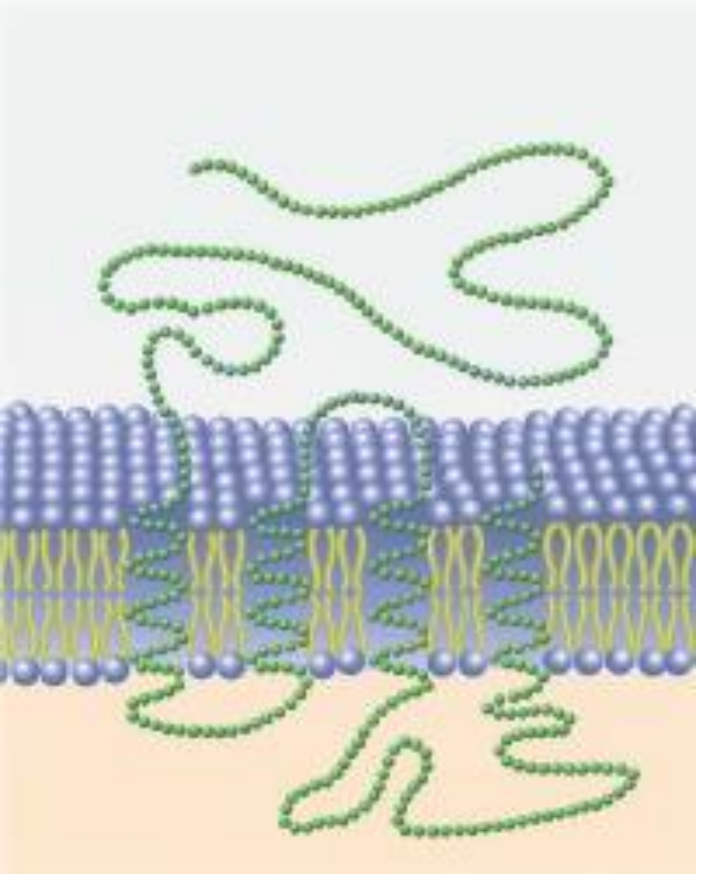

Lipids

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Medical Students- Summer Semester 2015

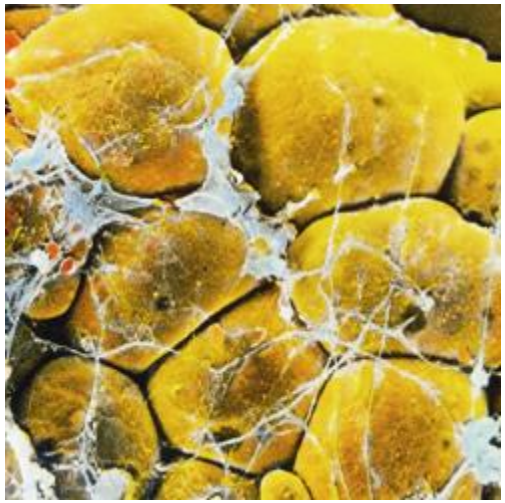
Images were taken Campbell textbook or McMurryetal

Lipids- Definition

- Naturally occurring organic molecules that are nonpolar and therefore dissolve in nonpolar organic solvents but not in water.
- Many lipids have hydrocarbon or modified hydrocarbon structure, properties, and behavior

Major role of lipids

- Energy storage from metabolism of food within fat cells (adipocytes).
- Separate the inside and outside of the cells as part of all cell membranes.
- Chemical messengers in the endocrine system and elsewhere.



Adipocytes

Lipid families

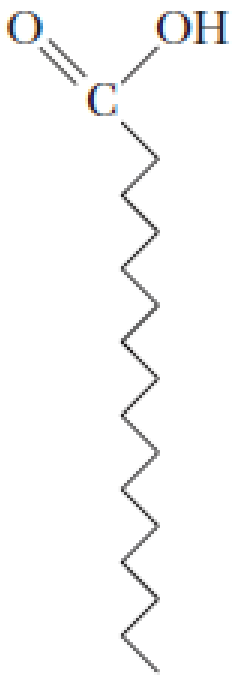
Fatty Acids

-Are long, unbranched hydrocarbon chains with a carboxylic acid group at one end.

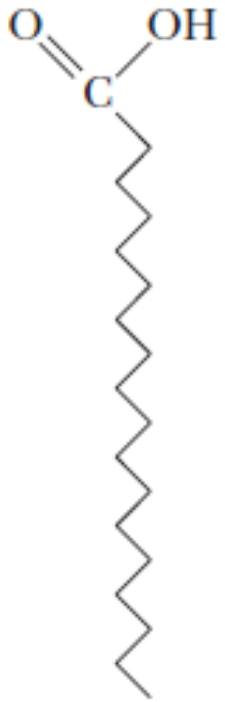
-Most have even numbers of carbon atoms.

-May or may not contain carbon carbon double bonds.

-Saturated fatty acids (without double bonds)



Palmitic acid

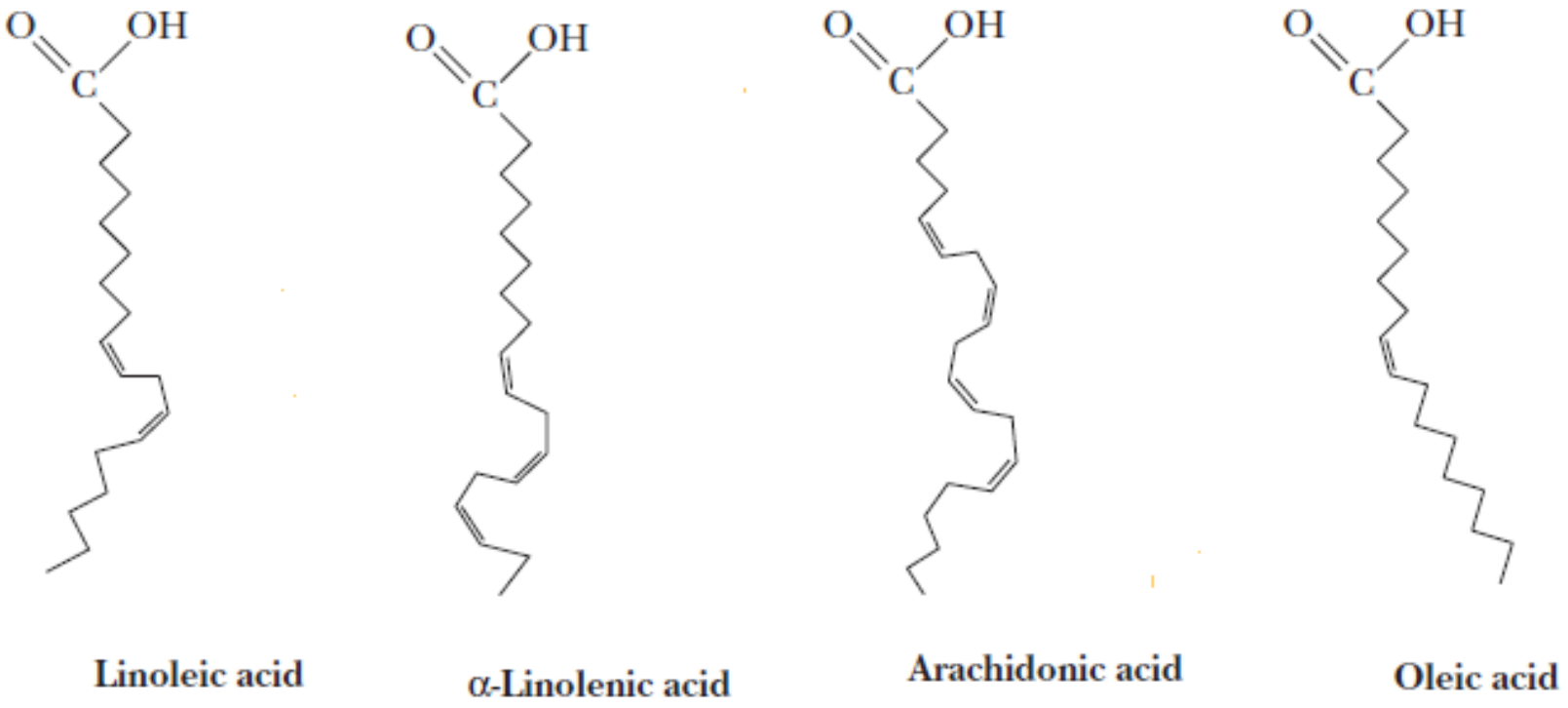


Stearic acid

Fatty Acids

-Unsaturated fatty acids (with double bonds)

- The stereochemistry at the double bond is usually cis rather than trans



Monounsaturated versus polyunsaturated fatty acids

Common fatty acids

Table 8.1

Typical Naturally Occurring Saturated Fatty Acids

Acid	Number of Carbon Atoms	Formula	Melting Point (°C)
Lauric	12	$CH_3(CH_2)_{10}CO_2H$	44
Myristic	14	$CH_3(CH_2)_{12}CO_2H$	58
Palmitic	16	$CH_3(CH_2)_{14}CO_2H$	63
Stearic	18	$CH_3(CH_2)_{16}CO_2H$	71
Arachidic	20	$CH_3(CH_2)_{18}CO_2H$	77

Table 8.2

Typical Naturally Occurring Unsaturated Fatty Acids

Acid	Number of Carbon Atoms	Degree of Unsaturation*	Formula	Melting Point (°C)
Palmitoleic	16	16:1—Δ^9	$CH_3(CH_2)_5CH{=}CH(CH_2)_7CO_2H$	–0.5
Oleic	18	18:1—Δ^9	$CH_3(CH_2)_7CH{=}CH(CH_2)_7CO_2H$	16
Linoleic	18	18:2—$\Delta^{9,12}$	$CH_3(CH_2)_4CH{=}CH(CH_2)CH{=}CH(CH_2)_7CO_2H$	–5
Linolenic	18	18:3—$\Delta^{9,12,15}$	$CH_3(CH_2CH{=}CH)_3(CH_2)_7CO_2H$	–11
Arachidonic	20	20:4—$\Delta^{5,8,11,14}$	$CH_3(CH_2)_4CH{=}CH(CH_2)_4(CH_2)_2CO_2H$	–50

*Degree of unsaturation refers to the number of double bonds. The superscript indicates the position of double bonds. For example, Δ9 refers to a double bond at the ninth carbon atom from the carboxyl end of the molecule.

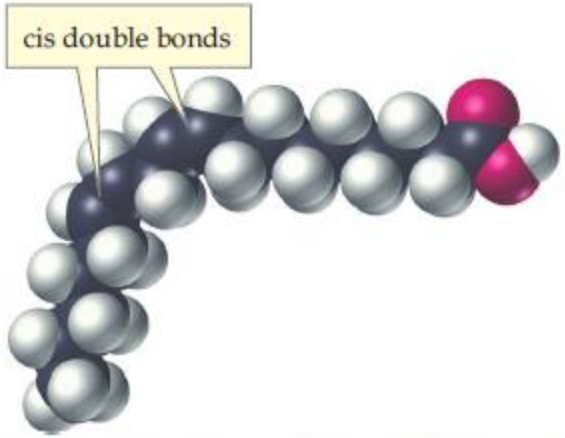
Properties of Fats and Oils

- Melting point decreases with the presence of more double bonds a fatty acid has.
- Vegetable **oils are lower melting than animal fats** because oils have more unsaturated fatty acids than animal **fats.**

A saturated fat has only single C-C bonds and appears straight

Stearic acid, an 18-carbon saturated fatty acid

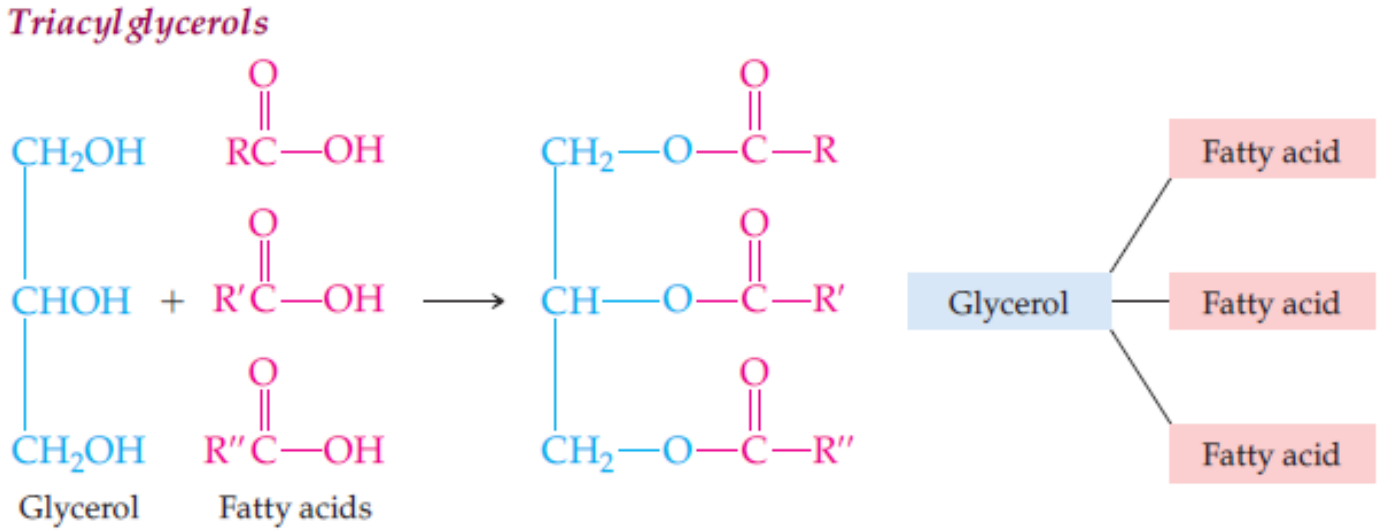
Unsaturated fats bend due to cis double bonds



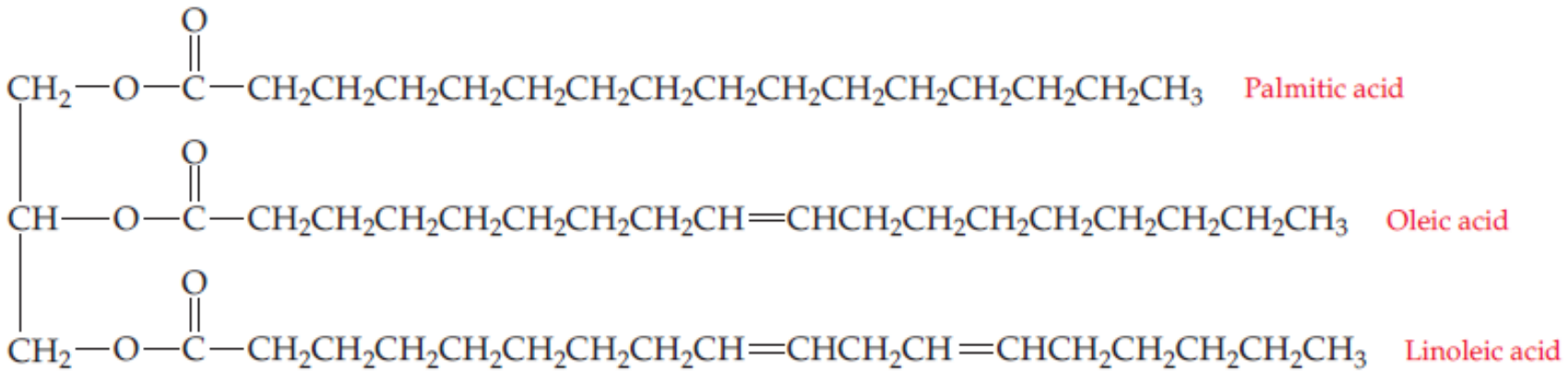
Linoleic acid, an 18-carbon unsaturated fatty acid

Triacylglycerols

- All fats and oils are composed of triesters of glycerol with three fatty acids.
- Glycerol (glycerine) is 1,2,3-propanetriol
- The 3 fatty acids can be the same or different.



Example of a triacylglycerol



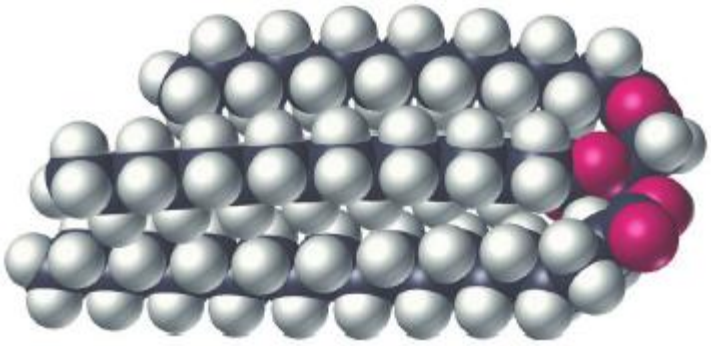
Oil and fat are mixtures of triacylglycerols

TABLE 24.2 Approximate Composition of Some Common Fats and Oils*

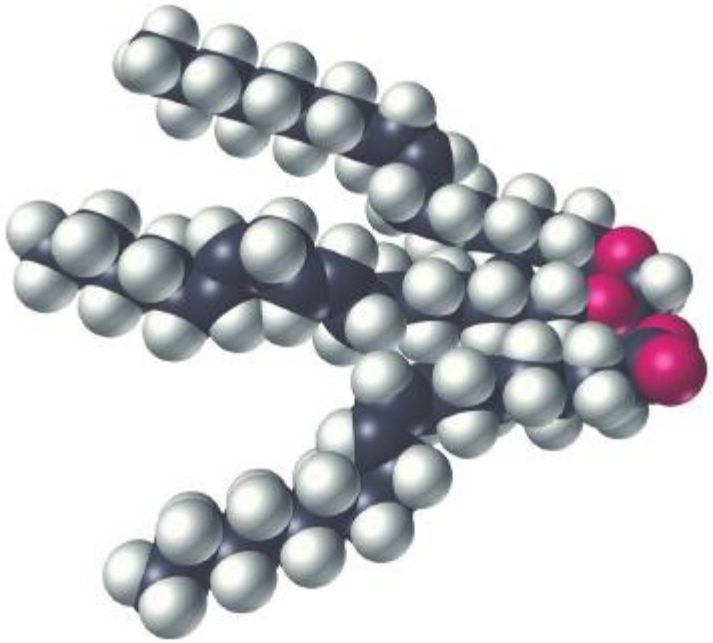
	SATURATED FATTY ACIDS (%)				UNSATURATED FATTY ACIDS (%)	
SOURCE	C_{12} LAURIC	C_{14} MYRISTIC	C_{16} PALMITIC	C_{18} STEARIC	C_{18} OLEIC	C_{18} LINOLEIC
Animal Fat						
Lard	—	1	25	15	50	6
Butter	2	10	25	10	25	5
Human fat	1	3	25	8	46	10
Whale blubber	—	8	12	3	35	10
Vegetable Oil						
Corn	—	1	8	4	46	42
Olive	—	1	5	5	83	7
Peanut	—	—	7	5	60	20
Soybean	—	—	7	4	34	53

*Where totals are less than 100%, small quantities of several other acids are present, with cholesterol also present in animal fats.

Triacylglycerols from a fat and an oil



A fat



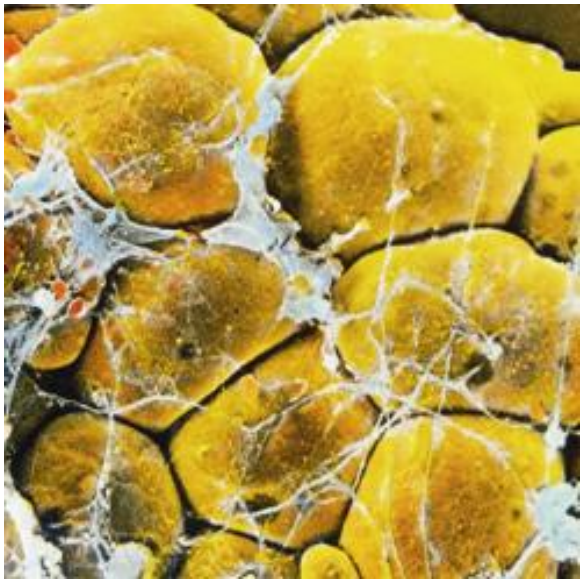
An oil

Properties of Triacylglycerols

- Uncharged, nonpolar, hydrophobic molecules.
- No ionic charges
- Solid triacylglycerols (fats) high proportion of saturated fatty acid chains
- Liquid triacylglycerols (oils) high proportion of unsaturated fatty acid chains

Roles of TAGs

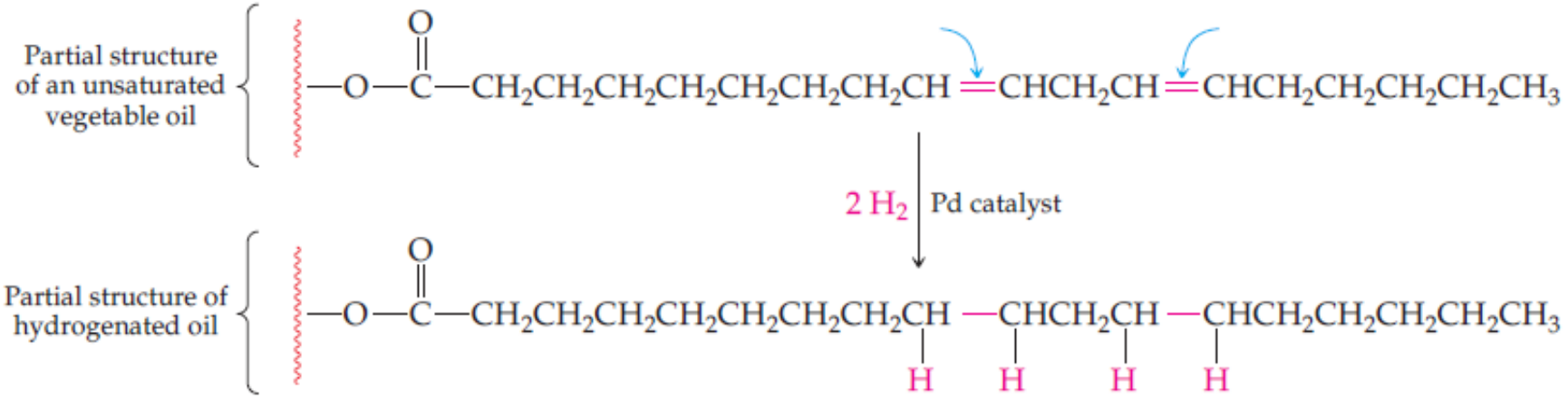
- The primary function of triacylglycerols is long-term storage of energy for the organism



- Adipose tissue provides thermal insulation and protective padding

Chemical Reactions of TAGs

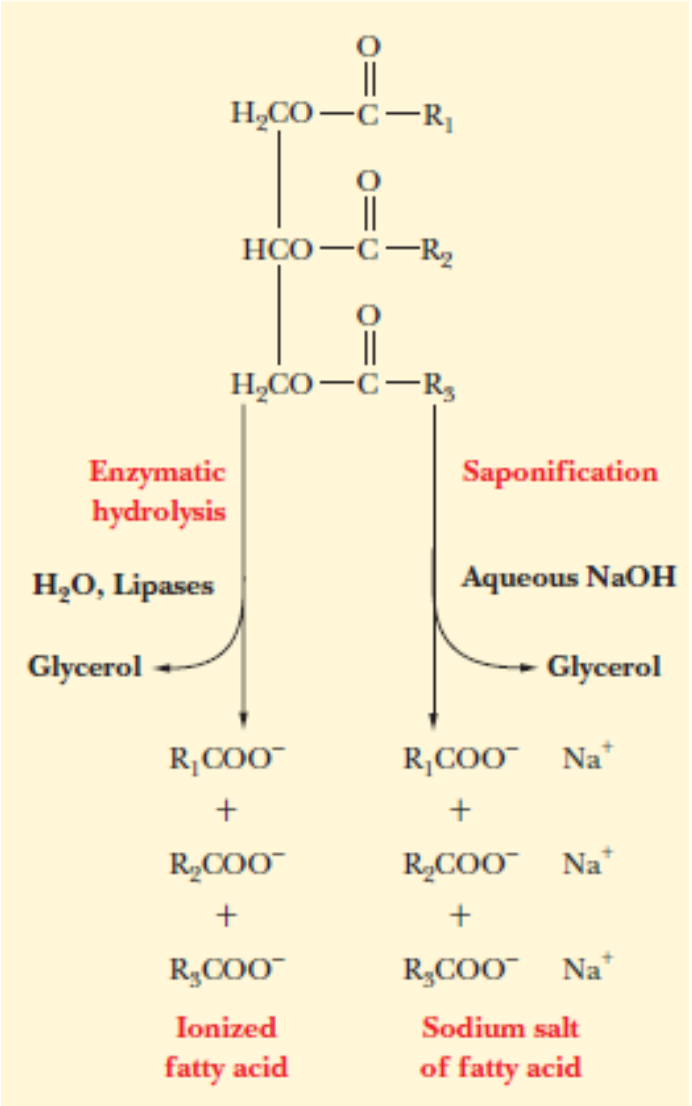
Hydrogenation



Margarine

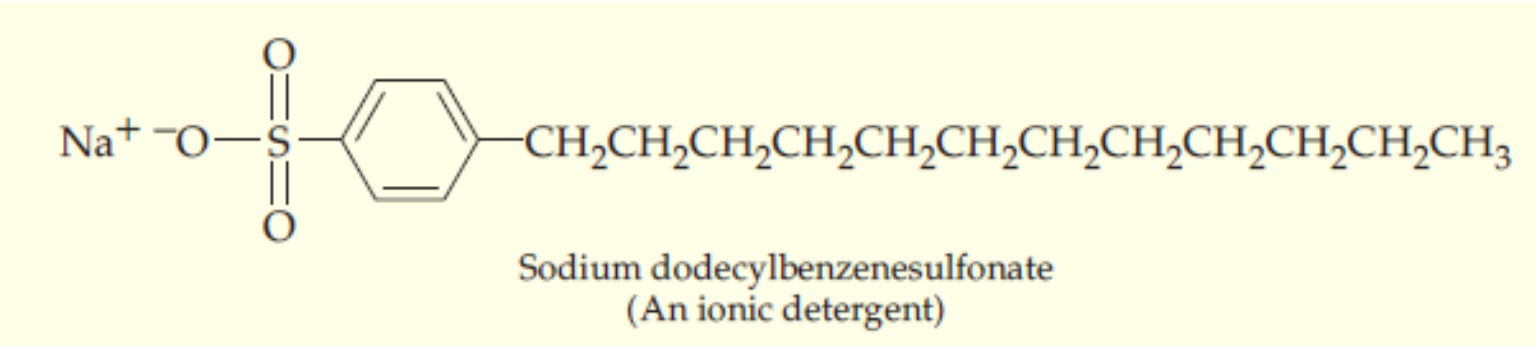
Hydrolysis of TAGs (Saponification)

- Esters can react with water (hydrolyzed) to form their carboxylic acids and alcohols.
- Lipases catalyze hydrolysis of dietary fats and oils in the body.
- Saponification is the hydrolysis of fats and oils by strong aqueous bases (NaOH or KOH)

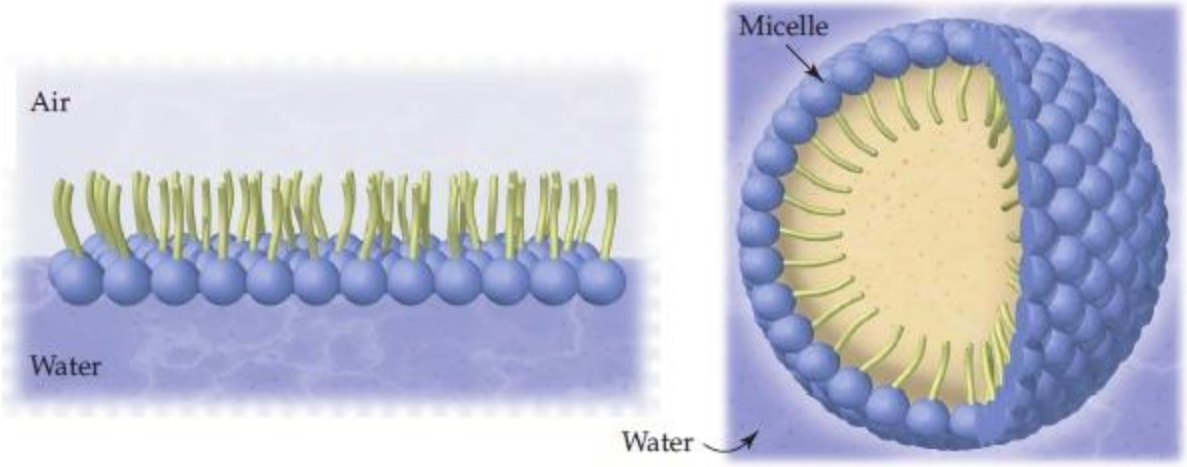


Detergents

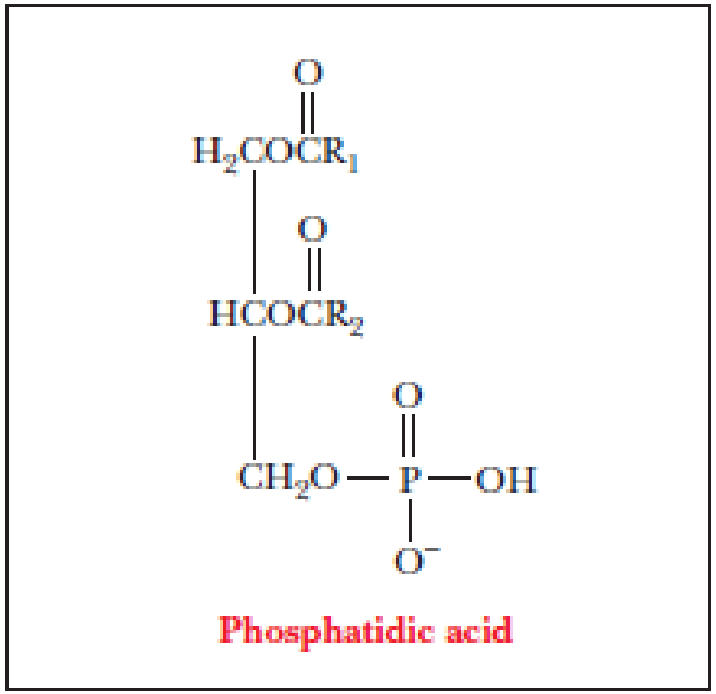
- Anything that washes away dirt

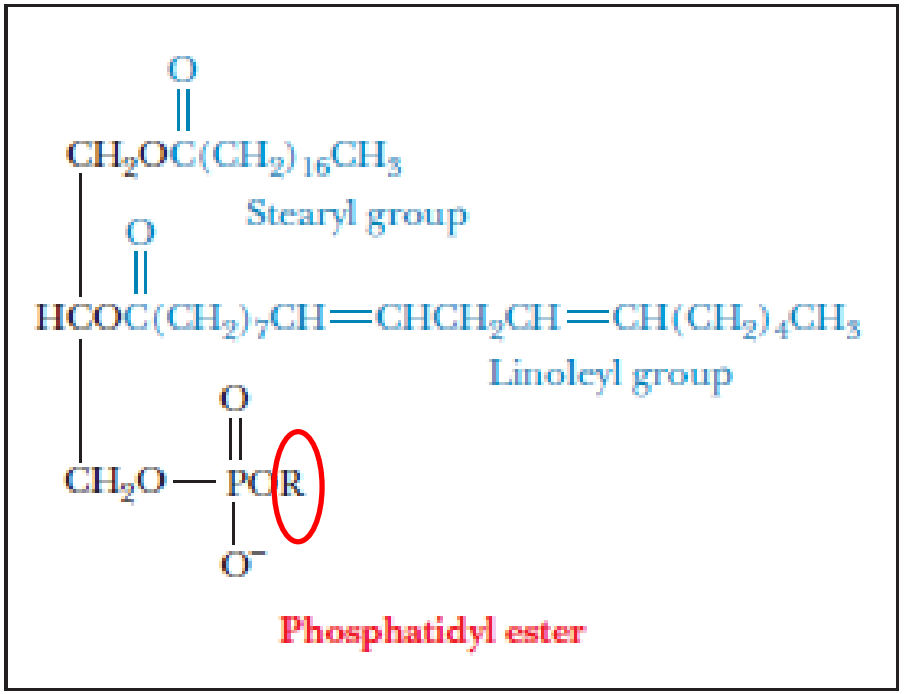


- How do soaps and detergents act?



Phosphoglycerols (Phosphatidyl esters) (Glycerophospholipids)





Phosphoric acid is triprotic and thus can form more than one ester linkage.

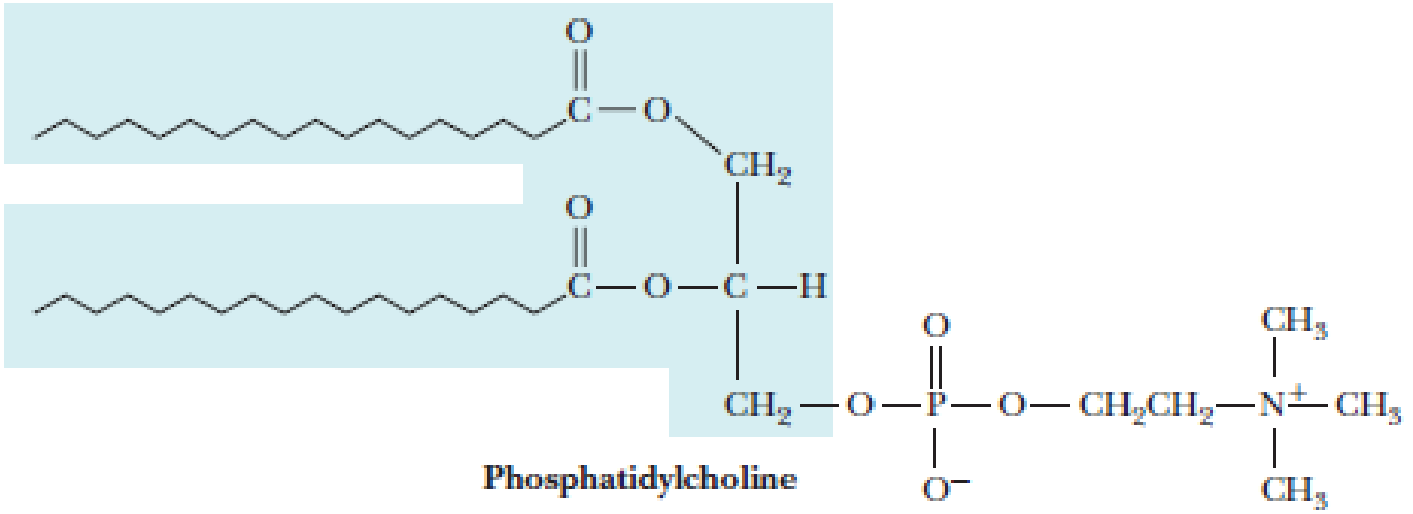
Different R groups result in different types of phosphoglycerols

Types of Phosphoglycerols

-The nature of the second alcohol esterified to the phosphoric acid determine the type of phosphoglycerol.

-Phosphoacylglycerols are important components of biological membranes.

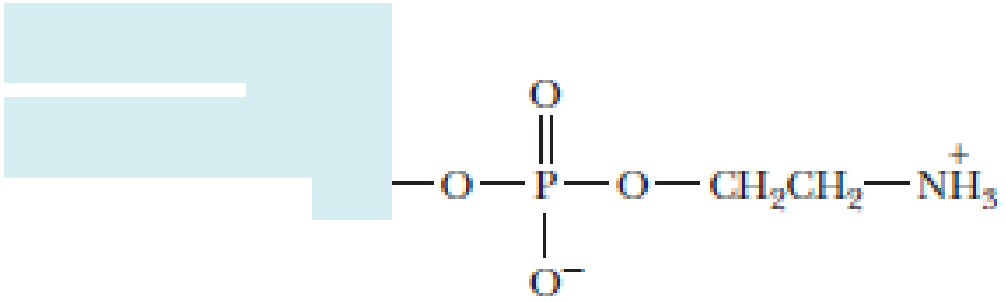
Phosphatidylcholine (lecithin)



Phosphatidylcholine

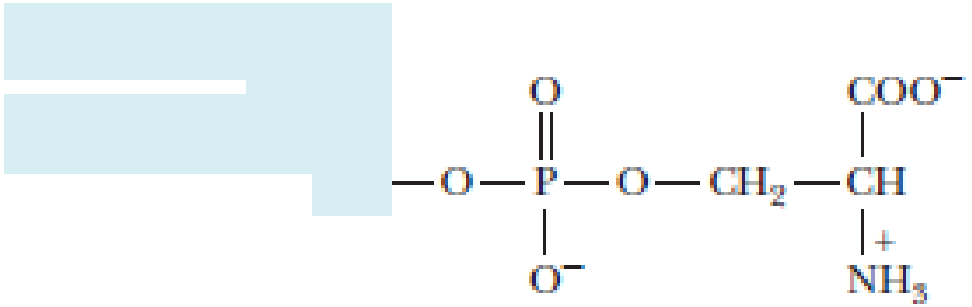
Types of Phosphoglycerols

Phosphatidylethanolamine (cephalin)



Phosphatidylethanolamine

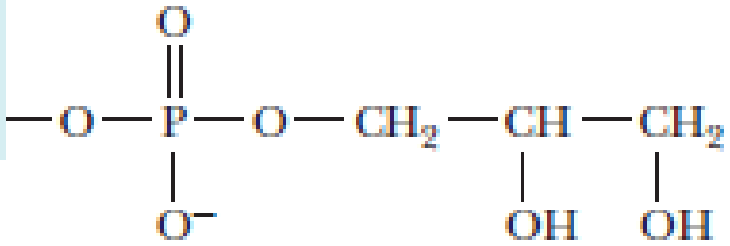
Phosphatidylserine



Phosphatidylserine

Types of Phosphoglycerols

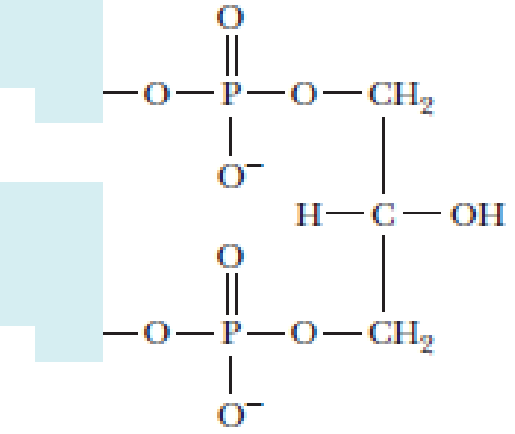
Phosphatidylglycerol



Phosphatidylglycerol

Diphosphatidylglycerol (Cardiolipin)

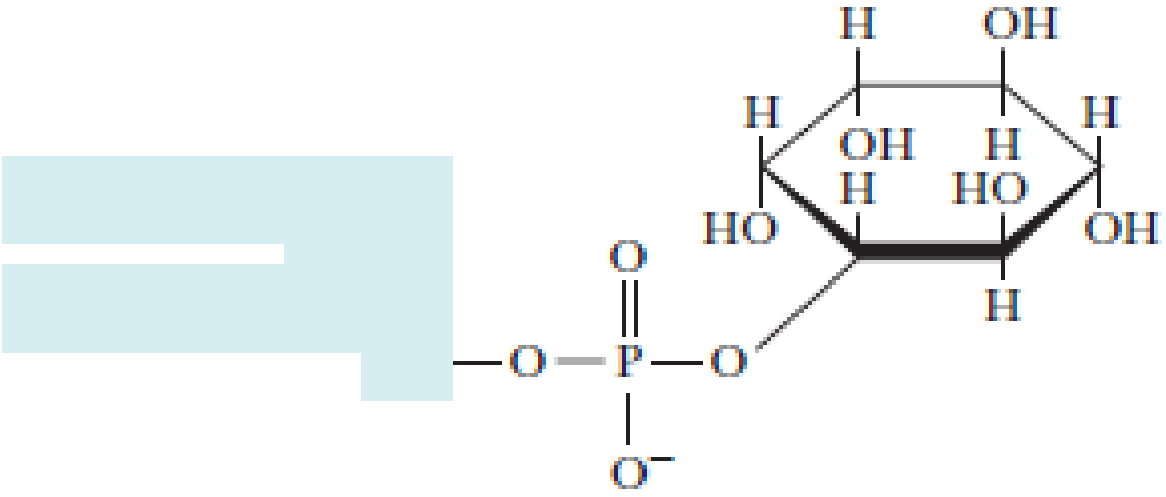
found almost exclusively in the inner mitochondrial membrane



Diphosphatidylglycerol (Cardiolipin)

Types of Phosphoglycerols

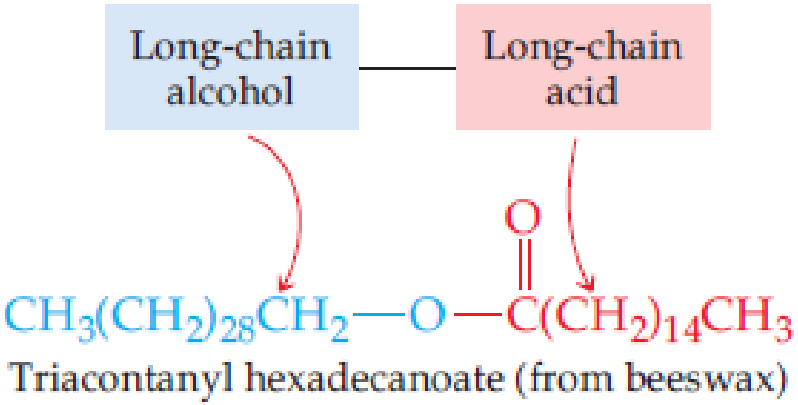
Phosphatidylinositol

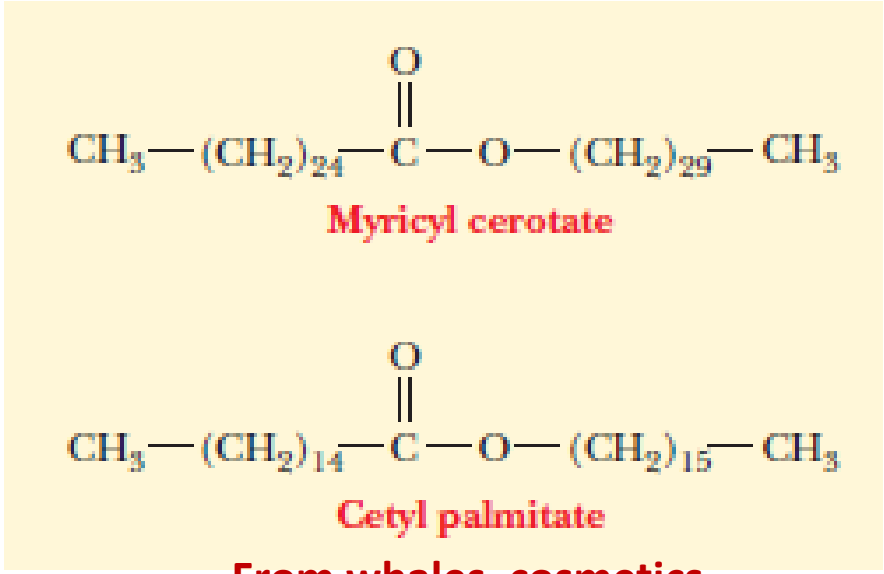


Phosphatidylinositol

Waxes

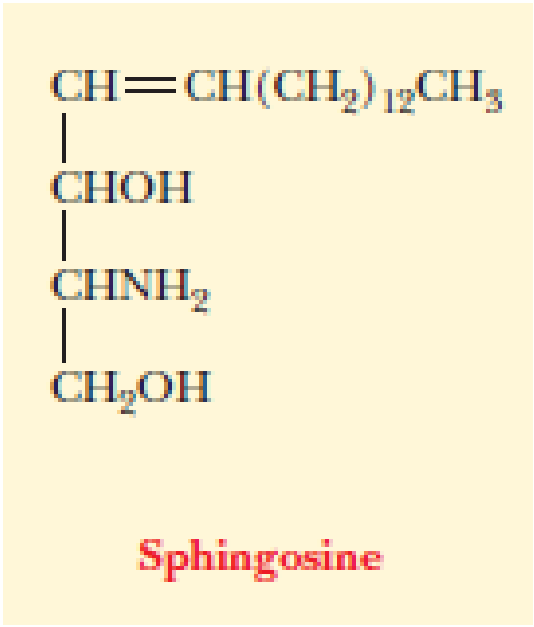
- **Waxes** are complex mixtures of esters of long-chain carboxylic acids and long chain.
- Beeswax, protective coatings on most fruits, aquatic birds feathers, etc



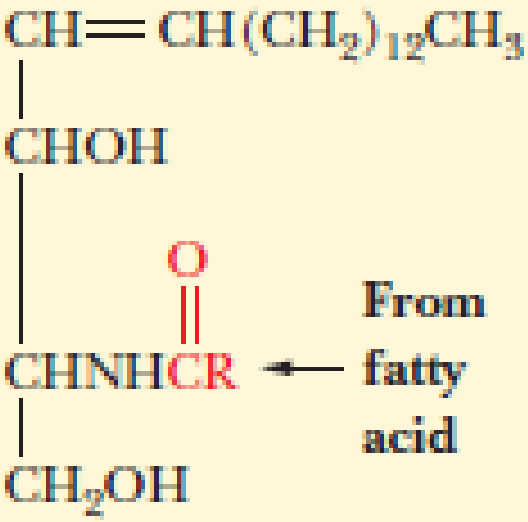


Sphingolipids

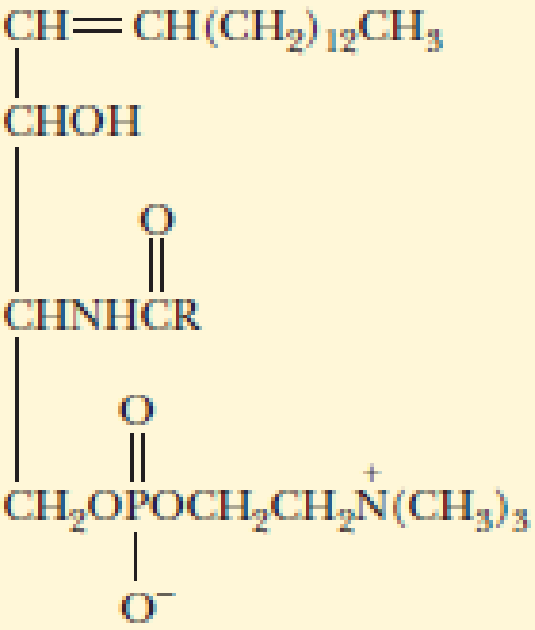
- Abundant in the nervous system



Sphingosine



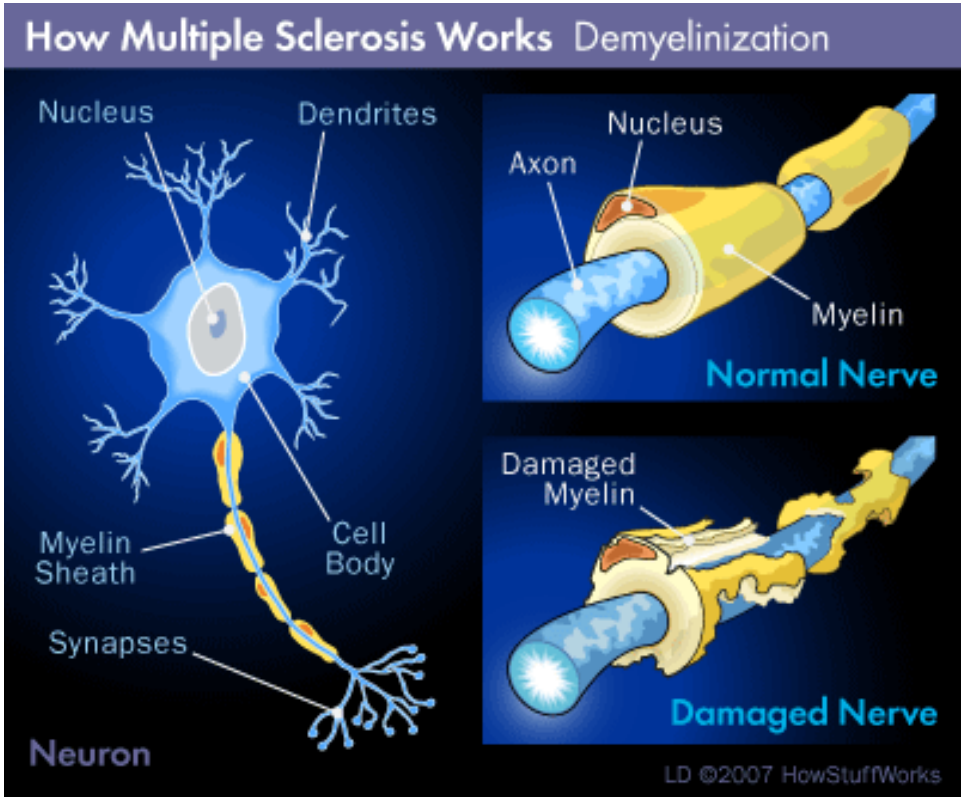
A ceramide
(*N*-acylsphingosine)



A sphingomyelin

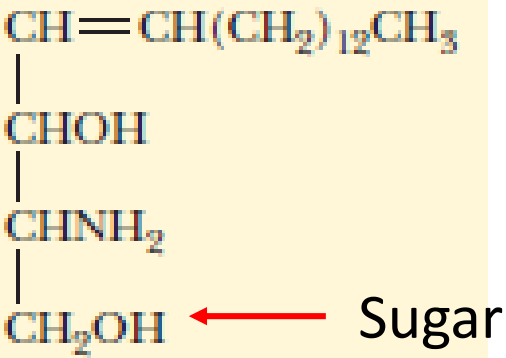
Sphingomyelin and multiple sclerosis (MS)

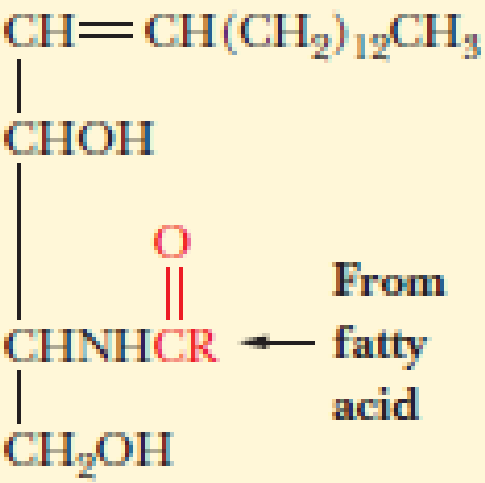
- Myelin sheath consists of many layers of plasma membrane (rich in lipids not proteins) that have been wrapped around the nerve cell.
- Loss of myelin leads to the slowing and eventual cessation of the nerve impulse.
- In MS, the myelin sheath is progressively destroyed by sclerotic plaques that affect the brain and spinal cord.
- Weakness, lack of coordination, and speech and vision problems

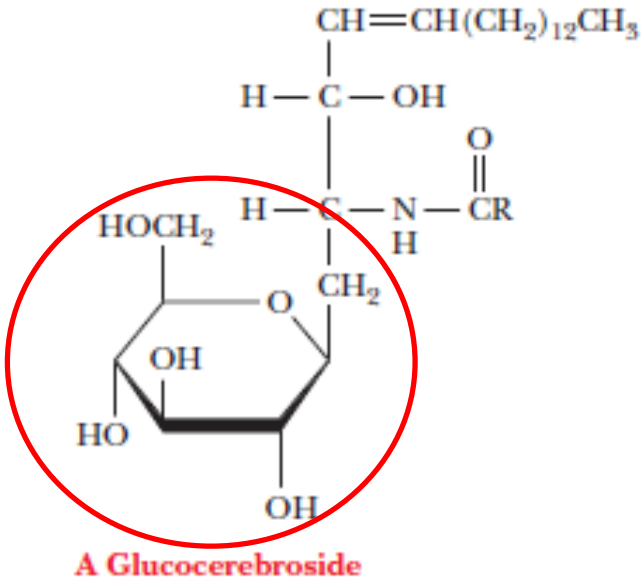


health.howstuffworks.com

Sphingolipids-Glycolipids







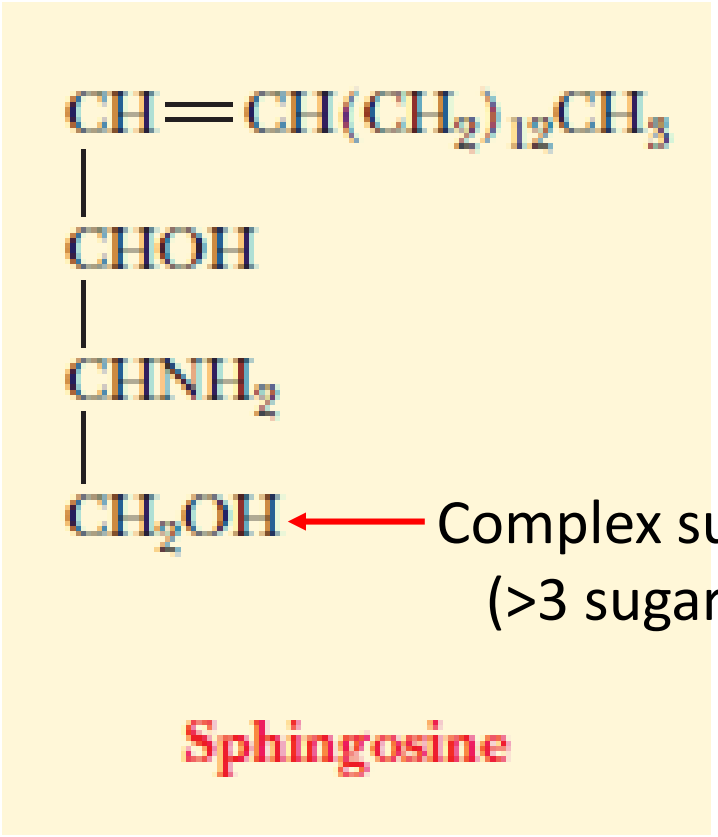
Glycolipids act as markers on cell membranes and play a role in tissue and organ specificity

Types of cerebrosides

Ceramide + glucose = glucocerebroside

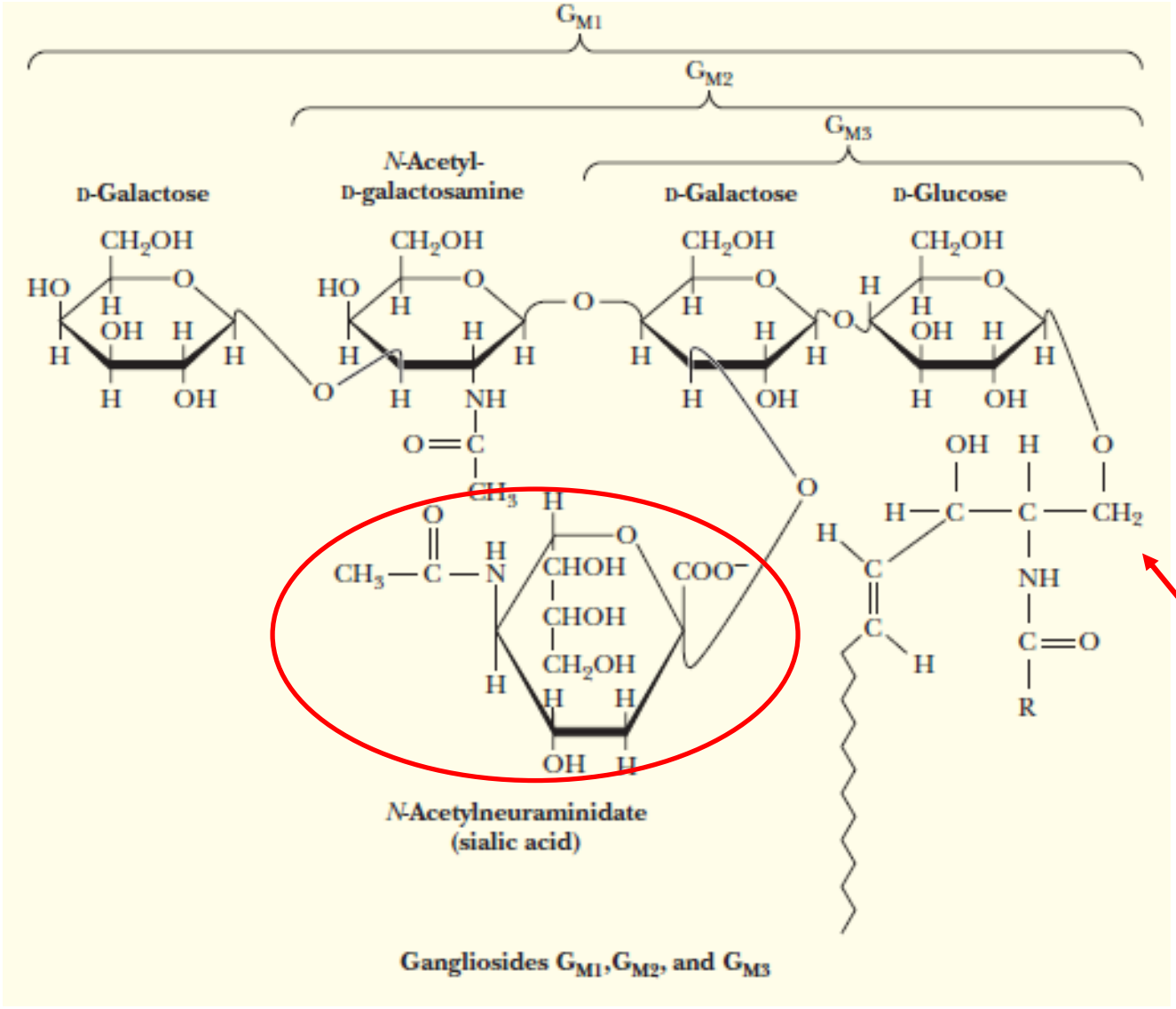
Ceramide + galactose= galactocerebroside

Glycolipids-Gangliosides



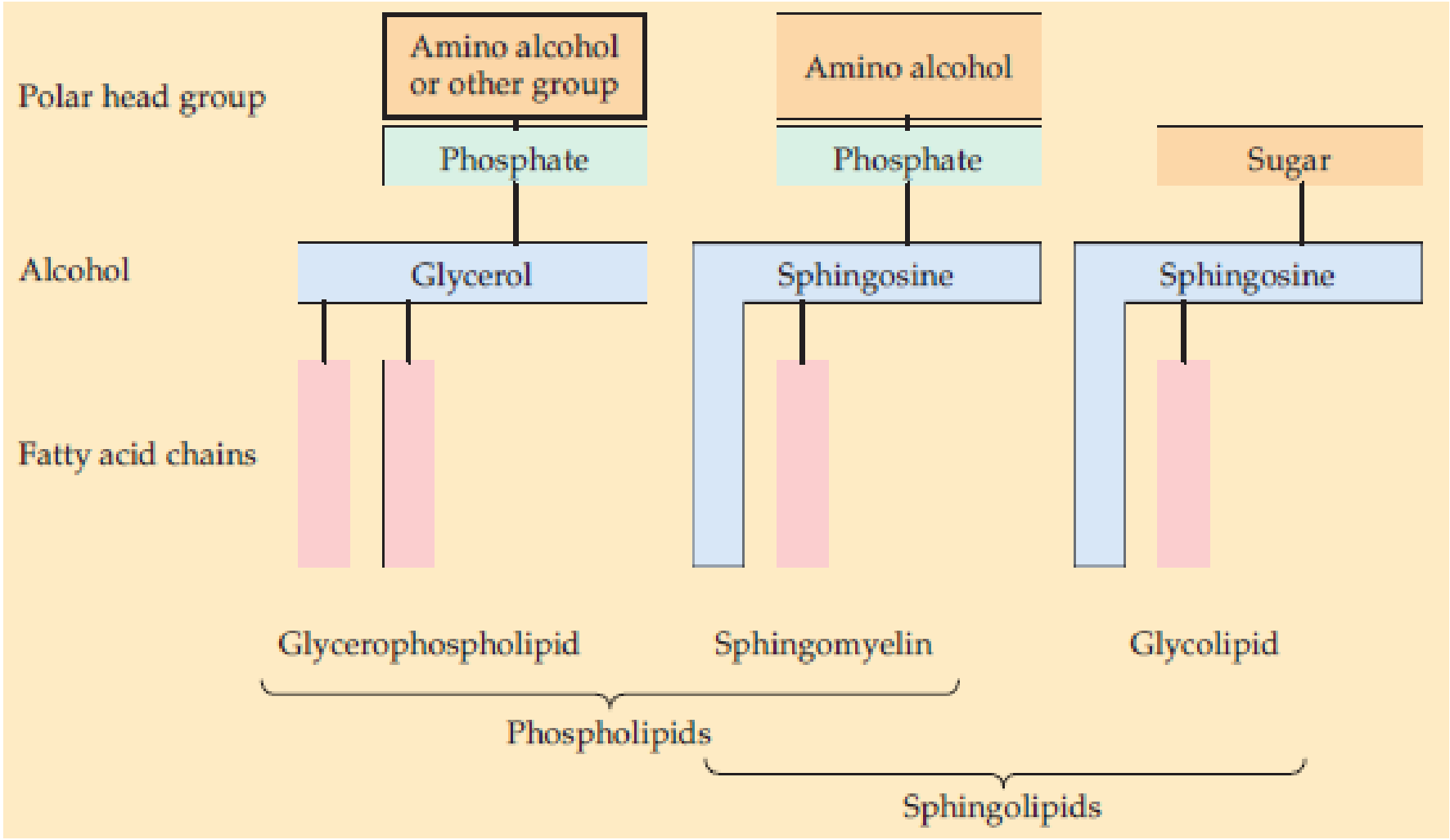
Gangliosides are present in large quantities in nerve tissues

Glycolipids-Gangliosides



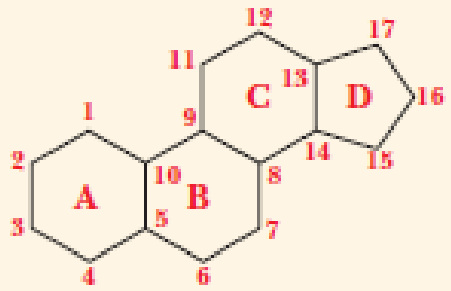
Sphingosine

Membrane lipids



Steroids

1



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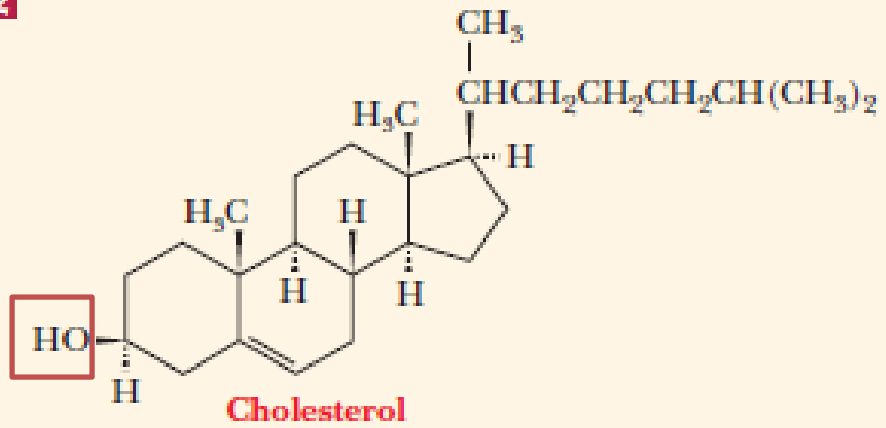
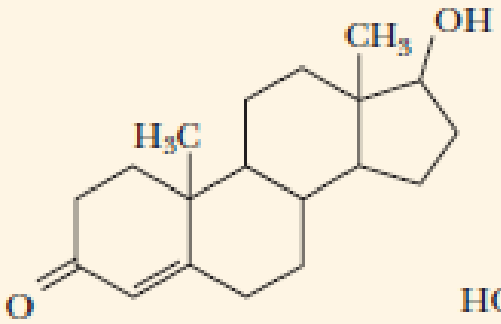
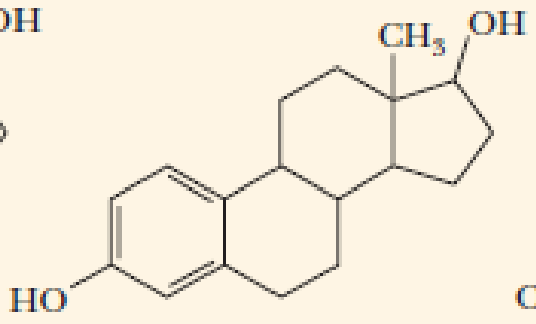


Cholesterol

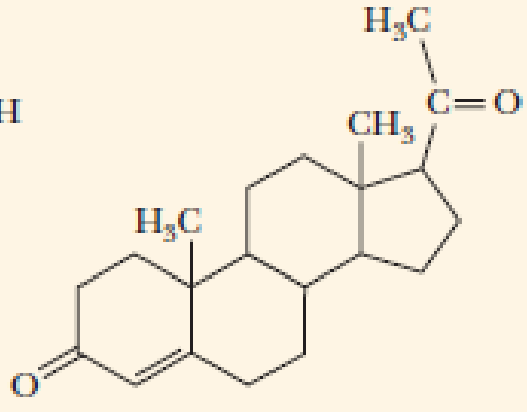
3 **Sex hormones**



Testosterone



Estradiol

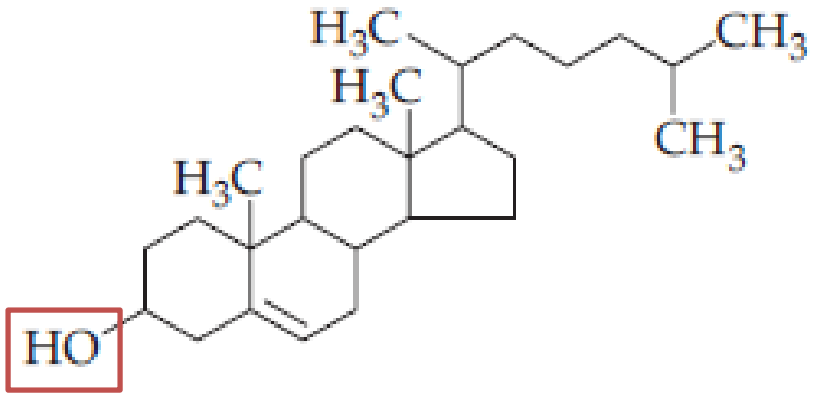


Progesterone

Cell Membrane Lipids

Cholesterol

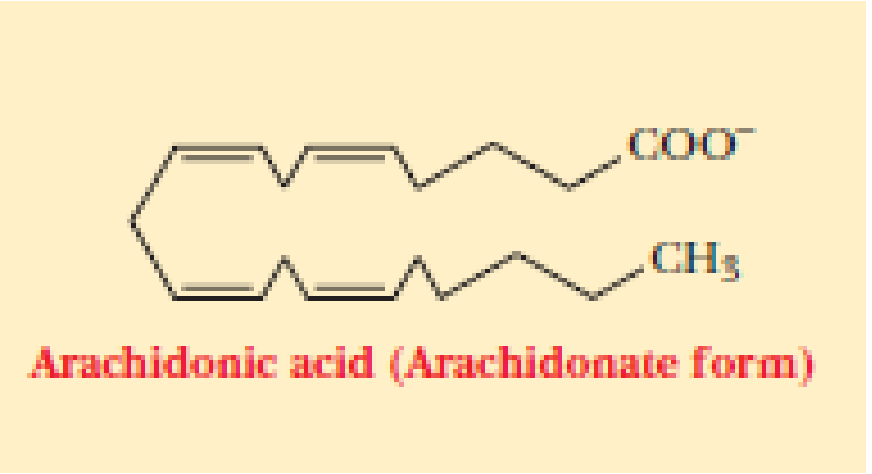
- A steroid
- 4 fused rings- flat shape
- Membrane fluidity
- A component of cell membranes
- A precursor of other steroids and of vitamin D3.



- Is modified in liver cells to produce bile acids, essential in the digestion of dietary fats.
- 800 mg/day
- Has a role in the development of atherosclerosis

Eicosanoids: Prostaglandins and Leukotrienes

- Local hormones (paracrine)
- Arachidonic acid derivatives (20:4)

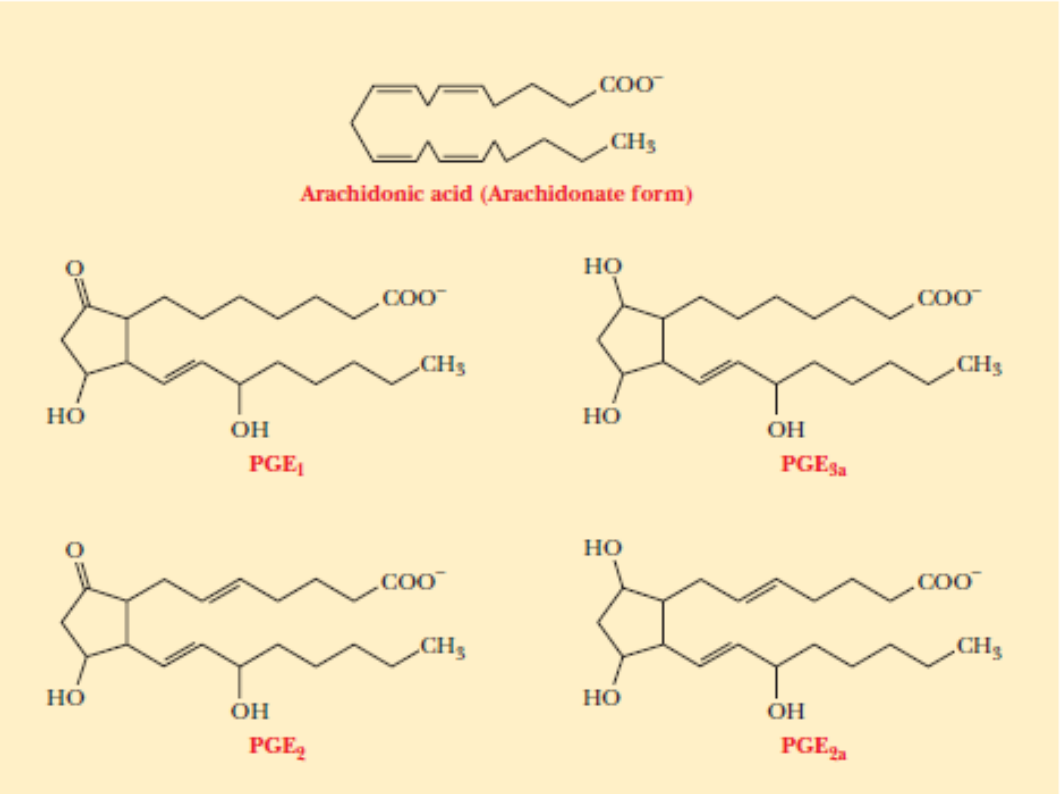


Arachidonic acid (Arachidonate form)

Prostaglandins (PGs)

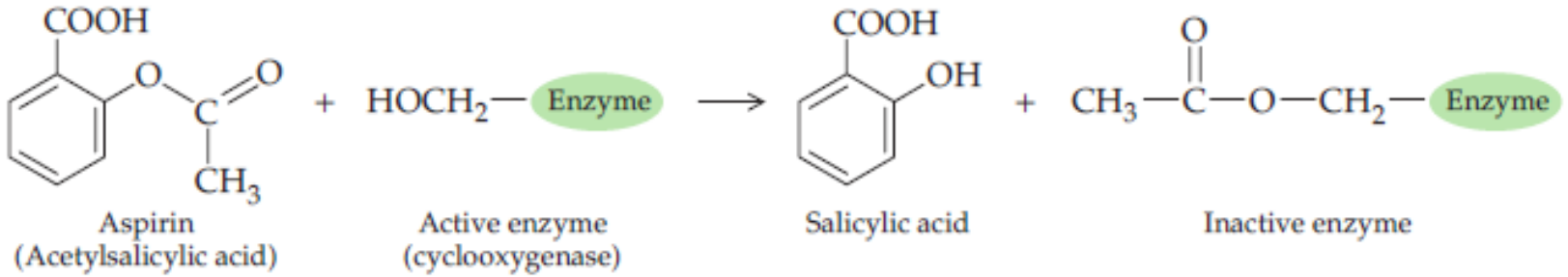
Different PGs differ in the numbers and positions of double bonds and oxygen-containing functional groups.

Functions: Control of blood pressure, stimulation of smooth-muscle contraction, induction of inflammation, and inhibit the aggregation of platelets.



Cortisone and other steroids also have anti-inflammatory effects because of their inhibition of PG synthesis.

Clinical application



Aspirin inhibits PG synthesis, particularly in blood platelets, accounting for its anti-inflammatory and fever-reducing properties.

Leukotrienes (LK)

- Function: constriction of smooth muscle, especially in the lungs.
- In asthma, allergic reactions to pollens increase LK C synthesis resulting in airway constrictions.
- Drugs that inhibit the synthesis of leukotriene C or block its receptors are used in the treatment of asthma

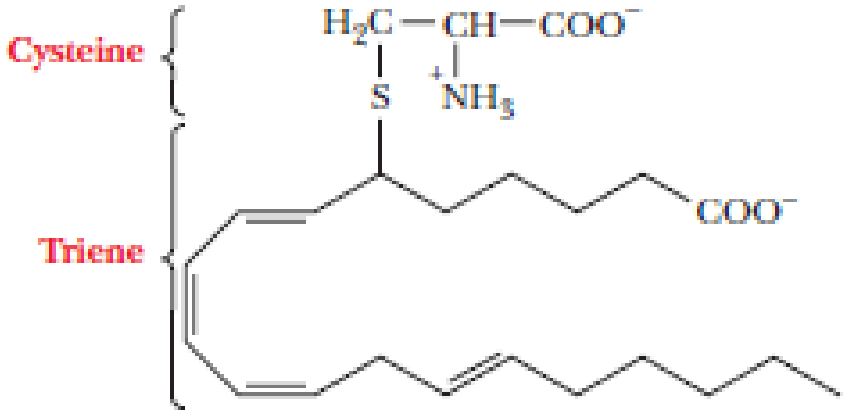


FIGURE 8.35 Leukotriene C.

Thromboxanes

- Arachidonic acid derivatives.
- They contain cyclic ethers.
- Ex. thromboxane A2 (TxA2) induces platelet aggregation and smooth-muscle contraction.

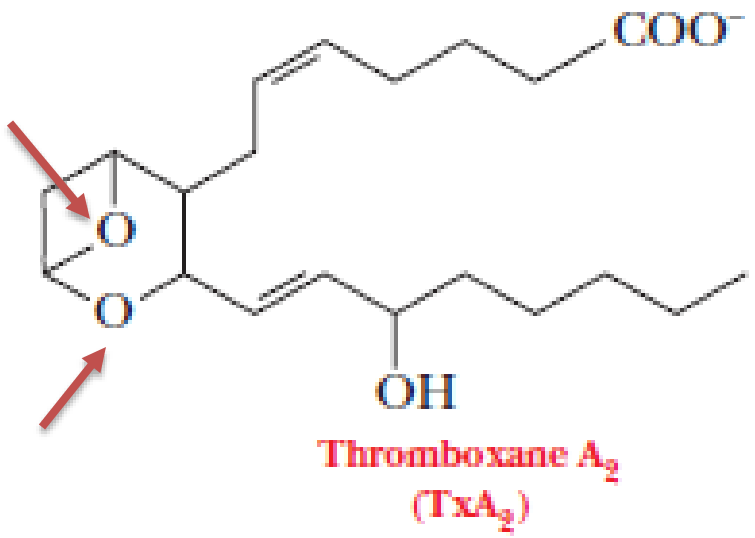


FIGURE 8.36 Thromboxane A_2.

Lipid-Soluble Vitamins

- Vitamin A, D, E and K
- Hydrophobic

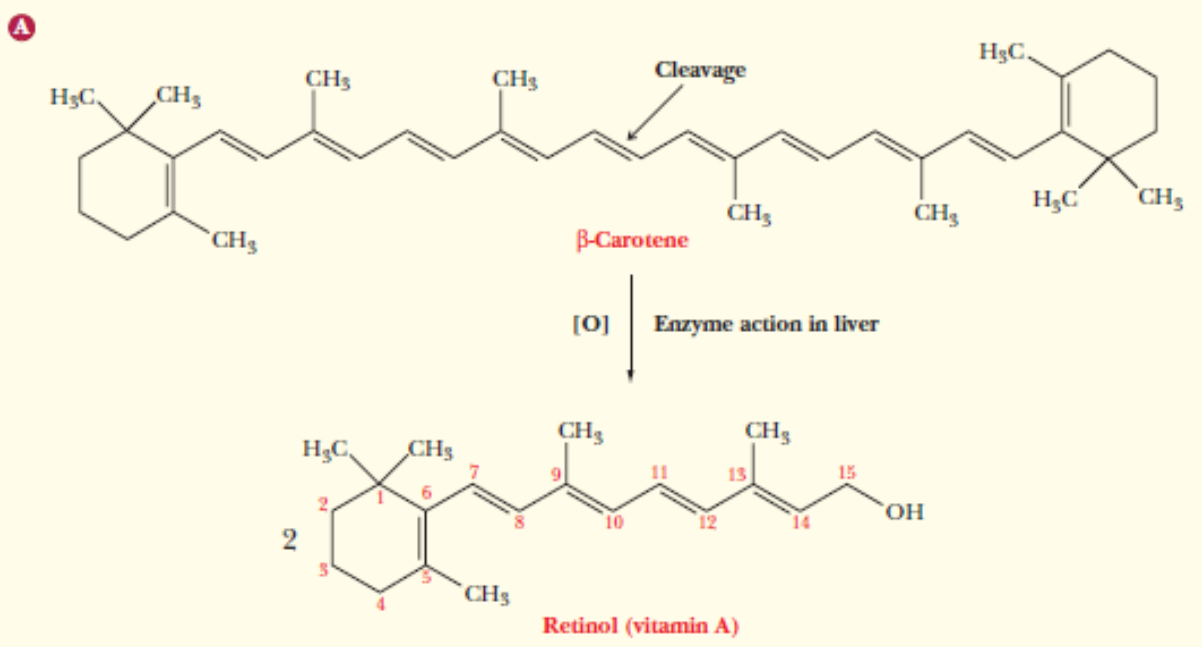
Table 8.3

Lipid-Soluble Vitamins and Their Functions

Vitamin	Function
Vitamin A	Serves as the site of the primary photochemical reaction in vision
Vitamin D	Regulates calcium (and phosphorus) metabolism
Vitamin E	Serves as an antioxidant; necessary for reproduction in rats and may be necessary for reproduction in humans
Vitamin K	Has a regulatory function in blood clotting

Lipid-Soluble Vitamins
Vitamin A or retinol

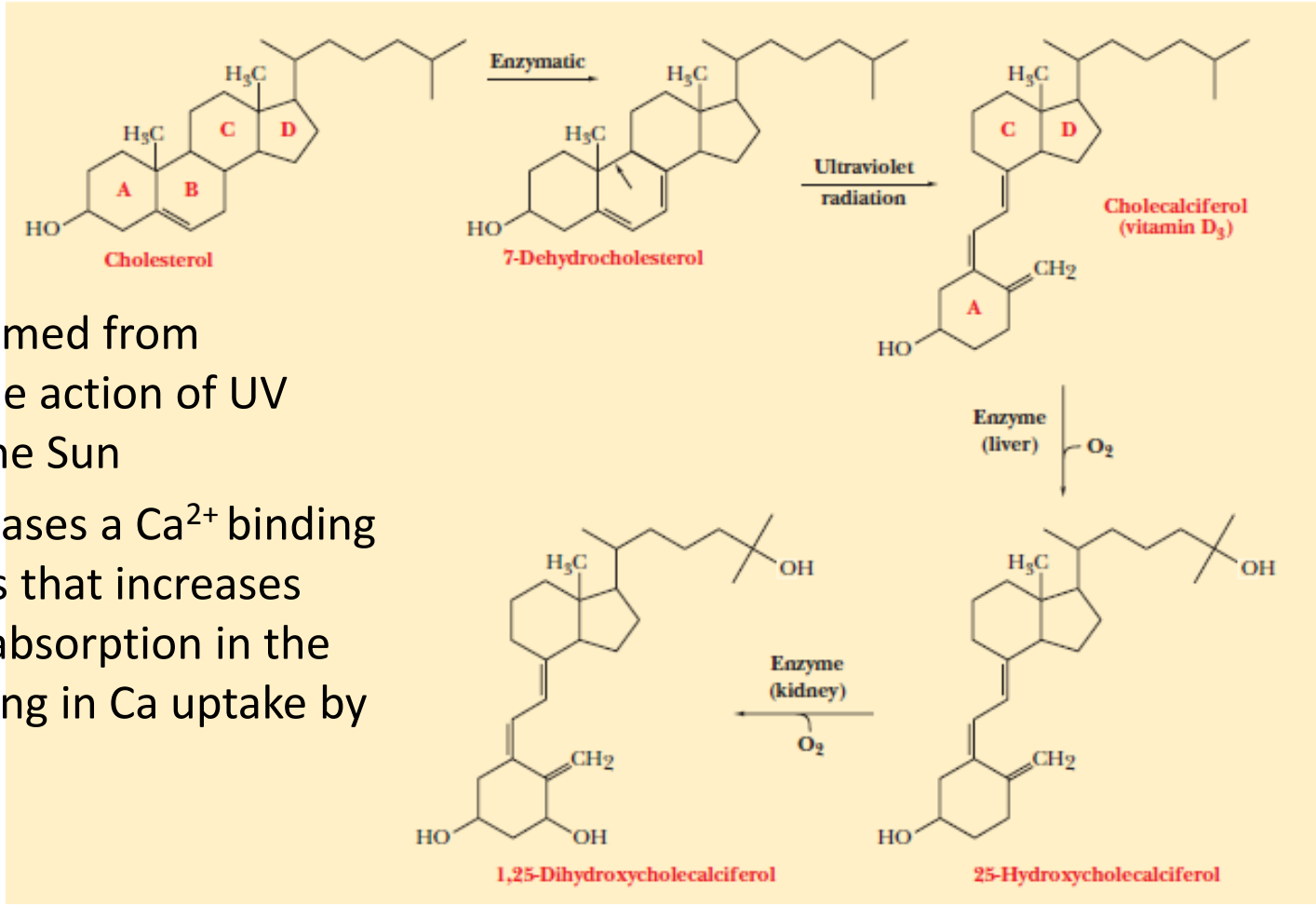
- **β-carotene** is the precursor of **vitamin A**
- **β-carotene is an** unsaturated hydrocarbon



- Vitamin A is oxidized to retinal that reacts with opsin to form rhodopsin

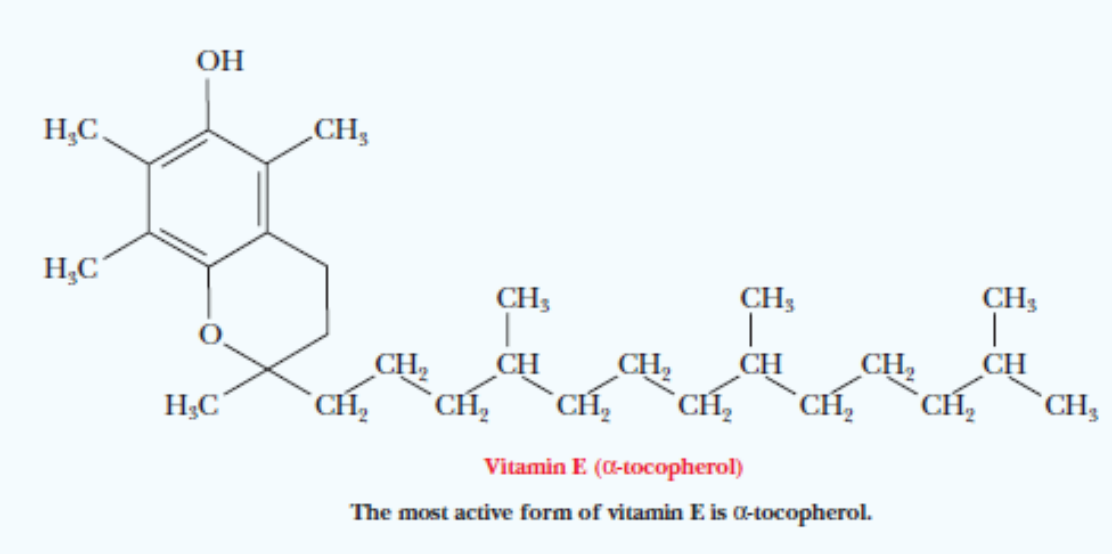
Lipid-Soluble Vitamins
Vitamin D

- Has several forms such as, vitamin D3 (cholecalciferol)



- Vitamin D3 is formed from cholesterol by the action of UV radiation from the Sun
- Vitamin D3 increases a Ca^{2+} binding protein synthesis that increases dietary calcium absorption in the intestines resulting in Ca uptake by the bones.
- Rickets

Lipid-Soluble Vitamins
Vitamin E

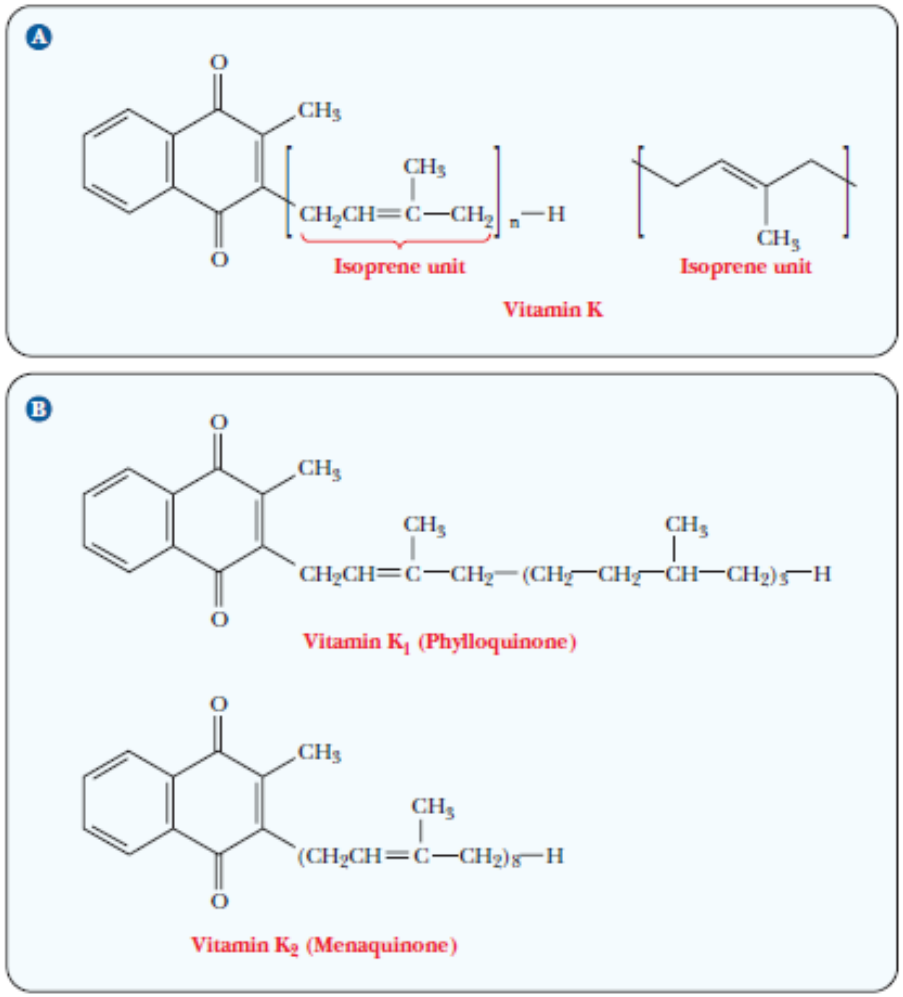


Vitamin E (α-tocopherol)

The most active form of vitamin E is α-tocopherol.

- The most active form of **vitamin E** is **α-tocopherol**
- An **antioxidant (**a good reducing agent) to protect important compounds, such as vitamin A, from degradation and to react with and remove **free radicals.**
- **b**
- A free radical are very reactive because it has at least one unpaired electron
- Free radicals play a role in the development of cancer and in the aging process.

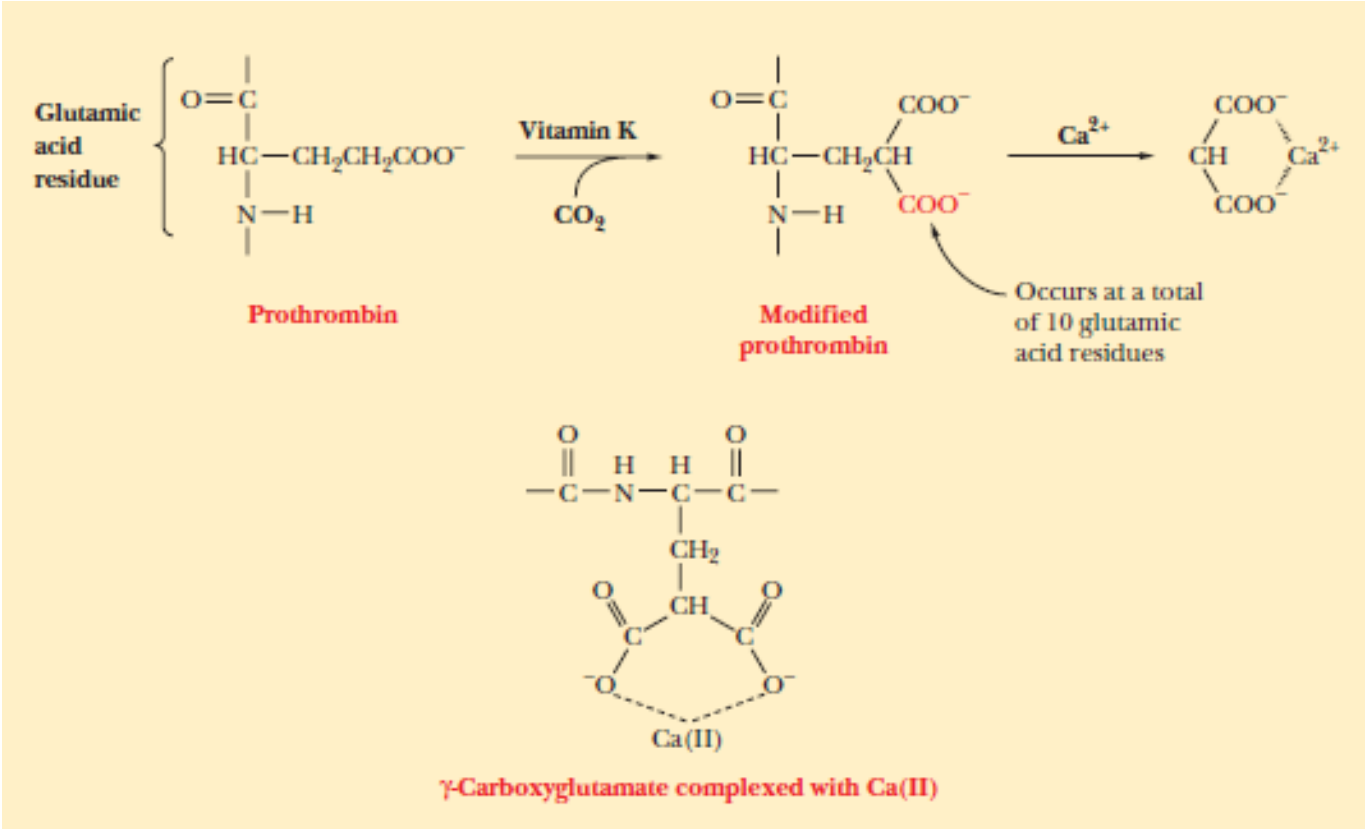
Lipid-Soluble Vitamins
Vitamin K



- From the Danish *Koagulation*
- A long unsaturated hydrocarbon side chain consists of repeating isoprene units
- The number of isoprene units determines the exact form of vitamin K.

Vitamin K and coagulation

- The anticoagulants, dicumarol and warfarin (a rat poison), are vitamin K antagonists



Biological membranes

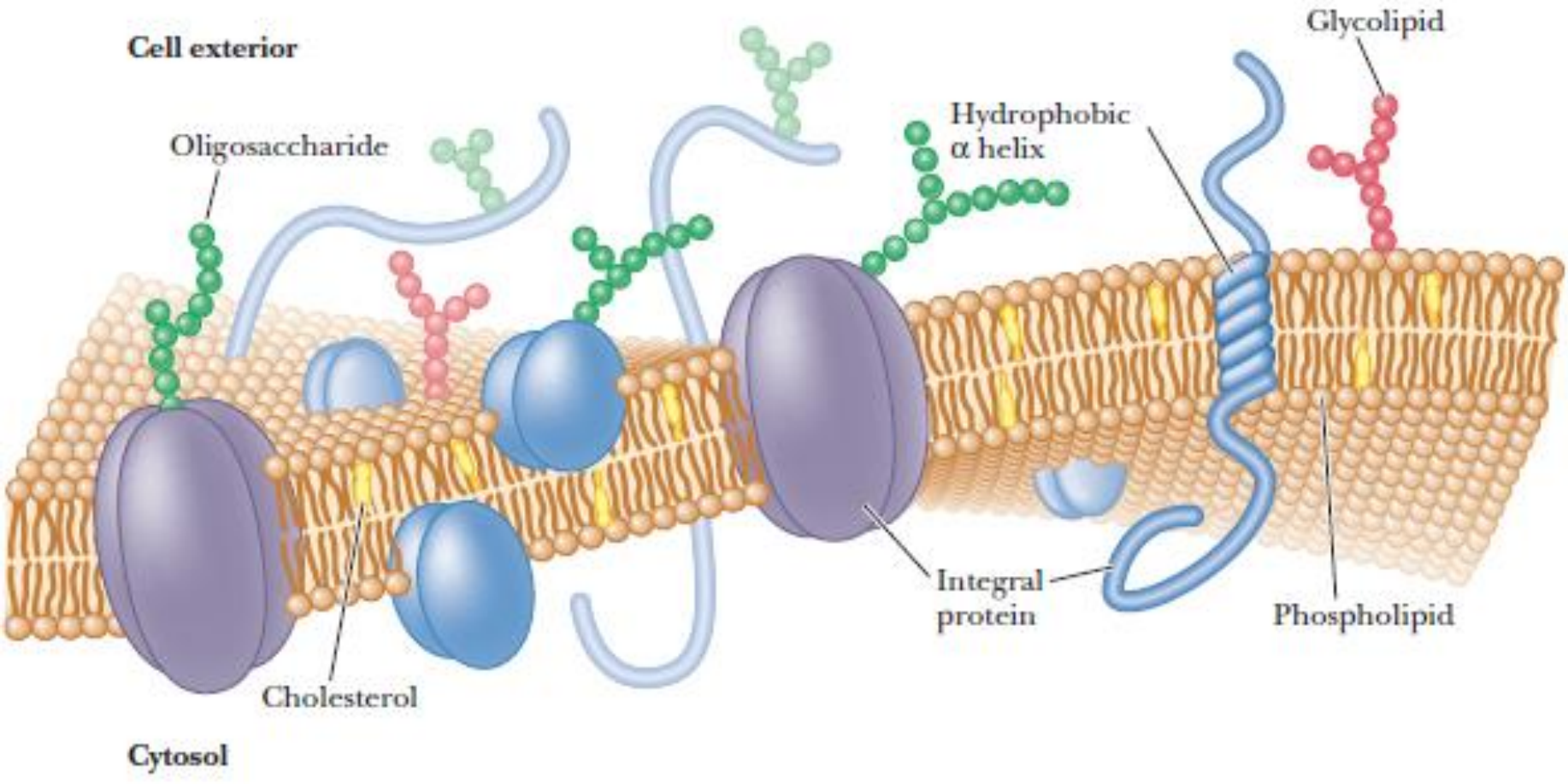
- Roles:
- 1. Separate cells from the external environment
- 2. Transport of specific substances into and out of cells.
- 3. Many important enzymes are found in membranes

- Phosphoglycerides are the principal lipid components of membranes

Lipid bilayer ≠ Cell membrane

- The protein component of a membrane can form 20% to 80% of its total weight

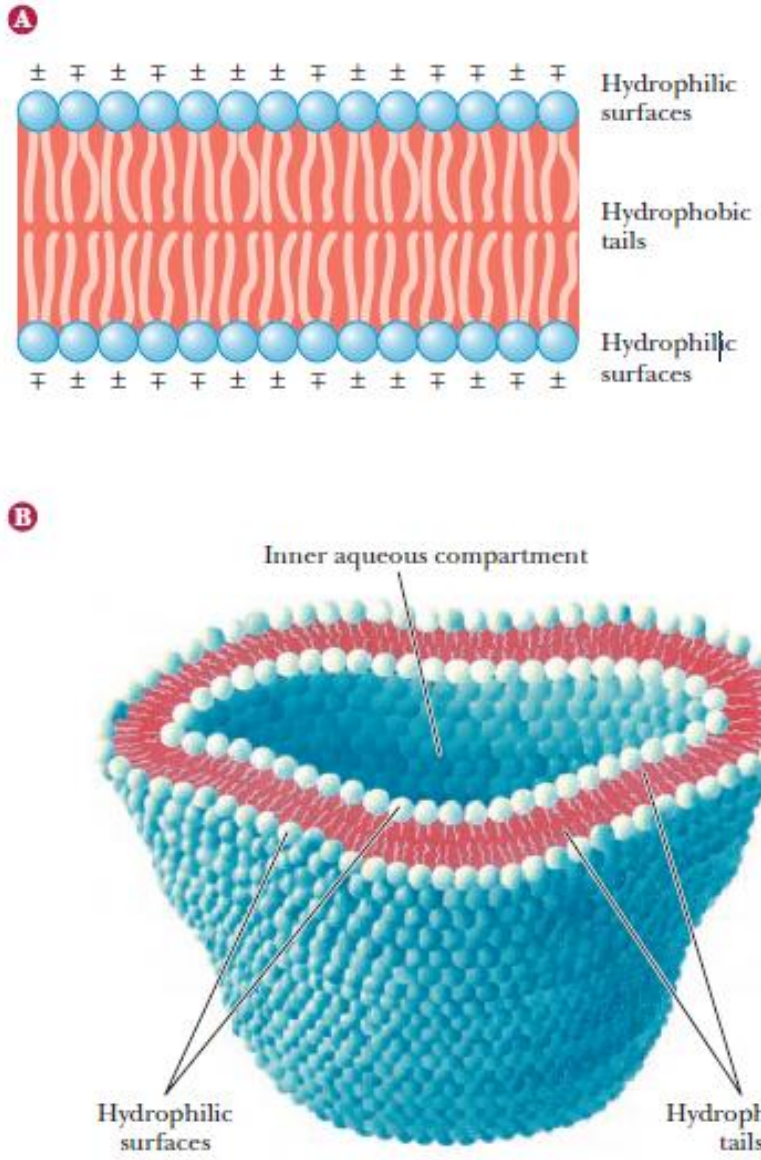
The structure of cell membrane: fluid-mosaic model



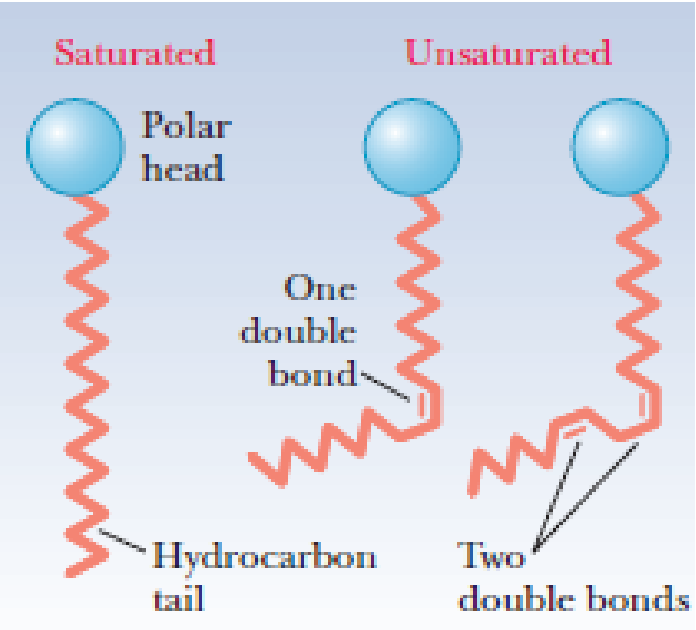
The lipid bilayer

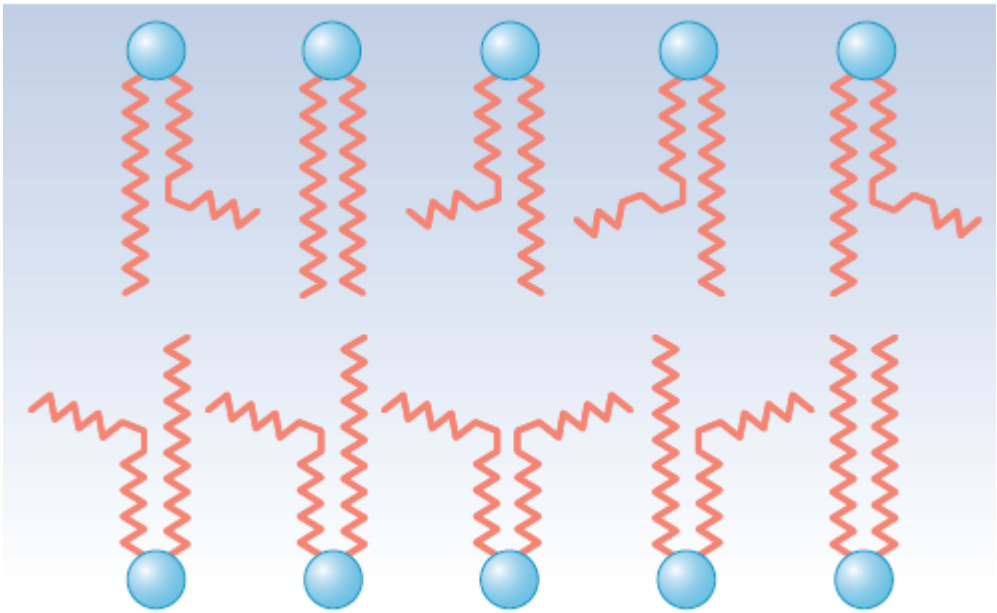
Bulkier molecules (e.g. cerebrosides) tend to occur in the outer layer, and smaller molecules tend to occur in the inner layer.

Because the bilayer is curved, the molecules of the inner layer are more tightly packed



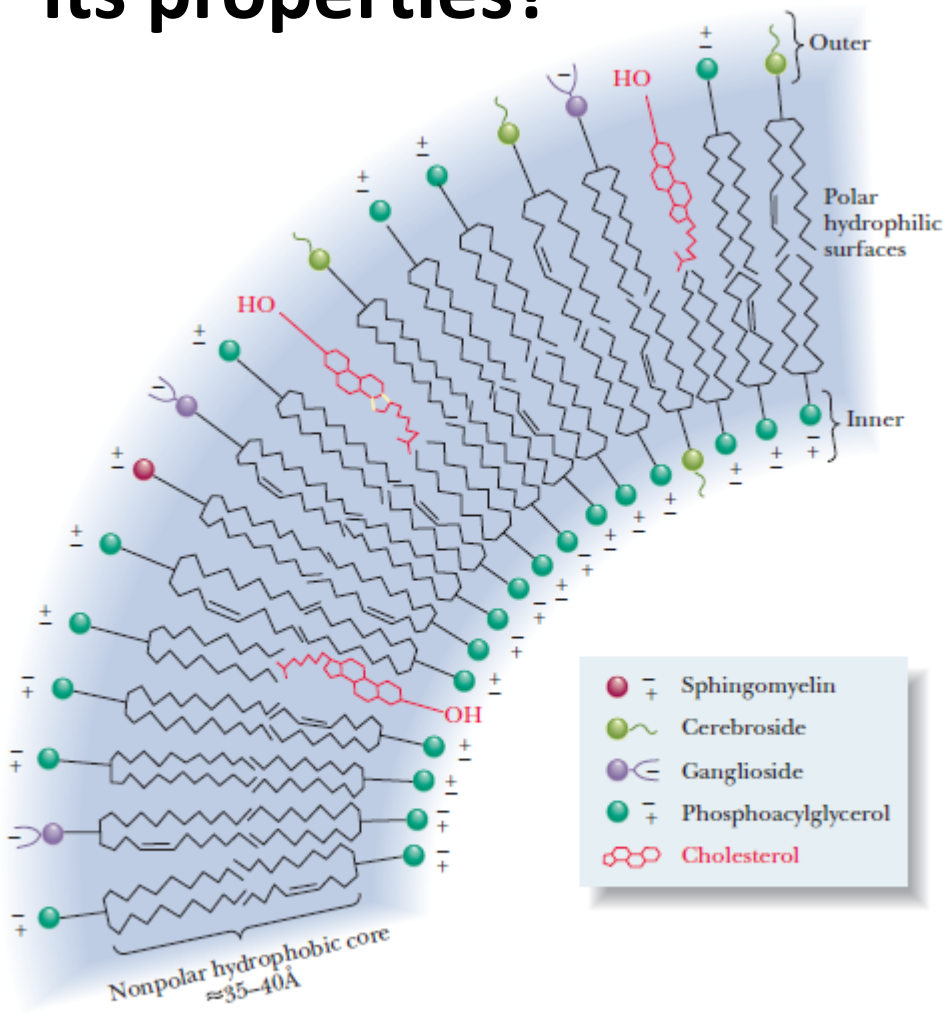
Fatty acids and membrane fluidity





Highly fluid membrane

How does the composition of the bilayer affect its properties?



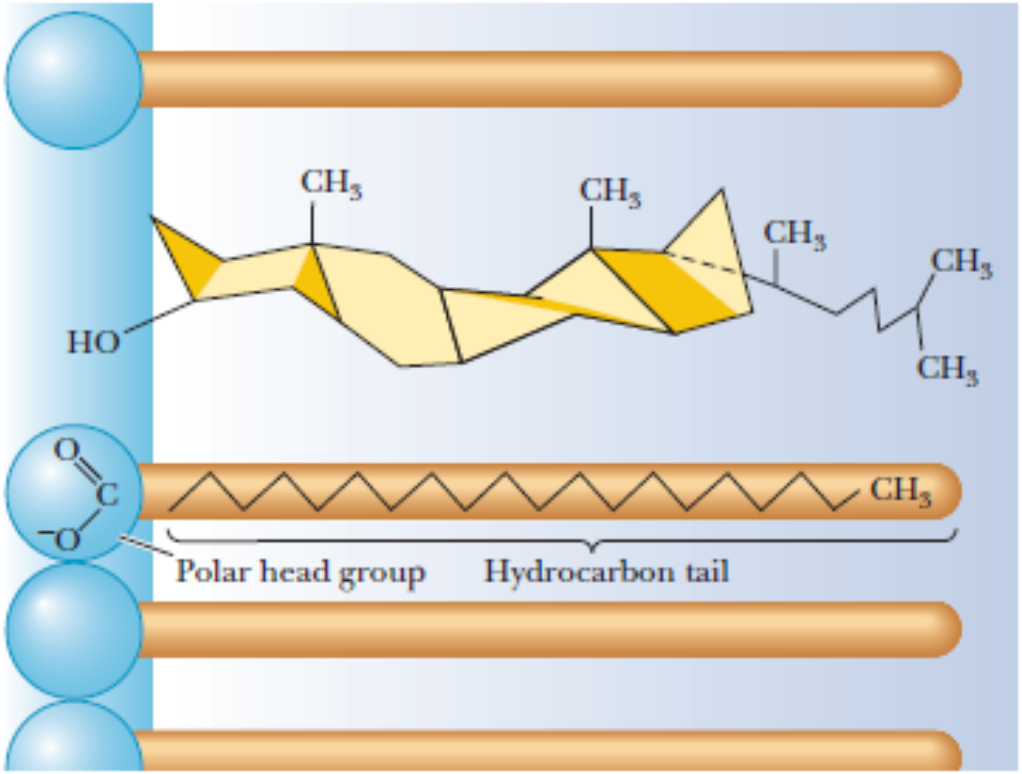
■ FIGURE 8.11 **Lipid bilayer asymmetry.** The compositions of the outer and inner layers differ; the concentration of bulky molecules is higher in the outer layer, which has more room.

-The bilayer's fluidity depends on its composition

-Saturated fatty acids, more packing and rigidity

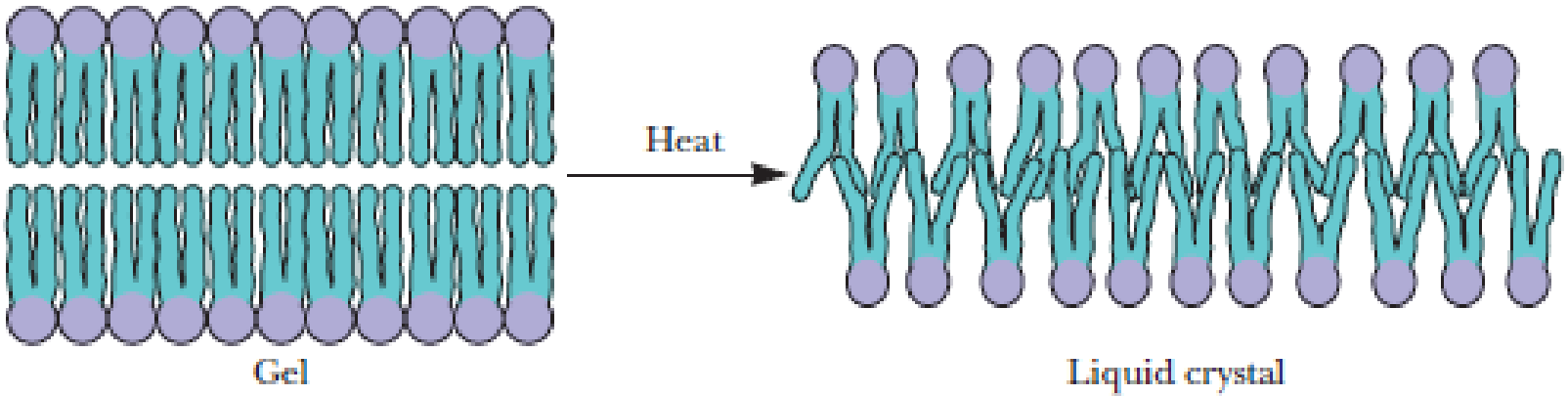
-The lipid bilayer components are always in motion (more movement in more fluid bilayers than rigid ones)

The effect of cholesterol on membrane fluidity



■ **FIGURE 8.14 Stiffening of the lipid bilayer by cholesterol.** The presence of cholesterol in a membrane reduces fluidity by stabilizing extended chain conformations of the hydrocarbon tails of fatty acids, as a result of van der Waals interactions.

Membrane gel-to-liquid crystalline phase transition



Lipid molecule movement within membranes

- Occasional “flip-flop” migration of lipid molecules from one layer of the bilayer to another.
- Lateral motion of lipid molecules within one of the two layers frequently takes place especially in more fluid bilayers.

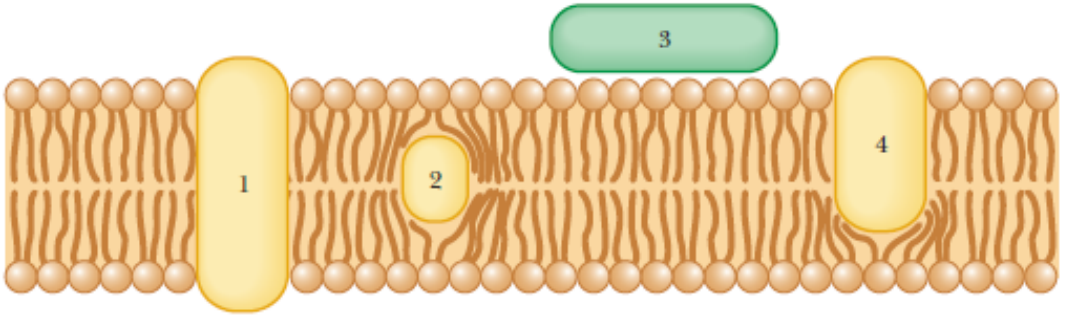
The Kinds of Membrane Proteins

1. Peripheral proteins on the surface of the membrane

- Are usually bound to the charged head groups of the lipid bilayer by polar interactions, electrostatic interactions, or both.
- Can be removed by mild treatment

2. Integral proteins within the lipid bilayer

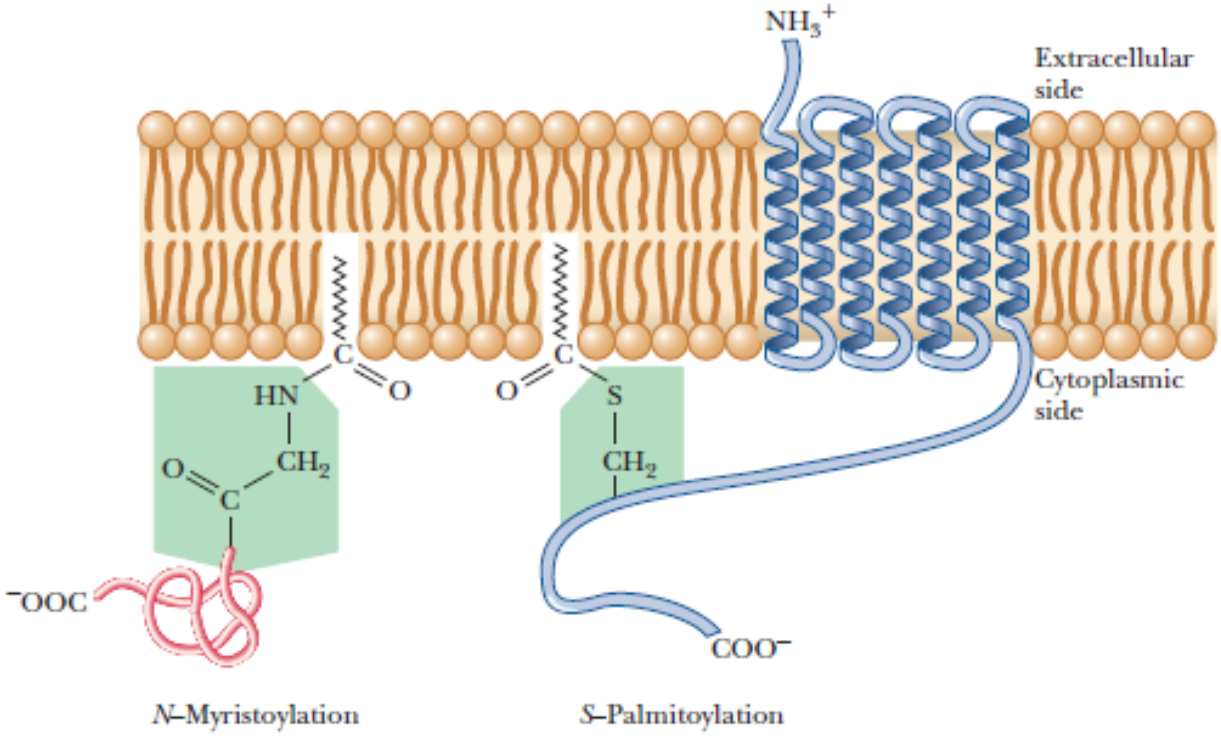
- Removal from membranes is difficult and needs harsh conditions, such as treatment with detergents or extensive sonication (these techniques result in denaturation)



■ FIGURE 8.16 **Some types of associations of proteins with membranes.** The proteins marked 1, 2, and 4 are integral proteins, and protein 3 is a peripheral protein. Note that the integral proteins can be associated with the lipid bilayer in several ways. Protein 1 transverses the membrane, protein 2 lies entirely within the membrane, and protein 4 projects into the membrane.

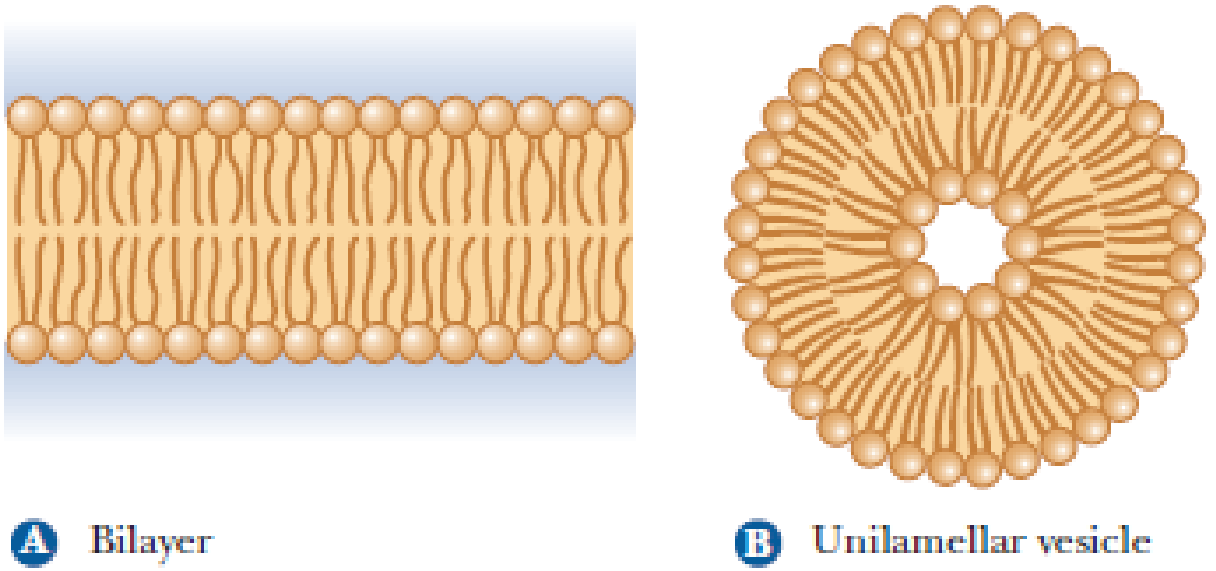
Protein Attachment to Membranes

- **Proteins span membranes** in the form of an a-helix or b-sheet.
- Proteins anchoring to lipids via **covalent bonds** from **cysteines** or free amino groups on the protein to lipid anchors.
- Lipid anchors: **myristoyl** and **palmitoyl groups**
- Proteins and lipids are **unevenly** distributed on the inner and outer layers of cell membranes



■ **FIGURE 8.17** **Certain proteins are anchored to biological membranes by lipid anchors.** Particularly common are the *N*-myristoyl- and *S*-palmitoyl anchoring motifs shown here. *N*-myristoylation always occurs at an *N*-terminal glycine residue, whereas thioester linkages occur at cysteine residues within the polypeptide chain. G-protein–coupled receptors, with seven transmembrane segments, may contain one (and sometimes two) palmitoyl anchors in thioester linkage to cysteine residues in the *C*-terminal segment of the protein.

Clinical application: Membranes and drug delivery



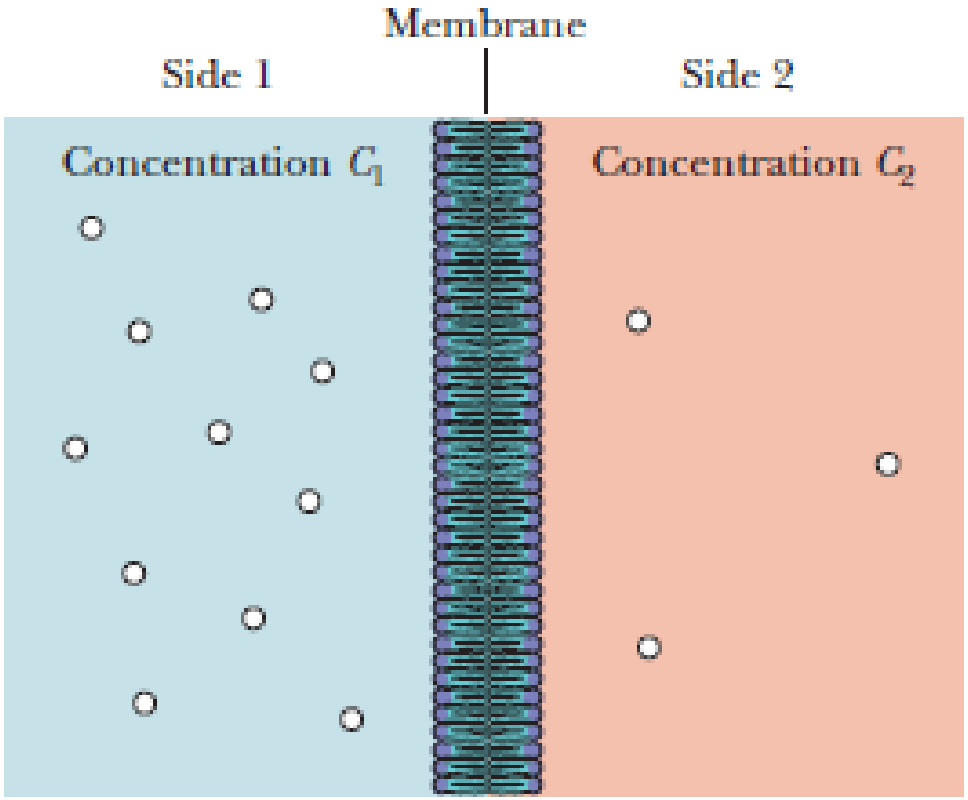
Example: a skin lotion to counteract the effects of UV light on DNA repair

The lotion contains liposomes filled with a viral DNA-repair enzyme, called T4 endonuclease V.

Functions of proteins

1. Structural boundaries and containers of all cells and of organelles
2. Transport through the lipid bilayer or membrane proteins.
3. Catalysis
4. Receptor property

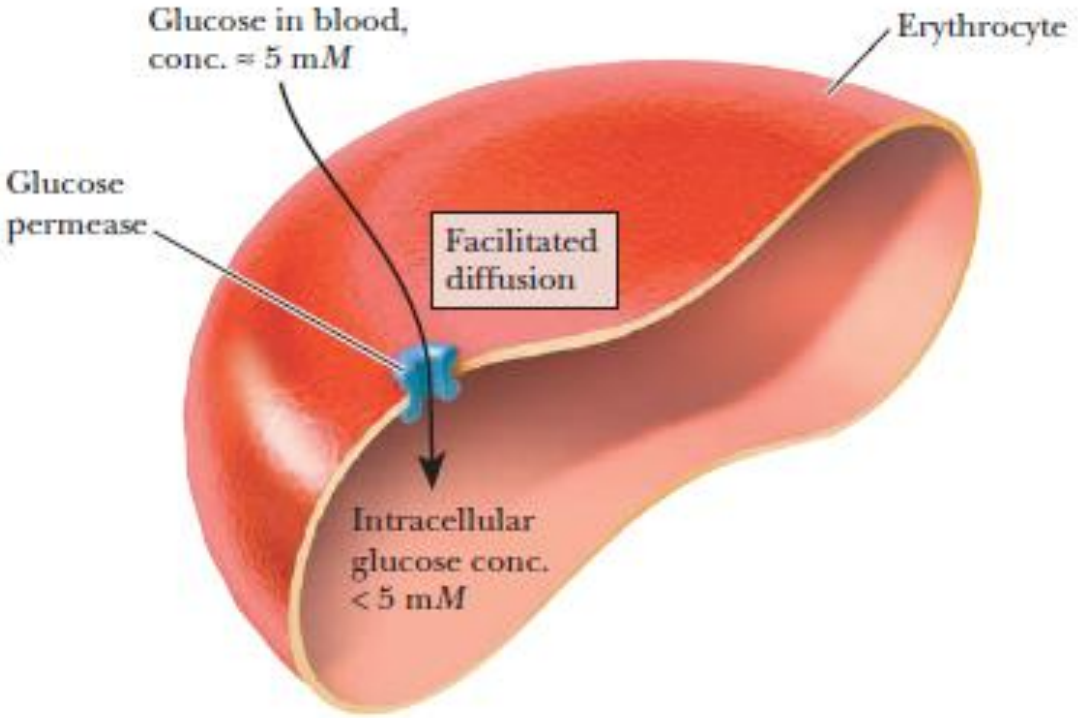
Transport through membranes

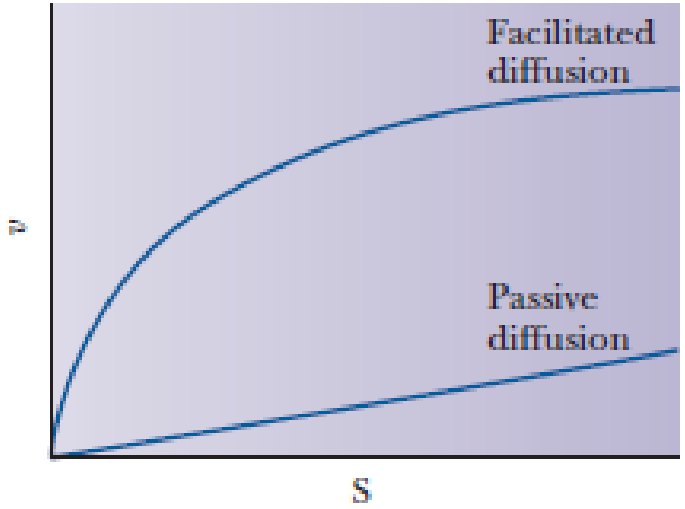


1. Passive transport including simple and facilitated diffusion

2. Active transport

Facilitated diffusion

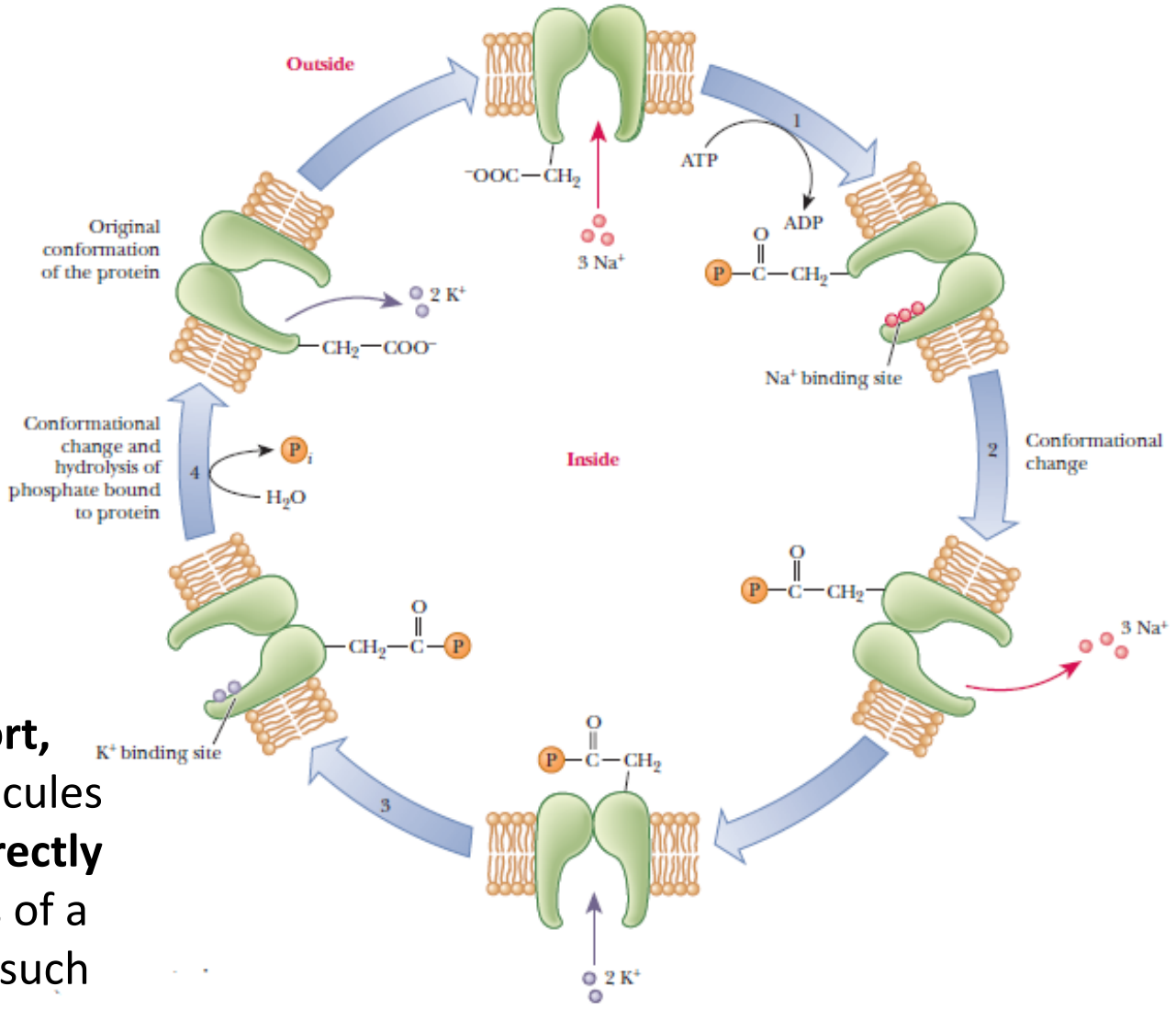




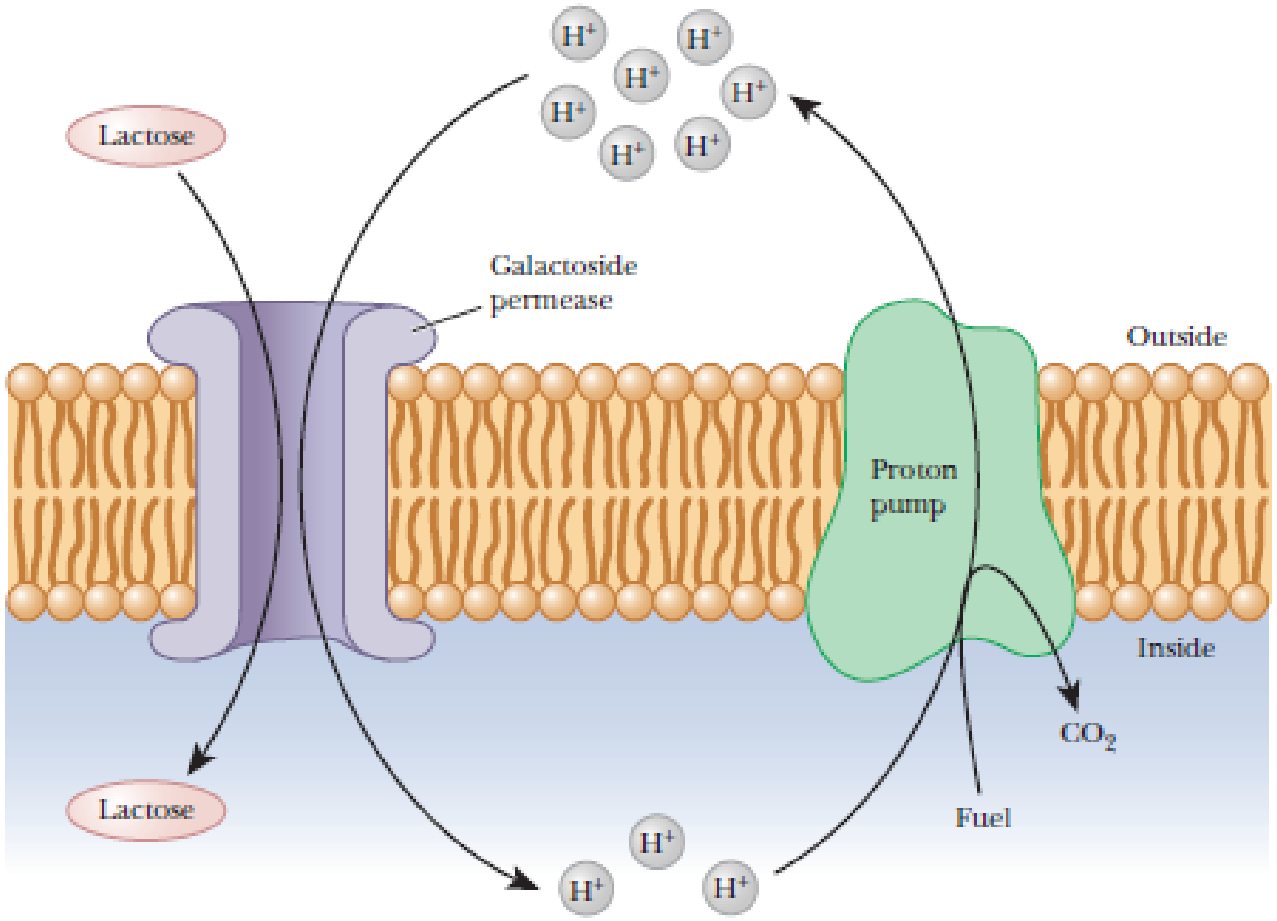
-Carrier proteins have several a-helical portions that span the membrane; or a b-barrel that forms the pore.
-The exterior of the helix (in contact with the lipid bilayer), is hydrophobic.
-The interior of the helix (through which ions pass) is hydrophilic.

Active transport

- A carrier protein and an energy source to move solutes against a gradient are needed
- EX. Na+/K+ pump (ATPase and a transport protein)
- **Primary active transport,** the movement of molecules against a gradient is **directly** linked to the hydrolysis of a high-energy molecule, such as ATP.



Secondary Active transport



How do membrane receptors work?

- Many receptors are tightly bound integral proteins, and their activity depends on the membrane environment.
- Receptors are often large oligomeric proteins (several subunits), with molecular weights of hundreds of thousands.
- Receptors have very few molecules in each cell, making their isolation and studying more difficult

How do membrane receptors work?

- LDL is a particle that consists of various lipids, cholesterol and phosphoglycerides, and a protein
- LDL is the principal carrier of cholesterol in the bloodstream
- Excess cholesterol inhibits LDL receptor synthesis and increases cholesterol concentration in blood.