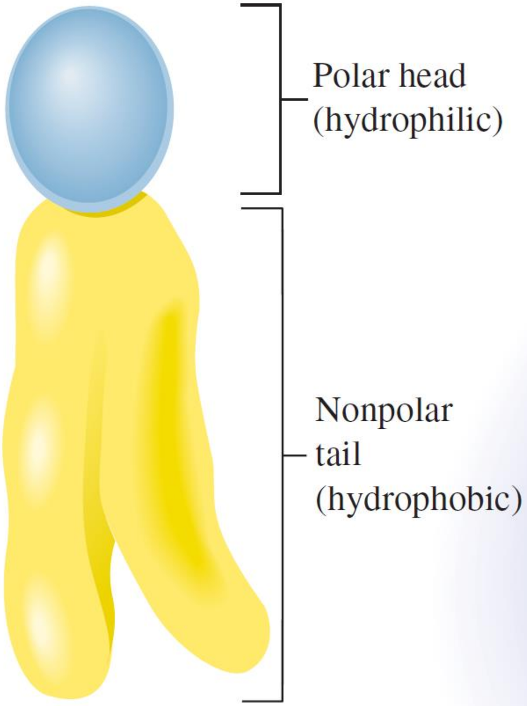
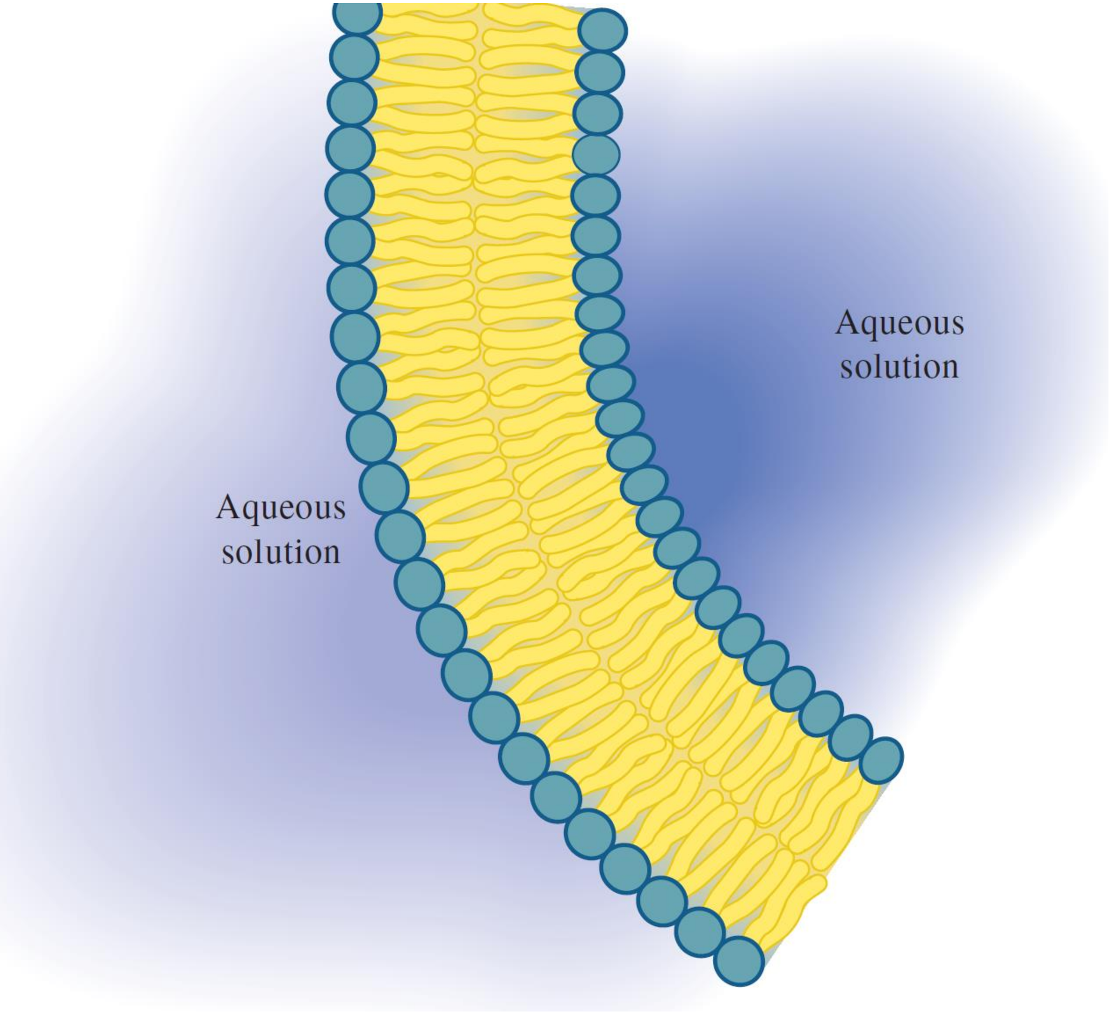
Lipids


Polar head
(hydrophilic)
Nonpolar
tail
(hydrophobic)


Aqueous
solution
Aqueous
solution

Lipids; Structure and Functions

❖Biological lipids are a chemically diverse group of compounds, the common and defining feature of which is their insolubility in water.

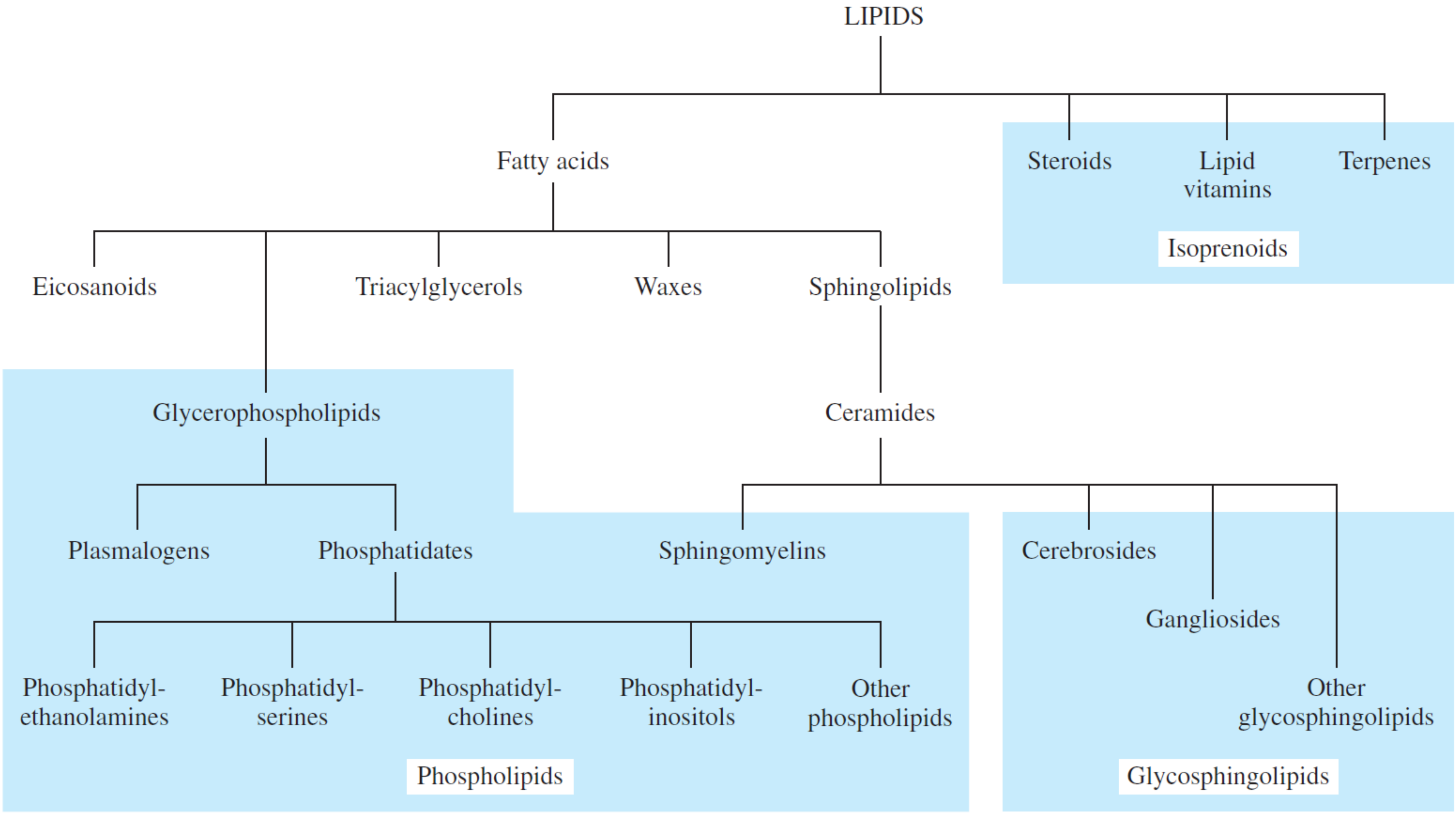
❖The biological functions of the lipids are as diverse as their chemistry.

❖Fats and oils are the principal stored forms of energy in many organisms.

❖Phospholipids and sterols are major structural elements of biological membranes.

❖Other lipids, although present in relatively small quantities, play crucial roles as

- enzyme cofactors,
- electron carriers,
- light-absorbing pigments,
- hydrophobic anchors for proteins,
- “chaperones” to help membrane proteins fold,
- emulsifying agents in the digestive tract,
- hormones, and intracellular messengers.



LIPIDS

Fatty acids

Steroids

Lipid vitamins

Terpenes

Isoprenoids

Eicosanoids

Triacylglycerols

Waxes

Sphingolipids

Glycerophospholipids

Ceramides

Plasmalogens

Phosphatidates

Sphingomyelins

Cerebrosides

Gangliosides

Phosphatidylethanolamines

Phosphatidylserines

Phosphatidylcholines

Phosphatidylinositols

Other phospholipids

Other glycosphingolipids

Phospholipids

Glycosphingolipids

Storage Lipids

- The fats and oils used almost universally as stored forms of energy in living organisms are derivatives of fatty acids.

- The fatty acids are hydrocarbon derivatives, at about the same low oxidation state (that is, as highly reduced) as the hydrocarbons in fossil fuels.

- The cellular oxidation of fatty acids (to CO_2 and H_2O), like the controlled, rapid burning of fossil fuels in internal combustion engines, is highly exergonic.

- Fatty acids are carboxylic acids with hydrocarbon chains ranging from 4 to 36 carbons long (C_4 to C_{36}).

- In some fatty acids, this chain is unbranched and fully saturated (contains no double bonds); in others the chain contains one or more double bonds .

TABLE 10–1 Some Naturally Occurring Fatty Acids: Structure, Properties, and Nomenclature

Carbon skeleton	Structure*	Systematic name†	Common name (derivation)	Melting point (°C)	Solubility at 30 °C (mg/g solvent)	
					Water	Benzene
12:0	$CH_3(CH_2)_{10}COOH$	*n*-Dodecanoic acid	Lauric acid (Latin *laurus*, “laurel plant”)	44.2	0.063	2,600
14:0	$CH_3(CH_2)_{12}COOH$	*n*-Tetradecanoic acid	Myristic acid (Latin *Myristica*, nutmeg genus)	53.9	0.024	874
16:0	$CH_3(CH_2)_{14}COOH$	*n*-Hexadecanoic acid	Palmitic acid (Latin *palma*, “palm tree”)	63.1	0.0083	348
18:0	$CH_3(CH_2)_{16}COOH$	*n*-Octadecanoic acid	Stearic acid (Greek *stear*, “hard fat”)	69.6	0.0034	124
20:0	$CH_3(CH_2)_{18}COOH$	*n*-Eicosanoic acid	Arachidic acid (Latin *Arachis*, legume genus)	76.5		
24:0	$CH_3(CH_2)_{22}COOH$	*n*-Tetracosanoic acid	Lignoceric acid (Latin *lignum*, “wood” + *cera*, “wax“)	86.0		
$16{:}1(\Delta^{9})$	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	*cis*-9-Hexadecenoic acid	Palmitoleic acid	1-0.5		
$18{:}1(\Delta^{9})$	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	*cis*-9-Octadecenoic acid	Oleic acid (Latin *oleum*, “oil”)	13.4		
$18{:}2(\Delta^{9,12})$	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-9,12-Octadecadienoic acid	Linoleic acid (Greek *linon*, “flax”)	1-5		
$18{:}3(\Delta^{9,12,15})$	$CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-,*cis*-9,12,15-Octadecatrienoic acid	α-Linolenic acid	−11		
$20{:}4(\Delta^{5,8,11,14})$	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_3COOH$	*cis*-,*cis*-,*cis*-,*cis*-5,8,11,14-Icosatetraenoic acid	Arachidonic acid	−49.5		

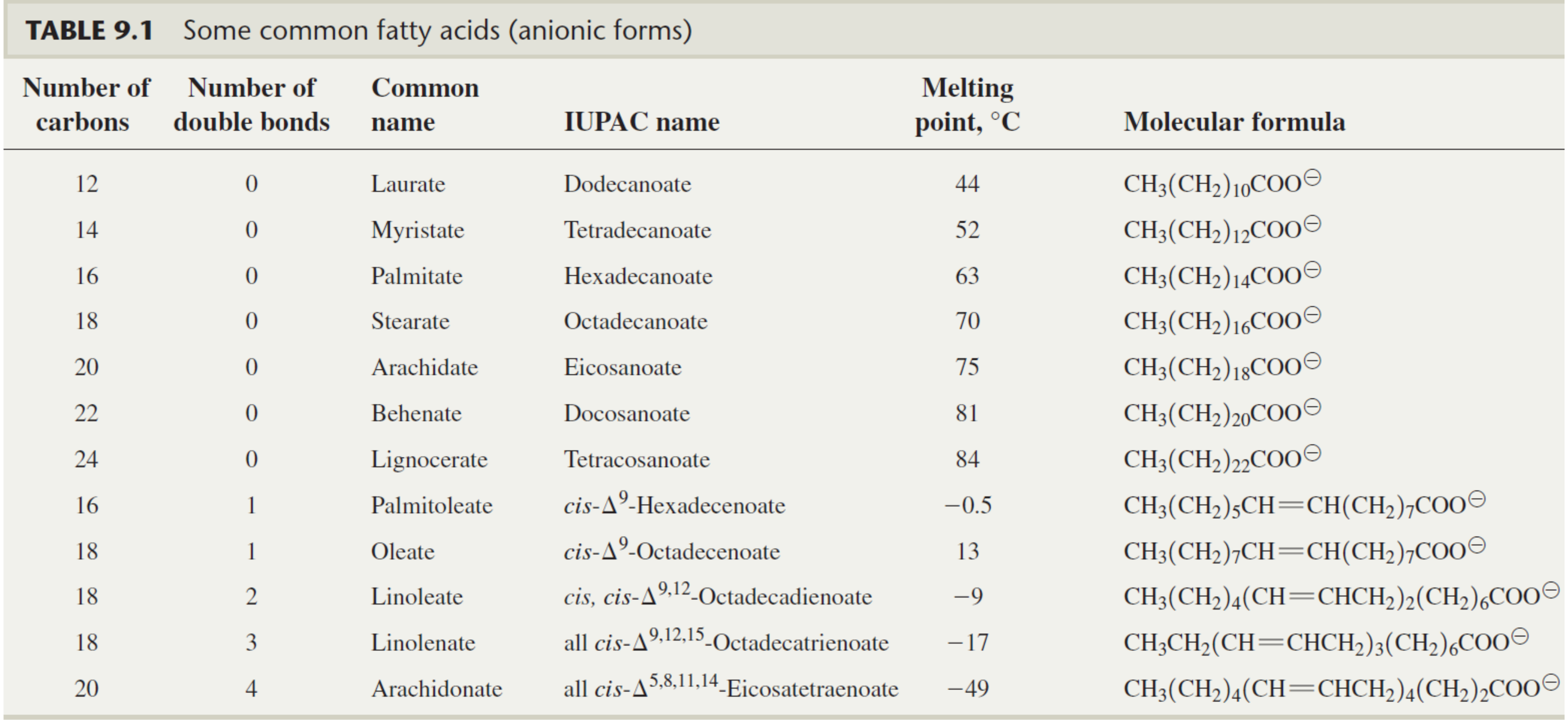
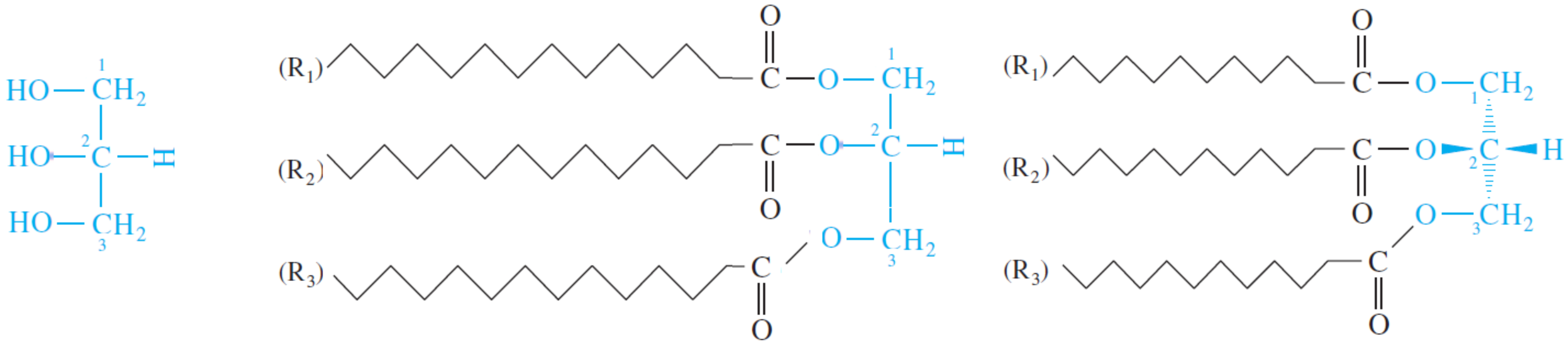


TABLE 9.1 Some common fatty acids (anionic forms)

Number of carbons	Number of double bonds	Common name	IUPAC name	Melting point, °C	Molecular formula
12	0	Laurate	Dodecanoate	44	$CH_3(CH_2)_{10}COO^{\ominus}$
14	0	Myristate	Tetradecanoate	52	$CH_3(CH_2)_{12}COO^{\ominus}$
16	0	Palmitate	Hexadecanoate	63	$CH_3(CH_2)_{14}COO^{\ominus}$
18	0	Stearate	Octadecanoate	70	$CH_3(CH_2)_{16}COO^{\ominus}$
20	0	Arachidate	Eicosanoate	75	$CH_3(CH_2)_{18}COO^{\ominus}$
22	0	Behenate	Docosanoate	81	$CH_3(CH_2)_{20}COO^{\ominus}$
24	0	Lignocerate	Tetracosanoate	84	$CH_3(CH_2)_{22}COO^{\ominus}$
16	1	Palmitoleate	*cis*-Δ^{9}-Hexadecenoate	−0.5	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COO^{\ominus}$
18	1	Oleate	*cis*-Δ^{9}-Octadecenoate	13	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COO^{\ominus}$
18	2	Linoleate	*cis, cis*-$\Delta^{9,12}$-Octadecadienoate	−9	$CH_3(CH_2)_4(CH{=}CHCH_2)_2(CH_2)_6COO^{\ominus}$
18	3	Linolenate	all *cis*-$\Delta^{9,12,15}$-Octadecatrienoate	−17	$CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6COO^{\ominus}$
20	4	Arachidonate	all *cis*-$\Delta^{5,8,11,14}$-Eicosatetraenoate	−49	$CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2COO^{\ominus}$



❖A simplified nomenclature for unbranched fatty acids specifies the chain length and number of double bonds, separated by a colon; for example, the 16-carbon saturated palmitic acid is abbreviated 16:0, and the 18-carbon oleic acid, with one double bond, is 18:1.

❖The positions of any double bonds are specified relative to the carboxyl carbon, numbered 1, by superscript numbers following **Δ**;

❖A 20-carbon fatty acid with one double bond between C-9 and C-10 (C-1 being the carboxyl carbon) and another between C-12 and C-13 is designated **$20{:}2(\Delta^{9,12})$** .

❖The most commonly occurring fatty acids have even numbers of carbon atoms in an unbranched chain of 12 to 24 carbons

- There is also a common pattern in the location of double bonds;

- in most monounsaturated fatty acids the double bond is between C-9 and C-10 (Δ9), and the other double bonds of polyunsaturated fatty acids are generally Δ12 and Δ15.

- Arachidonic acid is an exception to this generalization.

- The double bonds of polyunsaturated fatty acids are almost never conjugated (alternating single and double bonds, as in

$$-\mathrm{CH}{=}\mathrm{CH}-\mathrm{CH}{=}\mathrm{CH}-$$

- but are separated by a methylene group:

$$-\mathrm{CH}{=}\mathrm{CH}-\mathrm{CH_2}-\mathrm{CH}{=}\mathrm{CH}-$$

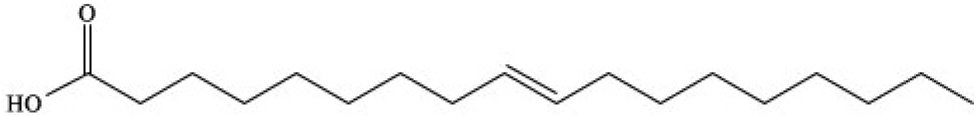
- In nearly all naturally occurring unsaturated fatty acids, the double bonds are in the cis configuration.

- Trans fatty acids are produced by fermentation in the rumen of dairy animals and are obtained from dairy products and meat.

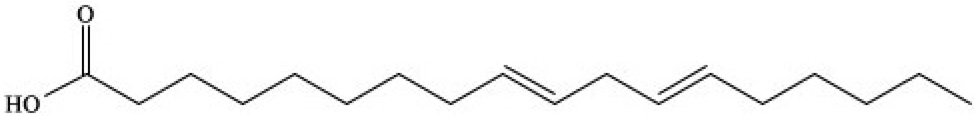
- Dietary trans fatty acids raise the level of triacylglycerols and of LDL (“bad”) cholesterol in the blood, and lower the level of HDL (“good”) cholesterol, and these changes alone are enough to increase the risk of coronary heart disease.

- But trans fatty acids may have further adverse effects. They seem, for example, to increase the body's inflammatory response, which is another risk factor for heart disease.

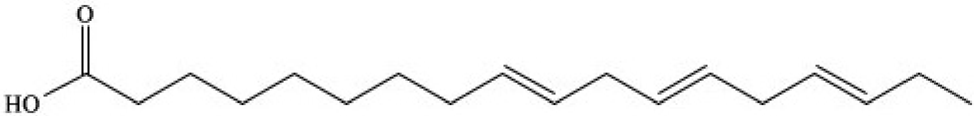
- In vertebrates, free fatty acids (unesterified fatty acids, with a free carboxylate group) circulate in the blood bound noncovalently to a protein carrier, serum albumin.



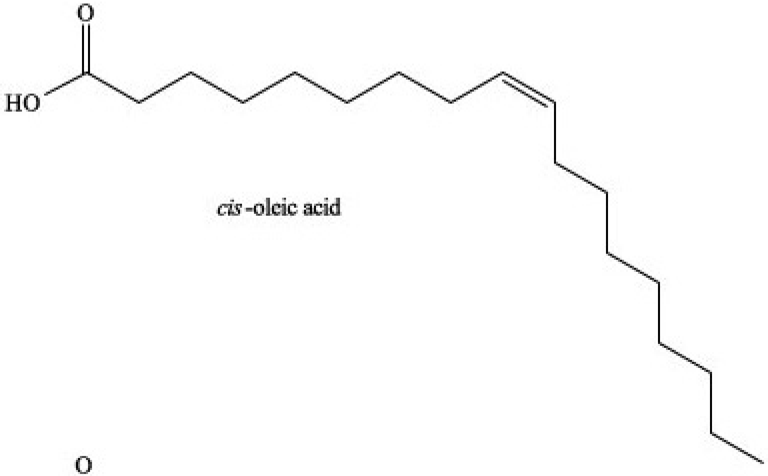
trans -oleic acid



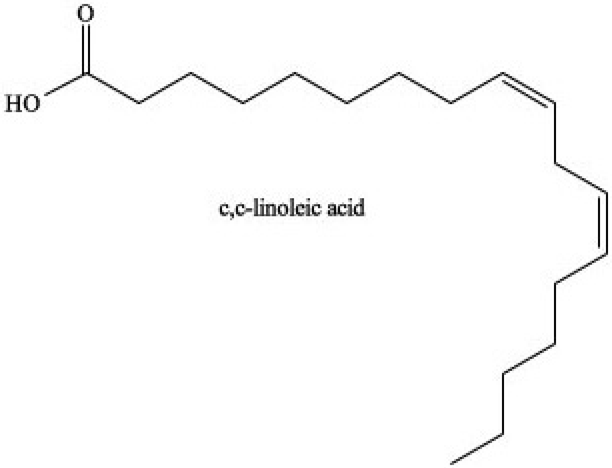
t,t-linoleic acid (linolelaidic acid)



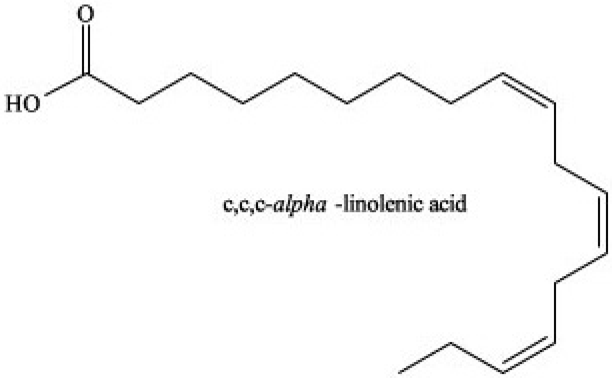
t,t,t- *alpha* -linolenic acid (linolenelaidic acid)



cis -oleic acid



c,c-linoleic acid



c,c,c-*alpha* -linolenic acid

- The physical properties of the fatty acids, and of compounds that contain them, are largely determined by the length and degree of unsaturation of the hydrocarbon chain.

- The nonpolar hydrocarbon chain accounts for the poor solubility of fatty acids in water.

- Lauric acid (12:0, Mr 200), for example, has a solubility in water of 0.063 mg/g—much less than that of glucose (Mr 180), which is 1,100 mg/g.

- The longer the fatty acyl chain and the fewer the double bonds, the lower is the solubility in water.

- The carboxylic acid group is polar (and ionized at neutral pH) and accounts for the slight solubility of short-chain fatty acids in water

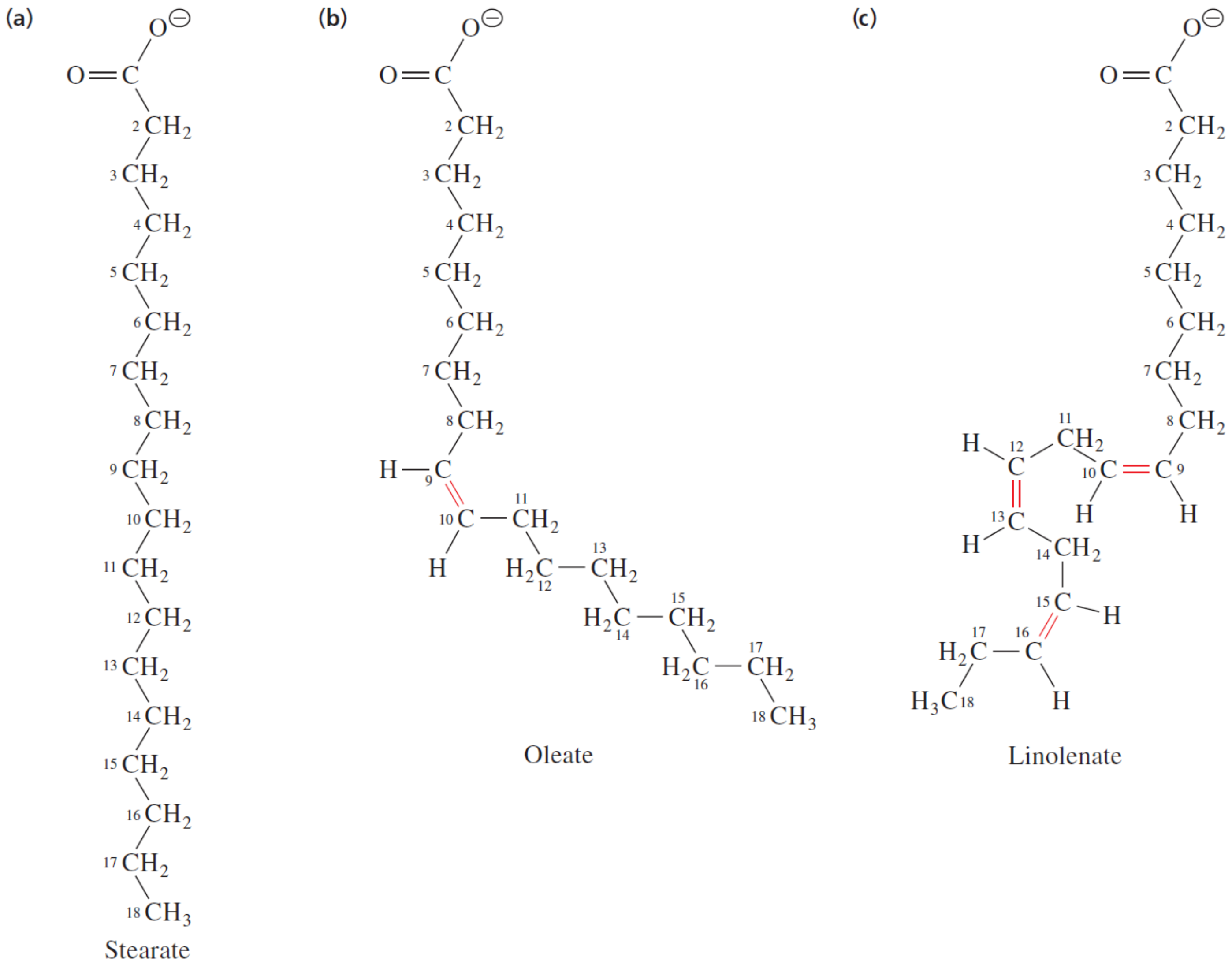
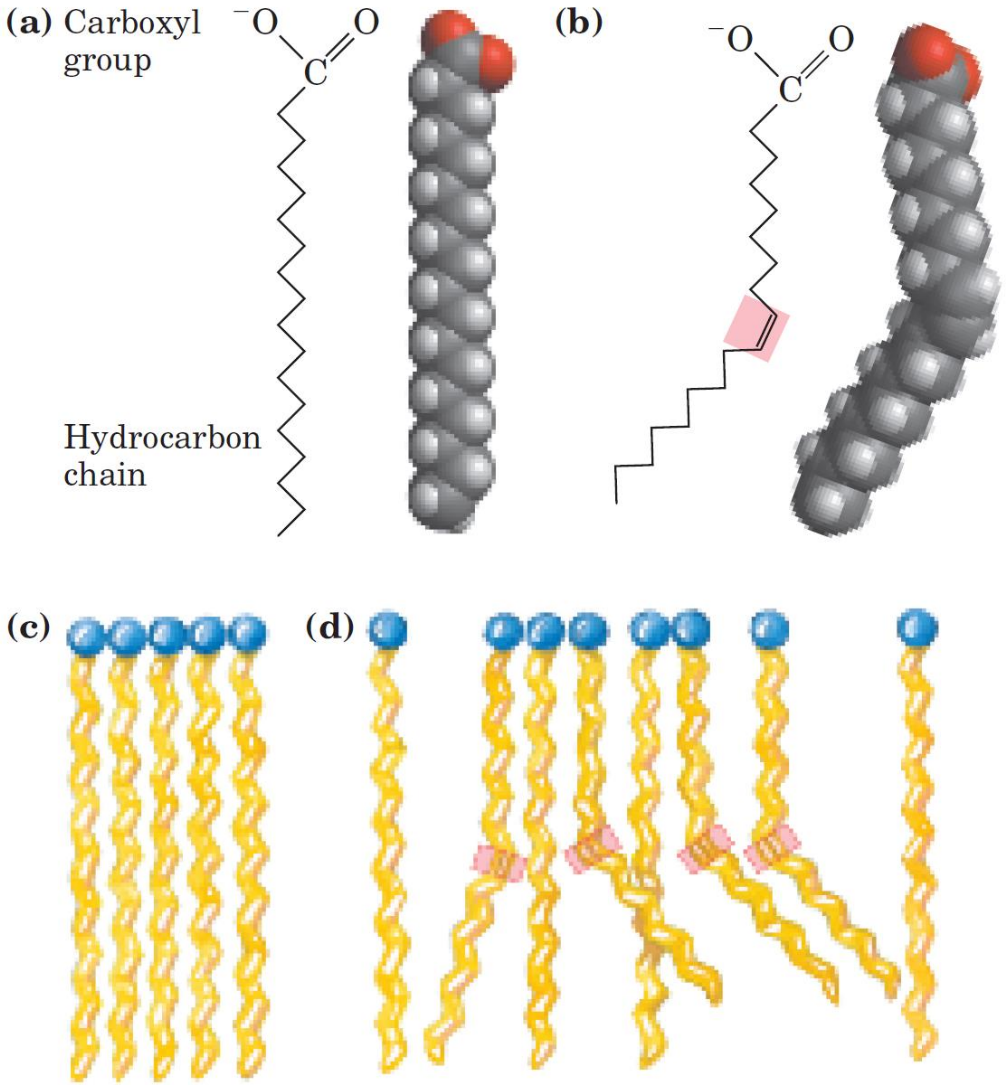


Figure 9.3 ▲
Chemical structures of three C_{18} fatty acids. **(a)** Stearate (octadecanoate), a saturated fatty acid. **(b)** Oleate (*cis*-Δ^9-octadecenoate), a monounsaturated fatty acid. **(c)** Linolenate (all-*cis*-$\Delta^{9,12,15}$-octadecatrienoate), a polyunsaturated fatty acid. The *cis* double bonds produce kinks in the tails of the unsaturated fatty acids. Linolenate is a very flexible molecule, and can assume a variety of conformations.

❖Melting points are also strongly influenced by the length and degree of unsaturation of the hydrocarbon chain.

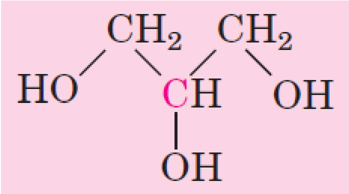


Saturated fatty acids

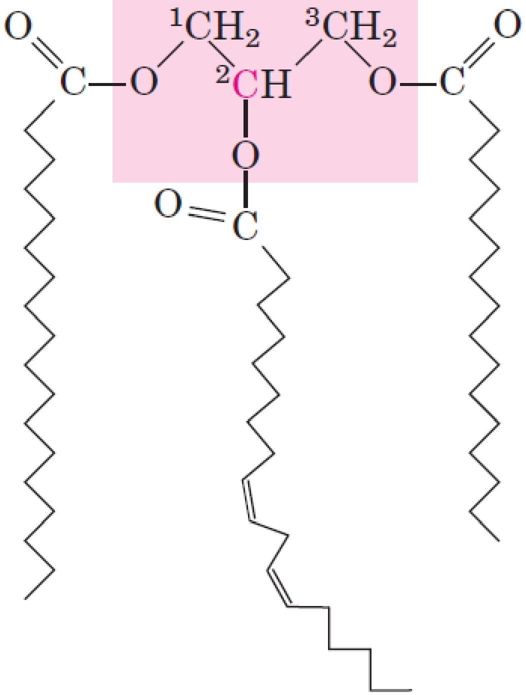
Mixture of saturated and unsaturated fatty acids

- The simplest lipids constructed from fatty acids are the **triacylglycerols**, also referred to as triglycerides, fats, or neutral fats.

- Triacylglycerols are composed of three fatty acids each in ester linkage with a single glycerol



Glycerol



1-Stearoyl, 2-linoleoyl, 3-palmitoyl glycerol,
a mixed triacylglycerol

❖Those containing the same kind of fatty acid in all three positions are called simple triacylglycerols and are named after the fatty acid they contain.

❖Simple triacylglycerols of 16:0, 18:0, and 18:1, for example, are tripalmitin, tristearin, and triolein, respectively.

❖Most naturally occurring triacylglycerols are mixed; they contain two or three different fatty acids.

❖To name these compounds unambiguously, the name and position of each fatty acid must be specified.

❖Because the polar hydroxyls of glycerol and the polar carboxylates of the fatty acids are bound in ester linkages, triacylglycerols are nonpolar, hydrophobic molecules, essentially insoluble in water.

Table 3.2 The fatty acid composition of some vegetable oils* (g per 100 g of total fatty acids)

	8:0	10:0	12:0	14:0	16:0	18:0	18:1 *n*-9	18:2 *n*-6	18:3 *n*-3	20:1+ 22:1	total
A. Major edible oil crops											
Cocoa butter					26	34	35	3			98
Coconut (3.4)	8	7	48	18	9	3	6	2			99
Corn (1.9)					13	3	31	52	1		100
Cottonseed (4.0)				1	24	3	19	53			100
Groundnut[a] (4.2)					13	3	37	41		2	96
Olive (2.7)					10	2	78	7	1		98
Palm (17.6)				1	43	4	41	10			99
Palm kernel (2.2)	4	4	45	18	9	3	15	2			100
Rape (Canola) (11.8)					4	2	56	26	10	2	100
Sesame (0.8)					9	6	38	45	1	1	100
Soybean (20.8)					11	4	22	53	8	1	99
Sunflower (9.3)					6	6	18	69			99
B. Major industrial oils											
Castor[b] (0.5)					1		3	4			98[b]
Linseed (0.7)					6	3	17	14	60		100
Rape (high erucic)					3	1	16	14	10	55	99
C. Other oils and fats of interest											
Avocado					20	1	60	18			99
Cuphea viscosissima	9	76	3	1	3		2	5			99
Evening primrose[c]					7	2	9	72			90[c]
Rice bran					16	2	42	37	1		98
Safflower (high oleic)					6	2	74	16			98
Safflower (high linoleic)					7	3	14	75			99

❖In most eukaryotic cells, triacylglycerols form a separate phase of microscopic, oily droplets in the aqueous cytosol, serving as depots of metabolic fuel.

❖In vertebrates, specialized cells called adipocytes, or fat cells, store large amounts of triacylglycerols as fat droplets that nearly fill the cell.

❖Triacylglycerols are also stored as oils in the seeds of many types of plants, providing energy and biosynthetic precursors during seed germination.

❖Adipocytes and germinating seeds contain lipases, enzymes that catalyze the hydrolysis of stored triacylglycerols, releasing fatty acids for export to sites where they are required as fuel.

- There are two significant advantages to using triacylglycerols as stored fuels, rather than polysaccharides such as glycogen and starch.

- First, the carbon atoms of fatty acids are more reduced than those of sugars, and oxidation of triacylglycerols yields more than twice as much energy, gram for gram, as the oxidation of carbohydrates.

- Second, because triacylglycerols are hydrophobic and therefore unhydrated, the organism that carries fat as fuel does not have to carry the extra weight of water of hydration that is associated with stored polysaccharides (2 g per gram of polysaccharide).

- Humans have fat tissue (composed primarily of adipocytes) under the skin, in the abdominal cavity, and in the mammary glands.

- In contrast, the human body can store less than a day’s energy supply in the form of glycogen.

- Carbohydrates such as glucose do offer certain advantages as quick sources of metabolic energy, one of which is their ready solubility in water.

- In some animals, triacylglycerols stored under the skin serve not only as energy stores but as insulation against low temperatures.

- Seals, walruses, penguins, and other warm-blooded polar animals are amply padded with triacylglycerols.

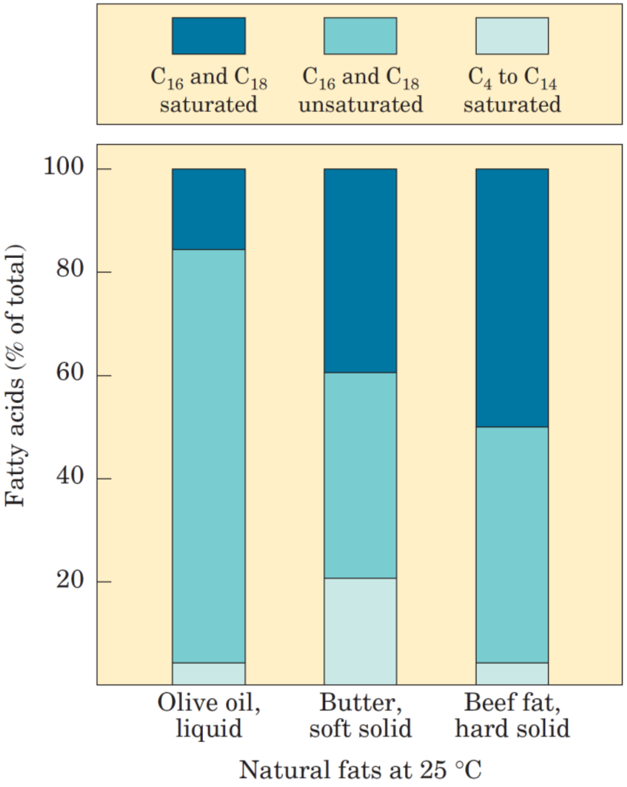
- In hibernating animals (bears, for example), the huge fat reserves accumulated before hibernation serve the dual purposes of insulation and energy storage

- Most natural fats, such as those in vegetable oils, dairy products, and animal fat, are complex mixtures of simple and mixed triacylglycerols.

- These contain a variety of fatty acids differing in chain length and degree of saturation.

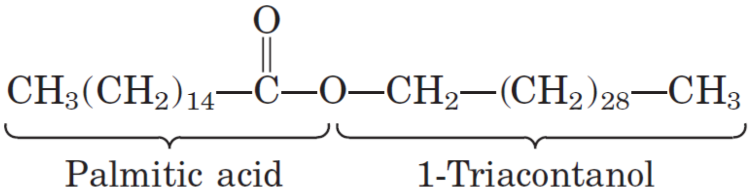
- When lipid-rich foods are exposed too long to the oxygen in air, they may spoil and become rancid.

- The unpleasant taste and smell associated with rancidity result from the oxidative cleavage of double bonds in unsaturated fatty acids, which produces aldehydes and carboxylic acids of shorter chain length and therefore higher volatility; these compounds pass readily through the air to your nose.



Waxes

- Biological waxes are esters of long-chain (C_{14} to C_{36}) saturated and unsaturated fatty acids with long-chain (C_{16} to C_{30}) alcohols.



$$\underbrace{\mathrm{CH_3(CH_2)_{14}}-\overset{\overset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}}_{\text{Palmitic acid}}-\underbrace{\mathrm{O}-\mathrm{CH_2}-(\mathrm{CH_2})_{28}-\mathrm{CH_3}}_{\text{1-Triacontanol}}$$

- Their melting points (60 to 100 °C) are generally higher than those of triacylglycerols.

- In plankton, the free-floating microorganisms at the bottom of the food chain for marine animals, waxes are the chief storage form of metabolic fuel.

- Waxes also serve a diversity of other functions related to their water-repellent properties and their firm consistency.

- Certain skin glands of vertebrates secrete waxes to protect hair and skin and keep it pliable, lubricated, and waterproof.

- Birds, particularly waterfowl, secrete waxes from their preen glands to keep their feathers water-repellent.

- The shiny leaves of holly, rhododendrons, poison ivy, and many tropical plants are coated with a thick layer of waxes, which prevents excessive evaporation of water and protects against parasites.

- Biological waxes find a variety of applications in the pharmaceutical, cosmetic, and other industries.

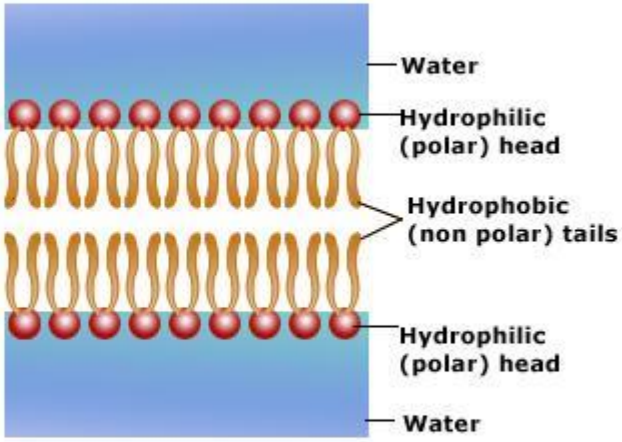
- Lanolin (from lamb’s wool), beeswax, carnauba wax (from a Brazilian palm tree), are widely used in the manufacture of lotions, ointments, and polishes.

Structural Lipids in Membranes

- The central architectural feature of biological membranes is a double layer of lipids, which acts as a barrier to the passage of polar molecules and ions.

- Membrane lipids are amphipathic: one end of the molecule is hydrophobic, the other hydrophilic.

- Their hydrophobic interactions with each other and their hydrophilic interactions with water direct their packing into sheets called membrane bilayers.



- Membrane lipids can be classified into five general classes
  - **Glycerophospholipids**, in which the hydrophobic regions are composed of two fatty acids joined to glycerol;
  - **Galactolipids and Sulfolipids**, which also contain two fatty acids esterified to glycerol, but lack the characteristic phosphate of phospholipids;
  - **Archaeal tetraether lipids**, in which two very long alkyl chains are ether-linked to glycerol at both ends;
  - **Sphingolipids**, in which a single fatty acid is joined to a fatty amine, sphingosine; and
  - **Sterols**, compounds characterized by a rigid system of four fused hydrocarbon rings

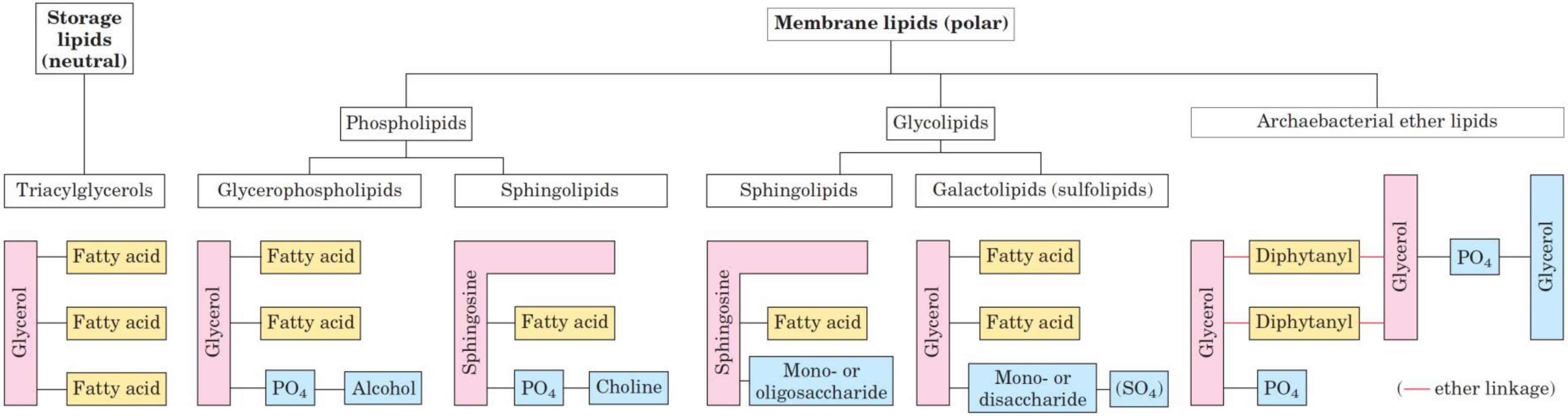
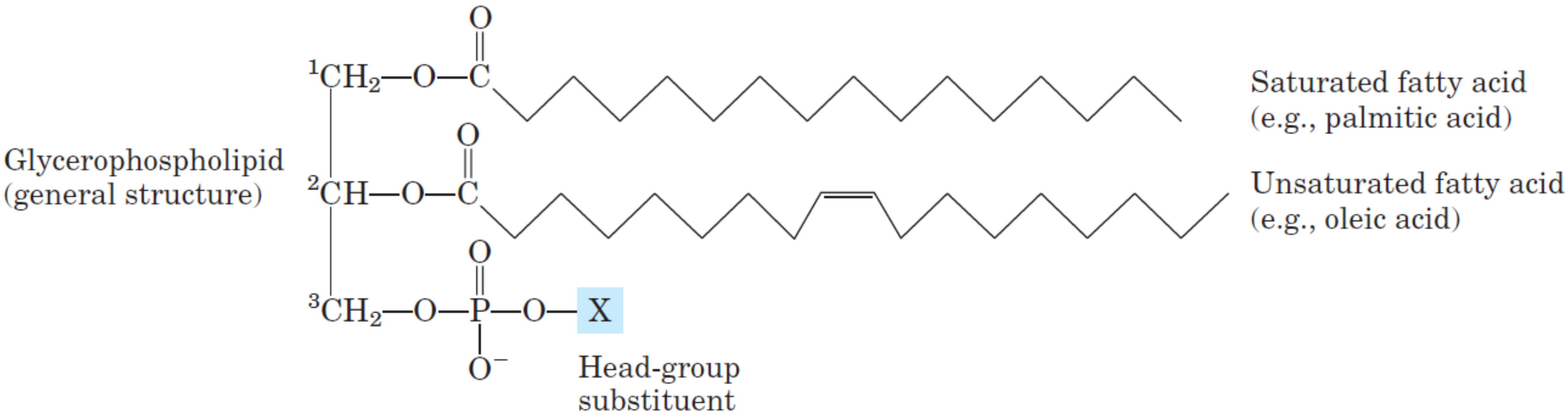


FIGURE 10–6 Some common types of storage and membrane lipids. All the lipid types shown here have either glycerol or sphingosine as the backbone (pink screen), to which are attached one or more long-chain alkyl groups (yellow) and a polar head group (blue). In triacylglycerols, glycerophospholipids, galactolipids, and sulfolipids, the alkyl groups are fatty acids in ester linkage. Sphingolipids contain a single fatty acid, in amide linkage to the sphingosine backbone. The membrane lipids of archaebacteria are variable; that shown here has two very long, branched alkyl chains, each end in ether linkage with a glycerol moiety. In phospholipids the polar head group is joined through a phosphodiester, whereas glycolipids have a direct glycosidic linkage between the head-group sugar and the backbone glycerol.

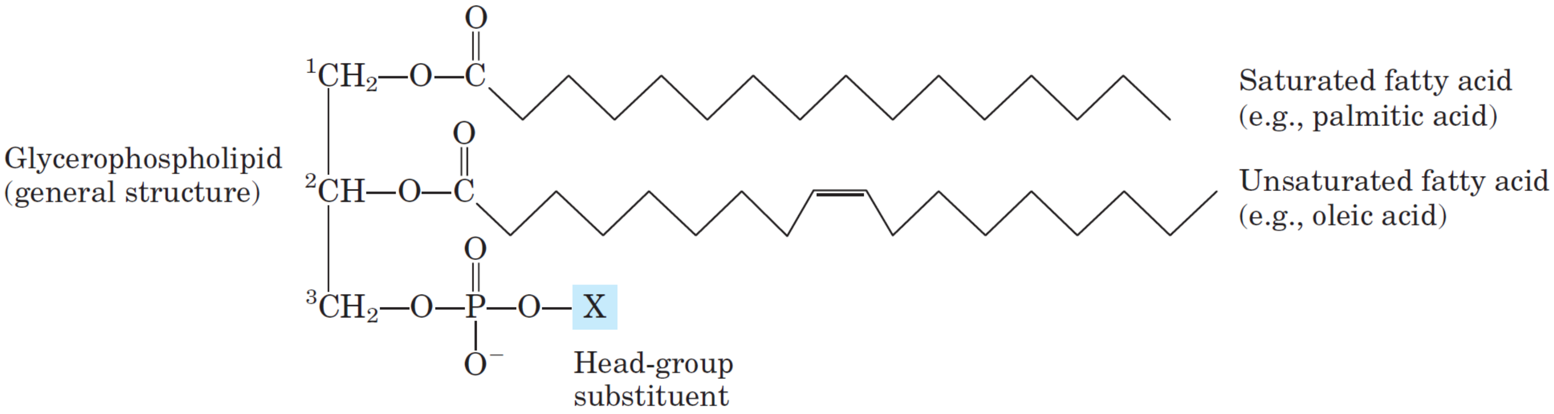
Glycerophospholipids

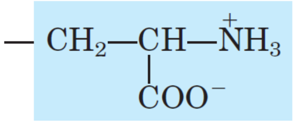
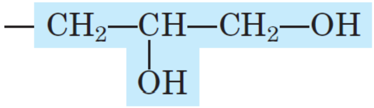
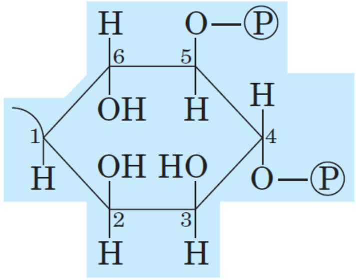
❖Glycerophospholipids, also called phosphoglycerides, are membrane lipids in which two fatty acids are attached in ester linkage to the first and second carbons of glycerol.

❖Also a highly polar or charged group is attached through a phosphodiester linkage to the third carbon.



❖Glycerol is prochiral; it has no asymmetric carbons, but attachment of phosphate at one end converts it into a chiral compound



Name of glycerophospholipid	Name of X	Formula of X	Net charge (at pH 7)
Phosphatidic acid	—	$-H$	−1
Phosphatidylethanolamine	Ethanolamine	$-CH_2-CH_2-\overset{+}{N}H_3$	0
Phosphatidylcholine	Choline	$-CH_2-CH_2-\overset{+}{N}(CH_3)_3$	0
Phosphatidylserine	Serine	 $-CH_2-\underset{COO^-}{\underset{\vert}{CH}}-\overset{+}{N}H_3$	−1
Phosphatidylglycerol	Glycerol	 $-CH_2-\underset{OH}{\underset{\vert}{CH}}-CH_2-OH$	−1
Phosphatidylinositol 4,5-bisphosphate	*myo*-Inositol 4,5-bisphosphate		−4

❖Glycerophospholipids are named as derivatives of the parent compound, phosphatidic acid (Fig. 10–9), according to the polar alcohol in the head group.

❖Phosphatidylcholine and phosphatidylethanolamine have choline and ethanolamine as their polar head groups, for example.

❖In all these compounds, the head group is joined to glycerol through a phosphodiester bond, in which the phosphate group bears a negative charge at neutral pH.

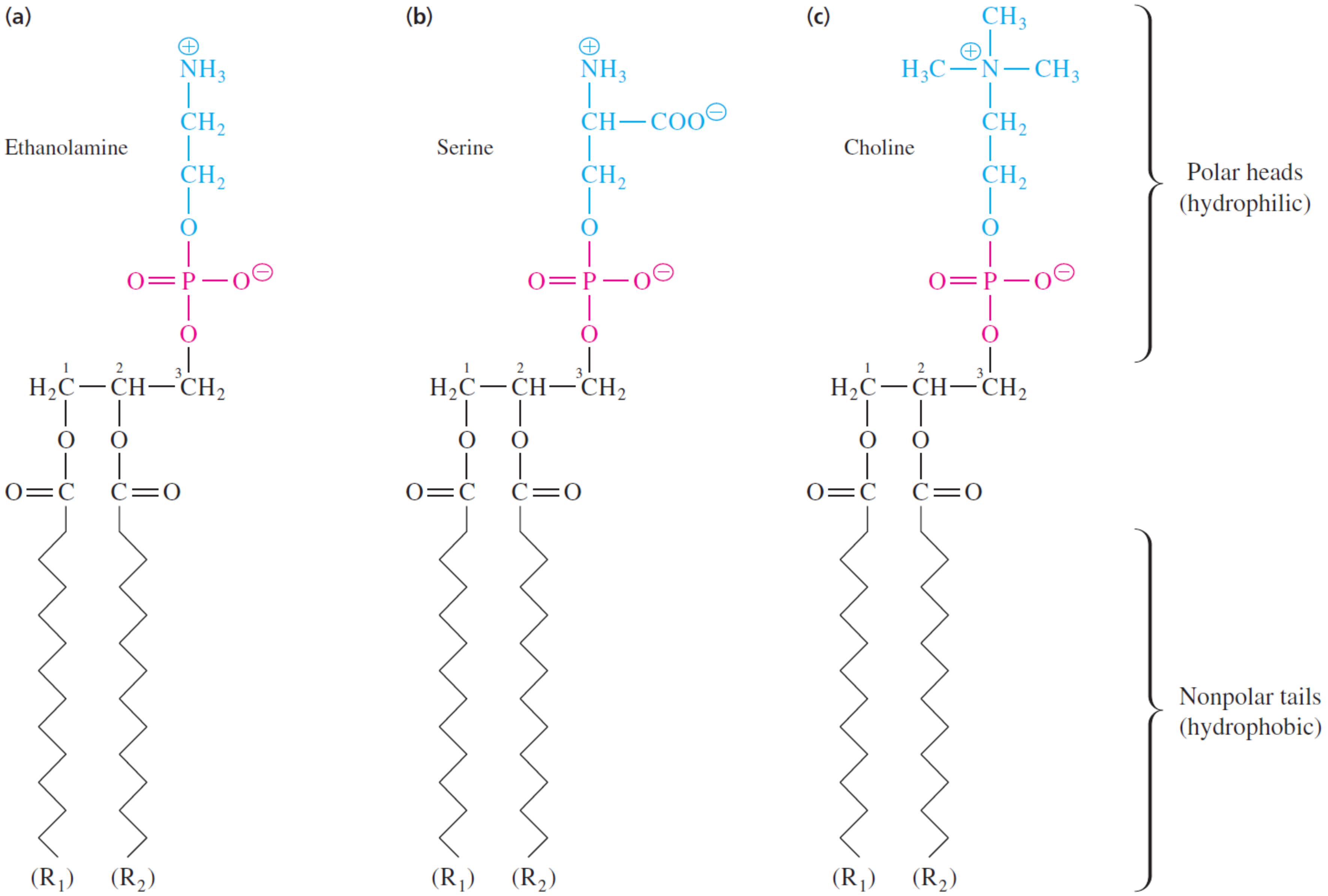
❖The polar alcohol may be negatively charged (as in phosphatidylinositol 4,5-bisphosphate), neutral (phosphatidylserine), or positively charged (phosphatidylcholine, phosphatidylethanolamine).

❖The fatty acids in glycerophospholipids can be any of a wide variety, so a given phospholipid (phosphatidylcholine for example) may consist of several molecular species, each with its unique complement of fatty acids.

❖The distribution of molecular species is specific for different organisms, different tissues of the same organism, and different glycerophospholipids in the same cell or tissue.

❖In general, glycerophospholipids contain a C16 or C18 saturated fatty acid at C-1 and a C18 or C20 unsaturated fatty acid at C-2.

❖With few exceptions, the biological significance of the variation in fatty acids and head groups is not yet understood.



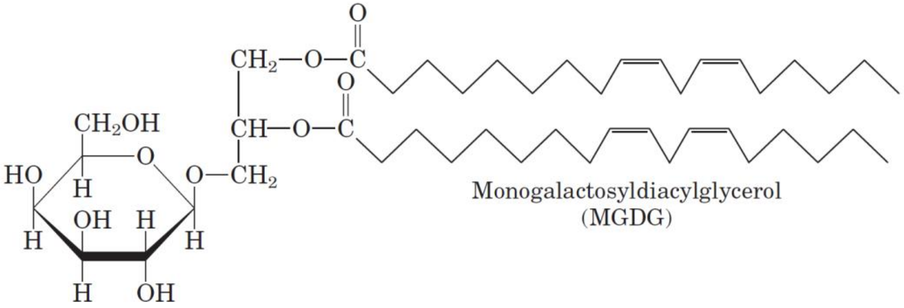
Phosphatidylethanolamine

Phosphatidylserine

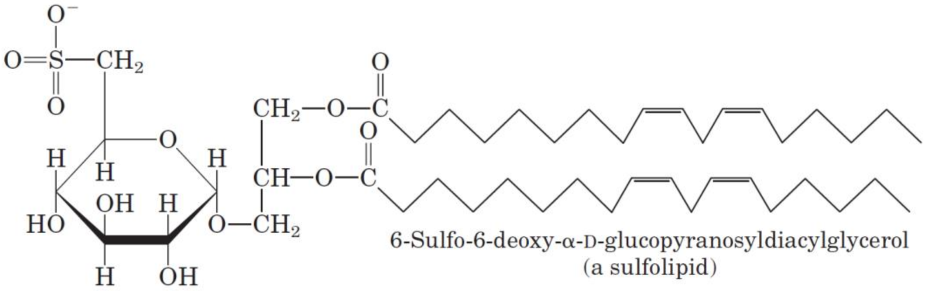
Phosphatidylcholine

Galaktolipitler ve Sulfolipitler

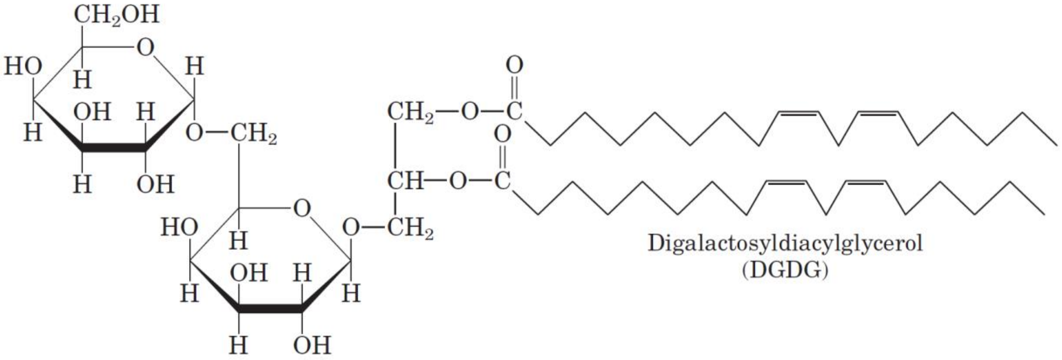
- The second group of membrane lipids are those that predominate in plant cells: the galactolipids, in which one or two galactose residues are connected by a glycosidic linkage to C-3 of a 1,2-diacylglycerol



Monogalactosyldiacylglycerol
(MGDG)



6-Sulfo-6-deoxy-α-D-glucopyranosyldiacylglycerol
(a sulfolipid)



Digalactosyldiacylglycerol
(DGDG)

❖Galactolipids are localized in the thylakoid membranes (internal membranes) of chloroplasts; they make up 70% to 80% of the total membrane lipids of a vascular plant, and are therefore probably the most abundant membrane lipids in the biosphere.

❖Phosphate is often the limiting plant nutrient in soil, and perhaps the evolutionary pressure to conserve phosphate for more critical roles favored plants that made phosphate-free lipids.

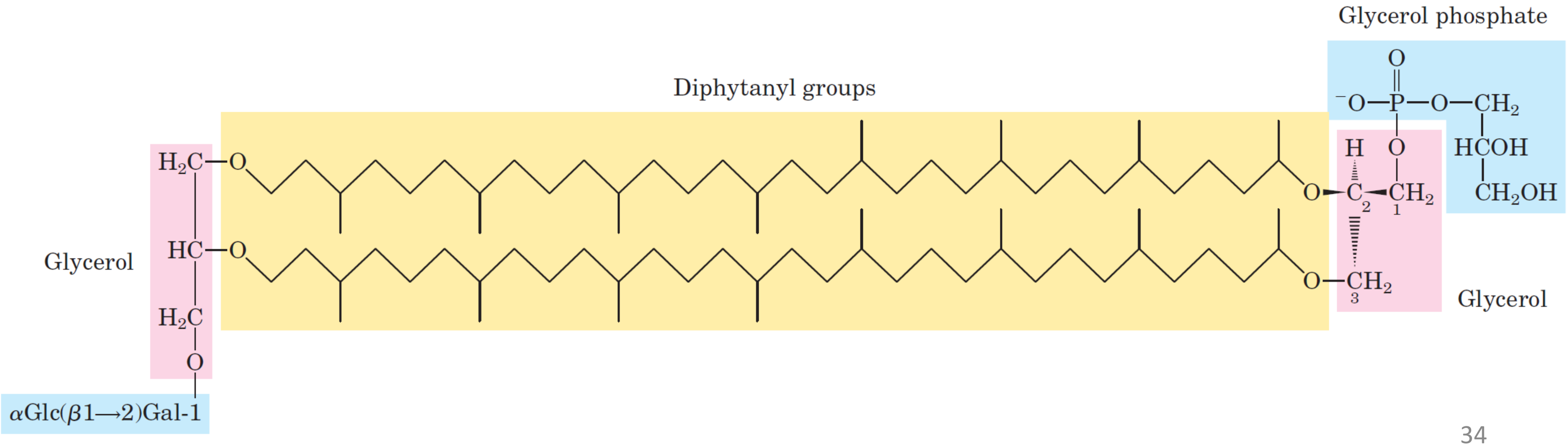
❖Plant membranes also contain sulfolipids, in which a sulfonated glucose residue is joined to a diacylglycerol in glycosidic linkage.

❖The sulfonate group bears a negative charge like that of the phosphate group in phospholipids.

Archaea Contain Unique Membrane Lipids

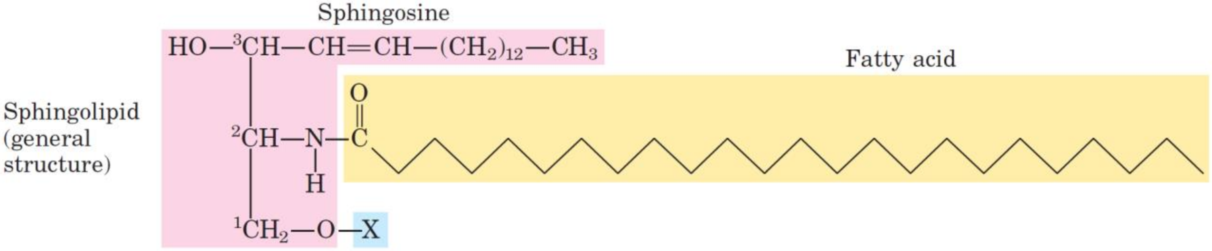
- Some archaea that live in ecological niches with extreme conditions—high temperatures (boiling water), low pH, high ionic strength, for example—have membrane lipids containing long-chain (32 carbons) branched hydrocarbons linked at each end to glycerol.

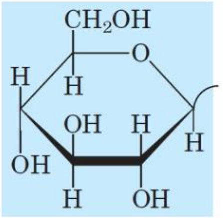
- These linkages are through ether bonds, which are much more stable to hydrolysis at low pH and high temperature than are the ester bonds found in the lipids of bacteria and eukaryotes.



Sphingolipids

- ❖Sphingolipids, the fourth large class of membrane lipids, also have a polar head group and two nonpolar tails, but unlike glycerophospholipids and galactolipids they contain no glycerol.



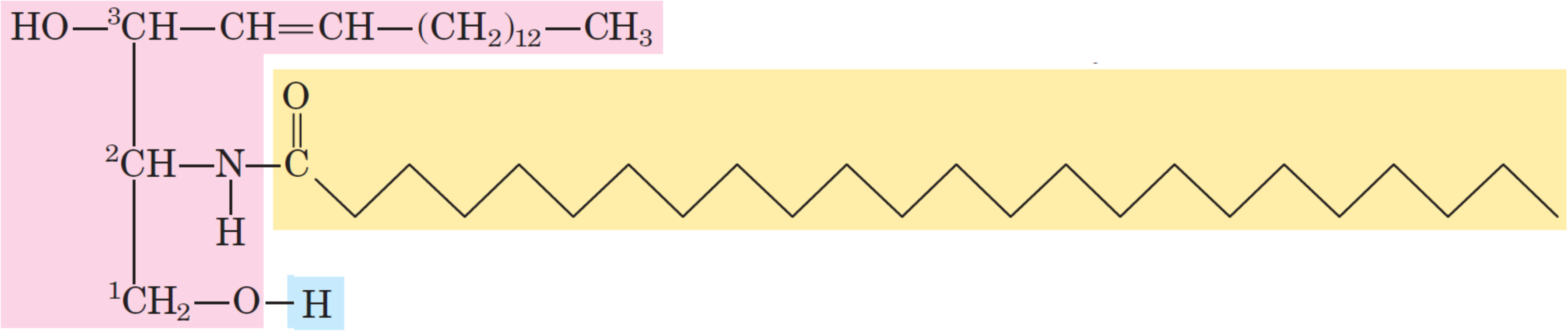
Name of sphingolipid	Name of X	Formula of X
Ceramide	—	—H
Sphingomyelin	Phosphocholine	$-\mathrm{P}(=\mathrm{O})(\mathrm{O}^-)-\mathrm{O}-\mathrm{CH_2}-\mathrm{CH_2}-\overset{+}{\mathrm{N}}(\mathrm{CH_3})_3$
Neutral glycolipids Glucosylcerebroside	Glucose	

- ❖Sphingolipids are composed of one molecule of the long-chain amino alcohol sphingosine (also called 4-sphingenine) or one of its derivatives, one molecule of a long-chain fatty acid, and a polar head group that is joined by a glycosidic linkage in some cases and a phosphodiester in others

- Carbons C-1, C-2, and C-3 of the sphingosine molecule are structurally analogous to the three carbons of glycerol in glycerophospholipids.

- When a fatty acid is attached in amide linkage to the -NH_2 on C-2, the resulting compound is a ceramide, which is structurally similar to a diacylglycerol.

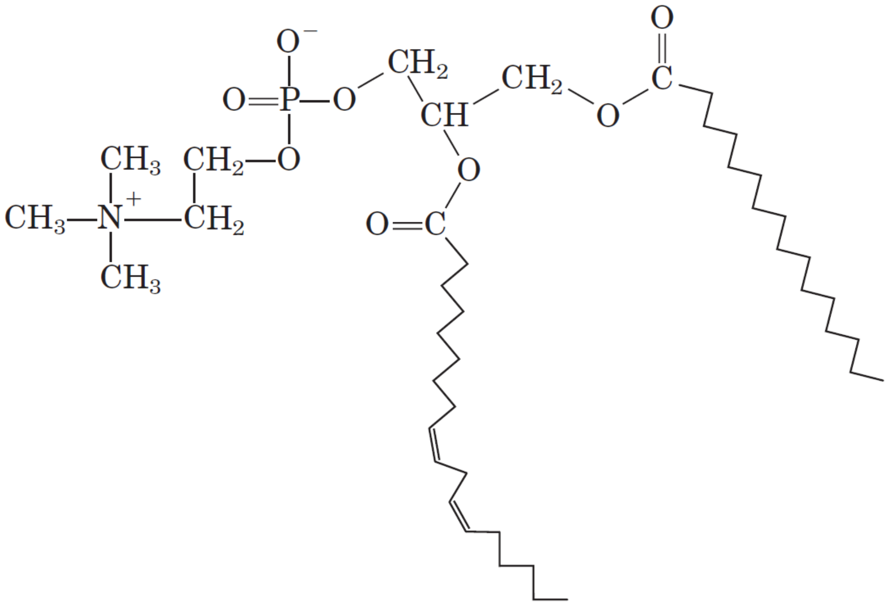
- Ceramide is the structural parent of all sphingolipids.



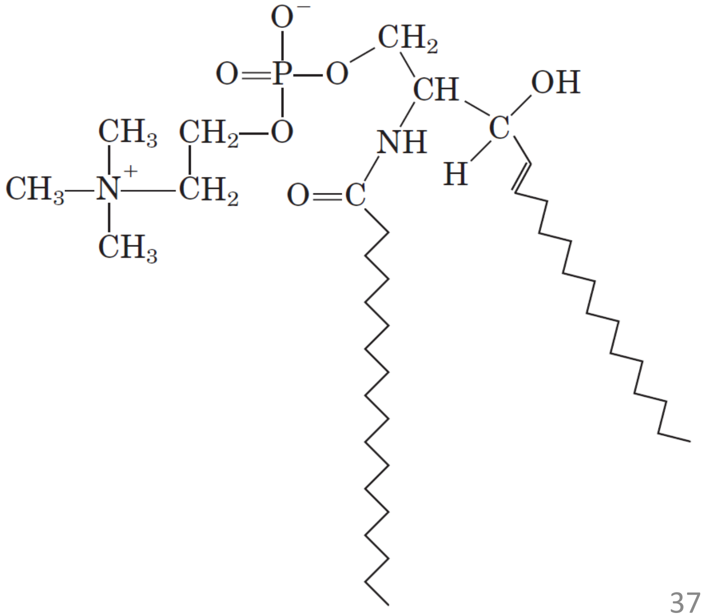
- There are three subclasses of sphingolipids, all derivatives of ceramide but differing in their head groups: **sphingomyelins**, **neutral (uncharged) glycolipids**, and **gangliosides**.

- Sphingomyelins contain phosphocholine or phosphoethanolamine as their polar head group and are therefore classified along with glycerophospholipids as phospholipids

Phosphatidylcholine



Sphingomyelin

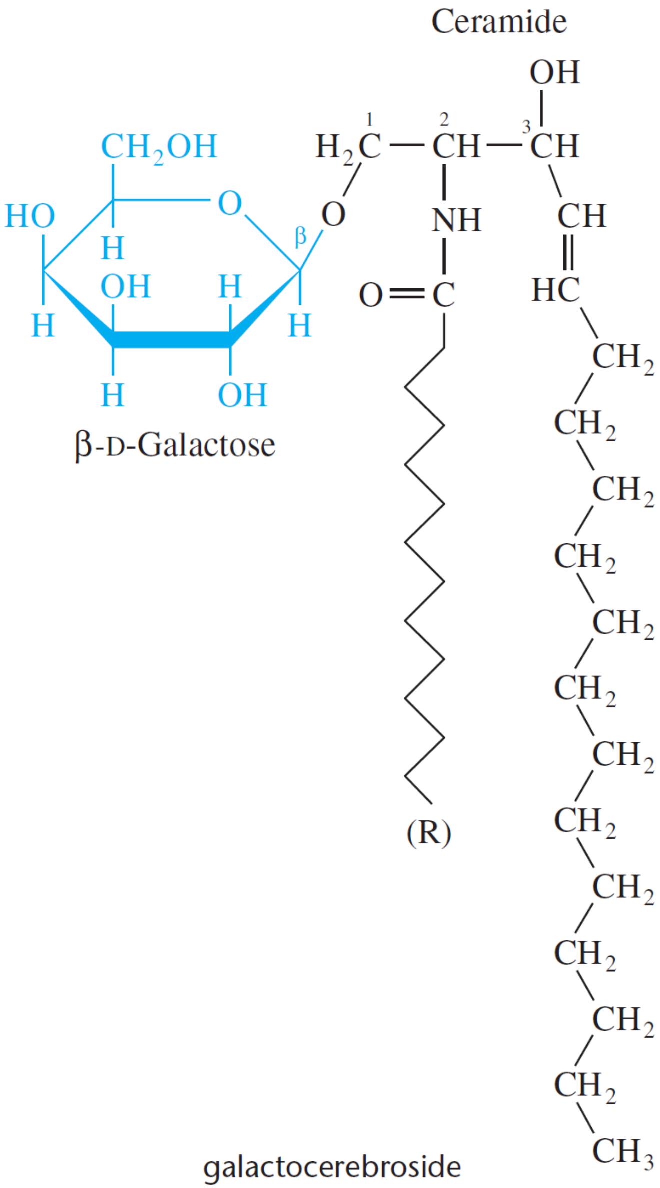


❖**Glycosphingolipids**, which occur largely in the outer face of plasma membranes, have head groups with one or more sugars connected directly to the —OH at C-1 of the ceramide moiety; they do not contain phosphate.

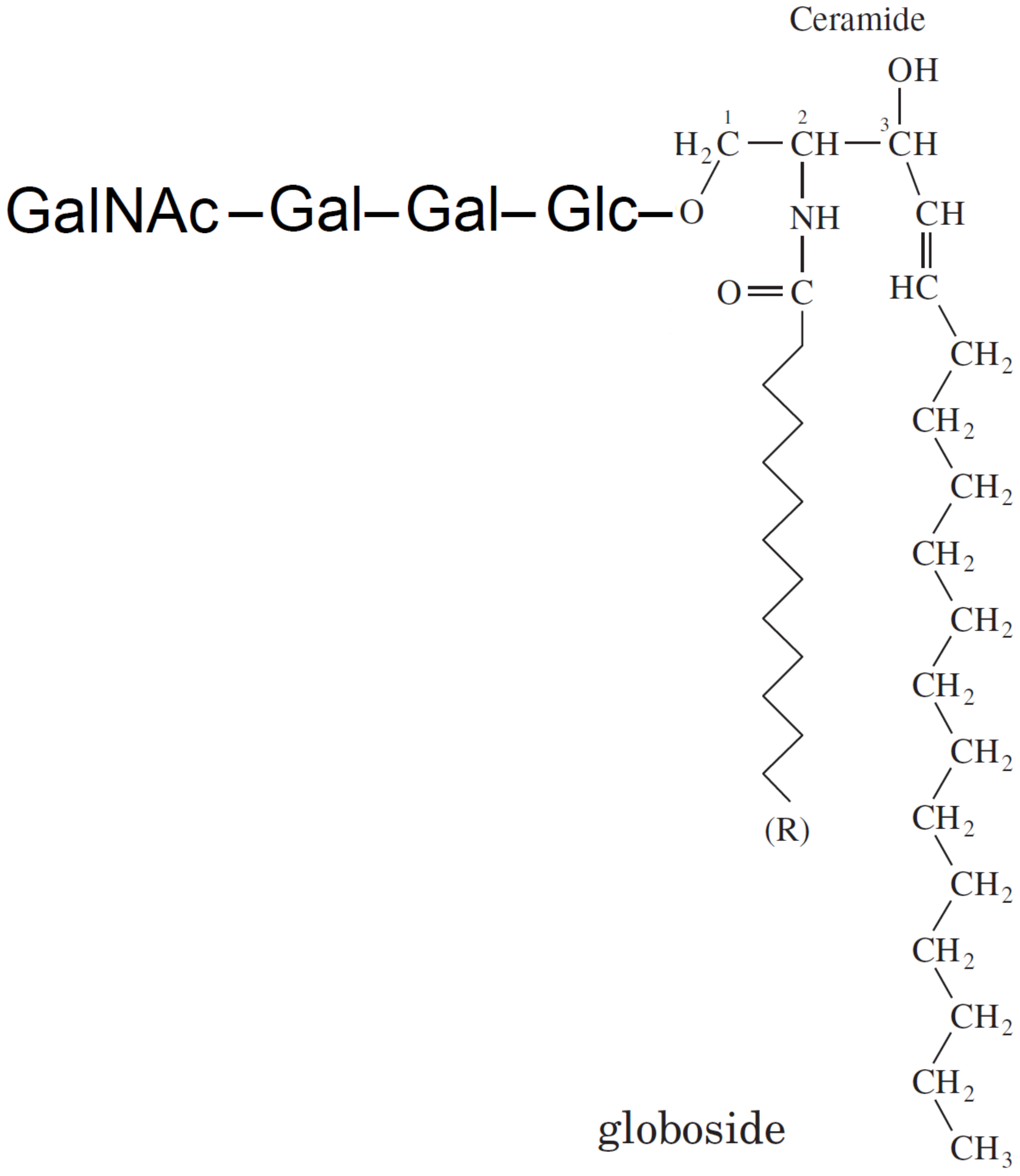
❖**Cerebrosides** have a single sugar linked to ceramide; those with galactose are characteristically found in the plasma membranes of cells in neural tissue, and those with glucose in the plasma membranes of cells in non-neural tissues.

❖**Globosides** are glycosphingolipids with two or more sugars, usually D-glucose, D-galactose, or N-acetyl-D-galactosamine.

❖Cerebrosides and globosides are sometimes called **neutral glycolipids**, as they have no charge at pH 7.



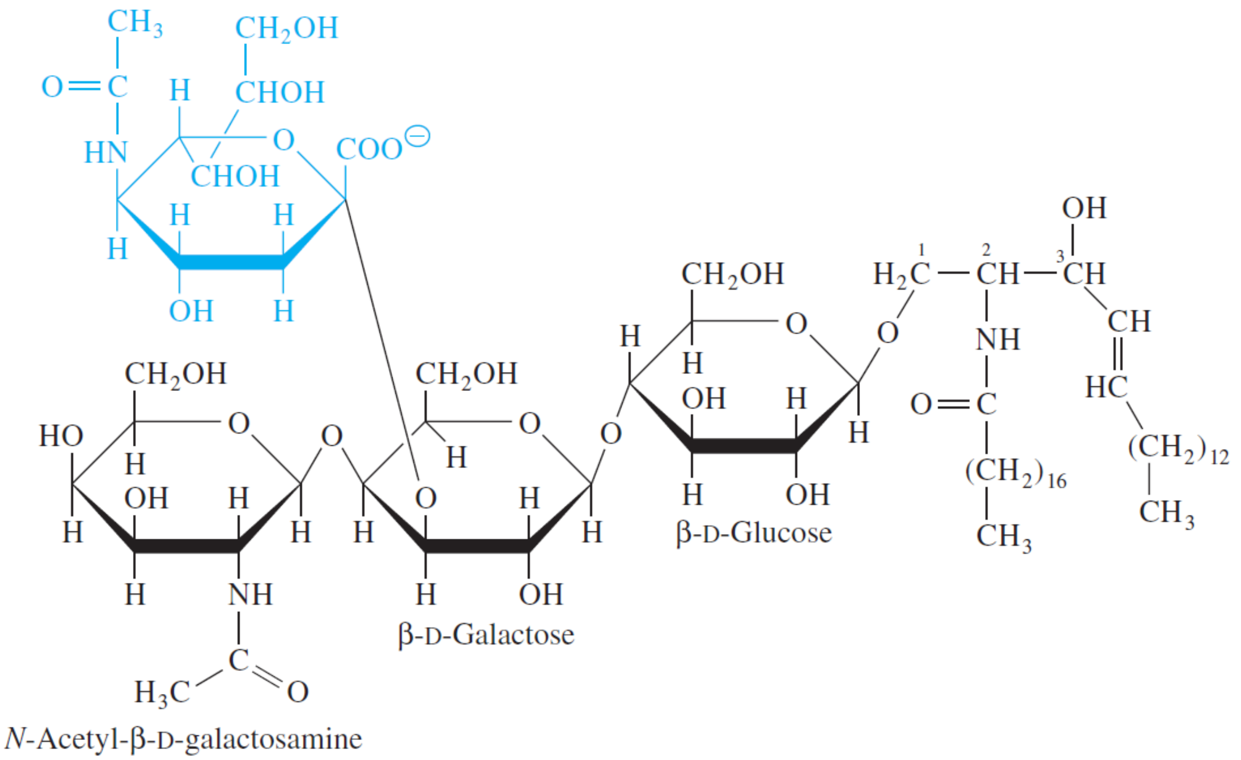
galactocerebroside

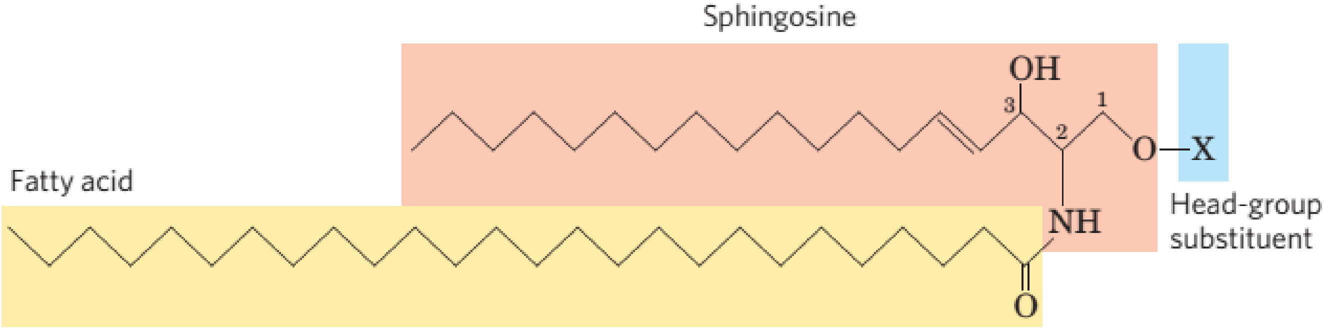


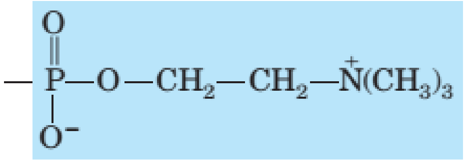
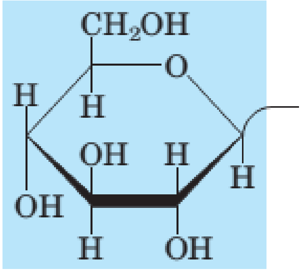
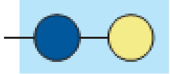
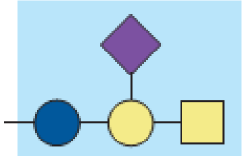
globoside

- **Gangliosides**, the most complex sphingolipids, have oligosaccharides as their polar head groups and one or more residues of N-acetylneuraminic acid (Neu5Ac), a sialic acid (often simply called “sialic acid”), at the termini.

- Sialic acid gives gangliosides the negative charge at pH 7 that distinguishes them from globosides.





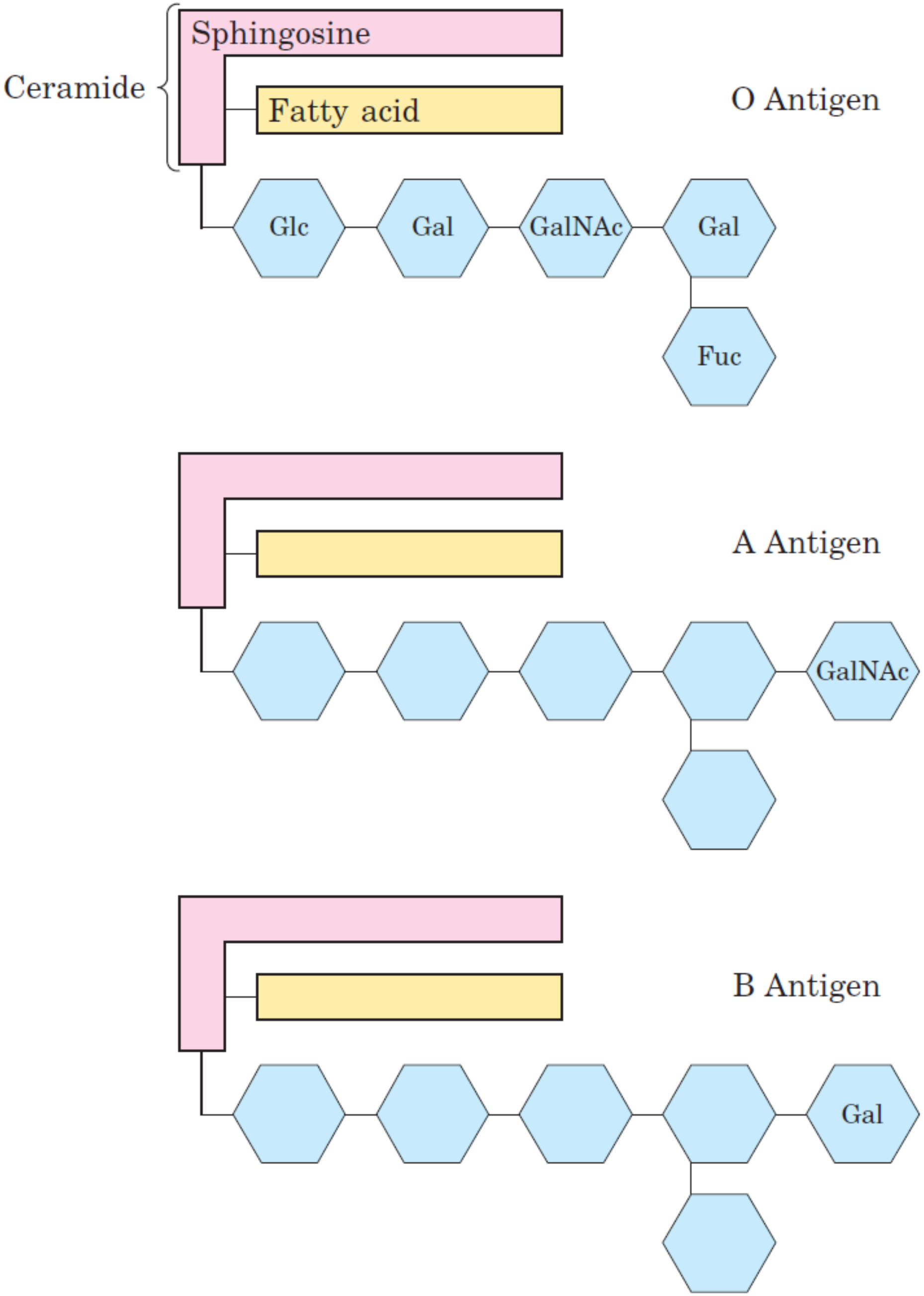
Name of sphingolipid	Name of X—O	Formula of X
Ceramide	—	$-\mathrm{H}$
Sphingomyelin	Phosphocholine	 $-\mathrm{P}(=\mathrm{O})(\mathrm{O}^-)-\mathrm{O}-\mathrm{CH_2}-\mathrm{CH_2}-\overset{+}{\mathrm{N}}(\mathrm{CH_3})_3$
Neutral glycolipids Glucosylcerebroside	Glucose	
Lactosylceramide (a globoside)	Di-, tri-, or tetrasaccharide	
Ganglioside GM2	Complex oligosaccharide	

- In humans, at least 60 different sphingolipids have been identified in cellular membranes.

- Many of these are especially prominent in the plasma membranes of neurons, and some are clearly recognition sites on the cell surface, but a specific function for only a few sphingolipids has been discovered thus far.

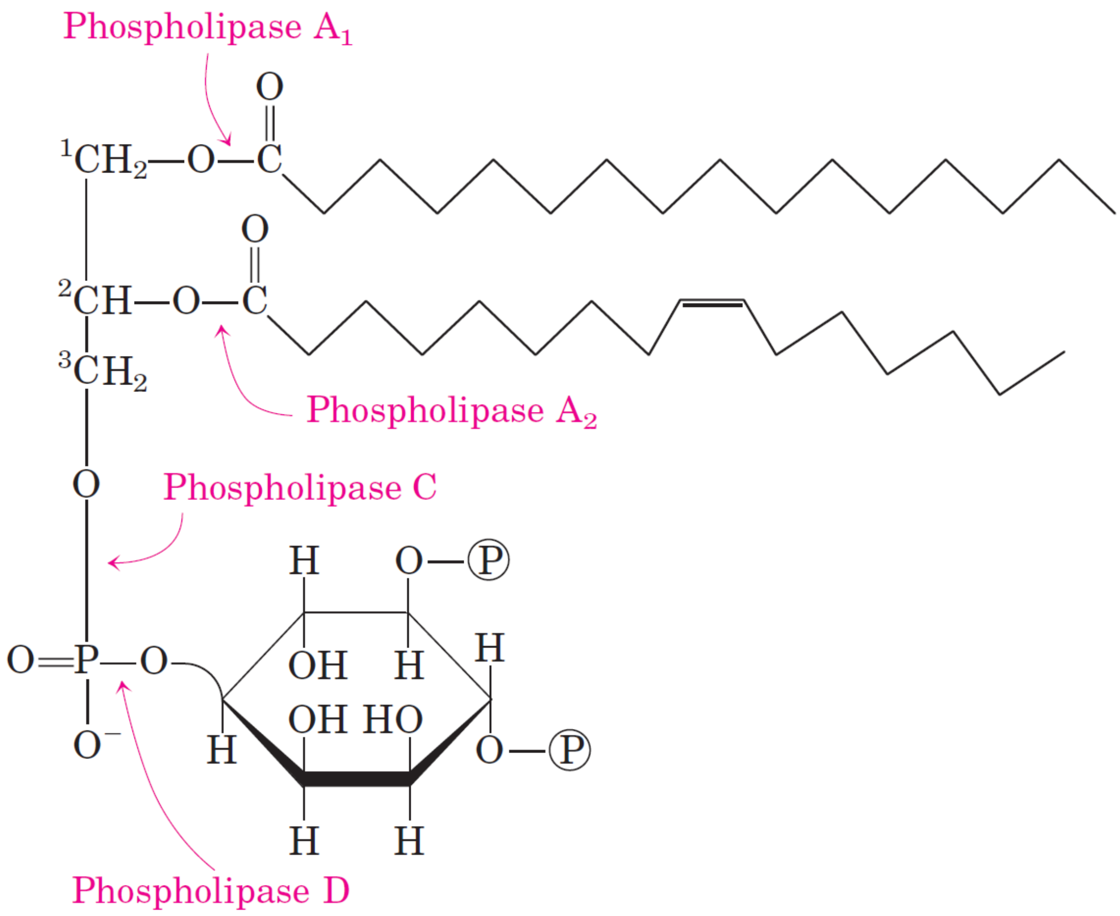
- The carbohydrate moieties of certain sphingolipids define the human blood groups and therefore determine the type of blood that individuals can safely receive in blood transfusions.

- Gangliosides are concentrated in the outer surface of cells, where they present points of recognition for extracellular molecules or surfaces of neighboring cells.


Ceramide
Sphingosine
Fatty acid
O Antigen
Glc
Gal
GalNAc
Gal
Fuc
A Antigen
GalNAc
B Antigen
Gal

- Most cells continually degrade and replace their membrane lipids.

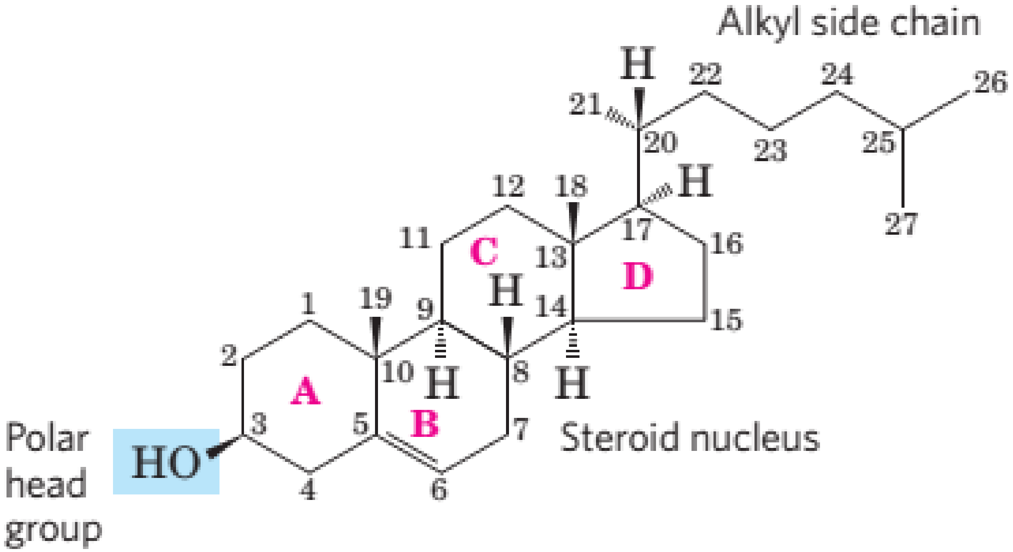
- For each hydrolyzable bond in a glycerophospholipid, there is a specific hydrolytic enzyme in the lysosome.



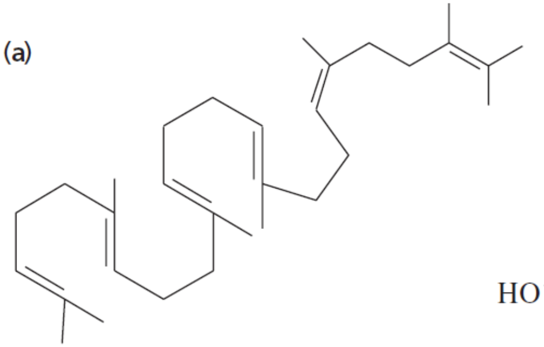
Sterols

- Sterols are structural lipids present in the membranes of most eukaryotic cells.

- The characteristic structure of this fifth group of membrane lipids is the steroid nucleus, consisting of four fused rings, three with six carbons and one with five (cyclopentanoperhydrophenantrene).

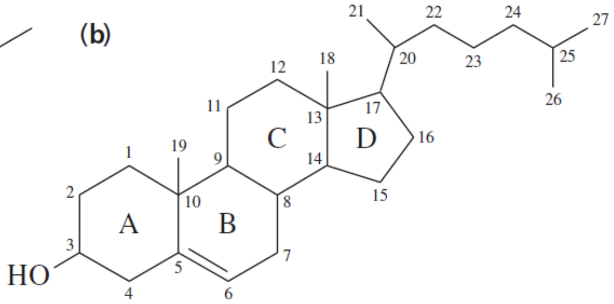


(a)



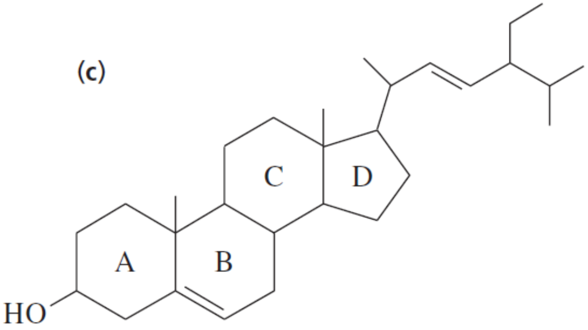
Squalene

(b)



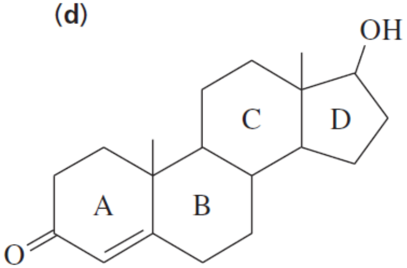
Cholesterol

(c)



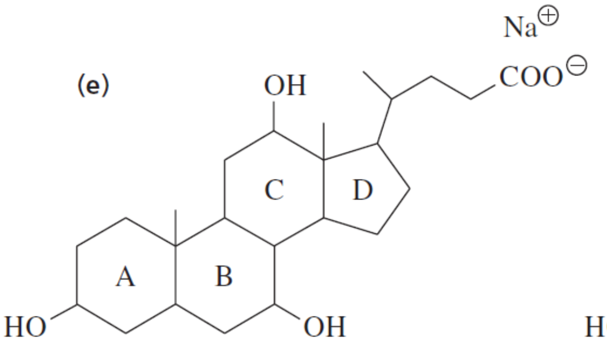
Stigmasterol
(a plant sterol)

(d)



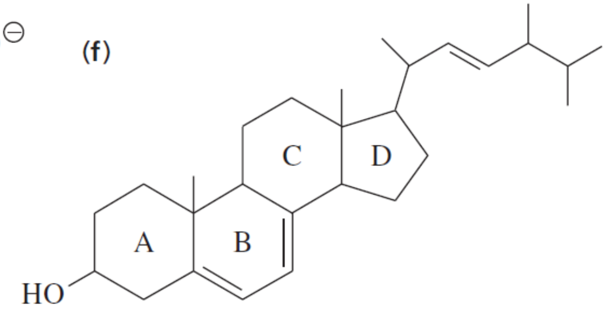
Testosterone
(a steroid hormone)

(e)



Sodium cholate
(a bile salt)

(f)



Ergosterol
(a sterol from fungi and yeast)

❖The steroid nucleus is almost planar and is relatively rigid; the fused rings do not allow rotation about C-C bonds.

❖**Cholesterol**, the major sterol in animal tissues, is amphipathic, with a polar head group (the hydroxyl group at C-3) and a nonpolar hydrocarbon body (the steroid nucleus and the hydrocarbon side chain at C-17), about as long as a 16-carbon fatty acid in its extended form.

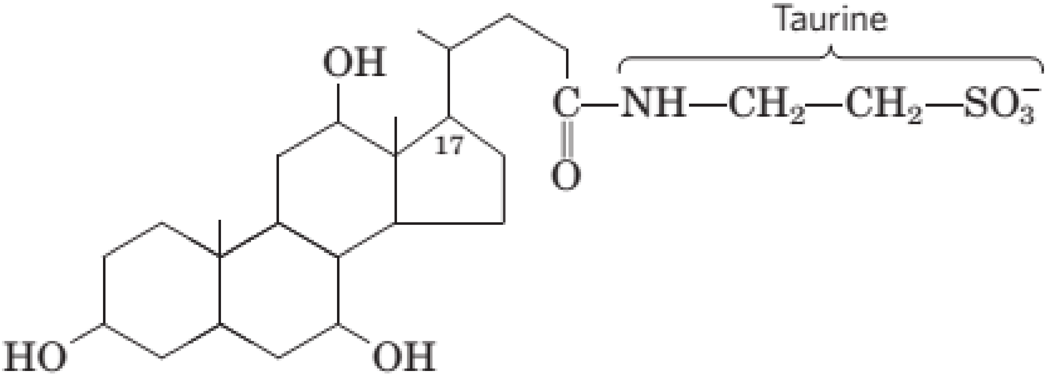
❖Similar sterols are found in other eukaryotes: stigmasterol in plants and ergosterol in fungi, for example.

❖Bacteria cannot synthesize sterols; a few bacterial species, however, can incorporate exogenous sterols into their membranes

- In addition to their roles as membrane constituents, the sterols serve as precursors for a variety of products with specific biological activities.

- Steroid hormones, for example, are potent biological signals that regulate gene expression.

- **Bile acids** are polar derivatives of cholesterol that act as detergents in the intestine, emulsifying dietary fats to make them more readily accessible to digestive lipases.



Taurocholic acid
(a bile acid)

Lipids as Signals, Cofactors, and Pigments

❖The two functional classes of lipids considered thus far (storage lipids and structural lipids) are major cellular components; membrane lipids make up 5% to 10% of the dry mass of most cells, and storage lipids more than 80% of the mass of an adipocyte.

❖With some important exceptions, these lipids play a passive role in the cell; lipid fuels are stored until oxidized by enzymes, and membrane lipids form impermeable barriers around cells and cellular compartments.

❖Another group of lipids, present in much smaller amounts, have active roles in the metabolic traffic as metabolites and messengers.

❖Some serve as potent signals—as hormones, carried in the blood from one tissue to another, or as intracellular messengers generated in response to an extracellular signal (hormone or growth factor).

- Others function as enzyme cofactors in electron-transfer reactions in chloroplasts and mitochondria, or in the transfer of sugar moieties in a variety of glycosylation reactions.

- A third group consists of lipids with a system of conjugated double bonds: pigment molecules that absorb visible light.

- Some of these act as light-capturing pigments in vision and photosynthesis; others produce natural colorations, such as the orange of pumpkins and carrots and the yellow of canary feathers.

- Finally, a very large group of volatile lipids produced in plants serve as signals that pass through the air, allowing plants to communicate with each other, and to invite animal friends and deter foes.

❖Phosphatidylinositol and its phosphorylated derivatives act at several levels to regulate cell structure and metabolism.

❖Membrane sphingolipids also can serve as sources of intracellular messengers.

❖Both ceramide and sphingomyelin are potent regulators of protein kinases.

❖Ceramide or its derivatives are involved in the regulation of cell division, differentiation, migration, and programmed cell death

- Eicosanoids are paracrine hormones, substances that act only on cells near the point of hormone synthesis instead of being transported in the blood to act on cells in other tissues or organs.

- These fatty acid derivatives have a variety of dramatic effects on vertebrate tissues.

- They are involved in reproductive function;
  - in the inflammation, fever, and pain associated with injury or disease;
  - in the formation of blood clots and the regulation of blood pressure;
  - in gastric acid secretion; and in various other processes important in human health or disease.

- All eicosanoids are derived from arachidonic acid (20:4($\Delta^{5,8,11,14}$)).

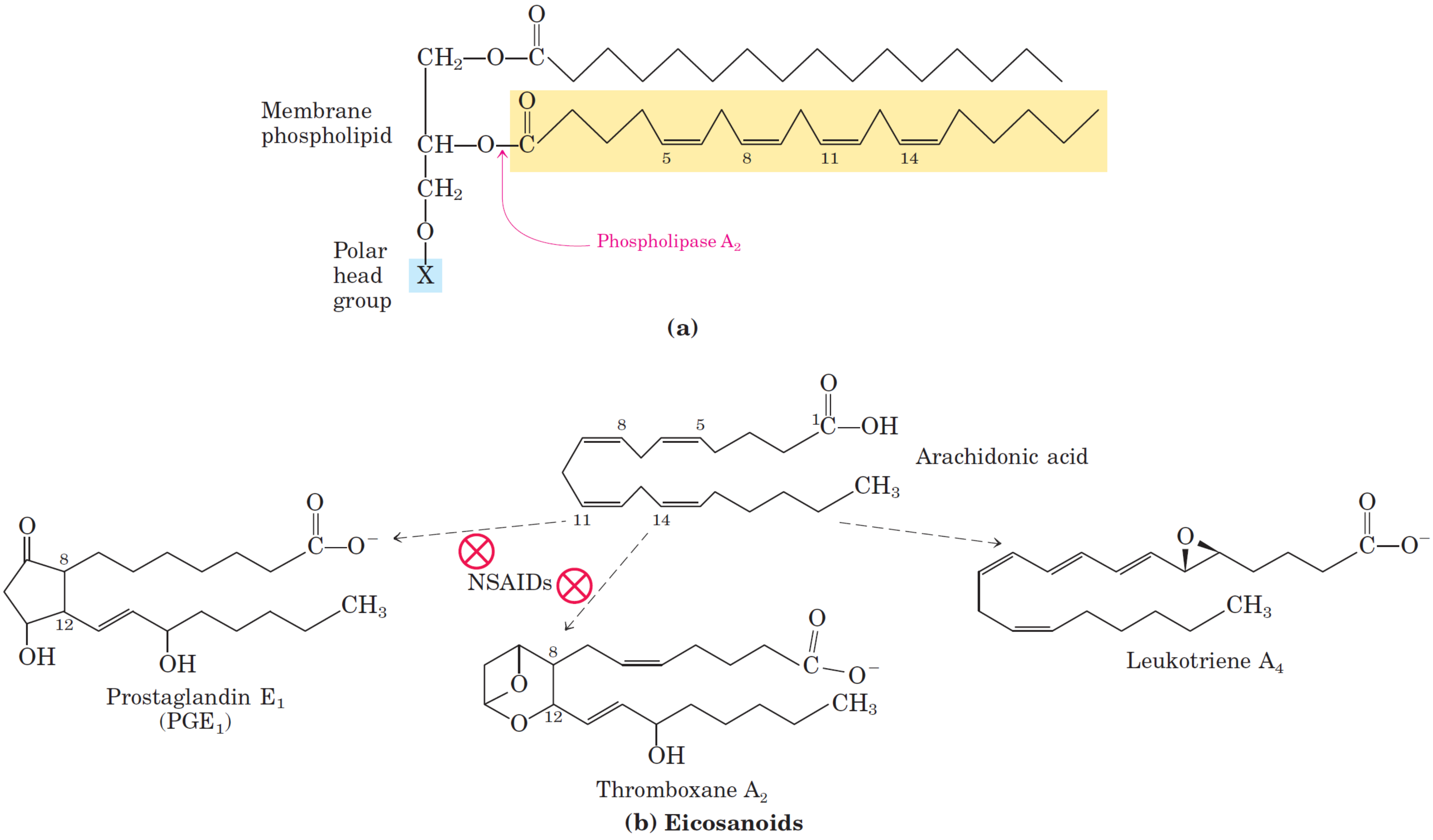
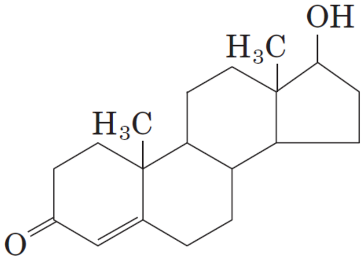


FIGURE 10–18 Arachidonic acid and some eicosanoid derivatives. (a) In response to hormonal signals, phospholipase A_2 cleaves arachidonic acid–containing membrane phospholipids to release arachidonic acid (arachidonate at pH 7), the precursor to various eicosanoids. **(b)** These compounds include prostaglandins such as PGE_1, in which C-8 and C-12 of arachidonate are joined to form the characteristic five-membered ring. In thromboxane A_2, the C-8 and C-12 are joined and an oxygen atom is added to form the six-membered ring. Leukotriene A_4 has a series of three conjugated double bonds. Nonsteroidal antiinflammatory drugs (NSAIDs) such as aspirin and ibuprofen block the formation of prostaglandins and thromboxanes from arachidonate by inhibiting the enzyme cyclooxygenase (prostaglandin H_2 synthase).

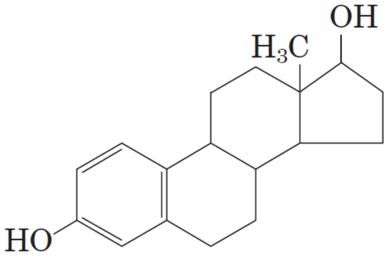
- Steroids are oxidized derivatives of sterols; they have the sterol nucleus but lack the alkyl chain attached to ring D of cholesterol, and they are more polar than cholesterol.

- Steroid hormones move through the bloodstream (on protein carriers) from their site of production to target tissues, where they enter cells, bind to highly specific receptor proteins in the nucleus, and trigger changes in gene expression and thus metabolism.

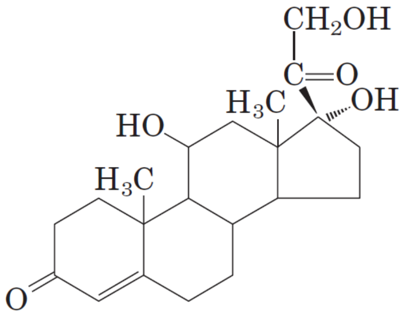
- The major groups of steroid hormones are the male and female sex hormones and the hormones produced by the adrenal cortex, cortisol and aldosterone



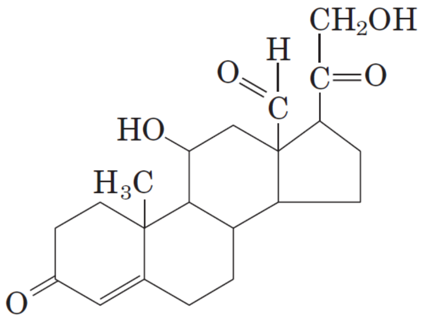
Testosterone



Estradiol



Cortisol

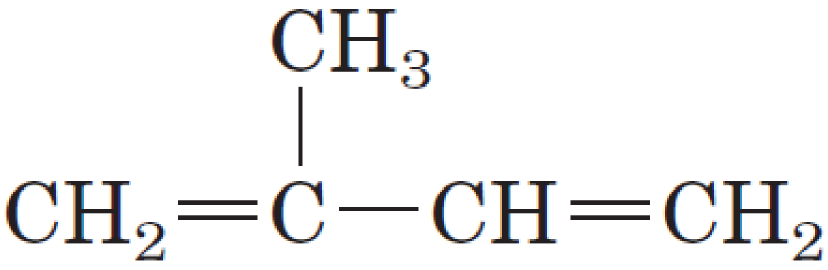


Aldosterone

- Plants produce literally thousands of different lipophilic compounds, volatile substances that are used to attract pollinators, to repel herbivores, to attract organisms that defend the plant against herbivores, and to communicate with other plants.

- Fat-soluble vitamins A, D, E, and K, all of which are isoprenoid compounds synthesized by the condensation of multiple isoprene units.

- Two of these (D and A) serve as hormone precursors.

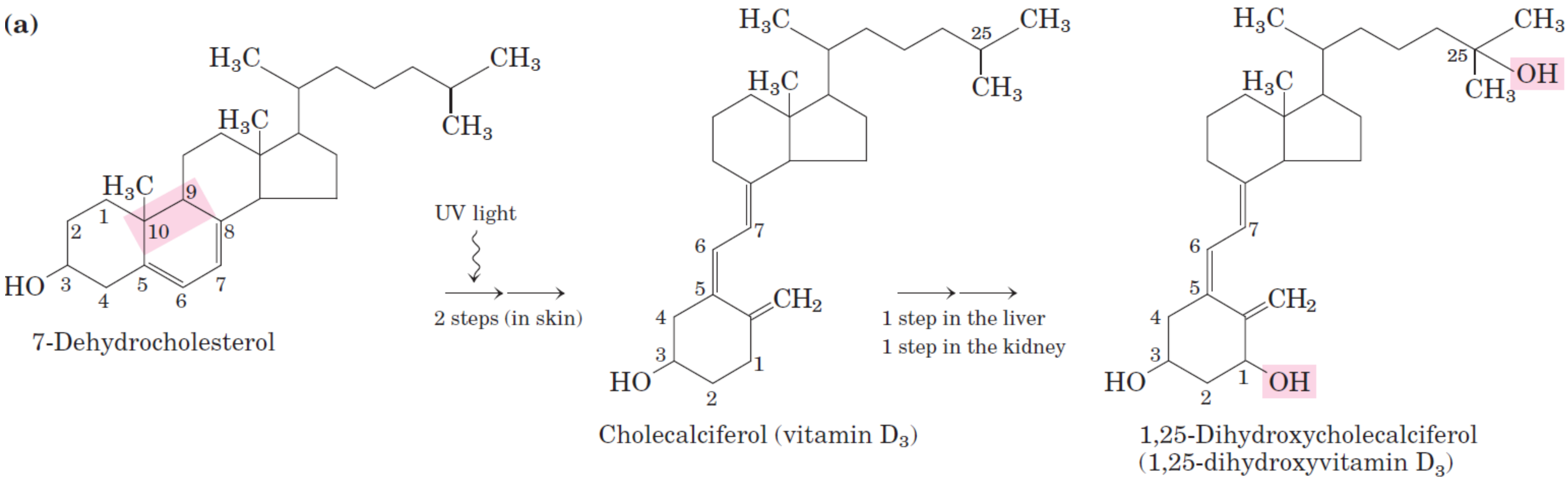


$$\mathrm{CH_2{=}\overset{\displaystyle CH_3}{\overset{|}{C}}{-}CH{=}CH_2}$$

Isoprene

- Vitamin D3, also called cholecalciferol, is normally formed in the skin from 7-dehydrocholesterol in a photochemical reaction driven by the UV component of sunlight.

- Vitamin D3 is not itself biologically active, but it is converted by enzymes in the liver and kidney to 1,25-dihydroxyvitamin D3 (calcitriol), a hormone that regulates calcium uptake in the intestine and calcium levels in kidney and bone.

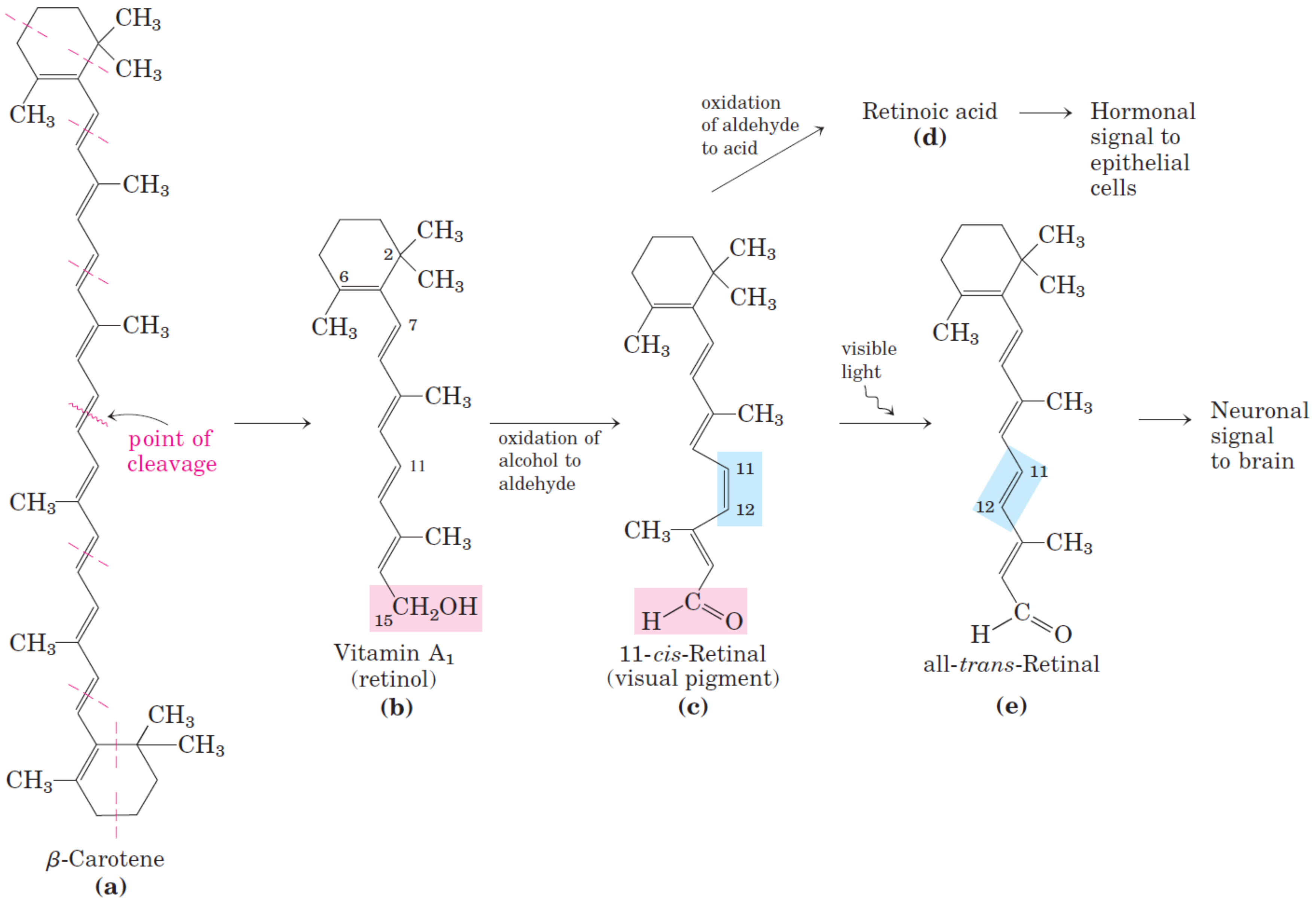


- Vitamin A (retinol), in its various forms, functions as a hormone and as the visual pigment of the vertebrate eye.

- Acting through receptor proteins in the cell nucleus, the vitamin A derivative retinoic acid regulates gene expression in the development of epithelial tissue, including skin.

- Retinoic acid is the active ingredient in the drug tretinoin (Retin-A), used in the treatment of severe acne and wrinkled skin.

- Retinal, another vitamin A derivative, is the pigment that initiates the response of rod and cone cells of the retina to light, producing a neuronal signal to the brain.



β-Carotene
(a)

Vitamin A$_1$
(retinol)
(b)

oxidation of alcohol to aldehyde

11-*cis*-Retinal
(visual pigment)
(c)

oxidation of aldehyde to acid

Retinoic acid
(d)

Hormonal signal to epithelial cells

visible light

all-*trans*-Retinal
(e)

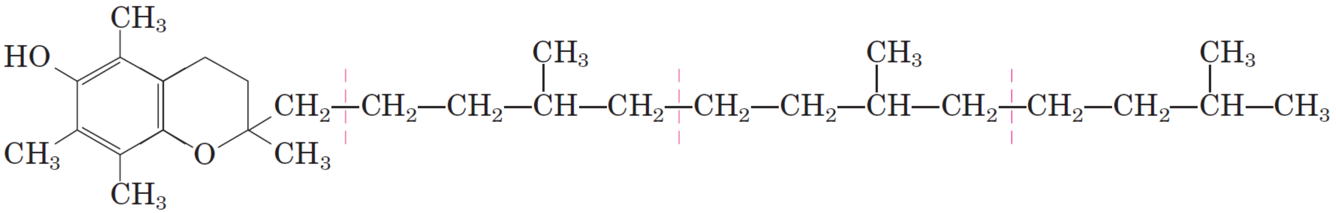
Neuronal signal to brain

- Vitamin E is the collective name for a group of closely related lipids called tocopherols, all of which contain a substituted aromatic ring and a long isoprenoid side chain.

- Because they are hydrophobic, tocopherols associate with cell membranes, lipid deposits, and lipoproteins in the blood.

- Tocopherols are biological antioxidants.

- The aromatic ring reacts with and destroys the most reactive forms of oxygen radicals and other free radicals, protecting unsaturated fatty acids from oxidation and preventing oxidative damage to membrane lipids, which can cause cell fragility.

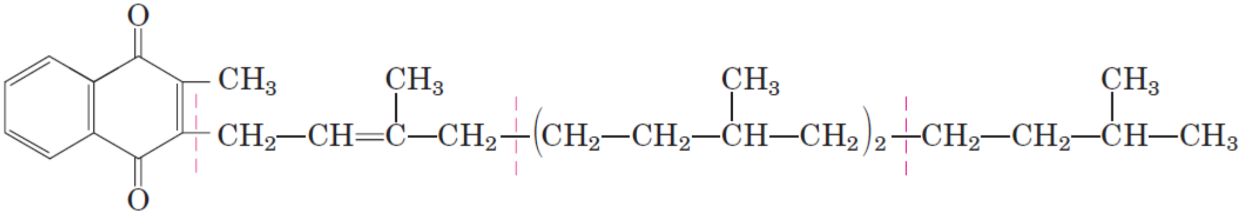


(a)
Vitamin E: an antioxidant

- The aromatic ring of vitamin K undergoes a cycle of oxidation and reduction during the formation of active prothrombin, a blood plasma protein essential in blood clotting.

- Prothrombin is a proteolytic enzyme that splits peptide bonds in the blood protein fibrinogen to convert it to fibrin, the insoluble fibrous protein that holds blood clots together

(b)
Vitamin K_1: a blood-clotting cofactor (phylloquinone)



Biological Membranes and Transport

- Cells are separated from the external world by a thin, fragile structure called the plasma membrane that is only 5 to 10 nm wide.

- 1. Compartmentalization. Membranes are continuous, unbroken sheets and, as such, inevitably enclose compartments.

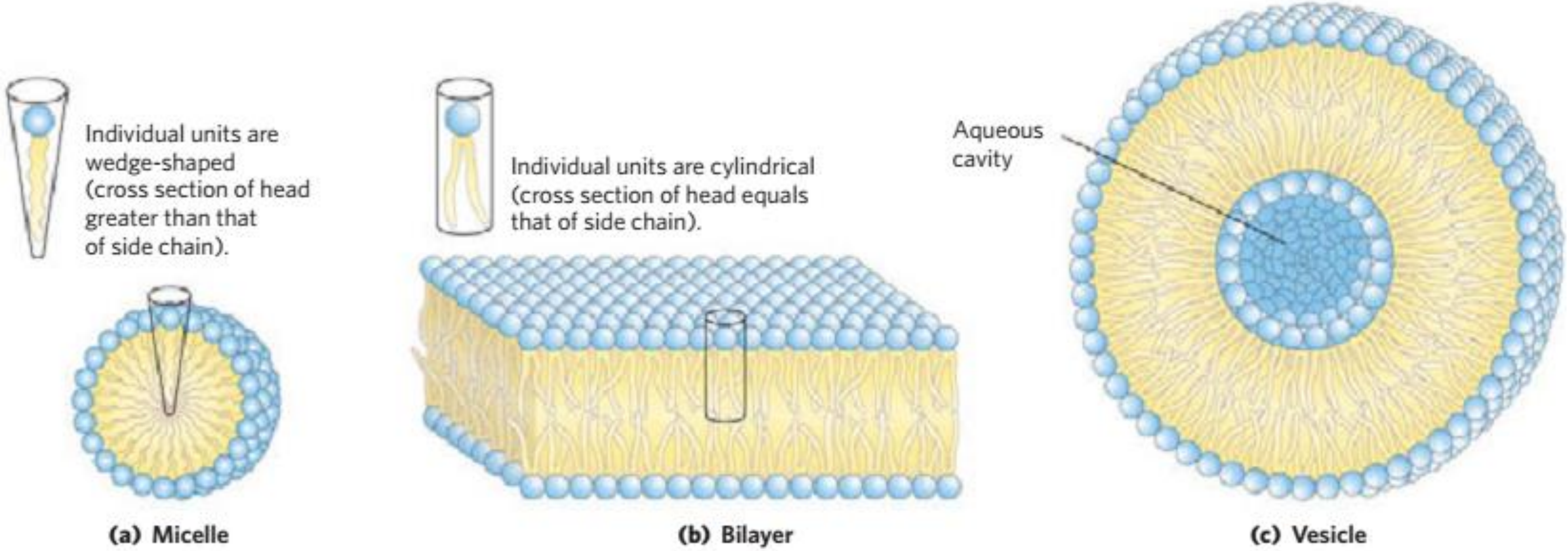
- 2. Scaffold for biochemical activities. Membranes not only enclose compartments but are also a distinct compartment themselves.

- 3. Providing a selectively permeable barrier. Membranes prevent the unrestricted exchange of molecules from one side to the other.

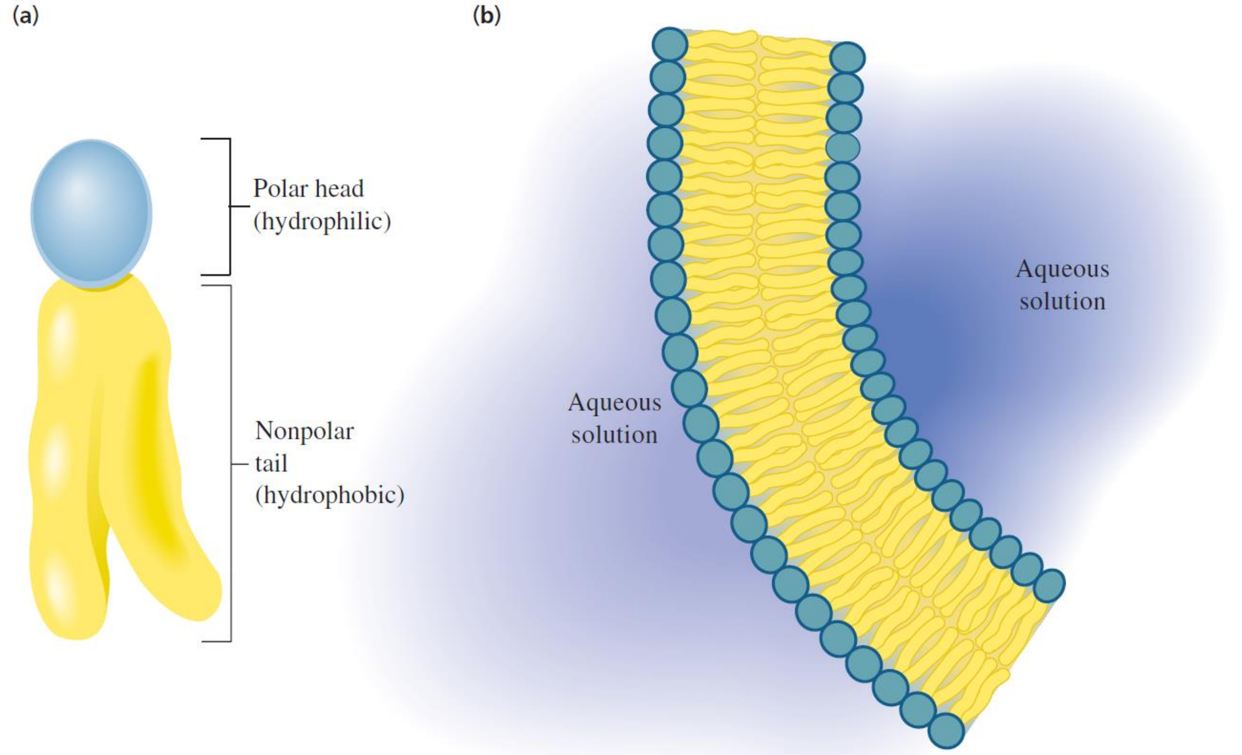
- 4. Transporting solutes.

- 5. Responding to external stimuli.

- 6. Intercellular interaction.



(a) Micelle **(b) Bilayer** **(c) Vesicle**



- Experiments conducted in the late 1960s led to a new concept of membrane structure, as detailed in the fluid mosaic model proposed in 1972 by S. Jonathan Singer and Garth Nicolson of the University of California, San Diego.

- In the **fluid-mosaic model**, which has served as the “central dogma” of membrane biology for more than three decades, the lipid bilayer remains the core of the membrane, but attention is focused on the physical state of the lipid.

- Unlike previous models, the bilayer of a fluid-mosaic membrane is present in a fluid state, and individual lipid molecules can move laterally within the plane of the membrane.

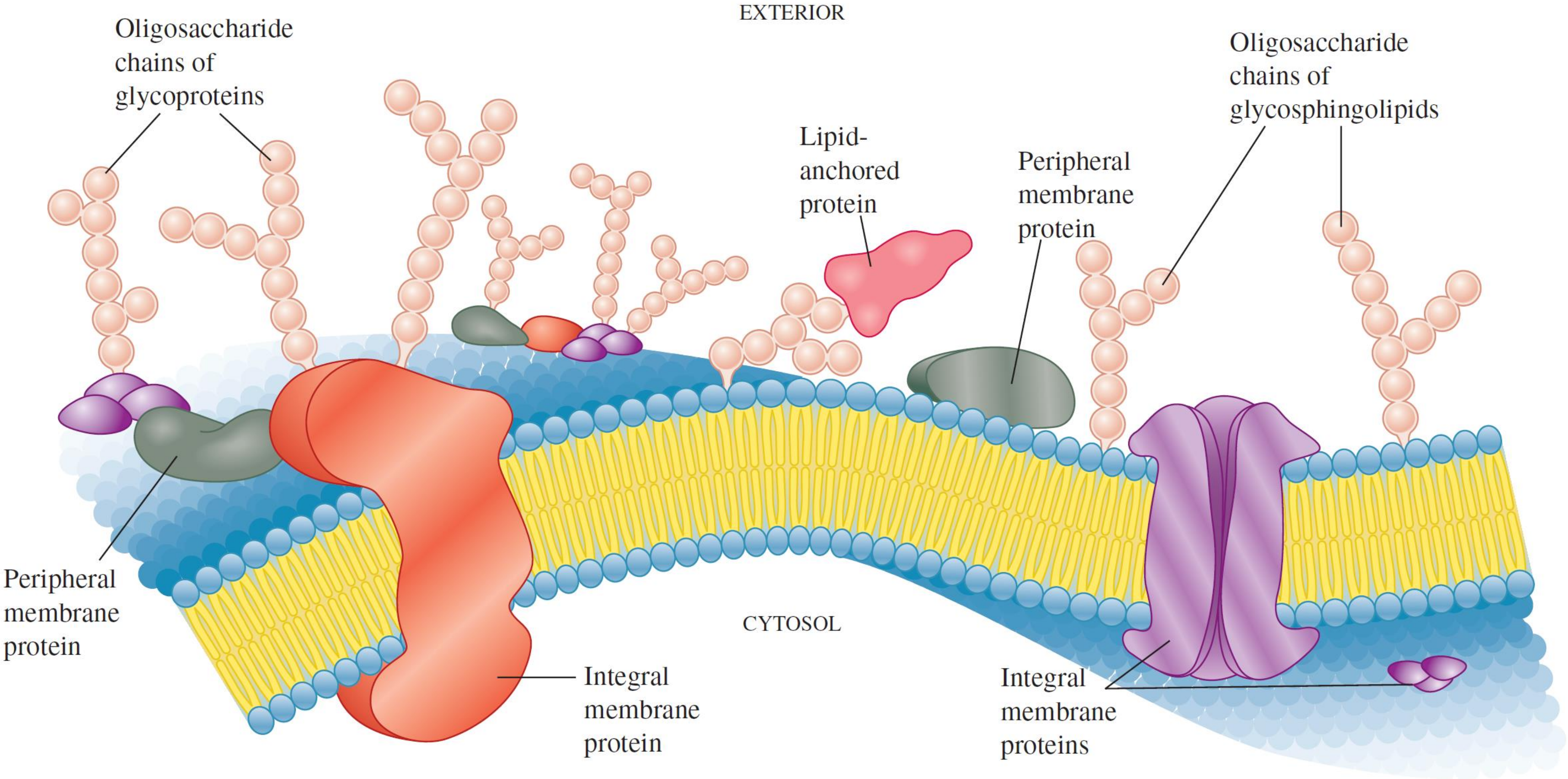
- The structure and arrangement of membrane proteins in the fluid-mosaic model differ from those of previous models in that they occur as a “mosaic” of discontinuous particles that penetrate the lipid sheet.

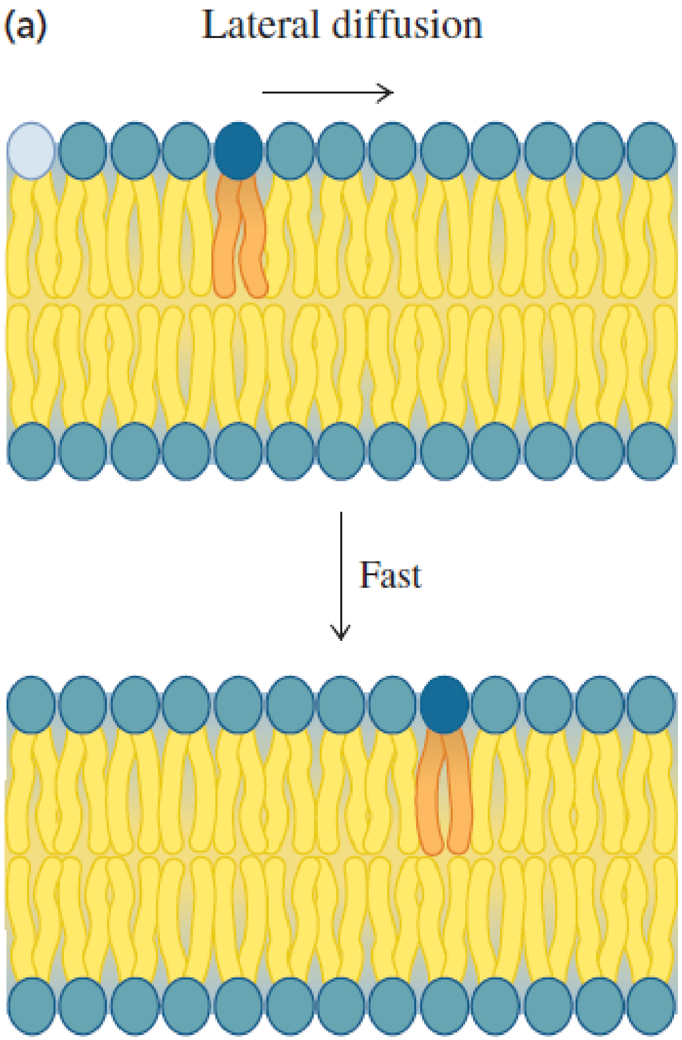
❖Most importantly, the fluid-mosaic model presents cellular membranes as dynamic structures in which the components are mobile and capable of coming together to engage in various types of transient or semipermanent interactions.

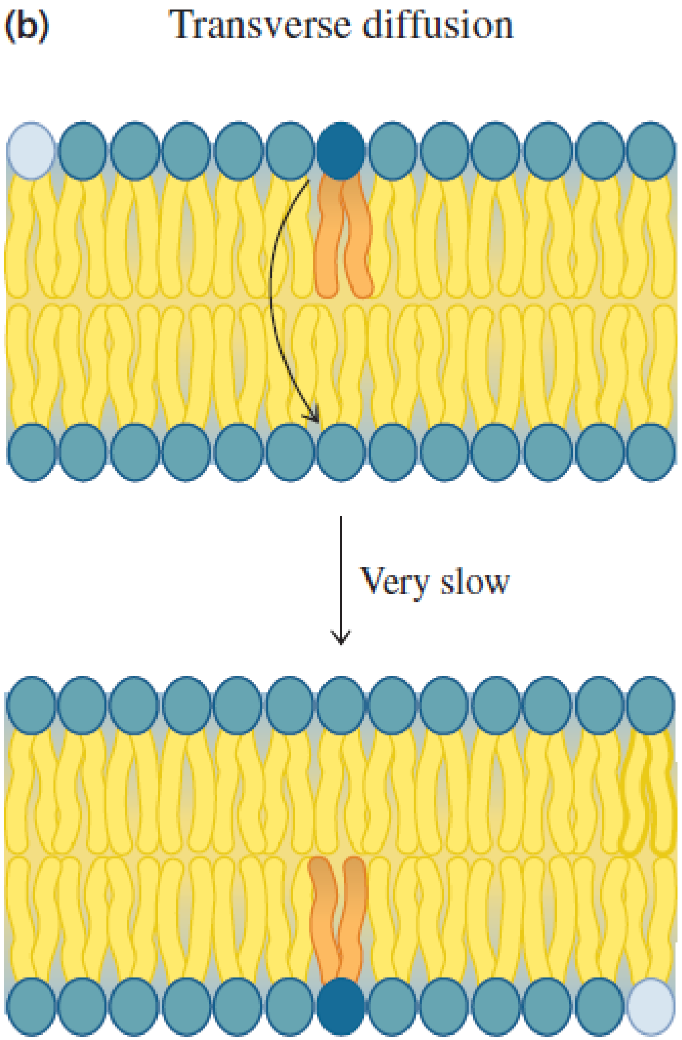
❖Membranes are lipid–protein assemblies in which the components are held together in a thin sheet by noncovalent bonds.

❖The ratio of lipid to protein in a membrane varies, depending on the type of cellular membrane (plasma vs. endoplasmic reticulum vs. Golgi), the type of organism (bacterium vs. plant vs. animal), and the type of cell (cartilage vs. muscle vs. liver).

❖Membranes also contain carbohydrates, which are attached to the lipids and proteins


EXTERIOR
Oligosaccharide chains of glycoproteins
Oligosaccharide chains of glycosphingolipids
Lipid-anchored protein
Peripheral membrane protein
Peripheral membrane protein
CYTOSOL
Integral membrane protein
Integral membrane proteins

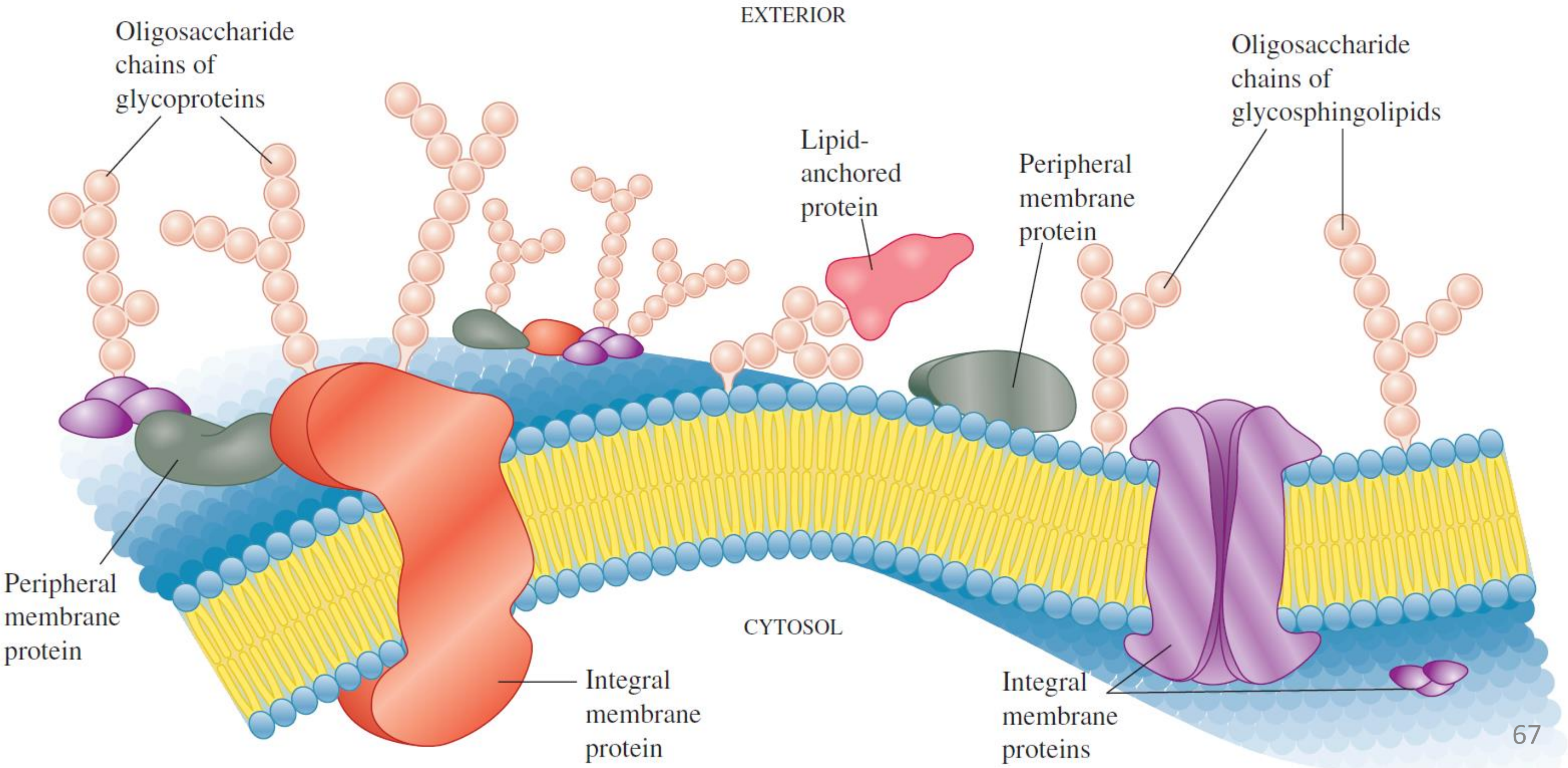

(a)
Lateral diffusion
Fast

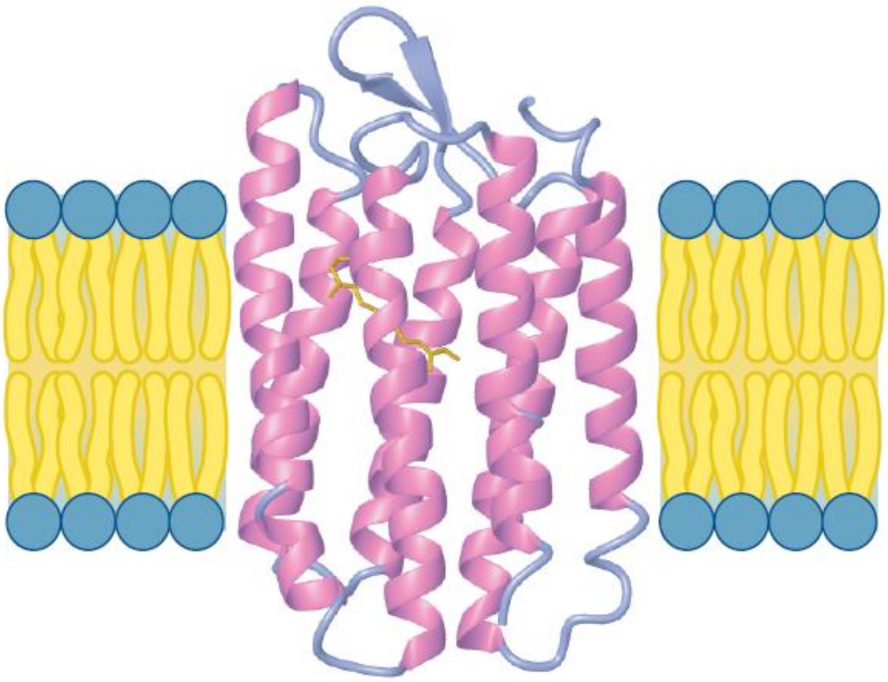

(b)
Transverse diffusion
Very slow

Membrane Proteins

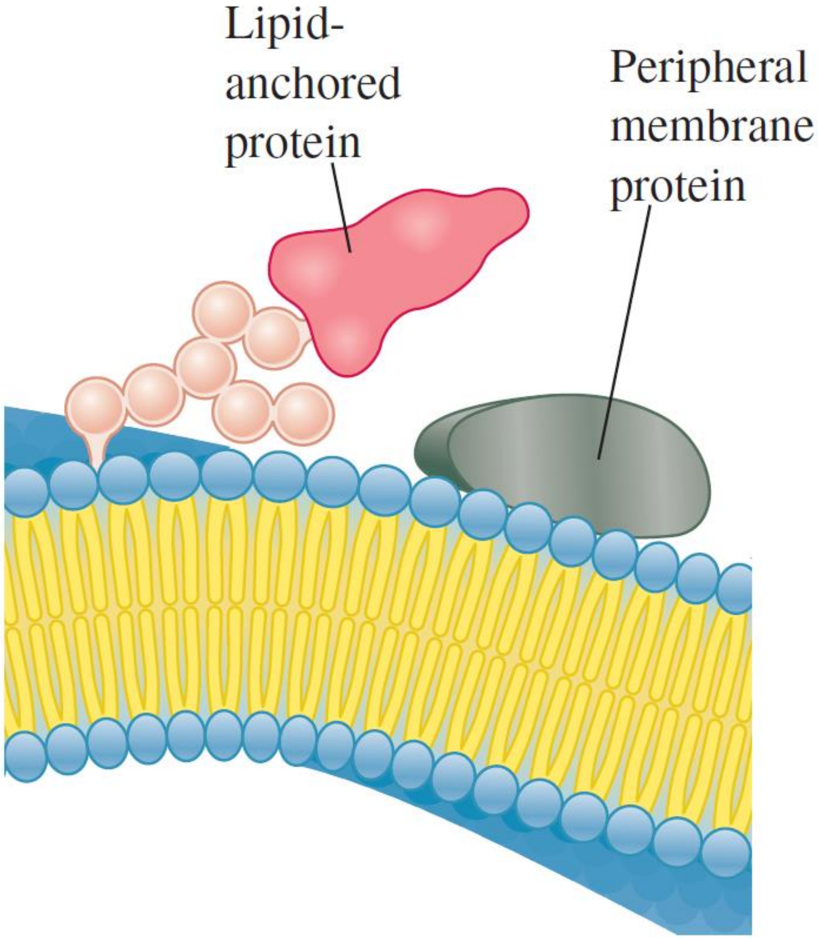
❖Depending on the cell type and the particular organelle within that cell, a membrane may contain hundreds of different proteins.

❖Membrane proteins can be grouped into three distinct classes distinguished by the intimacy of their relationship to the lipid bilayer.





Integral membrane proteins



❖Four basic mechanisms by which solute molecules move across membranes. The relative sizes of the letters indicate the directions of the concentration gradients.

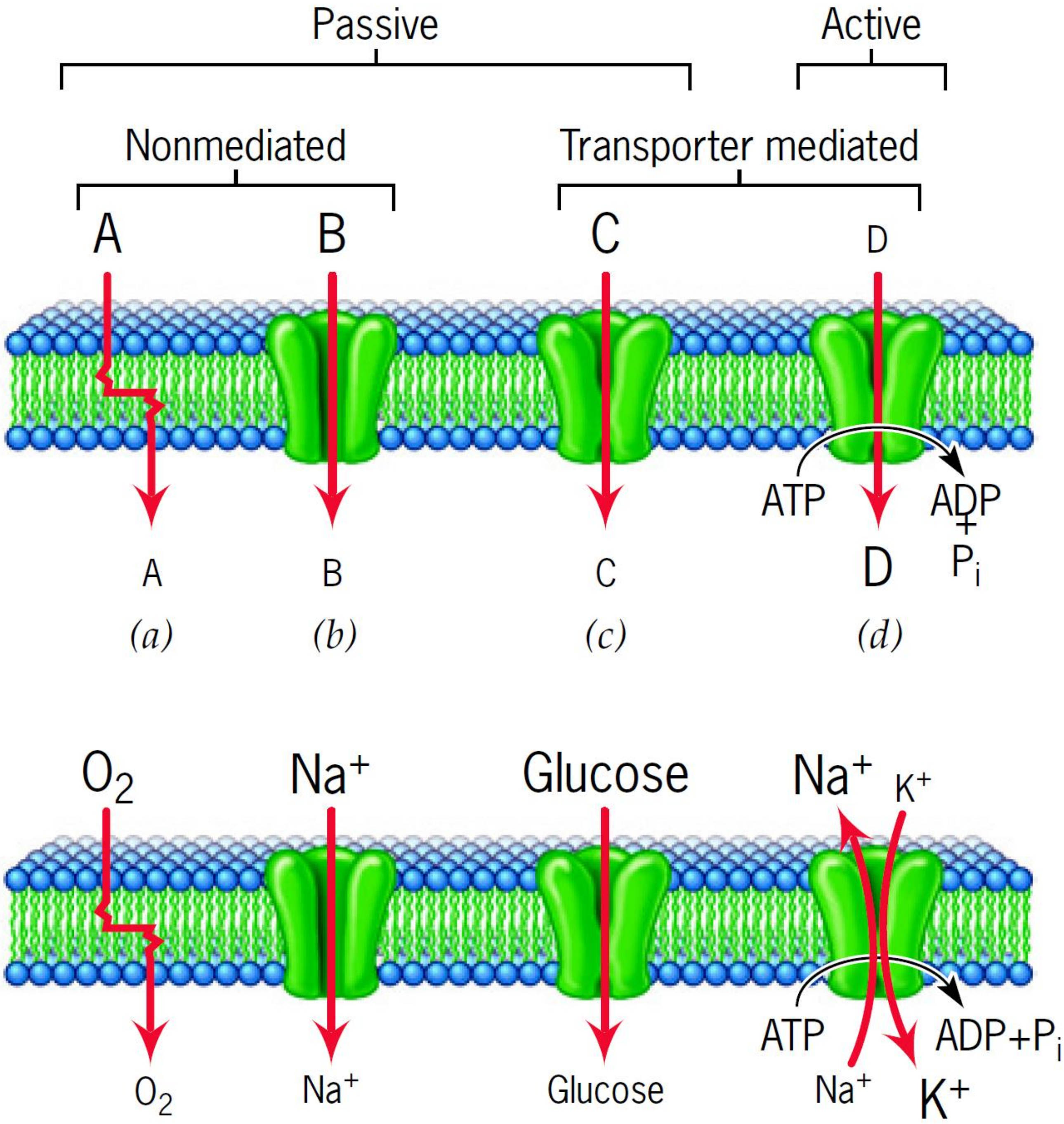
❖(a) Simple diffusion through the bilayer, which always proceeds from high to low concentration.

❖(b) Simple diffusion through an aqueous channel formed within an integral membrane protein or a cluster of such proteins. As in a, movement is always down a concentration gradient.

❖(c) Facilitated diffusion in which solute molecules bind specifically to a membrane protein carrier (a facilitative transporter). As in a and b, movement is always from high to low concentration.

❖(d) Active transport by means of a protein transporter with a specific binding site that undergoes a change in affinity driven with energy released by an exergonic process, such as ATP hydrolysis. Movement occurs against a concentration gradient.

❖(e) Examples of each type of mechanism as it occurs in the membrane of an erythrocyte.


Passive
Active
Nonmediated
Transporter mediated
A
B
C
D
ATP
ADP
+
P_i
A
B
C
D
(a)
(b)
(c)
(d)
O_2
Na^+
Glucose
Na^+
K^+
ATP
ADP+P_i
O_2
Na^+
Glucose
Na^+
K^+

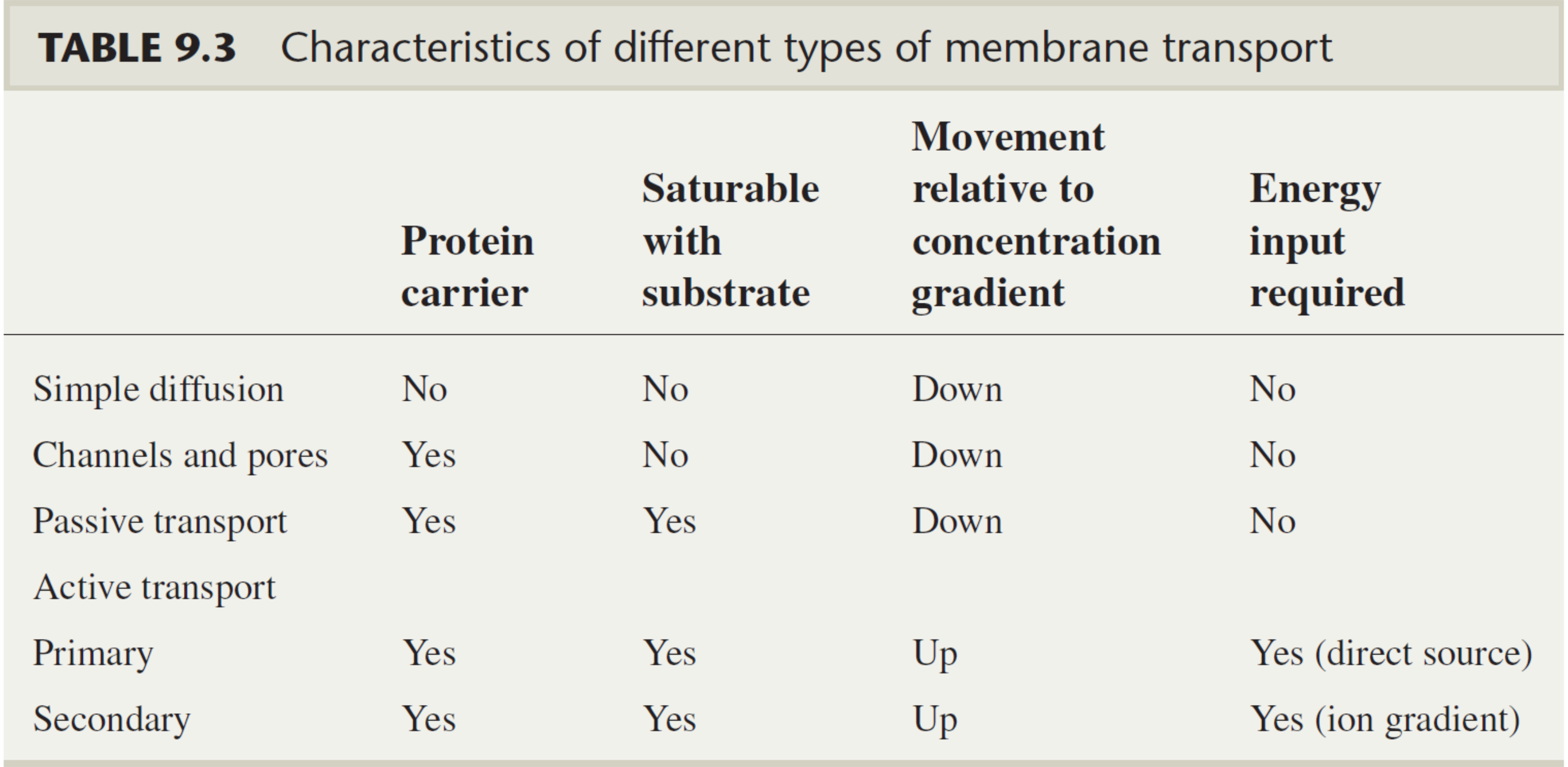
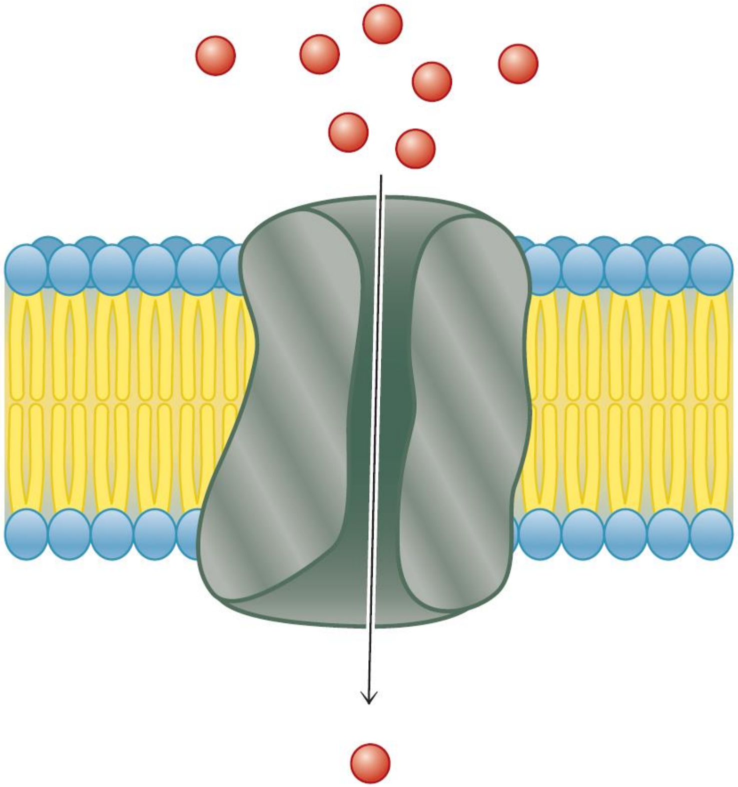
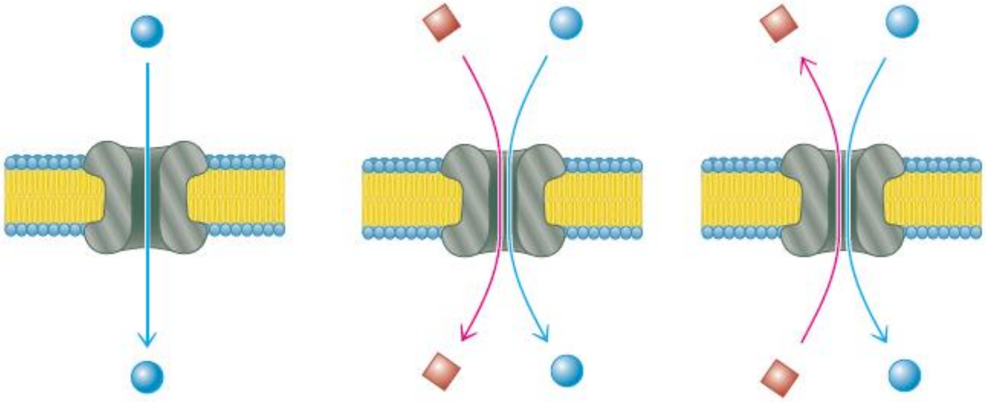


TABLE 9.3 Characteristics of different types of membrane transport

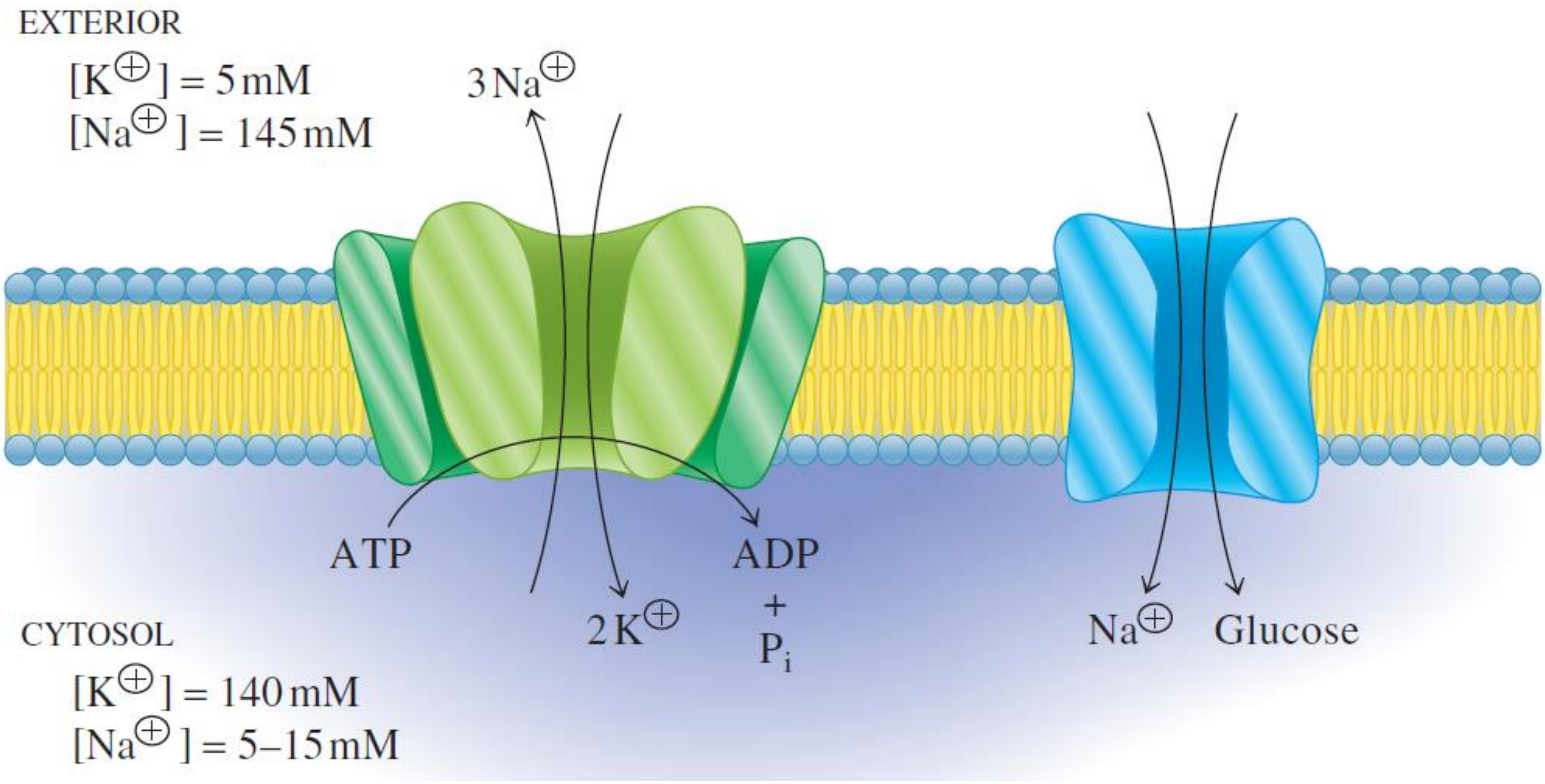
	Protein carrier	Saturable with substrate	Movement relative to concentration gradient	Energy input required
Simple diffusion	No	No	Down	No
Channels and pores	Yes	No	Down	No
Passive transport	Yes	Yes	Down	No
Active transport				
Primary	Yes	Yes	Up	Yes (direct source)
Secondary	Yes	Yes	Up	Yes (ion gradient)





Uniport. Symport. Antiport.

Types of passive and active transport.



EXTERIOR

$[K^{\oplus}] = 5\,\text{mM}$

$[Na^{\oplus}] = 145\,\text{mM}$

$3\,Na^{\oplus}$

ATP

$2\,K^{\oplus}$

ADP + P_i

$Na^{\oplus}$ Glucose

CYTOSOL

$[K^{\oplus}] = 140\,\text{mM}$

$[Na^{\oplus}] = 5\text{–}15\,\text{mM}$