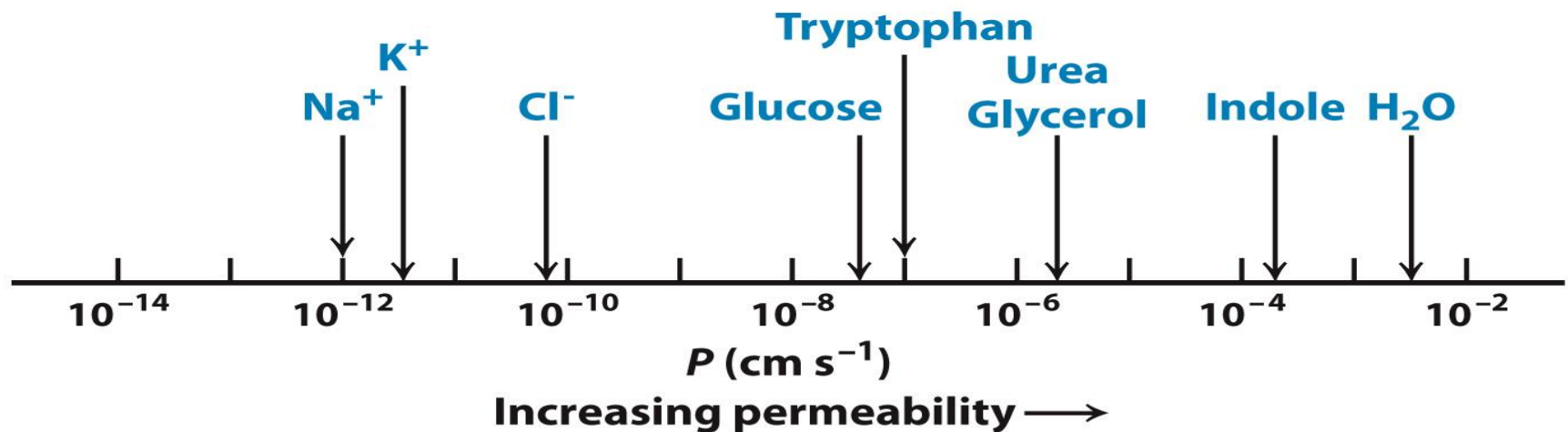


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While membrane lipids establish a permeability barrier, membrane proteins allow transport of molecules and information across the membrane.

Membranes vary in protein content from as little as 18% to as much as 75%.

Membrane proteins can be visualized by SDS-polyacrylamide gel electrophoresis.

The types of membrane proteins in a cell are a reflection of the biochemistry occurring inside the cell.

Integral membrane proteins are embedded in the hydrocarbon core of the membrane.

Peripheral membrane proteins are bound to the polar head groups of membrane lipids or to the exposed surfaces of integral membrane proteins.

Some proteins are associated with membranes by attachment to a hydrophobic moiety that is inserted into the membrane.

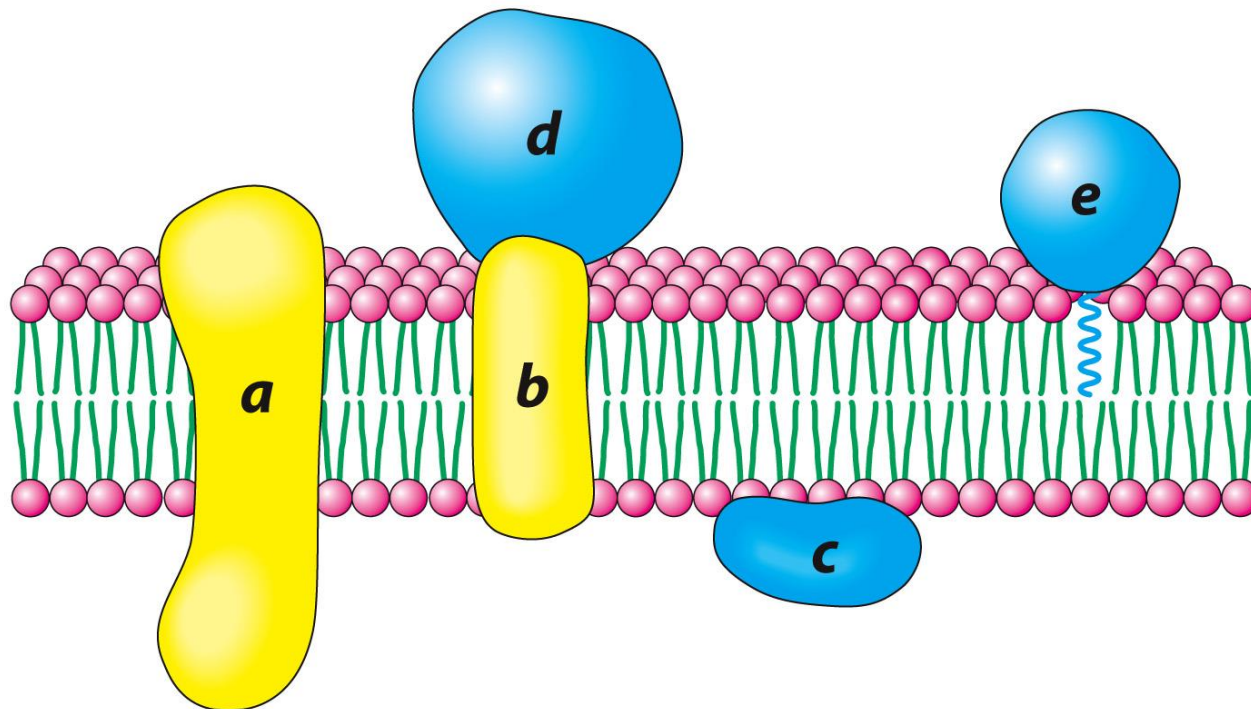


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Membrane-spanning α helices are a common structural feature of integral membrane proteins.

Bacteriorhodopsin, a light-powered proton pump, is an integral membrane protein composed of seven membrane-spanning helices.

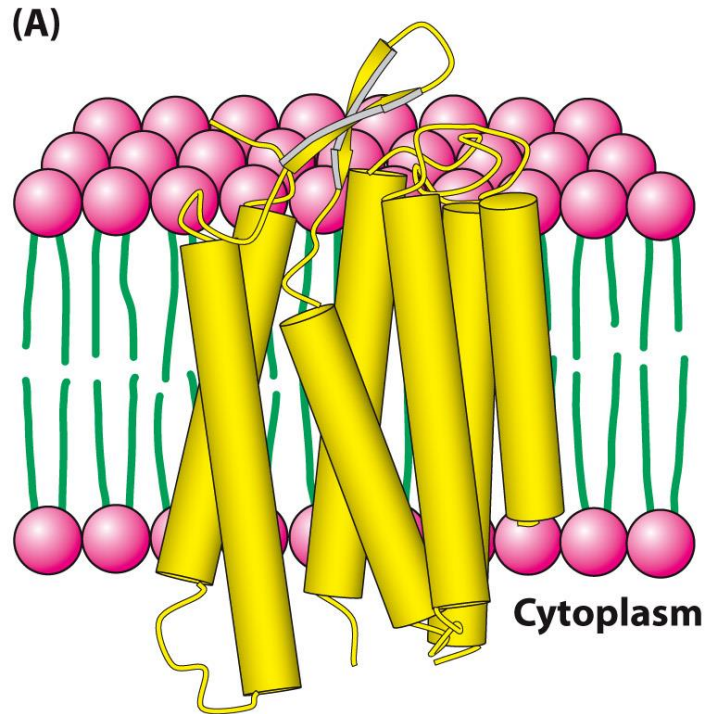
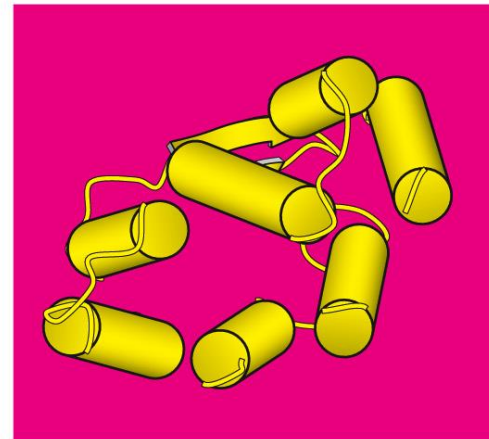


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Protein uses light energy to transfer protons across the membrane and generate proton gradient

Majority of AA in alfa helices are nonpolar

(B)



A Q I T G R P E W I W L A L G T A L M G L G T L Y F L V K G M G V S D P D A K K F Y A I T T L V P A
I A F T M Y L S M L L G Y G L T M V P F G G E Q N P I Y W A R Y A D W L F T T P L L L L D L A L L V
D A D Q G T I L A L V G A D G I M I G T G L V G A L T K V Y S Y R F V W W A I S T A A M L Y I L Y V
L F F G F T S K A E S M R P E V A S T F K V L R N V T V V L W S A Y V V V W L I G S E G A G I V P L
N I E T L L F M V L D V S A K V G F G L I L L R S R A I F G E A E A P E P S A D G A A A T S

Figure 12.18

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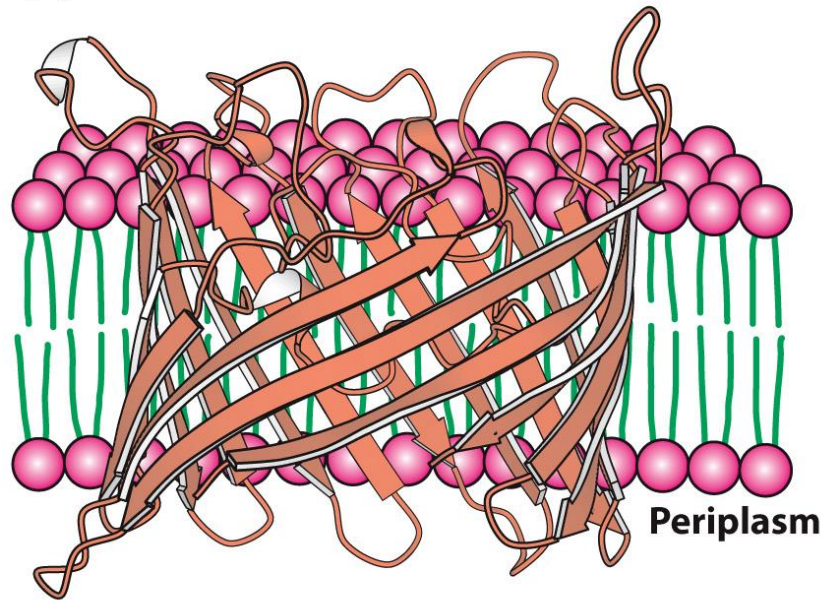
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Integral membrane proteins may also be composed of β strands that form a pore in the membrane.

The bacterial protein porin is an example of a β strand–rich integral membrane protein.

The outside surface of porin, which interacts with the hydrophobic interior of the membrane, is composed of hydrophobic amino acids. The inside is polar and filled with water.

(A)



(B)



Figure 12.19

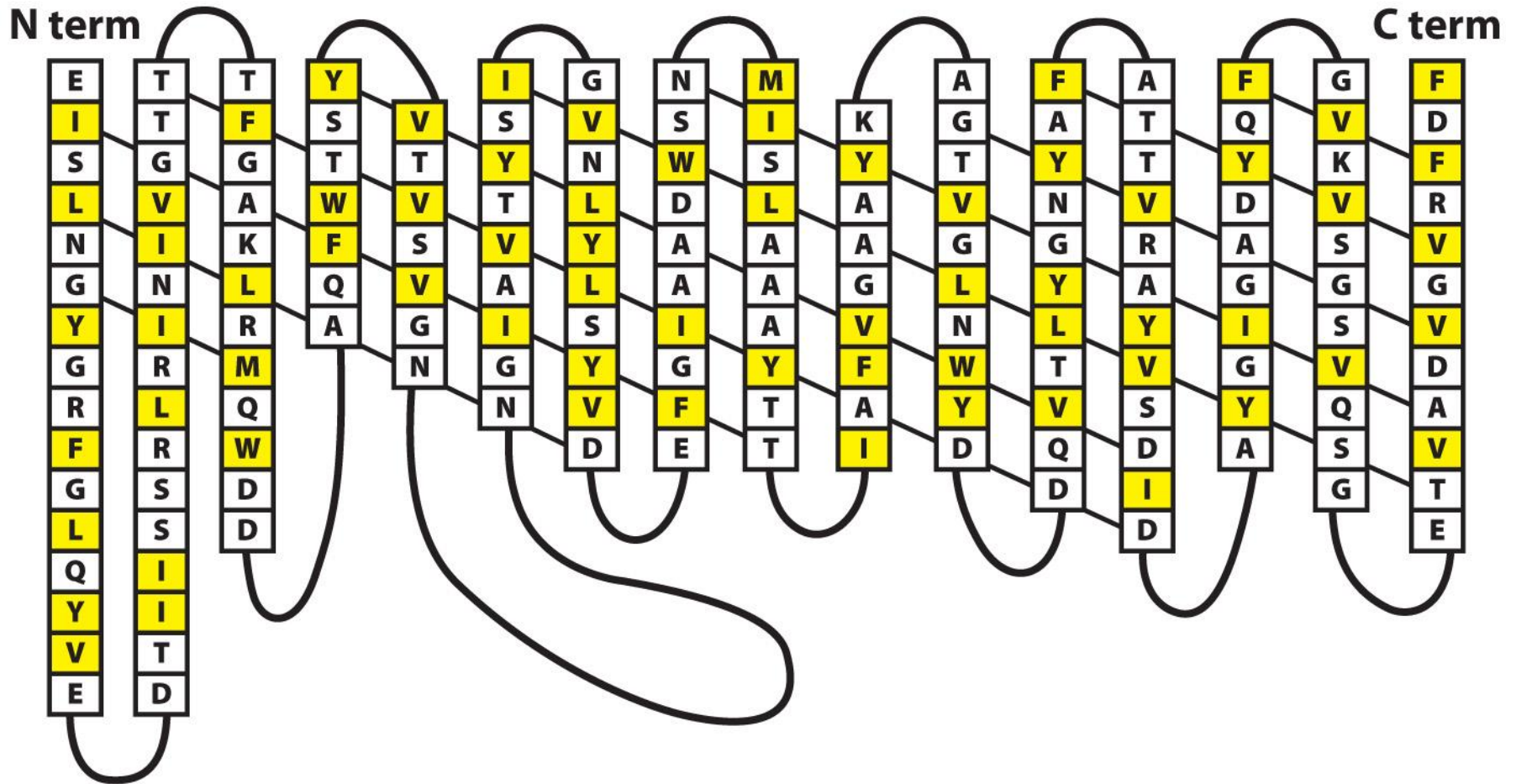


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β strands that tend to have hydrophobic and hydrophilic amino acids in adjacent positions

prostaglandin H₂ synthase-1

Only a portion of the enzyme prostaglandin H₂ synthase-1 is embedded in the membrane.

The cyclooxygenase (COX) activity of prostaglandin H₂ synthase-1 is dependent on a channel connecting the active site to the membrane interior.

Aspirin inhibits cyclooxygenase activity by obstructing the channel.

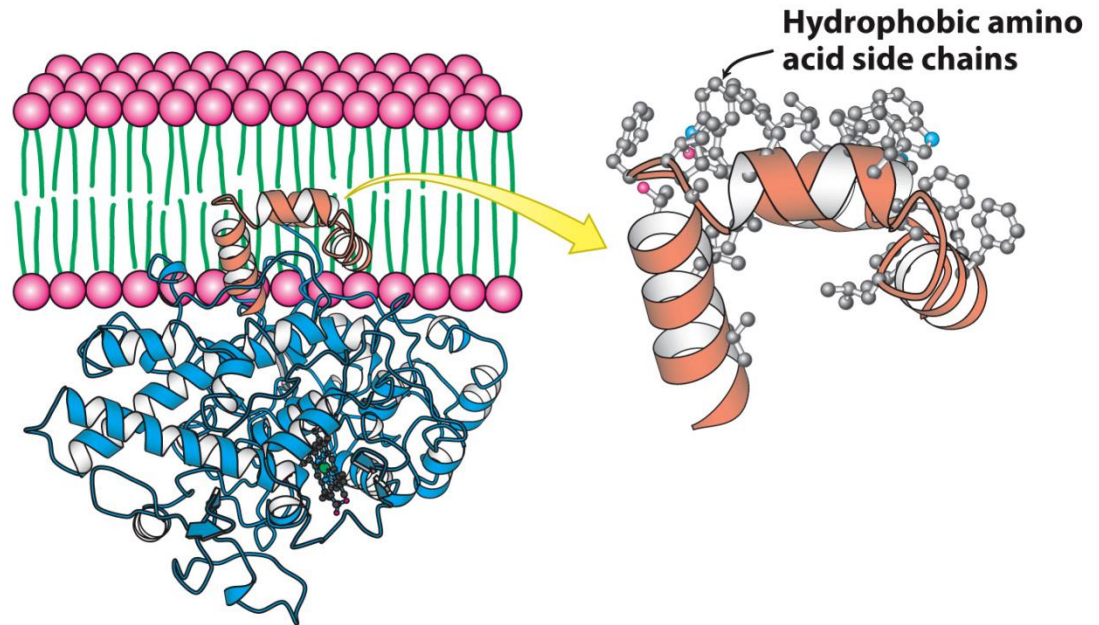
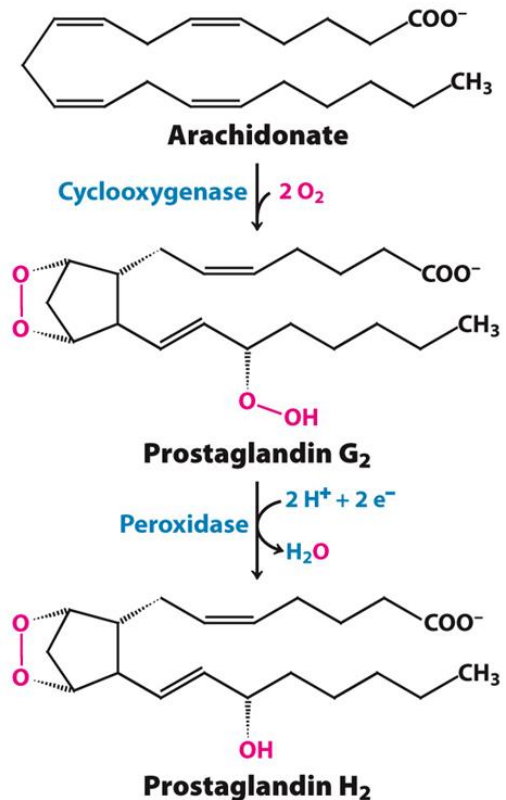
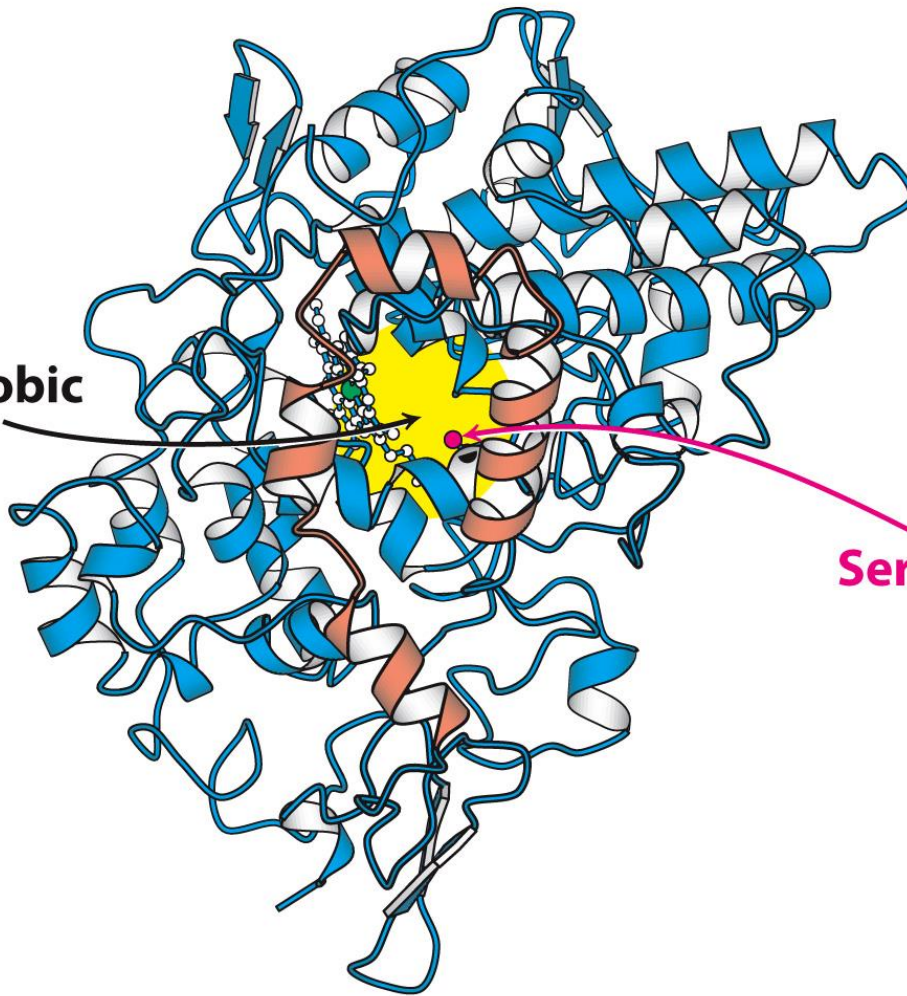
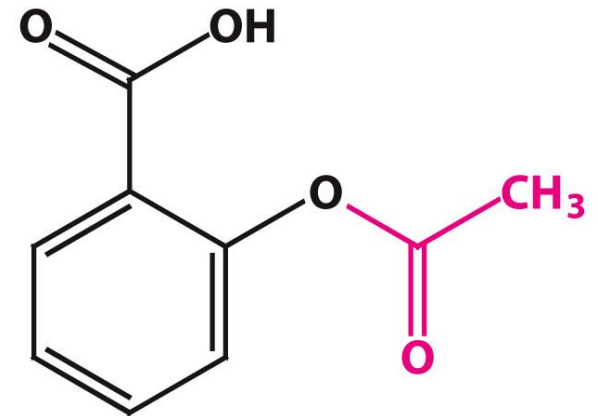


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Hydrophobic
channel



Ser 53



Aspirin
(Acetylsalicylic acid)

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Aspirin transfer the acetyl group to the ser residue that is along the path to the active site

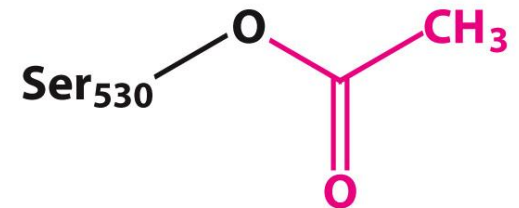
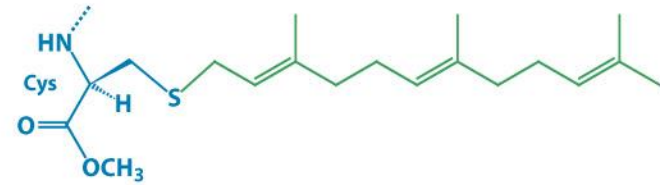


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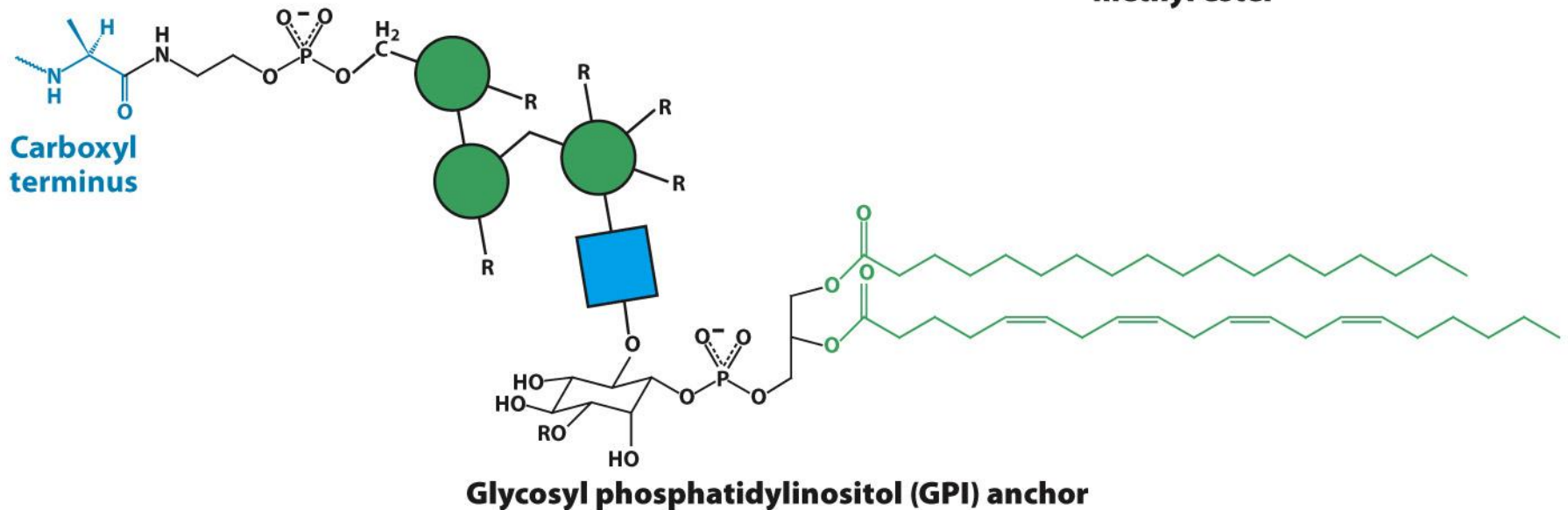
Hydrophilic proteins can be made to associate with the membrane by attaching a hydrophobic group.



S-Palmitoylcysteine



C-terminal S-farnesylcysteine methyl ester



Glycosyl phosphatidylinositol (GPI) anchor

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The green circles and blue square correspond to mannose and β-d-acetylglucosamine (GlcNAc), respectively

An α helix consisting of 20 residues can traverse a lipid bilayer.

Hydrophobicity of each amino acid is quantified by determining the free energy required to transfer the amino acid from a hydrophobic to a hydrophilic environment.

A protein sequence is examined by measuring the free energy of transferring each stretch of 20 amino acids, called a window, from a hydrophobic to a hydrophilic environment.

The free energy is plotted against the first amino acid of the window. Such a plot is called a hydrophathy plot.

Hydropathy plots can identify potential membrane-spanning helices.

TABLE 12.2 Polarity scale for identifying trans-membrane helices

Amino acid residue	Transfer free energy in kJ mol^{-1} (kcal mol^{-1})
Phe	15.5 (3.7)
Met	14.3 (3.4)
Ile	13.0 (3.1)
Leu	11.8 (2.8)
Val	10.9 (2.6)
Cys	8.4 (2.0)
Trp	8.0 (1.9)
Ala	6.7 (1.6)
Thr	5.0 (1.2)
Gly	4.2 (1.0)
Ser	2.5 (0.6)
Pro	-0.8 (-0.2)
Tyr	-2.9 (-0.7)
His	-12.6 (-3.0)
Gln	-17.2 (-4.1)
Asn	-20.2 (-4.8)
Glu	-34.4 (-8.2)
Lys	-37.0 (-8.8)
Asp	-38.6 (-9.2)
Arg	-51.7 (-12.3)

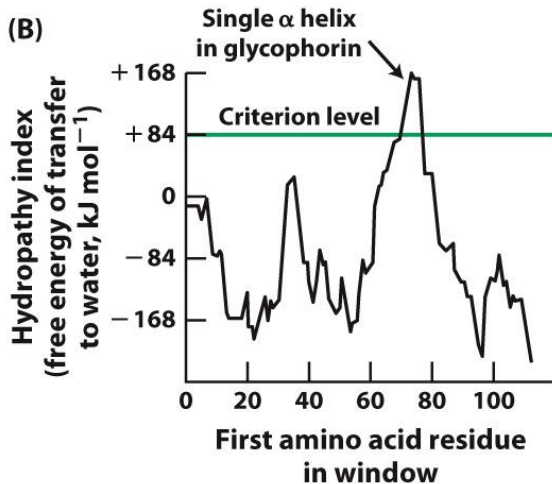
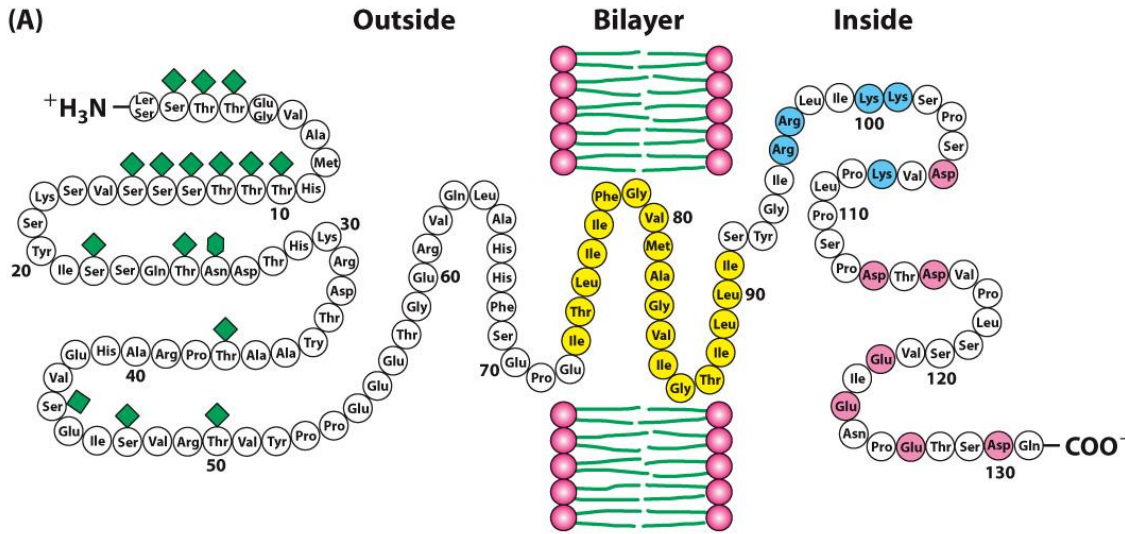
Source: Data from D. M. Engelman, T. A. Steitz, and A. Goldman. *Annu. Rev. Biophys. Biophys. Chem.* 15(1986):321-353.

Note: The free energies are for the transfer of an amino acid residue in an α helix from the membrane interior (assumed to have a dielectric constant of 2) to water.

Table 12.2

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Locating the membrane-spanning helix of glycophorin.



Hydropathy index larger than 84 kJ/mol indicates the presence of membrane spanning alpha helix

Membranes exhibits high fluidity

Fluorescence recovery after photobleaching (FRAP) is a technique that allows the measurement of lateral mobility of membrane components.

A membrane component is attached to a fluorescent molecule. On a very small portion of the membrane, the dye is subsequently destroyed by high-intensity light, thereby bleaching a portion of the membrane.

The mobility of the fluorescently labeled component is a function of how rapidly the bleached area recovers fluorescence. The average distance traveled S in time t depends on the diffusion constant D .

$$S = (4Dt)^{1/2}$$

Lateral diffusion of proteins depends on whether they are attached to other cellular or extracellular components.

Diffusion coefficient of lipids in various membrane is $1 \text{ } \mu\text{m}^2\text{s}^{-1}$

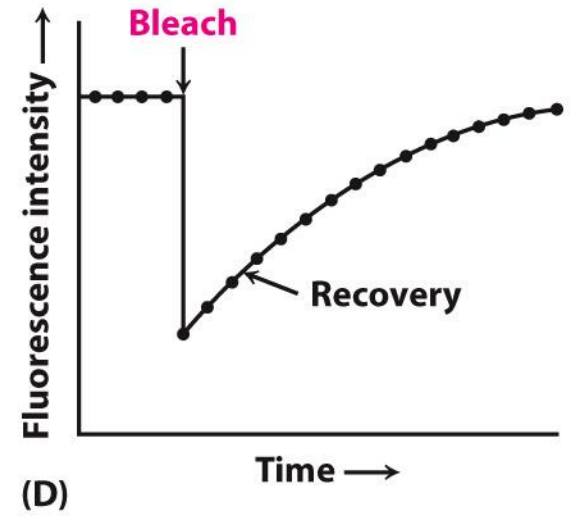
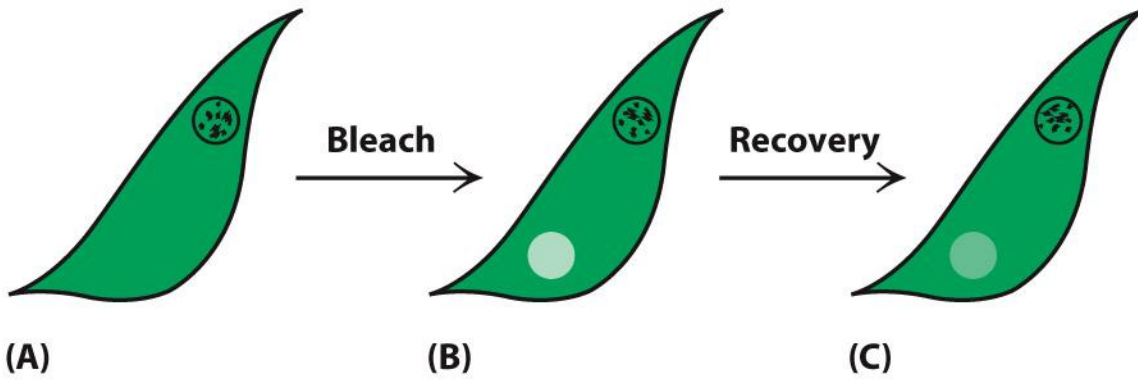


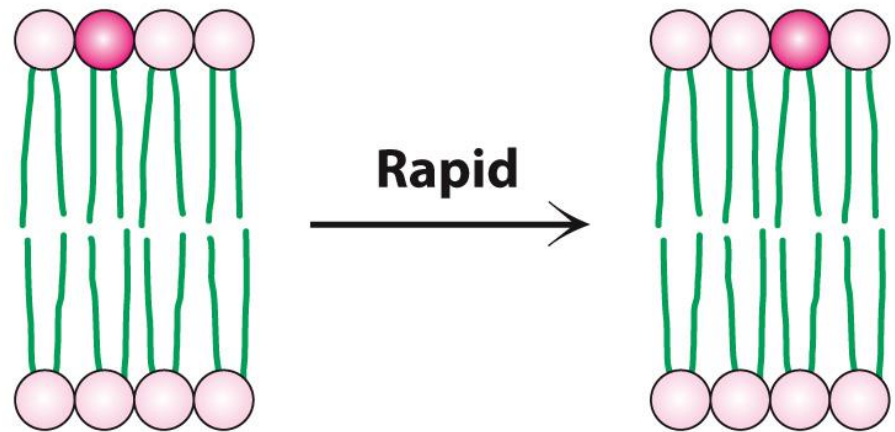
Figure 12.28
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The fluid mosaic model describes membranes as two-dimensional solutions of oriented lipids and globular proteins.

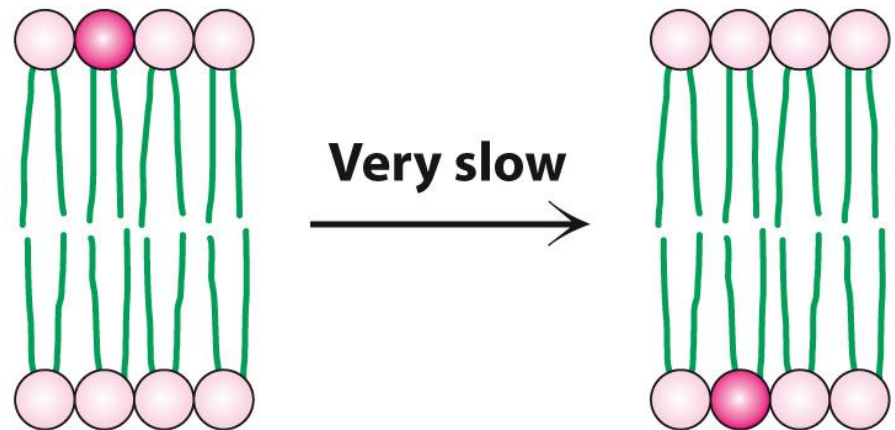
The lipids serve as a solvent and a permeability barrier.

Lipids rapidly diffuse laterally in membranes, although transverse diffusion or flip-flopping is very rare without the assistance of enzymes.

The prohibition of transverse diffusion accounts for the stability of membrane asymmetry.



Lateral diffusion



**Transverse diffusion
(flip-flop)**

Figure 12.29

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Membrane processes depend on the fluidity of the membrane.

The temperature at which a membrane transitions from being highly ordered to very fluid is called the melting temperature (T_m).

The melting temperature is dependent on the length of the fatty acids in the membrane lipid and the degree of cis unsaturation.

Cholesterol helps to maintain proper membrane fluidity in membranes in animals.

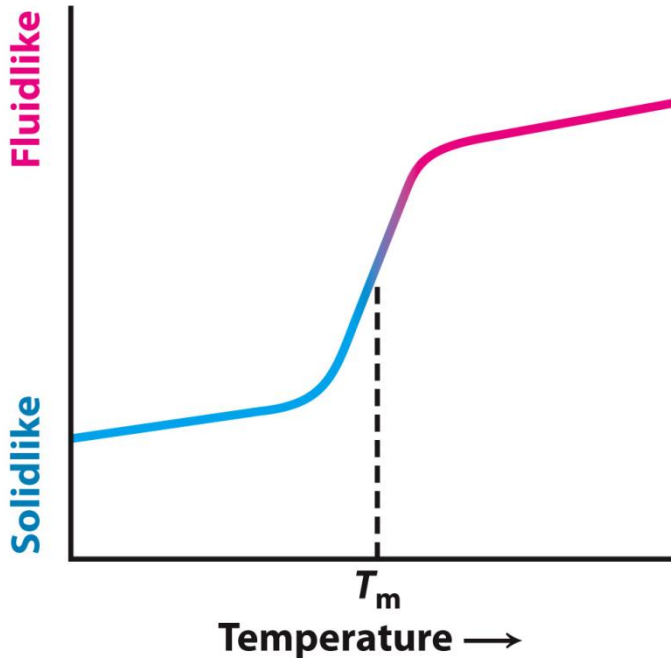
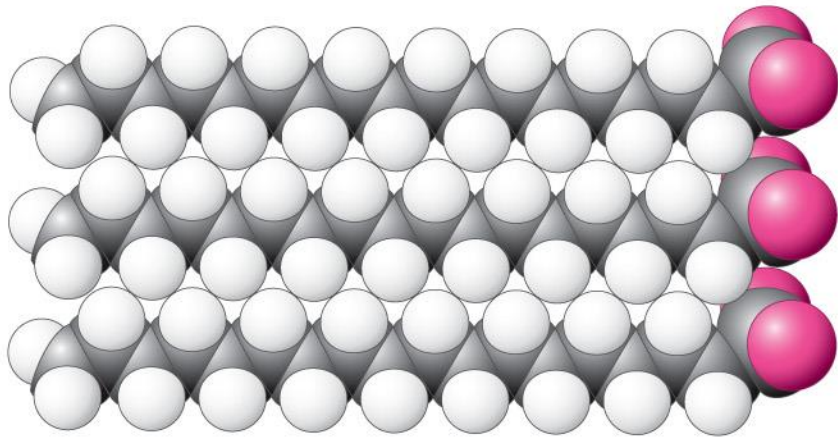


TABLE 12.3 The melting temperature of phosphatidylcholine containing different pairs of identical fatty acid chains

Number of carbons	Number of double bonds	Fatty acid		
		Common name	Systematic name	T_m (°C)
22	0	Behenate	<i>n</i> -Docosanoate	75
18	0	Stearate	<i>n</i> -Octadecanoate	58
16	0	Palmitate	<i>n</i> -Hexadecanoate	41
14	0	Myristate	<i>n</i> -Tetradecanoate	24
18	1	Oleate	<i>cis</i> - Δ^9 -Octadecenoate	-22

Table 12.3
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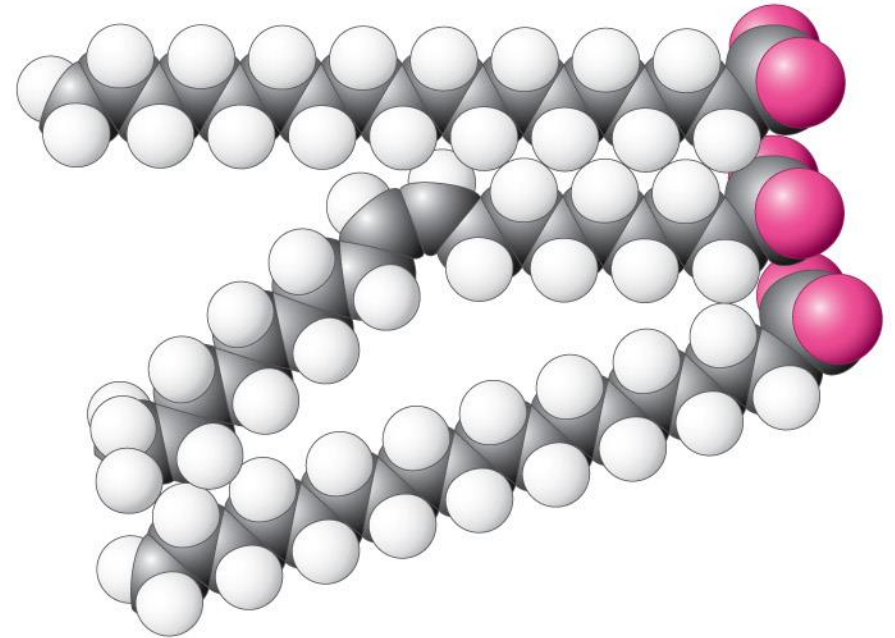
three molecules of stearate (C18, saturated)



(A)

Figure 12.31

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(B)

a molecule of oleate (C18, unsaturated)
between two molecules of stearate

Cholesterol

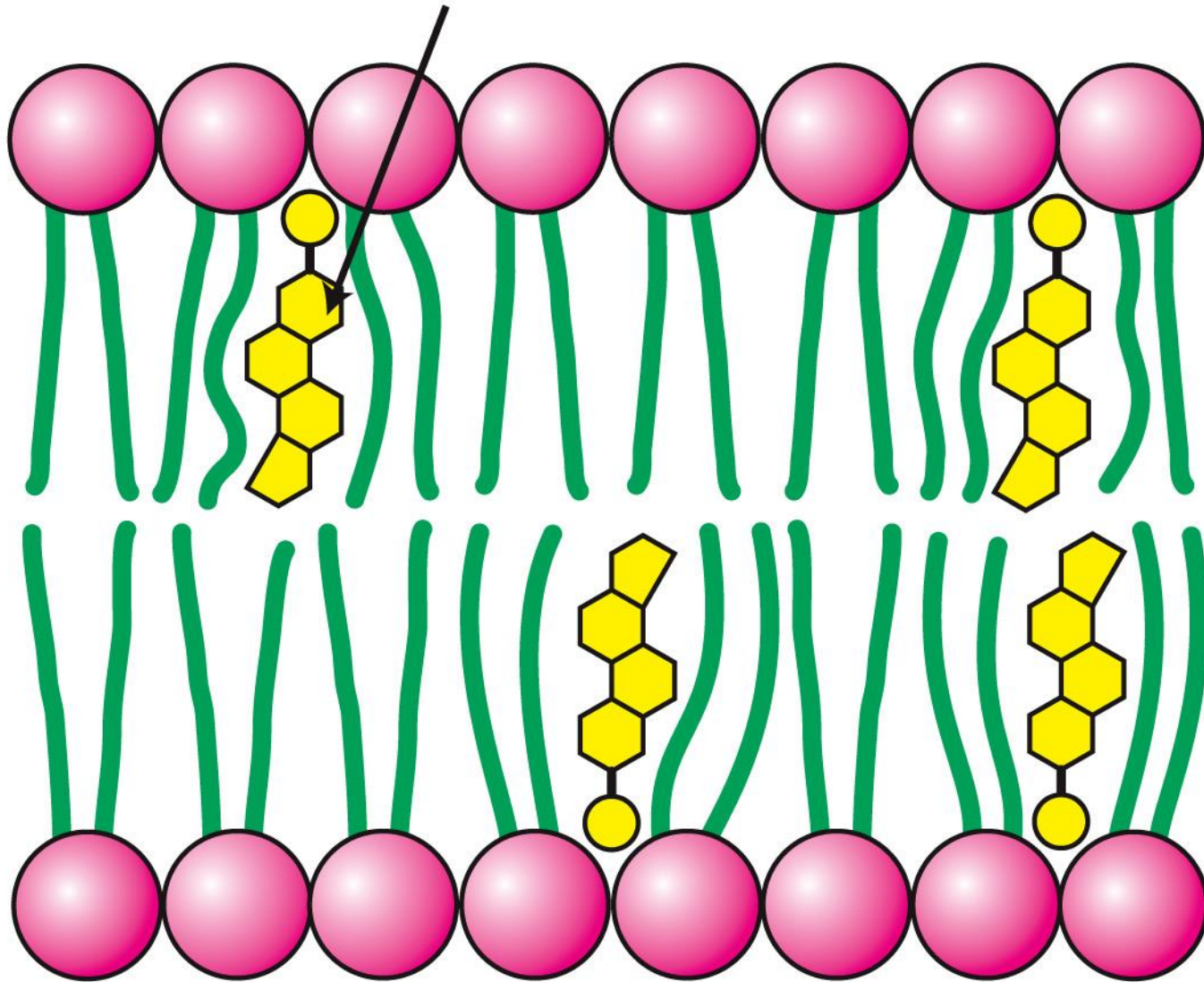


Figure 12.32

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Lipid rafts are highly dynamic complexes formed between cholesterol and specific lipids

Cholesterol forms complexes with sphingolipids, glycolipids, and some GPI-anchored proteins.

Such complexes, which concentrate in defined regions of the membrane, are called lipid rafts.

Lipid rafts may function in signal transduction.