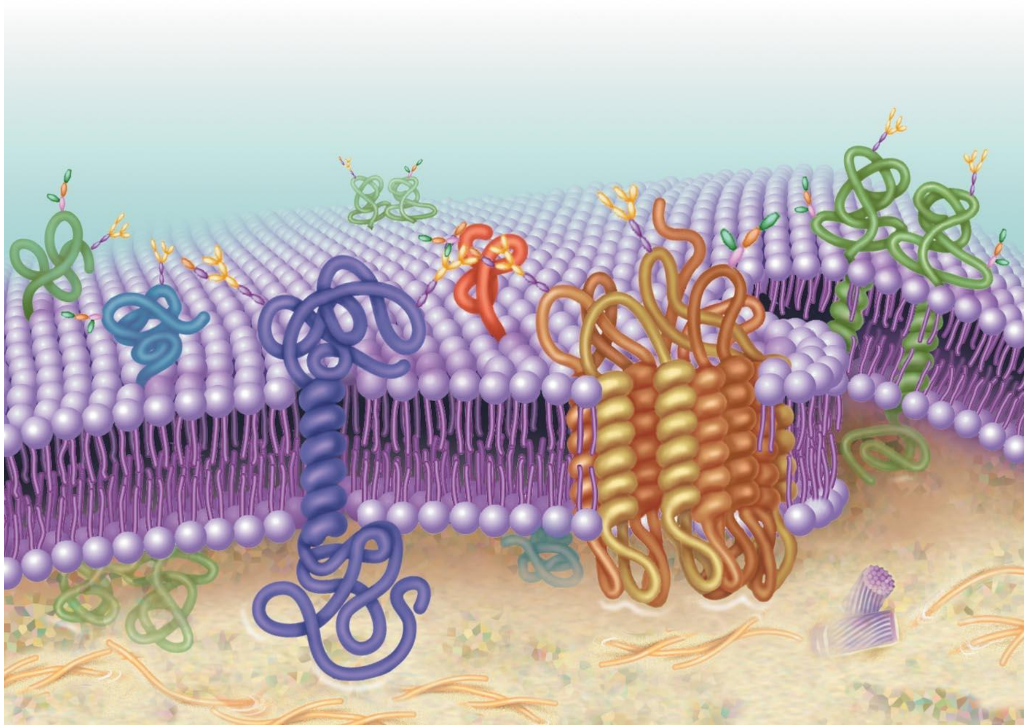
Chapter 11. *Lipids and Membranes*

- **Section 11.1:** Lipid Classes
- **Section 11.2:** Membranes



Section 11.1: Lipid Classes

- **Lipids** are defined as substances from living things that dissolve in nonpolar solvents and a broad group of naturally-occurring molecules which includes fats, waxes, sterols, fat-soluble vitamins (such as vitamins A, D, E and K), monoglycerides, diglycerides, triglycerides, phospholipids, and others.

- The main biological functions of lipids include stored form of energy, structural elements of biological membranes (phopholipids) and important signaling molecules.

- Lipids may be broadly defined as hydrophobic or amphiphilic small molecules. The amphiphilic nature of some lipids allows them to form structures such as vesicles, liposomes, or membranes in an aqueous environment.

- Lipid is sometimes used as a synonym for fats that are a subgroup of lipids called triglycerides. Lipids also encompass molecules such as fatty acids and their derivatives (including tri-, di-, and monoglycerides and phospholipids), as well as cholesterol.

Lipids can be subdivided into the following classes:

1. **Fatty acids**
2. **Triacylglycerols**
3. **Wax esters**
4. **Phospholipids**
5. **Sphingolipids**
6. **Isoprenoids**

https://www.youtube.com/watch?v=dUEtwL_aV9U

Fatty Acids

- **Fatty acid** is an unbranched-chain carboxylic acid, most commonly of 12~20 carbons, derived from hydrolysis of animal fats, vegetable oils, or phosphodiacylglycerols of biological membranes.
- Monocarboxylic acids that typically contain hydrocarbon chains of variable lengths (12 to 20 or more carbons)
- Numbered from the carboxylate end, and the a-carbon is adjacent to the carboxylate group
- Terminal methyl carbon is denoted the omega (w) carbon
- Important in triacylglycerols and phospholipids

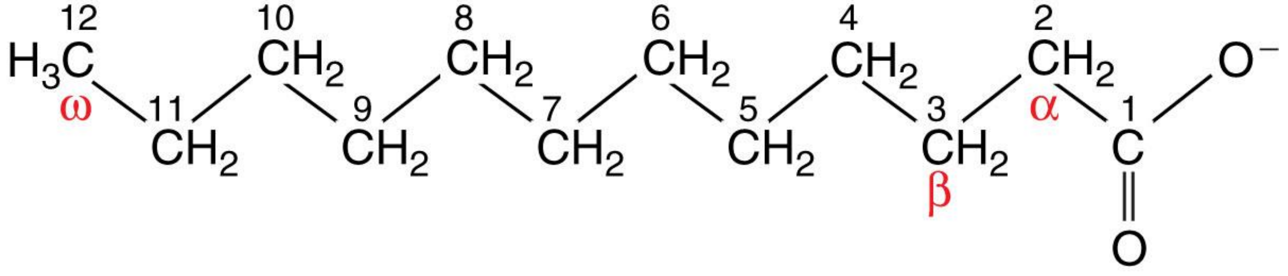
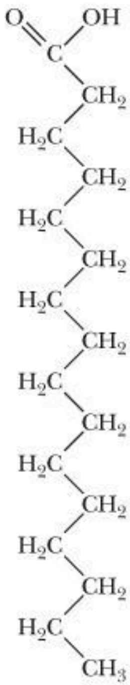


Figure 11.1 Fatty Acid Structure

TABLE 11.1 Examples of Fatty Acids

Common Name	Structure	Abbreviation
Saturated Fatty Acids		
Myristic acid	$CH_3(CH_2)_{12}COOH$	14:0
Palmitic acid	$CH_3(CH_2)_{12}CH_2CH_2COOH$	16:0
Stearic acid	$CH_3(CH_2)_{12}CH_2CH_2CH_2CH_2COOH$	18:0
Arachidic acid	$CH_3(CH_2)_{12}CH_2CH_2CH_2CH_2CH_2CH_2COOH$	20:0
Lignoceric acid	$CH_3(CH_2)_{12}CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2COOH$	24:0
Cerotic acid	$CH_3(CH_2)_{12}CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2COOH$	26:0
Unsaturated Fatty Acids		
Palmitoleic acid	$CH_3(CH_2)_5\overset{H}{C}{=}\overset{H}{C}(CH_2)_7COOH$	$16{:}1^{\Delta 9}$
Oleic acid	$CH_3(CH_2)_7\overset{H}{C}{=}\overset{H}{C}(CH_2)_7COOH$	$18{:}1^{\Delta 9}$
Linoleic acid	$CH_3(CH_2)_4\overset{H}{C}{=}\overset{H}{C}{-}CH_2{-}\overset{H}{C}{=}\overset{H}{C}(CH_2)_7COOH$	$18{:}2^{\Delta 9,12}$
α-Linolenic acid	$CH_3CH_2\overset{H}{C}{=}\overset{H}{C}{-}CH_2{-}\overset{H}{C}{=}\overset{H}{C}{-}CH_2{-}\overset{H}{C}{=}\overset{H}{C}(CH_2)_7COOH$	$18{:}3^{\Delta 9,12,15}$
γ-Linolenic acid	$CH_3(CH_2)_3{-}\left(CH_2{-}\overset{H}{C}{=}\overset{H}{C}\right)_3{-}(CH_2)_4{-}COOH$	$18{:}3^{\Delta 6,9,12}$
Arachidonic acid	$CH_3(CH_2)_3{-}\left(CH_2{-}\overset{H}{C}{=}\overset{H}{C}\right)_4{-}(CH_2)_3COOH$	$20{:}4^{\Delta 5,8,11,14}$



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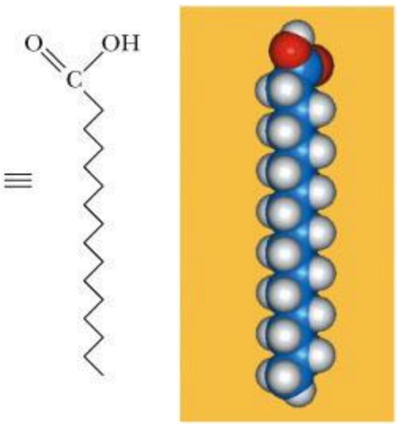
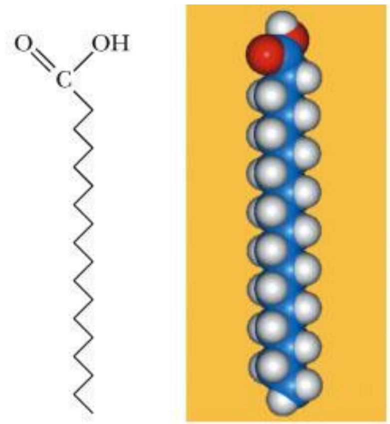
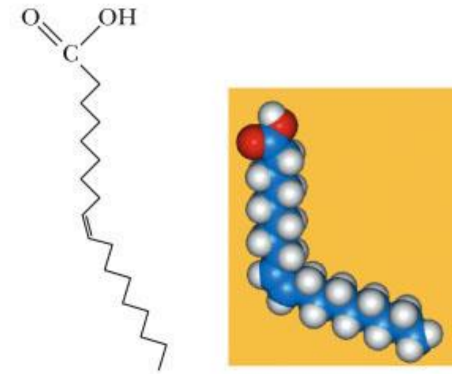


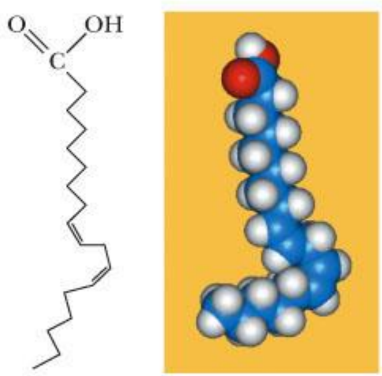
Palmitic acid



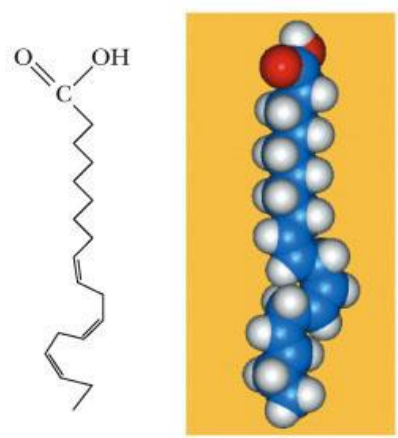
Stearic acid



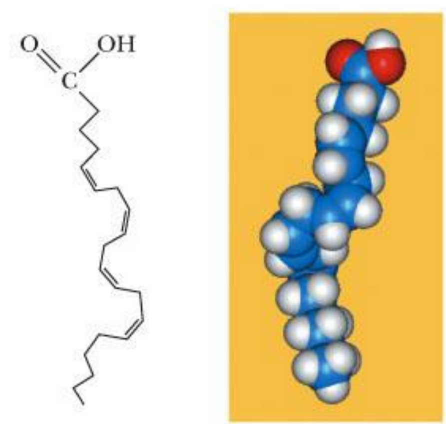
Oleic acid



Linoleic acid



α-Linolenic acid



Arachidonic acid

- Most naturally occurring fatty acids have an even number of carbons in an unbranched chain
- Fatty acids that contain only single carbon-carbon bonds are **saturated**
- Fatty acids that contain one or more double bonds are **unsaturated**
    - Can occur in two isomeric forms: **cis** (like groups on the same side) and **trans** (like groups are on opposite sides)

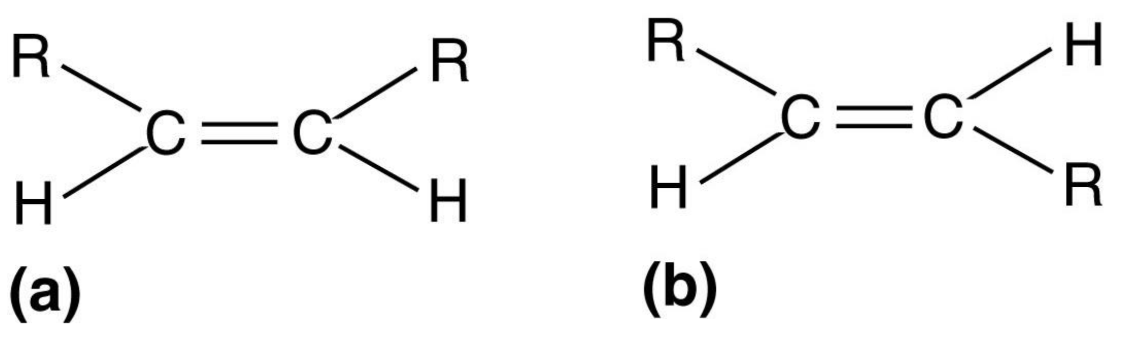


Figure 11.2 Isomeric Forms of Unsaturated Molecules

- The double bonds in most naturally occurring fatty acids are ***cis*** and cause a **kink** in the fatty acid chain
- Unsaturated fatty acids are liquid at room temperature; saturated fatty acids are usually solid
  - **Monounsaturated** fatty acids have one double bond while **polyunsaturated** fats have two or more

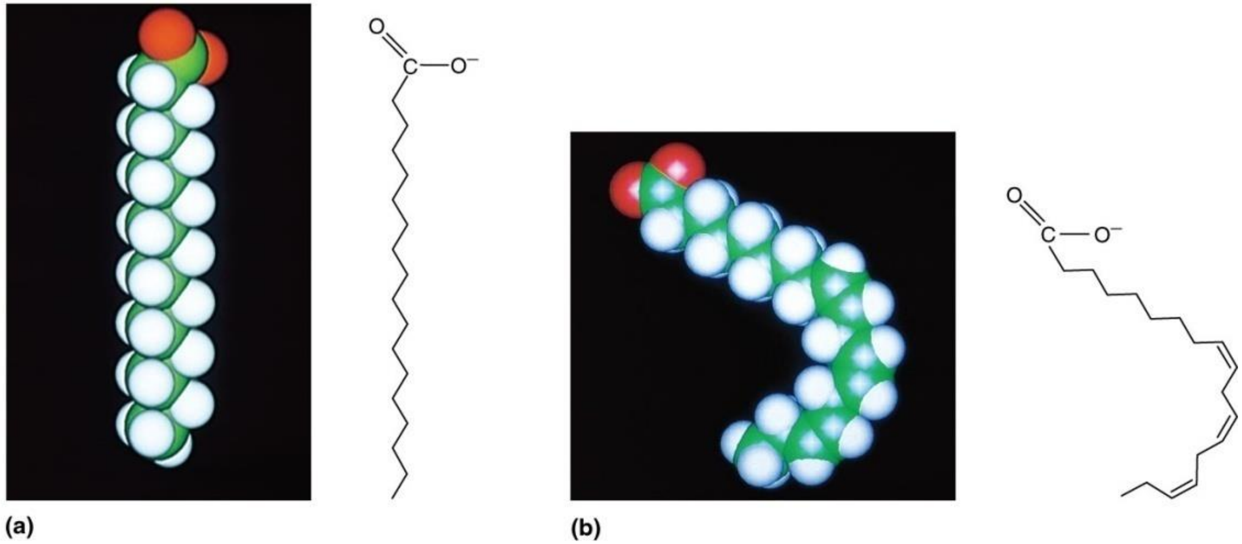


Figure 11.3 Space-Filling and Conformational Models

Eicosanoids

- A diverse group of powerful, hormone-like (generally **autocrine**) molecules produced in most mammalian tissues
- Include prostaglandins, thromboxanes, and leukotrienes
  - Mediate a wide variety of physiological processes: smooth muscle contraction, inflammation, pain perception, and blood flow regulation
- Eicosonoids are often derived from arachidonic acid or eicosapentaenoic acid (EPA)
- **Prostaglandins** contain a cyclopentane ring and hydroxyl groups at C-11 and C-15
  - Prostaglandins are involved in inflammation, digestion, and reproduction

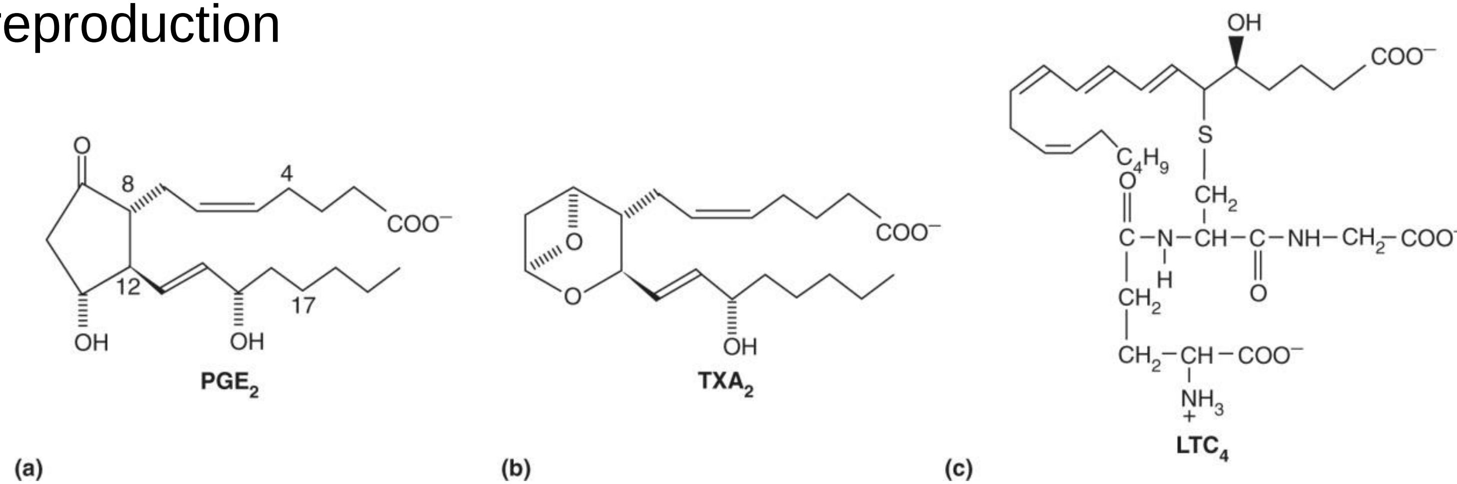
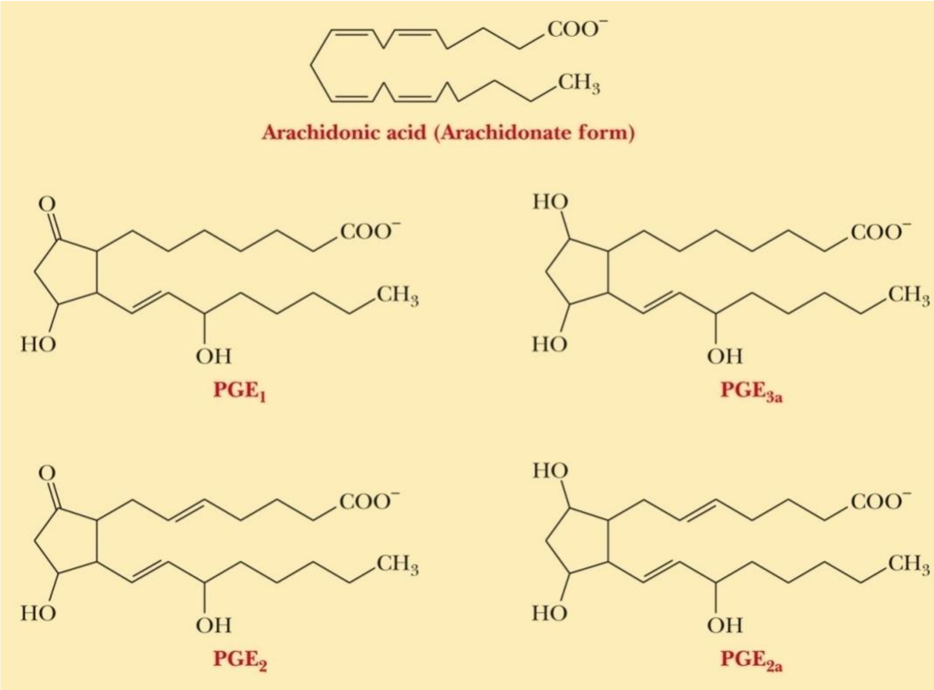


Figure 11.4a Eicosanoids

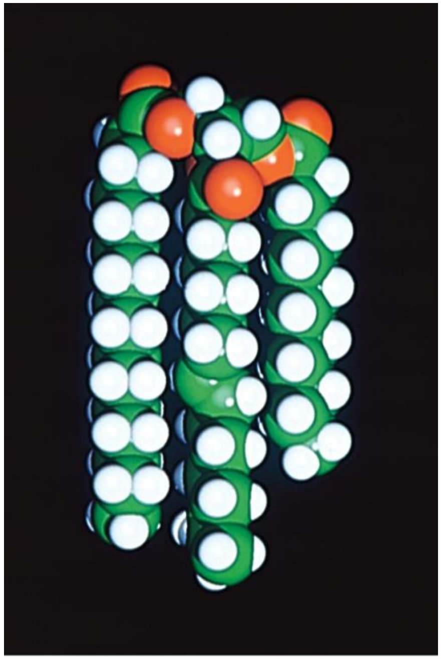
Prostaglandins

- **Prostaglandins:** a family of compounds that have the 20-carbon skeleton of prostanoic acid
- First detected in seminal fluid…from prostate
- The metabolic precursor is arachidonic acid (20 carbon atoms: 4 double bonds)
- Functions of prostaglandins are control of blood pressure, stimulation of smooth muscle contraction and induction of inflammation.
- Aspirin, cortisone and other steroids have anti-inflammatory actions by inhibiting the synthesis of prostaglandins.



Triacylglycerols are fatty acid esters of glycerol

- Triacylglycerols are esters of glycerol with three fatty acids.
- Neutral fats because they have no charge
- Contain fatty acids of varying lengths and can be a mixture of saturated and unsaturated
- Depending on fatty acid composition, can be termed fats or oils
- Fats are solid at room temperature and have a high saturated fatty acid composition. Oils are liquid at room temperature and have a high unsaturated fatty acid composition



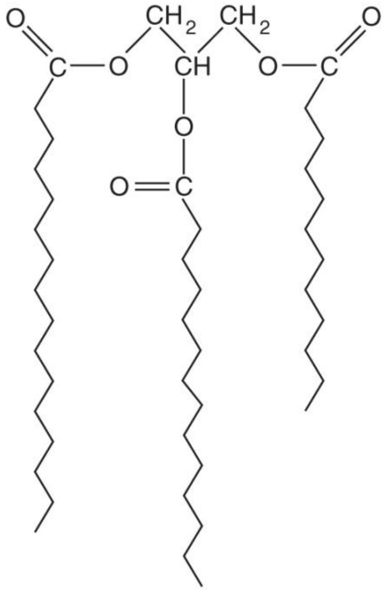


Figure 11.6 Space-Filling and Conformational Models of a Triacylglycerol

Triacylglycerols

Roles in animals: energy storage (also in plants), insulation at low temperatures, and water repellent for some animals' feathers and fur

- Better storage form of energy for two reasons:
  1. Hydrophobic and coalesce into droplets; store an equivalent amount of energy in about one-eighth the space
  2. More reduced and thus can release more electrons per molecule when oxidized

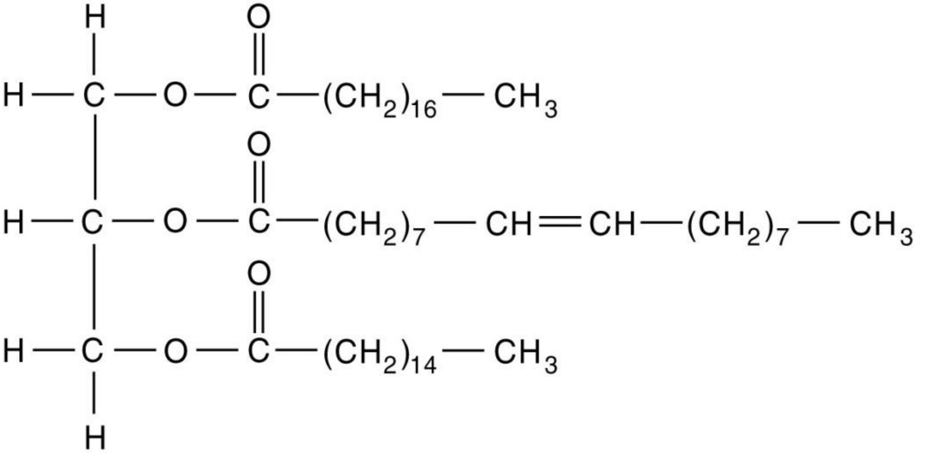
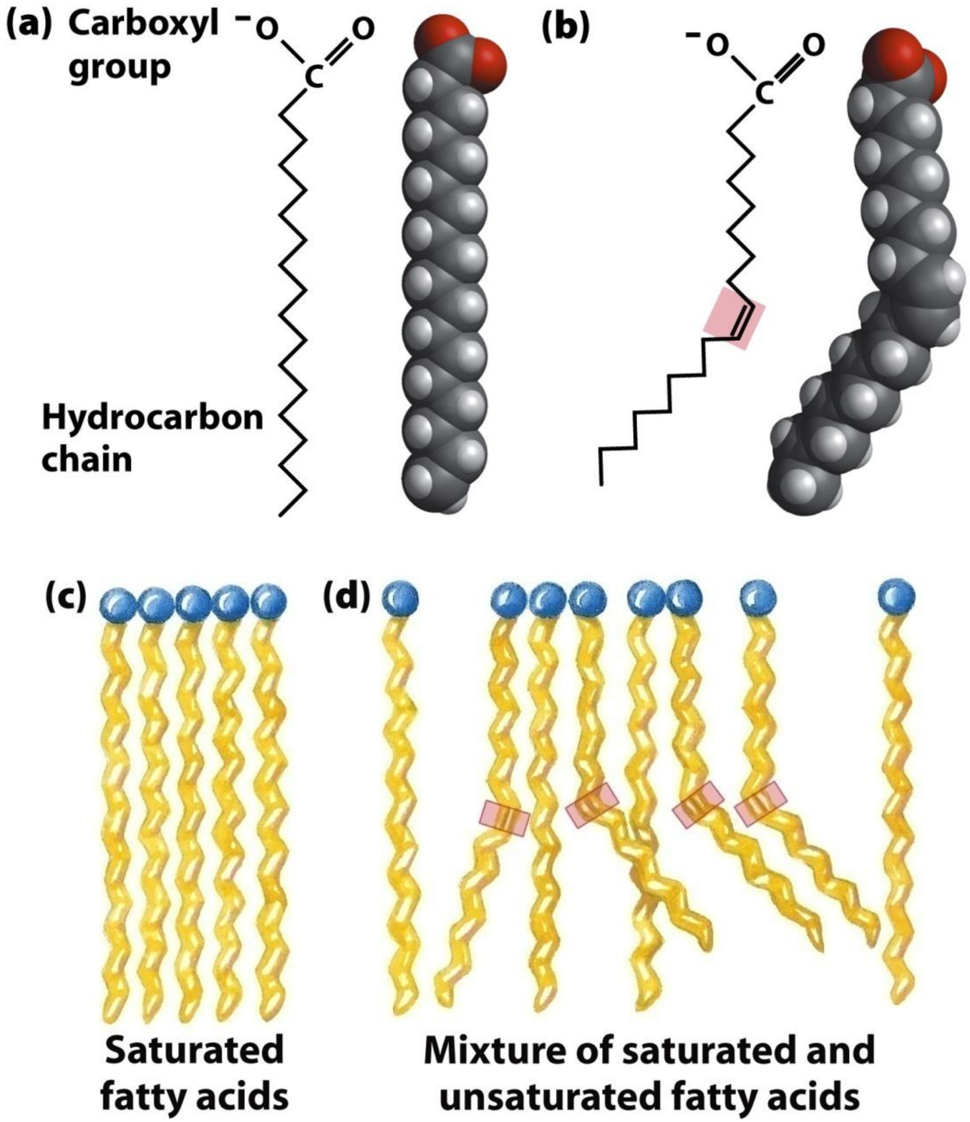


Figure 11.5 Triacylglycerol



Packing of fatty acids into stable aggregates

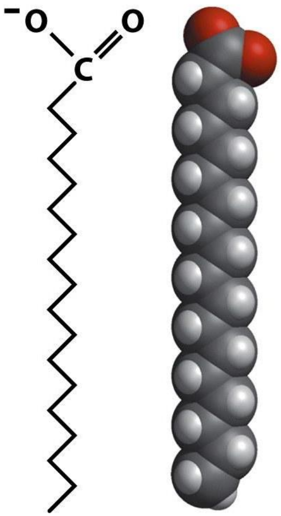
Physical properties of fatty acids are largely determined by the length and degree of unsaturation of hydrocarbon chain.

- Poor solubility due to nonpolar hydrocarbon chains.
- FA that contain C=C are *unsaturated*: If contain only C-C bonds, they are *saturated*.
- The longer carbon chain and the fewer double bonds, the lower the solubility.
- The carboxylic group is polar and accounts for the slight solubility in water.
- The degree of packing of fatty acids affects their melting points.
- Saturated fatty acids with carbons (12 to 24) are *waxy*, whereas unsaturated fatty acids of these lengths are *oily* liquids.

Typical Naturally Occurring Saturated Fatty Acids

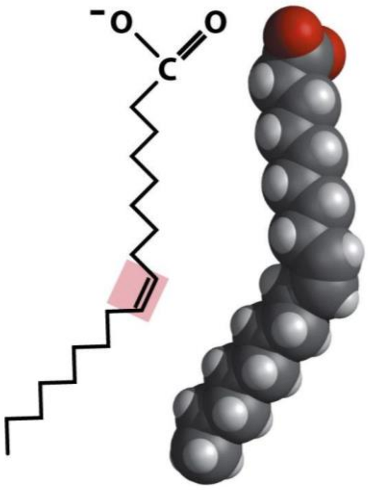
Acid	Number of Carbon Atoms	Formula	Melting Point (°C)
Lauric	12	$CH_3(CH_2)_{10}CO_2H$	44
Myristic	14	$CH_3(CH_2)_{12}CO_2H$	58
Palmitic	16	$CH_3(CH_2)_{14}CO_2H$	63
Stearic	18	$CH_3(CH_2)_{16}CO_2H$	71
Arachidic	20	$CH_3(CH_2)_{18}CO_2H$	77

Fully saturated forms



- Flexible due to free rotation around each carbon-carbon bond
- Minimized steric hinderance
- Crystalline arrays due to tight packing
- High melting point

Unsaturated forms



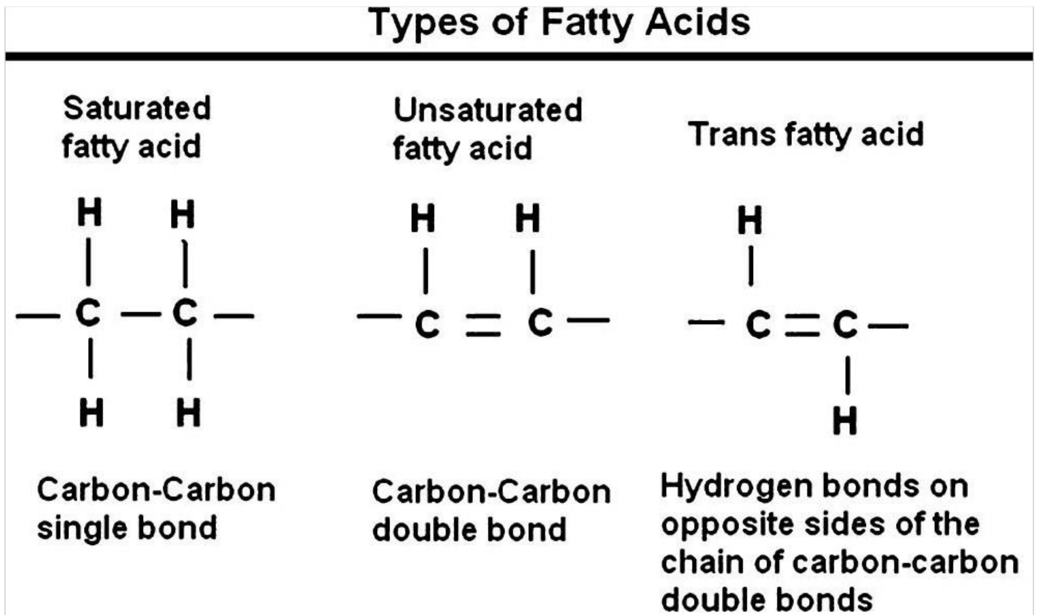
- A *cis* bond forces a ***kink*** in the hydrocarbon chain.
- Weak intermolecular interactions
- Low melting points due to poorly ordered array

- In most unsaturated fatty acids, the ***cis*** isomer predominates; the ***trans*** isomer is rare.

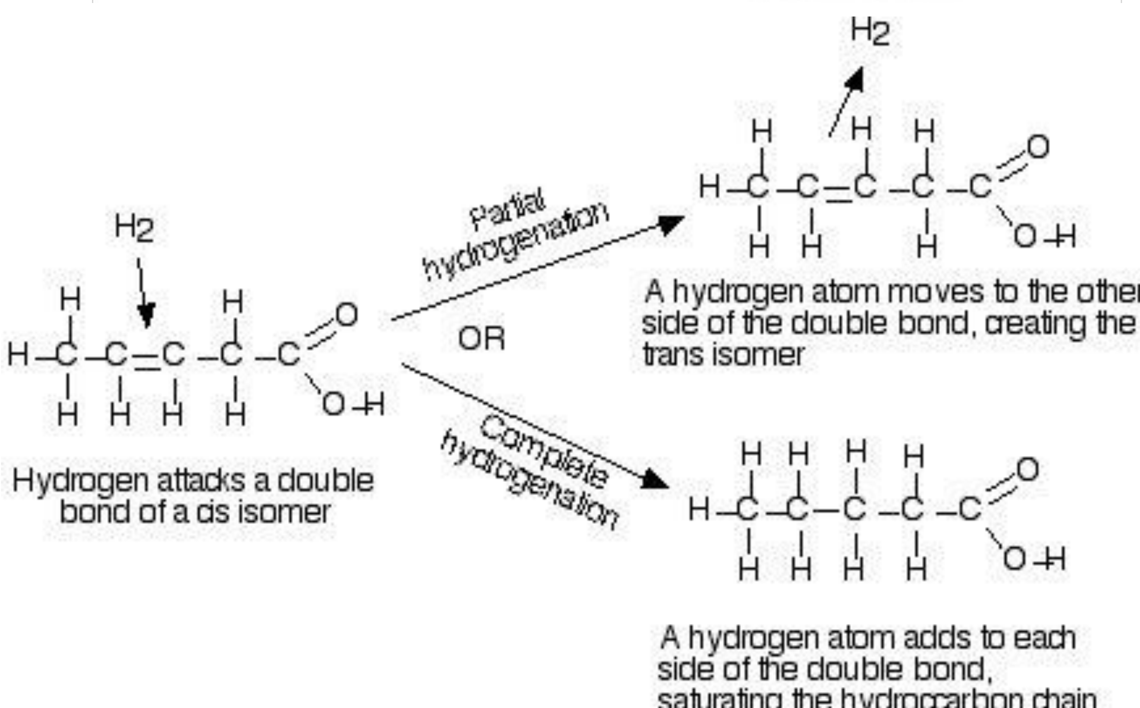
- **Unsaturated** fatty acids have lower melting points than their saturated counterparts; the greater the degree of unsaturation, the lower the melting point

Typical Naturally Occurring Unsaturated Fatty Acids

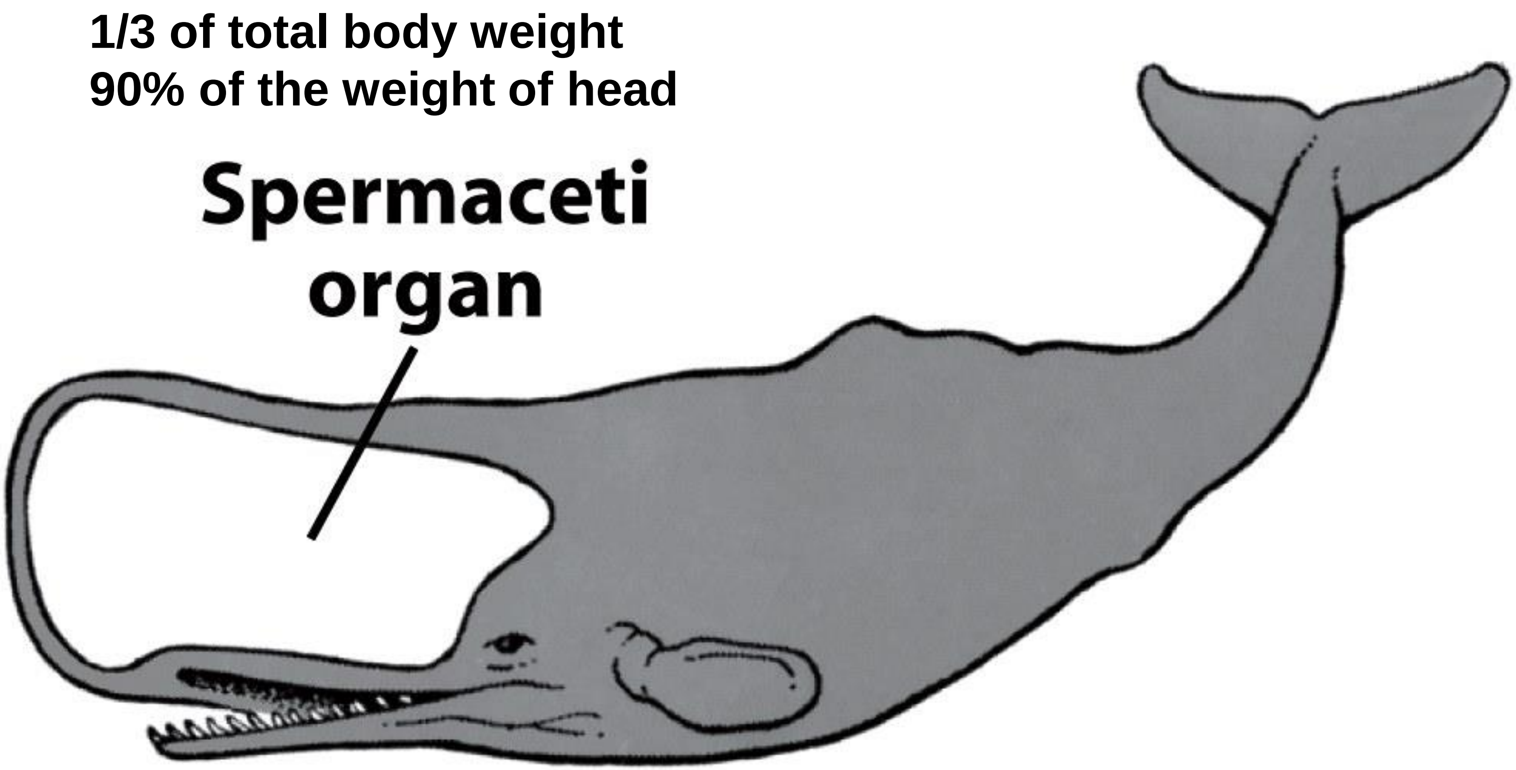
Acid	Number of Carbon Atoms	Degree of Unsaturation*	Formula	Melting Point (°C)
Palmitoleic	16	16:1—Δ^{9}	$CH_3(CH_2)_5CH{=}CH(CH_2)_7CO_2H$	−0.5
Oleic	18	18:1—Δ^{9}	$CH_3(CH_2)_7CH{=}CH(CH_2)_7CO_2H$	16
Linoleic	18	18:2—$\Delta^{9,12}$	$CH_3(CH_2)_4CH{=}CH(CH_2)CH{=}CH(CH_2)_7CO_2H$	−5
Linolenic	18	18:3—$\Delta^{9,12,15}$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



Types of Fatty Acids
Saturated fatty acid
Unsaturated fatty acid
Trans fatty acid
Carbon-Carbon single bond
Carbon-Carbon double bond
Hydrogen bonds on opposite sides of the chain of carbon-carbon double bonds



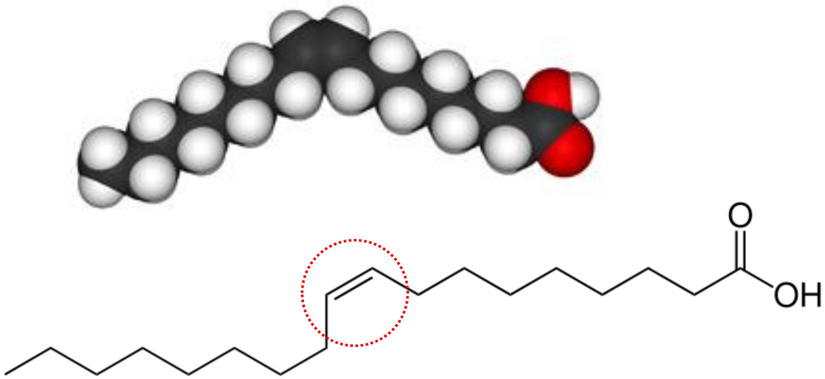
H2
Hydrogen attacks a double bond of a cis isomer
Partial hydrogenation
OR
Complete hydrogenation
A hydrogen atom moves to the other side of the double bond, creating the trans isomer
A hydrogen atom adds to each side of the double bond, saturating the hydrocarbon chain



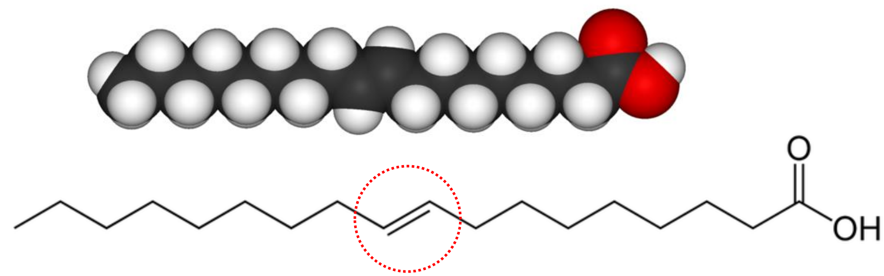
The mixture of triacylglycerols and waxes containing an abundance of unsatataturated fatty acids is liquid at the normal resting body temperature, but it becomes to crystallize at about 31°C and becomes solid when the temperature drops several more degrees.

Partial hydrogenation of cooking oils produces *trans* fatty acids

Cis unsaturated fatty acid that comprises 55–80% of olive oil.



Trans unsaturated fatty acid often found in partially hydrogenated vegetable oils



Longer shelf-life

Increased stability at high temperature

High melting points

Margarine (solid at room temperature)

Wax Esters

- **Waxes** are complex mixtures of nonpolar lipids
- Protective coatings on the leaves, stems, and fruits of plants and on the skin and fur of animals
- Wax esters composed of long-chain fatty acids and long-chain alcohols are prominent constituents of most waxes
  - Examples include carnuba (melissyl cerotate) and beeswax

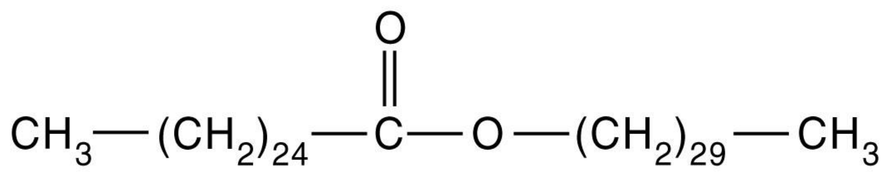
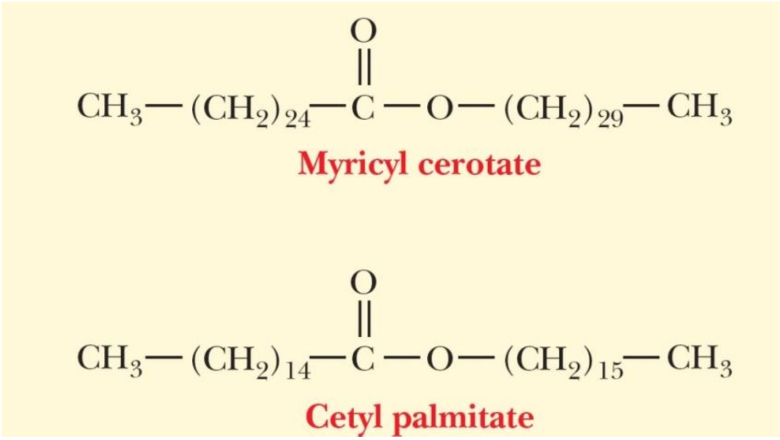
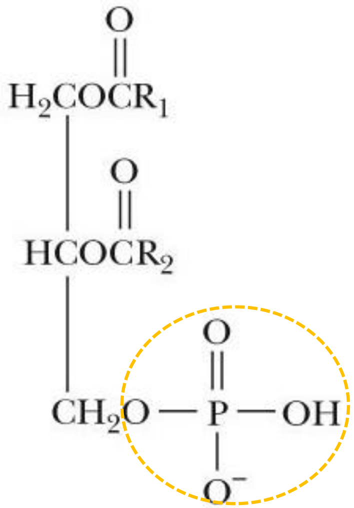


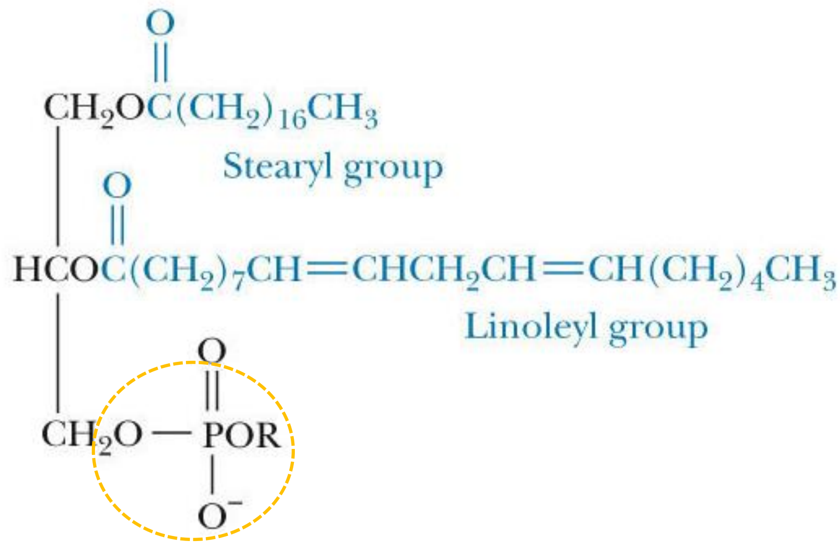
Figure 11.8 The Wax Ester Melissyl Cerotate



Phosphoacylglycerols (Phospholipids)



Phosphatidic acid



Phosphatidyl ester

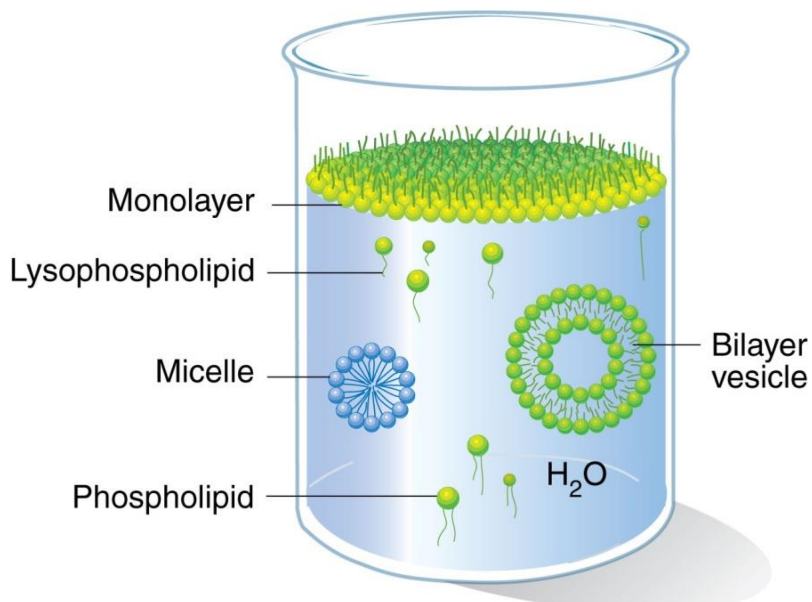


Figure 11.9 Phospholipid Molecules in Aqueous Solution

Phospholipids

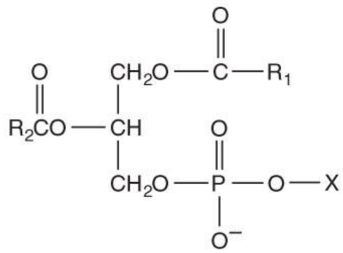
- Amphipathic with a polar head group (phosphate and other polar or charged groups) and hydrophobic fatty acids
- Act in membrane formation, emulsification, and as a surfactant
- Spontaneously rearrange into ordered structures when suspended in water
- When one alcohol group of glycerol is esterified by a phosphoric acid rather than by a carboxylic acid, phosphatidic acid produced.
- Phosphoacylglycerols (phosphoglycerides) are the second most abundant group of naturally occurring lipids, and they are found in plant and animal membranes.
- Simplest phosphoglyceride is phosphatidic acid composed of glycerol-3-phosphate and two fatty acids

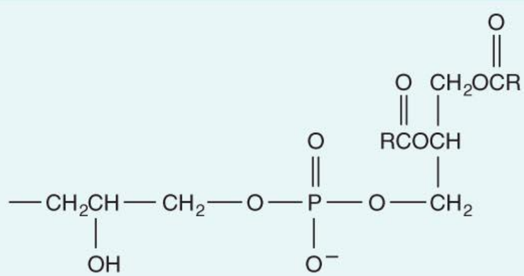
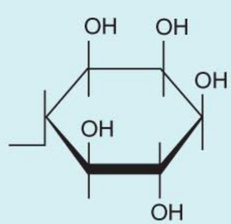
Phospholipids

Two types of phospholipids: phosphoglycerides & sphingomyelins

- **Sphingomyelins** contain sphingosine instead of glycerol (also classified as sphingolipids)
- **Phosphoglycerides** contain a glycerol, fatty acids, phosphate, and an alcohol
  - Simplest phosphoglyceride is phosphatidic acid composed of glycerol-3-phosphate and two fatty acids
  - Phosphatidylcholine (lecithin) is an example of alcohol esterified to the phosphate group as choline

TABLE 11.2 Major Classes of Phosphoglycerides

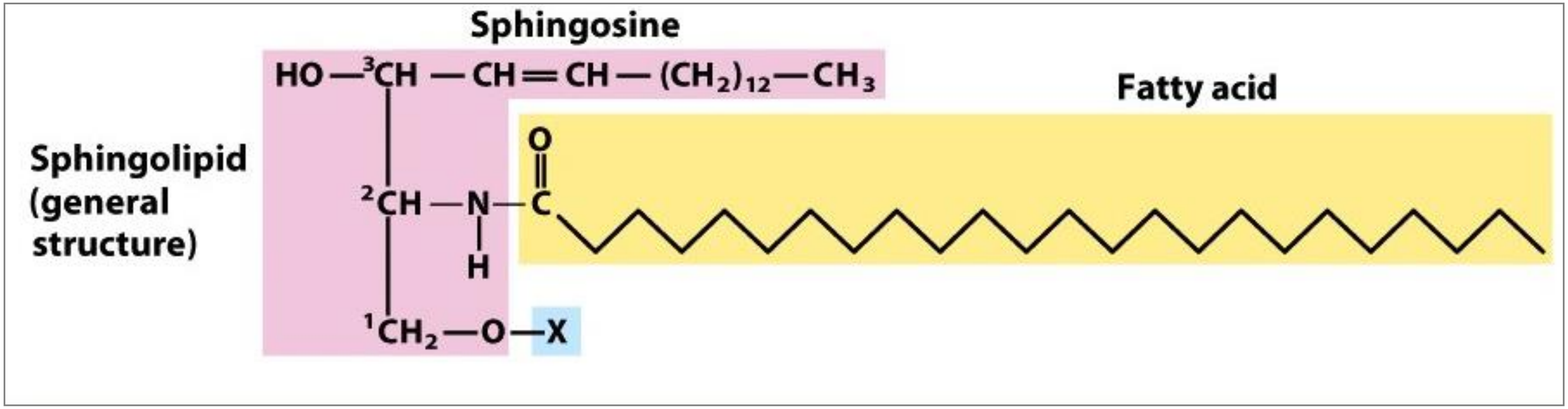


X Substituent		
Name of X-OH	**Formula of X**	**Name of Phospholipid**
Water	—H	Phosphatidic acid
Choline	$—CH_2CH_2\overset{+}{N}(CH_3)_3$	Phosphatidylcholine (lecithin)
Ethanolamine	$—CH_2CH_2\overset{+}{N}H_3$	Phosphatidylethanolamine (cephalin)
Serine	$—CH_2—CH(\overset{+}{N}H_3)COO^-$	Phosphatidylserine
Glycerol	$—CH_2CH(OH)CH_2OH$	Phosphatidylglycerol
Phosphatidylglycerol		Diphosphatidylglycerol (cardiolipin)
Inositol		Phosphatidylinositol

Sphingolipids

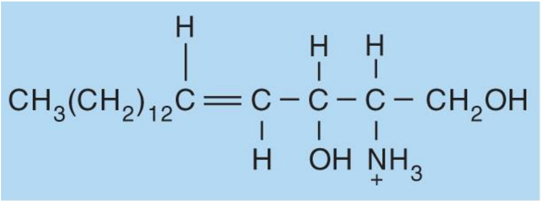
Sphingolipids are composed of one molecule of the long chain amino alcohol **sphingosine**, one molecule of long chain fatty acid and a polar head group.

- No glycerol
- Contain sphingosine, a long-chain amino alcohol
- Found in plants and animals
- Abundant in nervous system
- Bares structural similarity to phospholipids

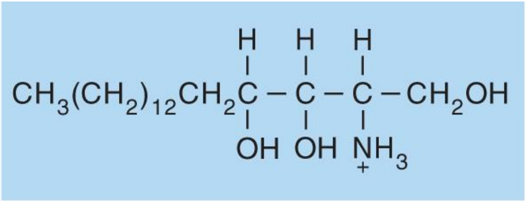


Sphingolipids are derivatives of sphingosine

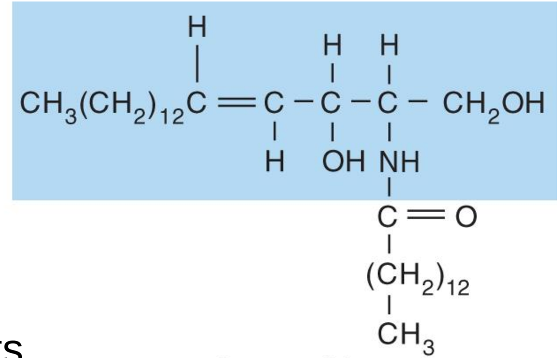
- Important components of animal and plant membranes
- Sphingosine (long-chain amino alcohol) and ceramide in animal cells



Sphingosine



Phytosphingosine



A ceramide

Figure 11.12 Sphingolipid Components

Sphingomyelin is found in most cell membranes, but is most abundant in the myelin sheath of nerve cells

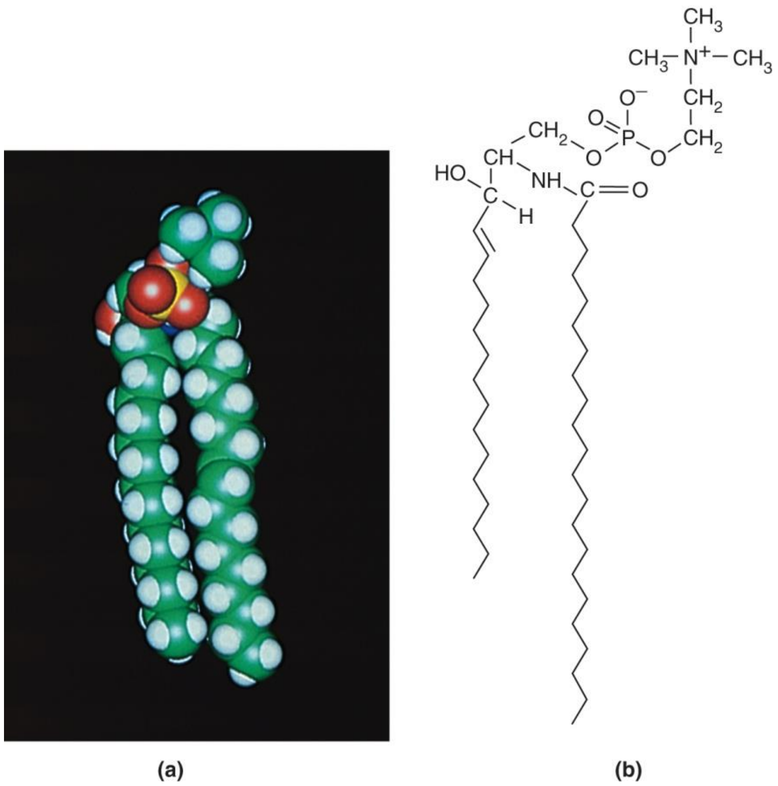
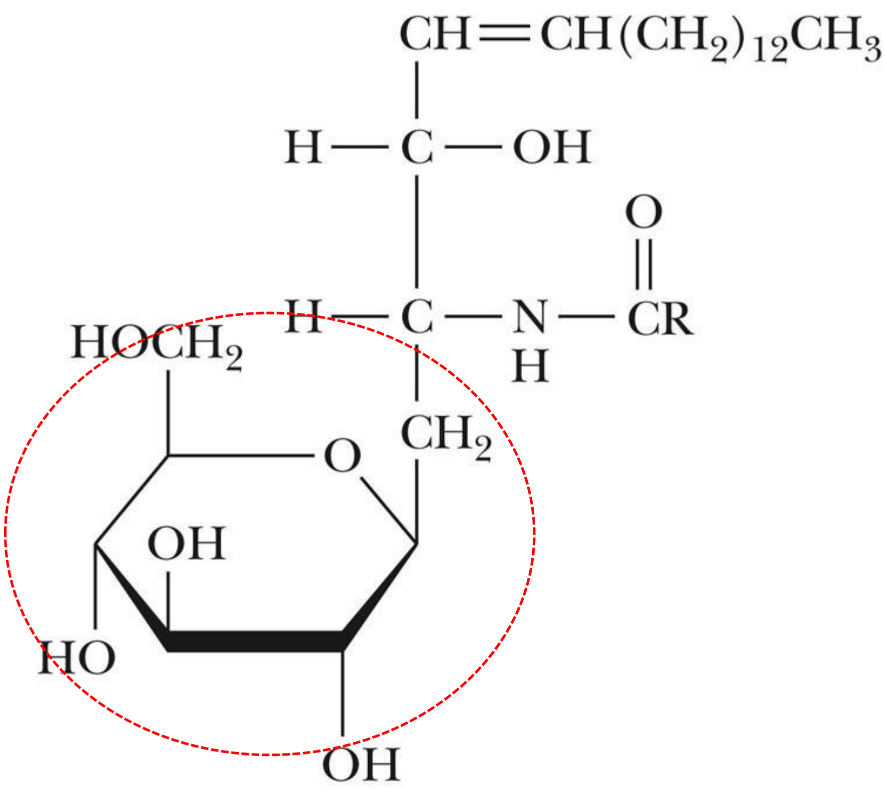


Figure 11.13 Space-Filling and Conformational Models of Sphingolmyelin

Glycolipids

Glycolipid is a compound in which a *carbohydrate* is bound to an -OH of the lipid.



A Glucocerebroside

- In most cases, sugar is either glucose or galactose
  - Many glycolipids are derived from **ceramides**.
- Glycolipids with complex carbohydrate moiety that contains more than 3 sugars are known as ***gangliosides***.

The ceramides are also precursors of **glycolipids**

- A monosaccharide, disacchaaride, or oligosaccharide attached to a ceramide through an O-glycosidic bond
- Most important classes are cerebrosides, sulfatides, and gangliosides (may bind bacteria and their toxins)

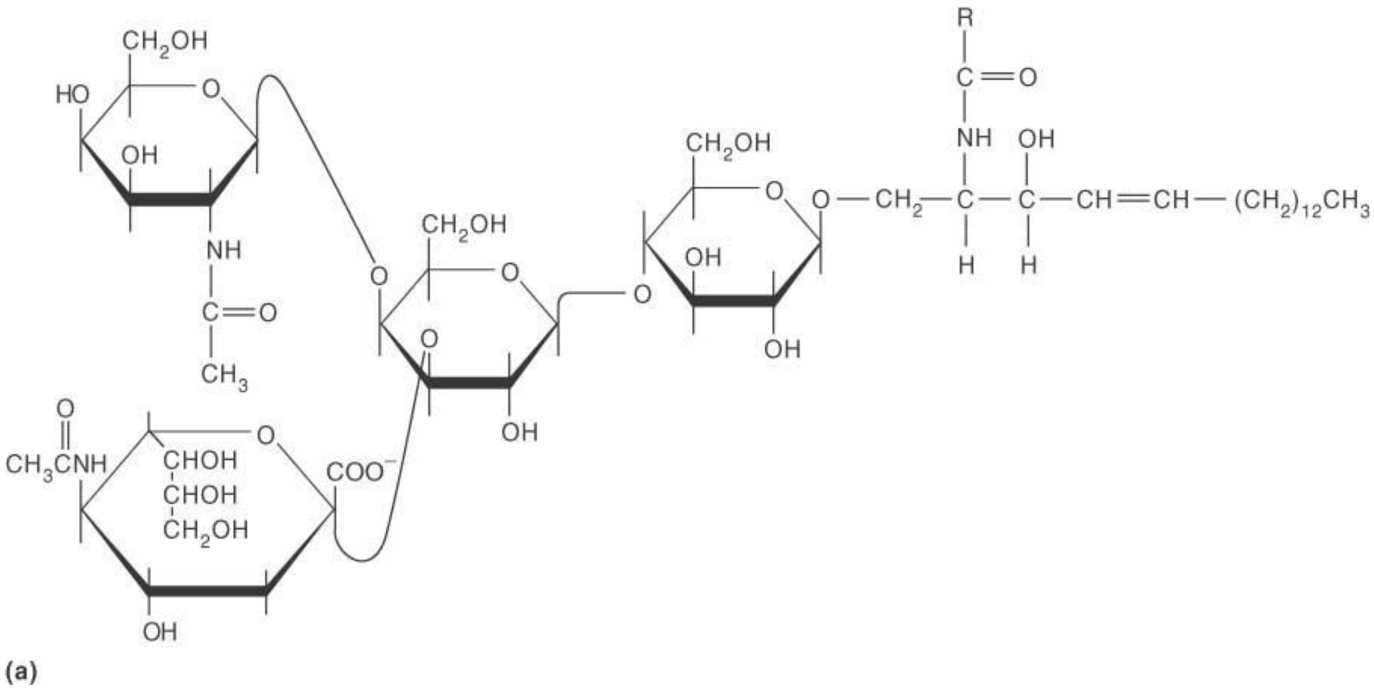
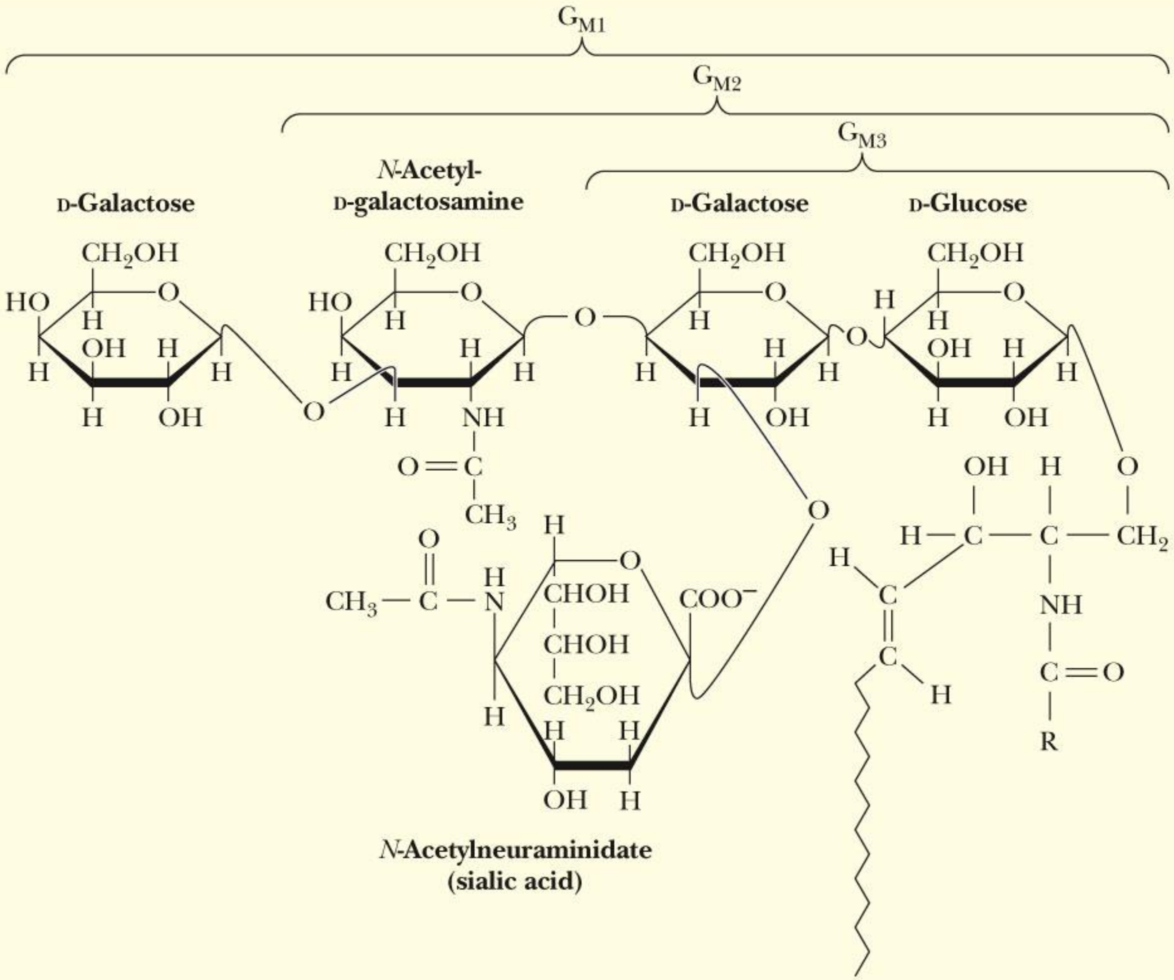
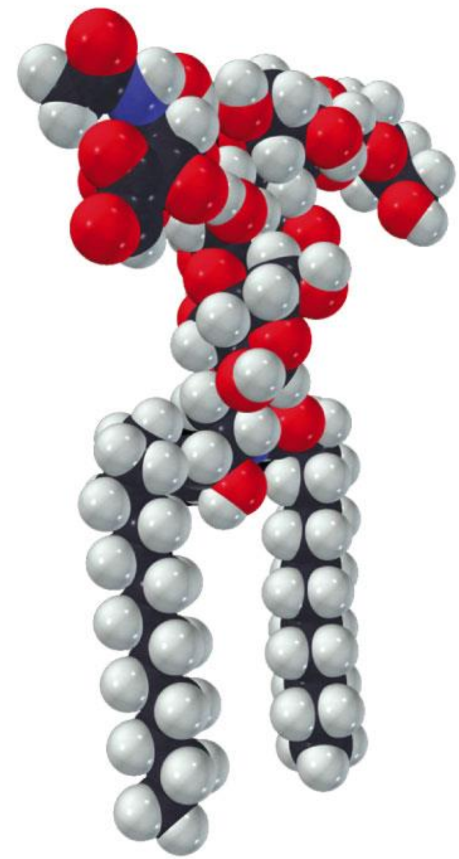


Figure 11.14a Selected Glycolipids



Gangliosides G_{M1}, G_{M2}, and G_{M3}



Gangliosides

Isoprenoids

- Vast array of biomolecules containing repeating five-carbon structural units, or **isoprene units**
- Isoprenoids consist of terpenes and steroids
- **Terpenes** are classified by the number of isoprene units they have
  - Monoterpenes (used in perfumes), sesquiterpines (e.g., citronella), tetraterpenes (e.g., **carotenoids**)

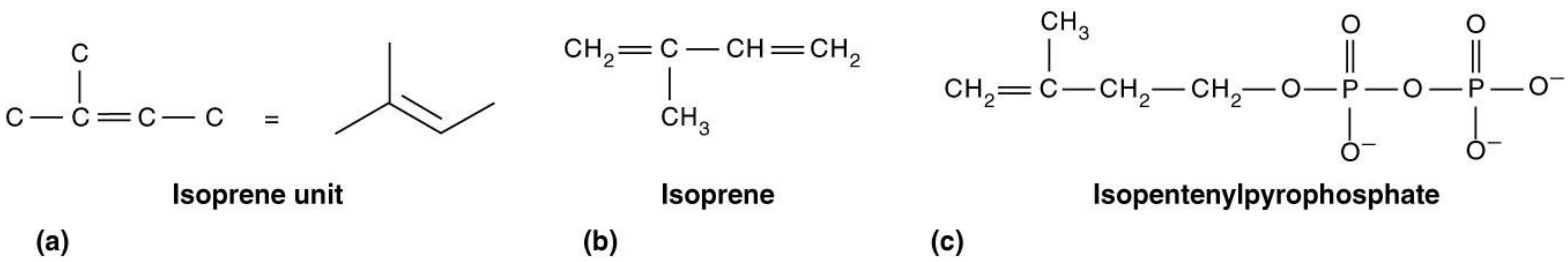
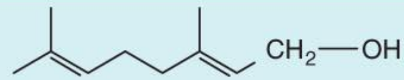
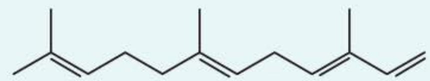
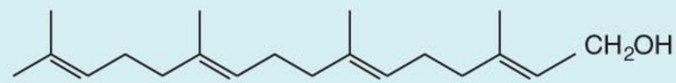
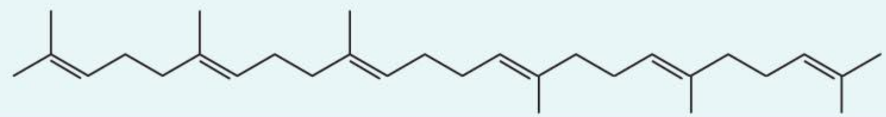
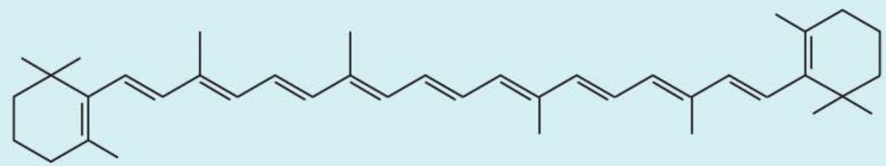
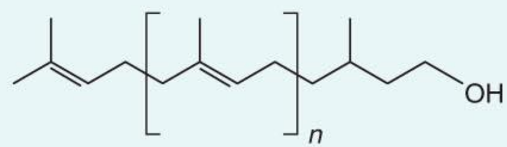
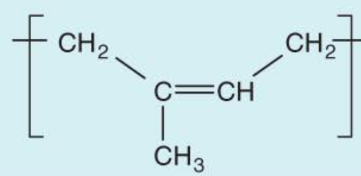


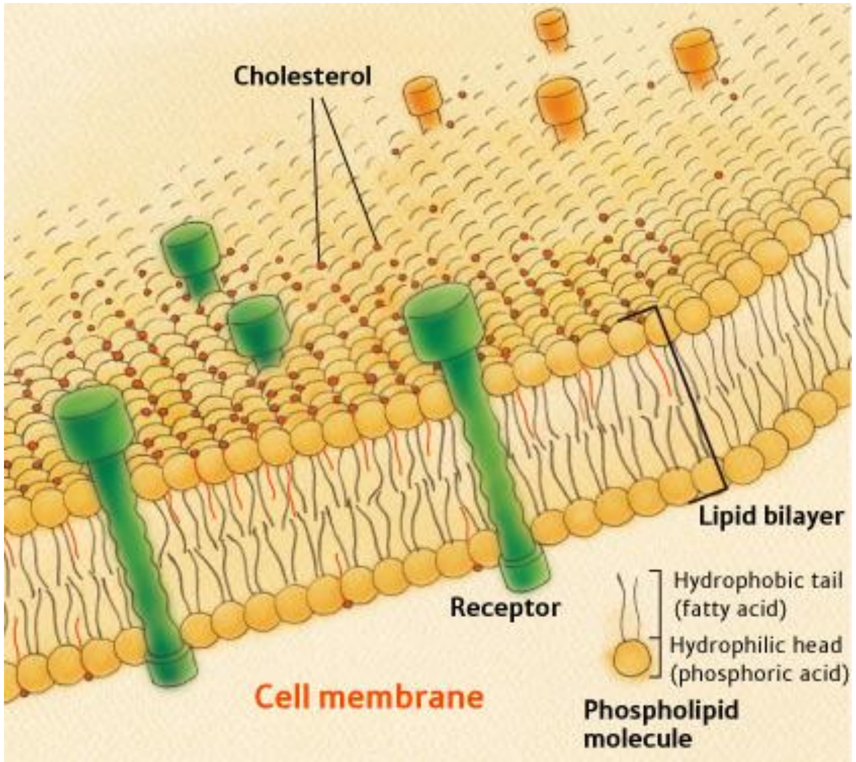
Figure 11.15 Isoprene

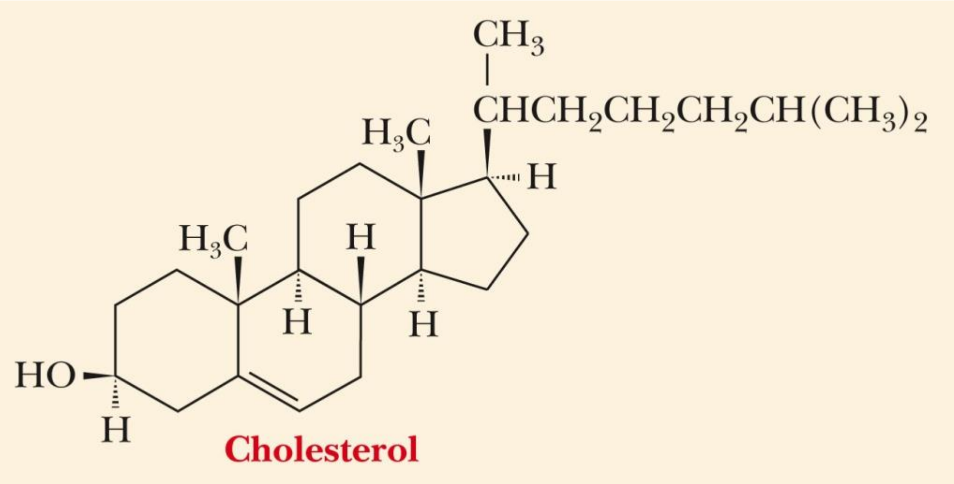
TABLE 11.4 Examples of Terpenes

Type	Number of Isoprene Units	Example: Name	Example: Structure
Monoterpene	2	Geraniol	
Sesquiterpene	3	Farnesene	
Diterpene	4	Phytol	
Triterpene	6	Squalene	
Tetraterpene	8	*β*-Carotene	
Polyterpene	9–24	Dolichol	
	Thousands	Rubber	

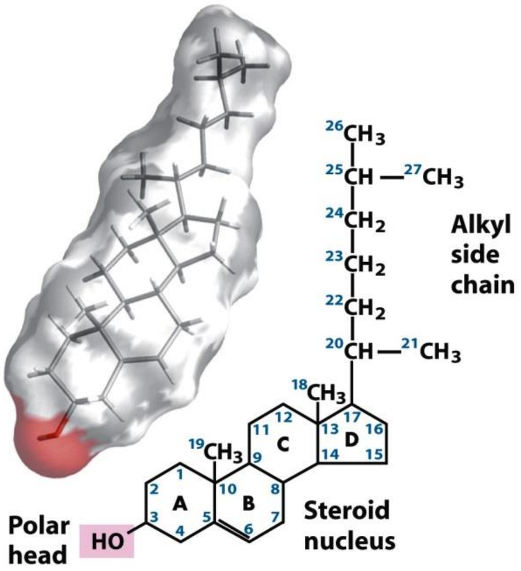
Steroids

- **Steroid** is a group of lipids that have fused-ring structure of **3** six-membered rings, and **1** five-membered ring.
- Steroid is structural lipids in the membrane of most eukaryotic cells.
- Rigid due to no rotation about C-C bonds
- The steroid of most interest in our discussion of biological membranes is cholesterol.





- **Cholesterol** is an important molecule in animal cells that is classified as a **sterol**, because C-3 is oxidized to a hydroxyl group
  - Essential in animal membranes; a precursor of all steroid hormones, vitamin D, and bile salts
  - Usually stored in cells as a fatty acid ester
- The term steroid is commonly used to describe all derivatives of the steroid ring structure



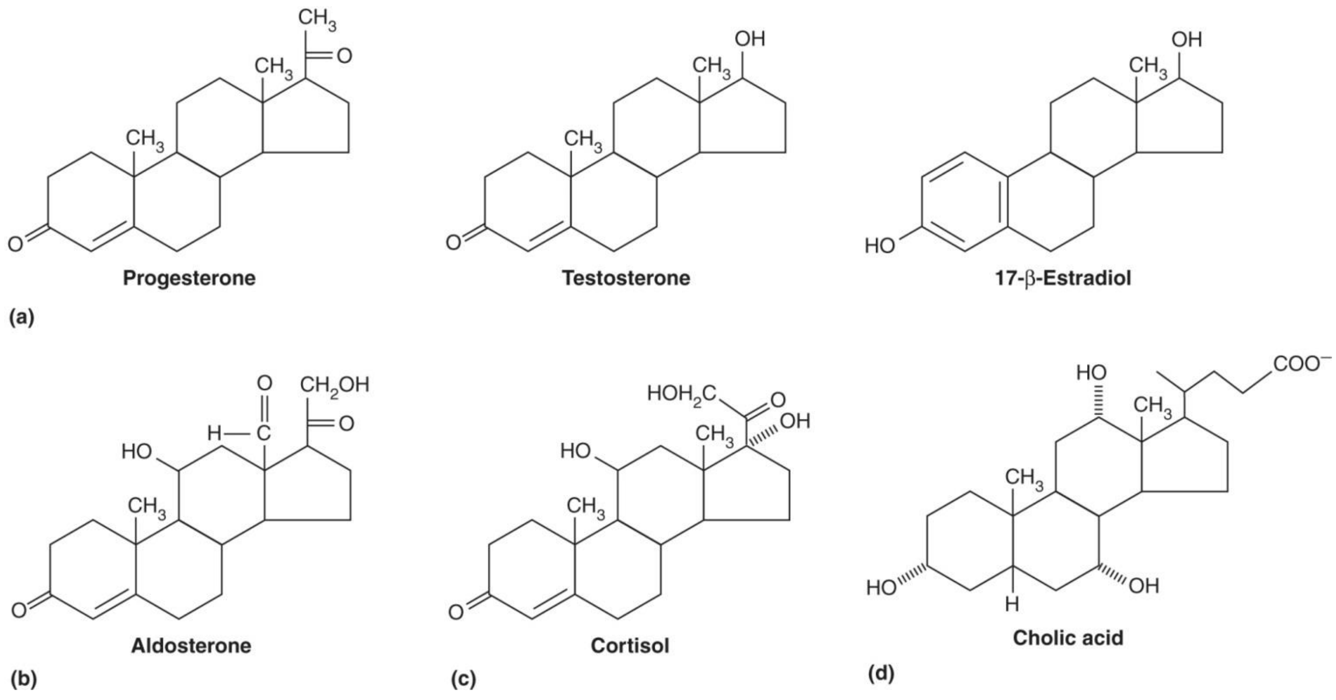


Figure 11.19 Animal Steroids

Sex hormones

- **Androgens:** male sex hormones
  - synthesized in the testes
  - responsible for the development of male secondary sex characteristics
  - Testosterone

- **Estrogens:** female sex hormones
  - synthesized in the ovaries
  - responsible for the development of female secondary sex characteristics and control of the menstrual cycle

Lipoproteins

- Term most often applied to a group of molecular complexes found in the blood plasma of mammals
- Transport lipid molecules through the bloodstream from organ to organ
- Protein components (apolipoproteins) for lipoproteins are synthesized in the liver or intestine

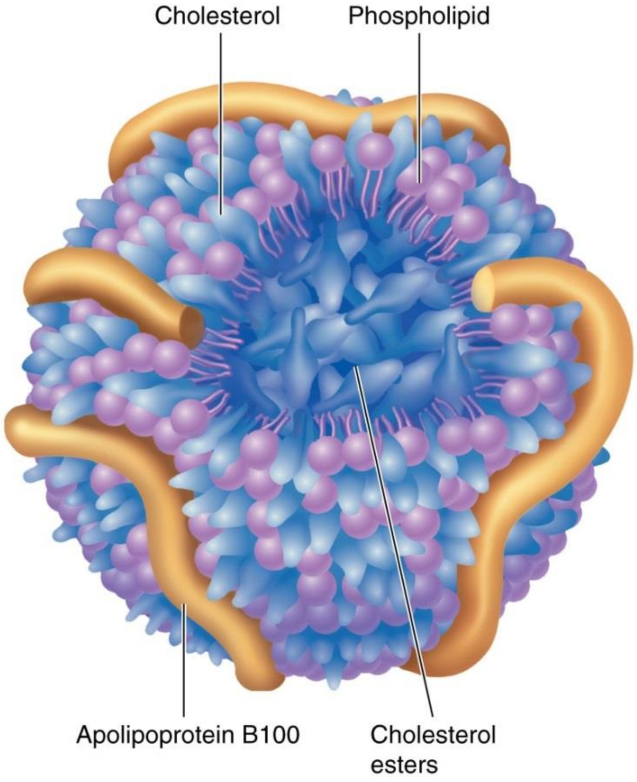


Figure 11.21 Plasma Lipoproteins

- Five classes of apolipoproteins (A, B, C, D, and E)
- There are different types of lipoproteins with different ratios of lipid and protein components

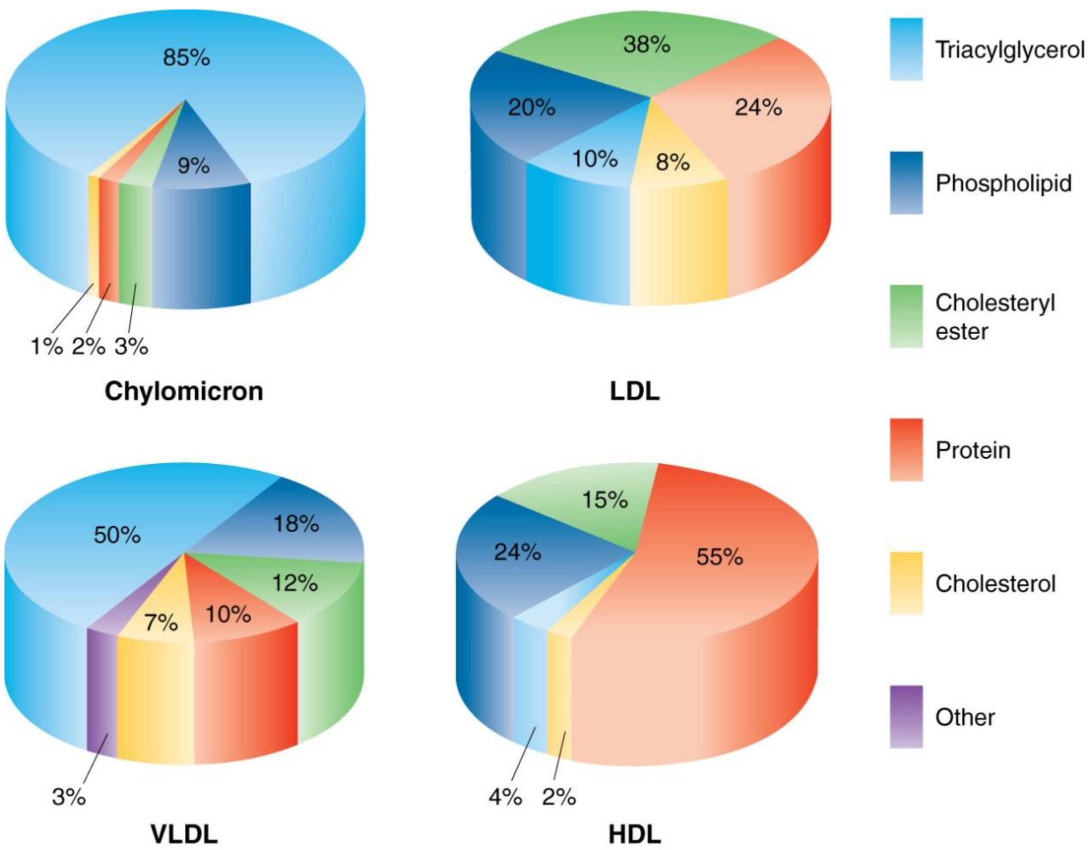


Figure 11.22 Proportional (Relative) Mass of Cholesterol, Cholesterol Ester, Phospholipid, and Protein Molecules in Four Major Classes of Plasma Lipoproteins

- Lipoproteins are classified according to their density:
  - **Chylomicrons** are large lipoproteins of extremely low density that transport triacylglycerol and cholesteryl esters (synthesized in the intestines)
  - **Very low density lipoproteins** (VLDL) are synthesized in the liver and transport lipids to the tissues
  - **Low density lipoproteins** (LDL) are principle transporters of cholesterol and cholesteryl esters to tissues
  - **High density lipoprotein** (HDL) is a protein-rich particle produced in the liver and intestine that seems to be a scavenger of excess cholesterol from membranes

- HDL also scavenges cholesteryl esters that are produced by lecithin:cholesterol acetyltransferase
- HDL transports these excess cholesteryl esters to the liver where they are turned into bile acids
    - HDL is considered "good cholesterol"

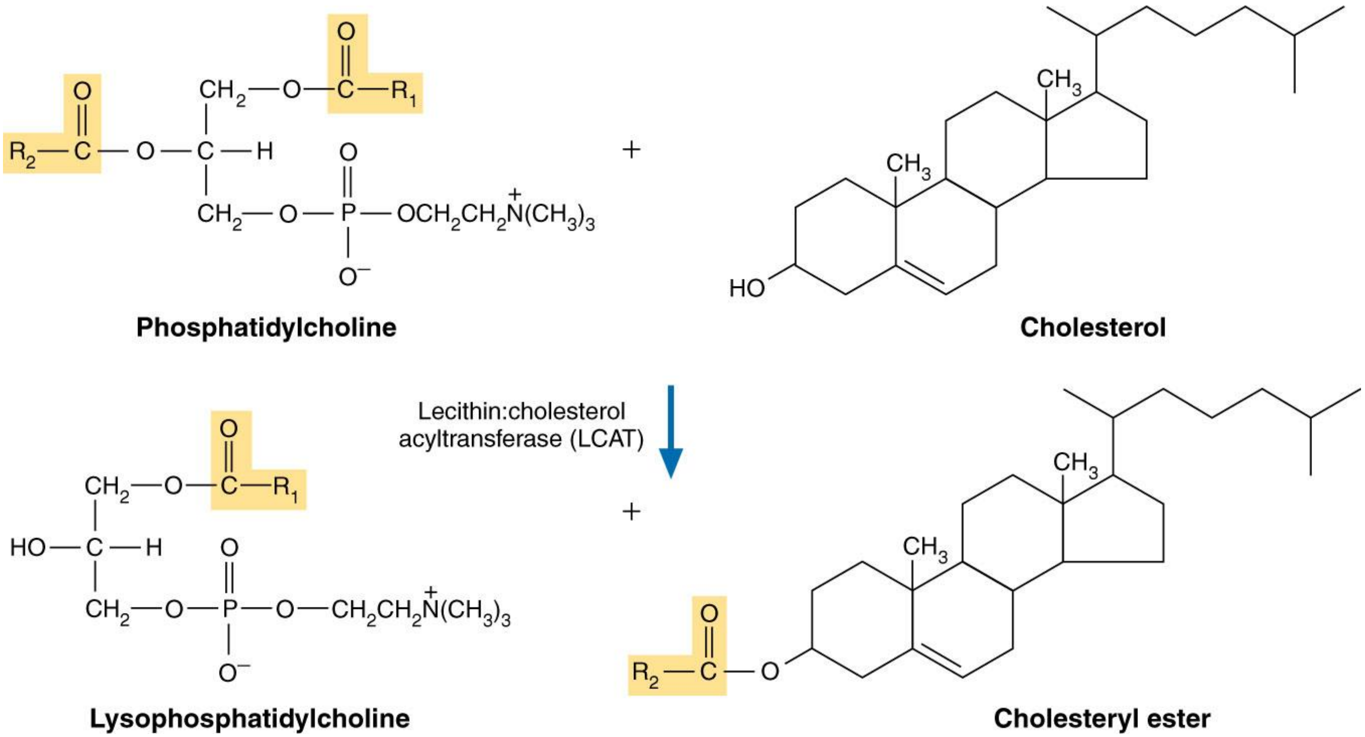


Figure 11.23 Reaction Catalyzed by Lecithin: Cholesterol Acetyltransferase (LCAT)

Section 11.2: Membranes

A membrane is a noncovalent heteropolymer of **lipid bilayer** and associated proteins (**fluid mosaic model**)

Membrane Structure

Proportions of lipid, protein, and carbohydrate vary considerably among cell types and organelles

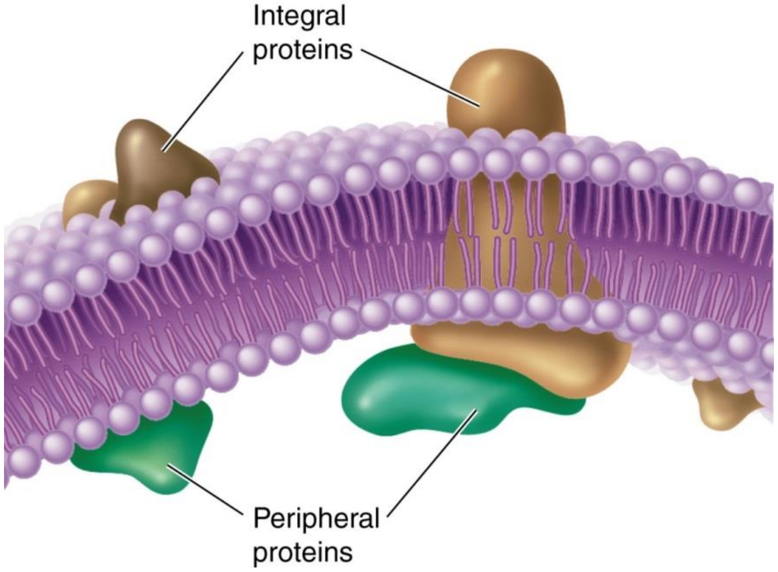
TABLE 11.5 Chemical Composition of Some Cell Membranes

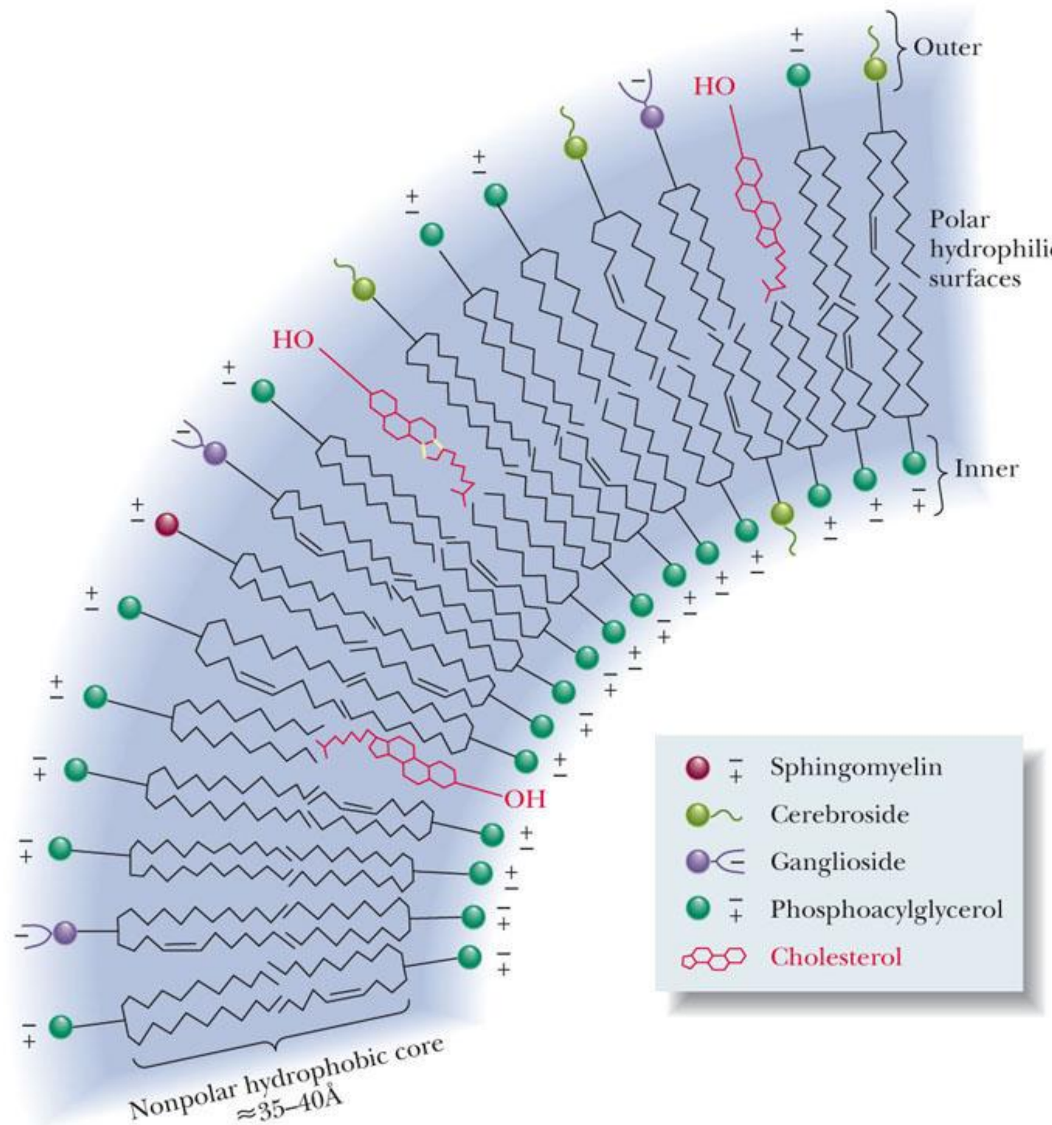
Membrane	Protein (%)	Lipid (%)	Carbohydrate (%)
Human erythrocyte plasma membrane	49	43	8
Mouse liver cell plasma membrane	46	54	2–4
Amoeba plasma membrane	54	42	4
Mitochondrial inner membrane	76	24	1–2
Spinach chloroplast lamellar membrane	70	30	6
Halobacterium purple membrane	75	25	0

Source: G. Guidotti, Membrane Proteins, *Annu. Rev. Biochem.* 41:731, 1972.

Membrane bilayers

- Both inner and outer layers of bilayer contain mixtures of lipids.
- Compositions on inside and outside of lipid bilayer can be different.
- This is what distinguishes the layers.
- Plant membranes have a higher percentage of unsaturated fatty acids than animal membranes.
- The presence of cholesterol is characteristic of animal rather than plant membranes.
- *Animal membranes are less fluid (more rigid) than plant membranes.*
- The membranes of prokaryotes, which contain no appreciable amounts of steroids, are the most fluid.





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

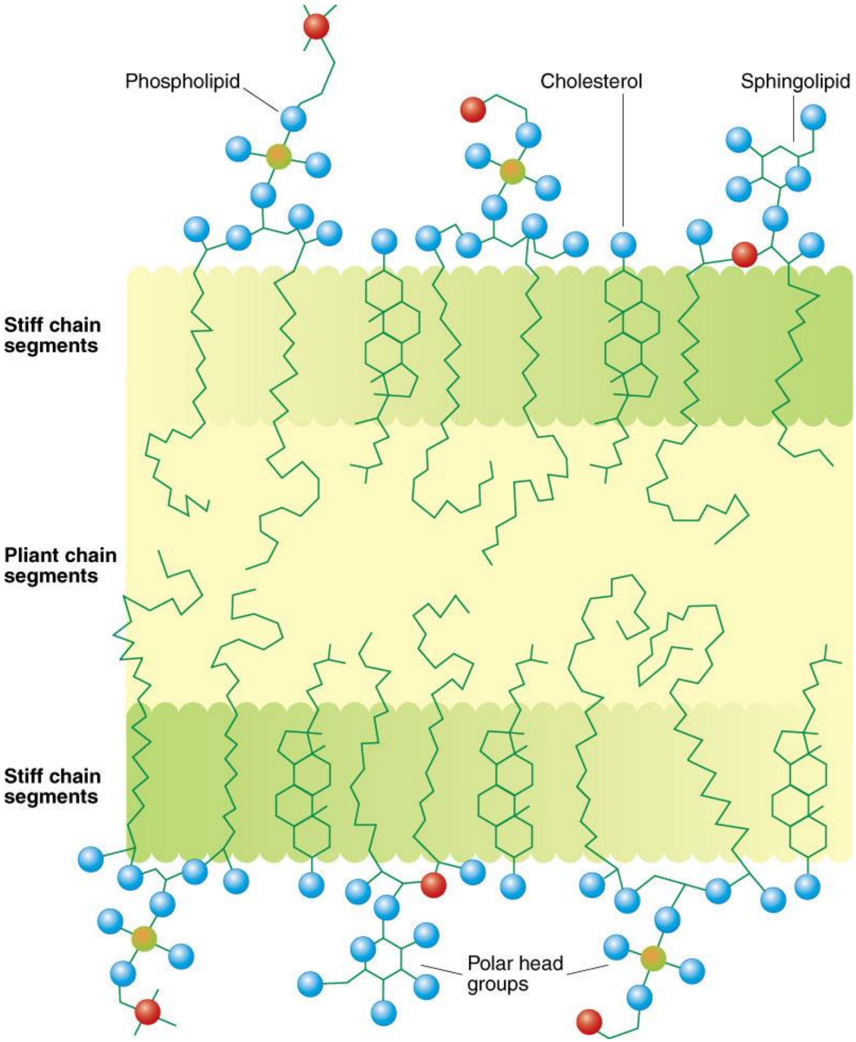


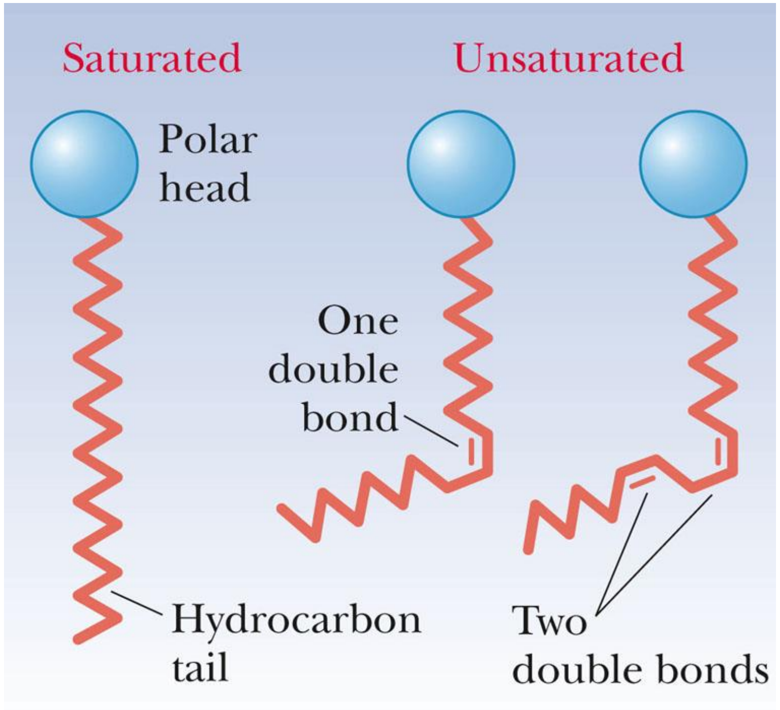
Figure 11.24 Diagrammatic View of a Lipid Bilayer

- The movement of molecules from one side of a membrane to the other requires a **flipase.**
- Membrane fluidity largely depends on the percentage of unsaturated fatty acids and cholesterol.
- Cholesterol contributes to stability with its rigid ring system and fluidity with its flexible hydrocarbon tail

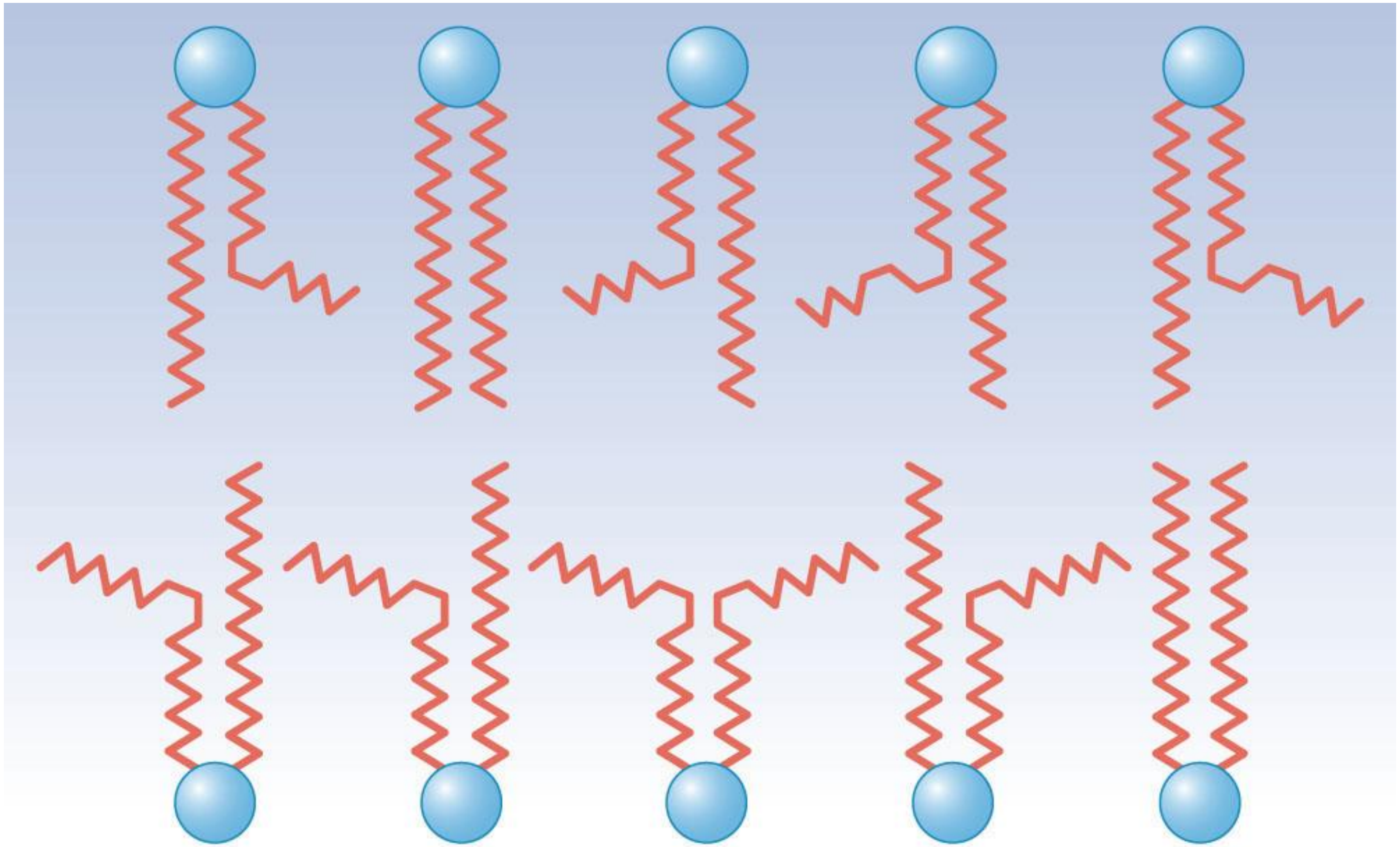
- **Selective permeability** is provided by the hydrophobic chains of the lipid bilayer, which is impermeable to most all molecules (except small nonpolar molecules)
  - Membrane proteins help regulate the movement of ionic and polar substances
  - Small nonpolar substances may diffuse down their concentration gradient
- **Self-sealing** is a result of the lateral flow of lipid molecules after a small disruption
- **Asymmetry** of biological membranes is necessary for their function
  - The lipid composition on each side of the membrane is different

Effect of Double Bonds on the Conformations of Fatty Acids

- **Kink** in hydrocarbon chain
- Causes **disorder** in packing against other chains
- This disorder causes greater **fluidity** in membranes with *cis*-double bonds *vs* saturated fatty acid chains



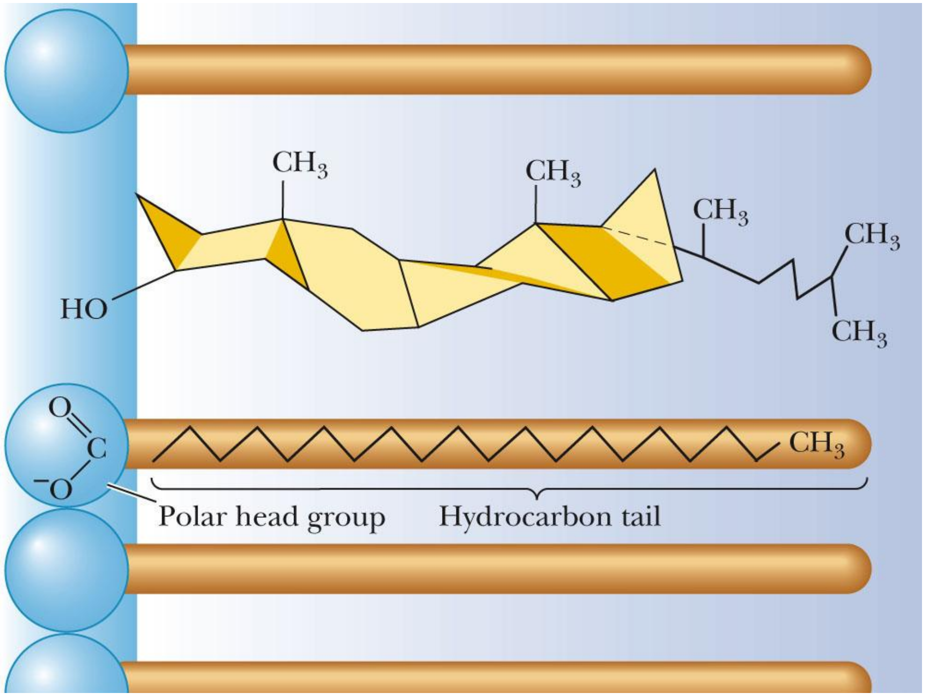
Unsaturated fatty acids have kinks in their tails.



Schematic drawing of a portion of a highly fluid phospholipid bilayer. The kinks in the unsaturated side chains prevent close packing of the hydrocarbon portions of the phospolipids.

Cholesterol reduces Fluidity

- Presence of cholesterol reduces fluidity by stabilizing extended chain conformations of hydrocarbon tails of FA.
- Due to hydrophobic interactions



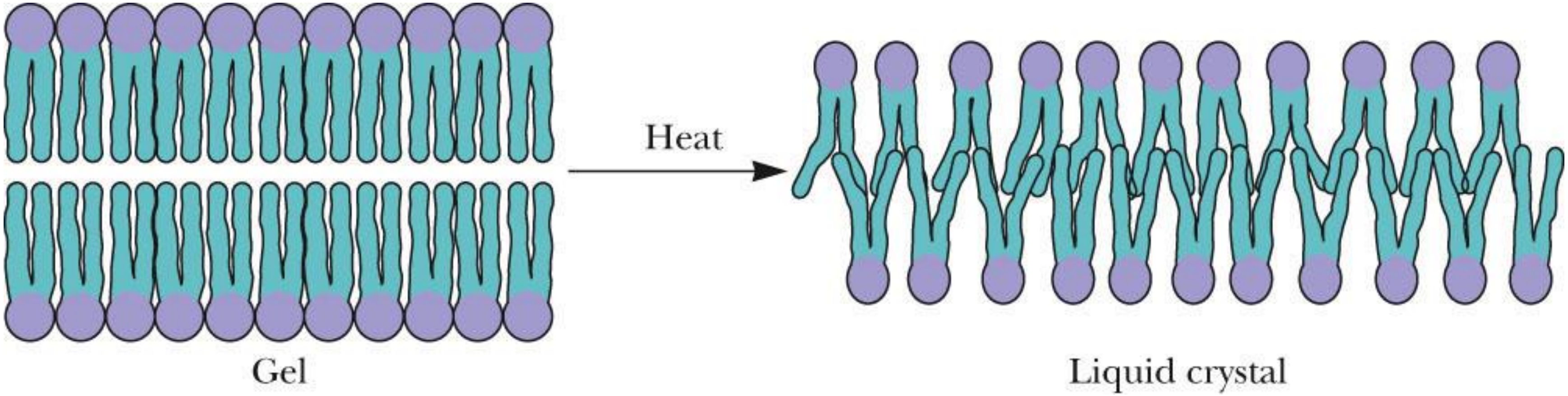
Stiffening of the lipid bilayer by cholesterol. The presence of cholesterol in a membrane reduces fluidity by stabilizing extended chain conformations of the hydrocarbon tails of fatty acids, as a result of *van der Waals* interactions.

Transition temperature in lipid bilayer

- With heat, membranes become more disordered; the transition temperature is higher for more rigid membranes; it is lower for less rigid membranes

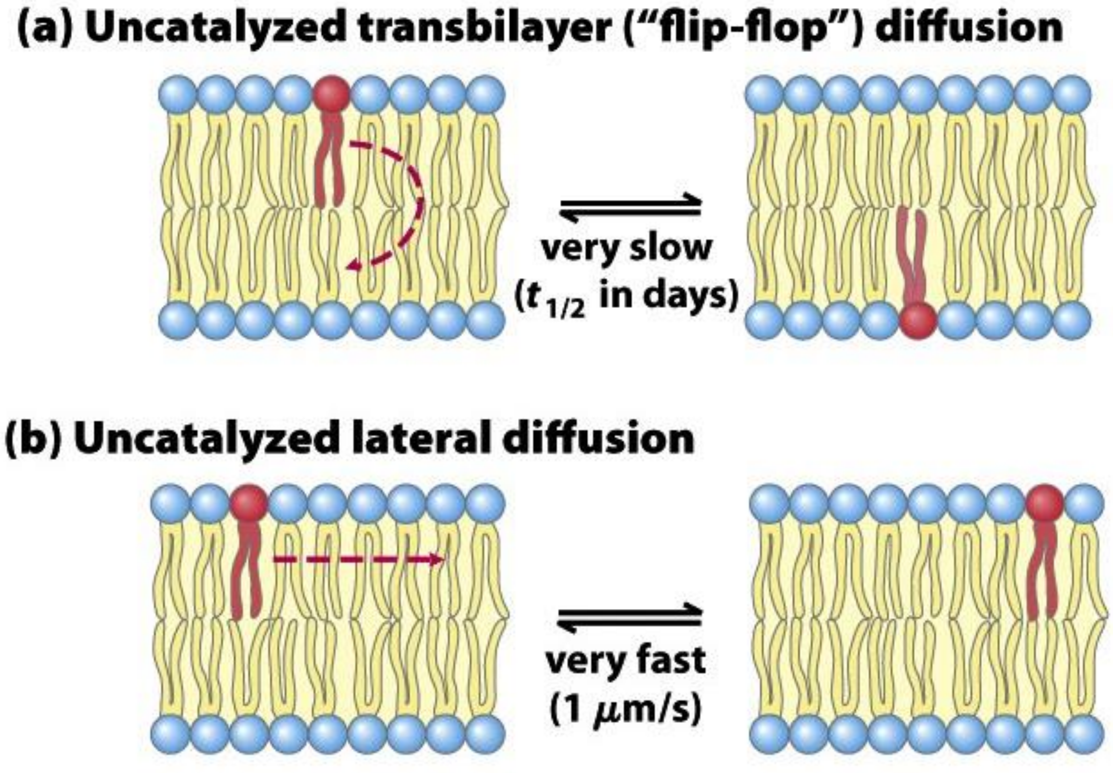
- Surface area increases and thickness decreases as a temperature goes through a phase transition.

- Mobility of the lipid chains increases dramatically.

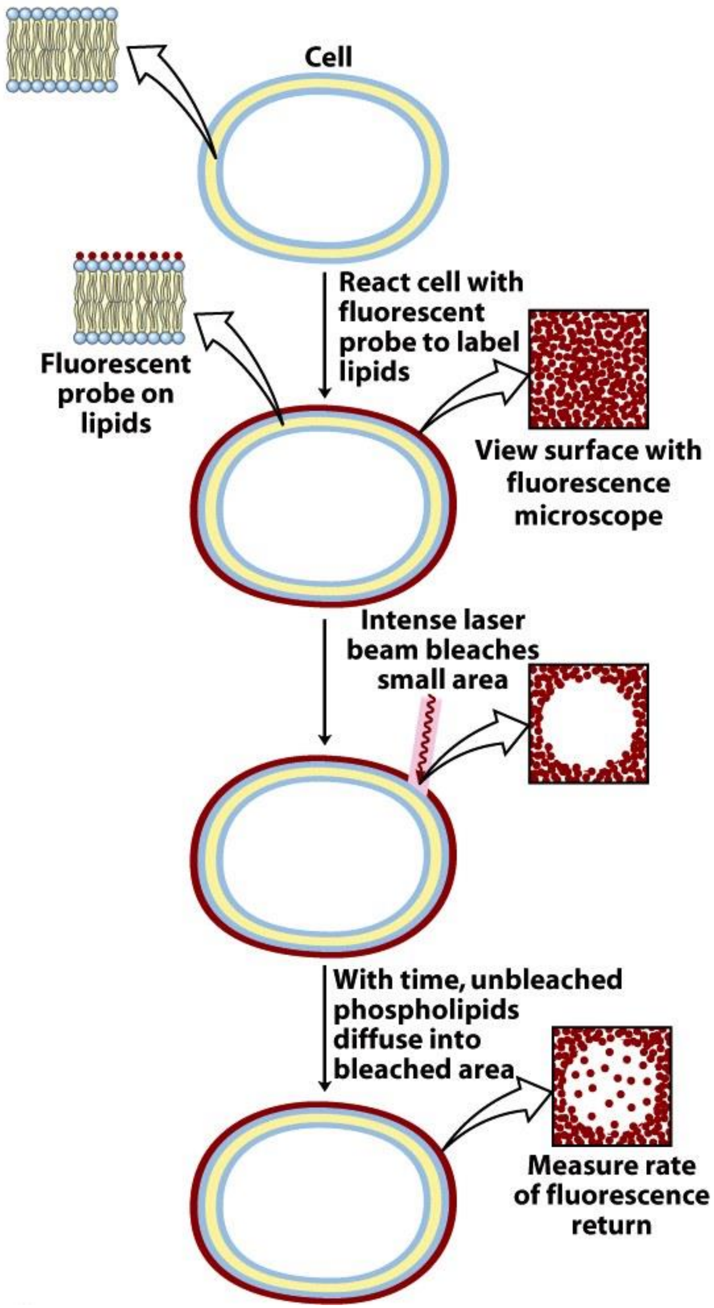


Gel-to-liquid crystalline phase transition, which occurs when a membrane is warmed through the transition temperature.

- There is little tendency for 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 takes place, however, especially in more fluid bilayers.



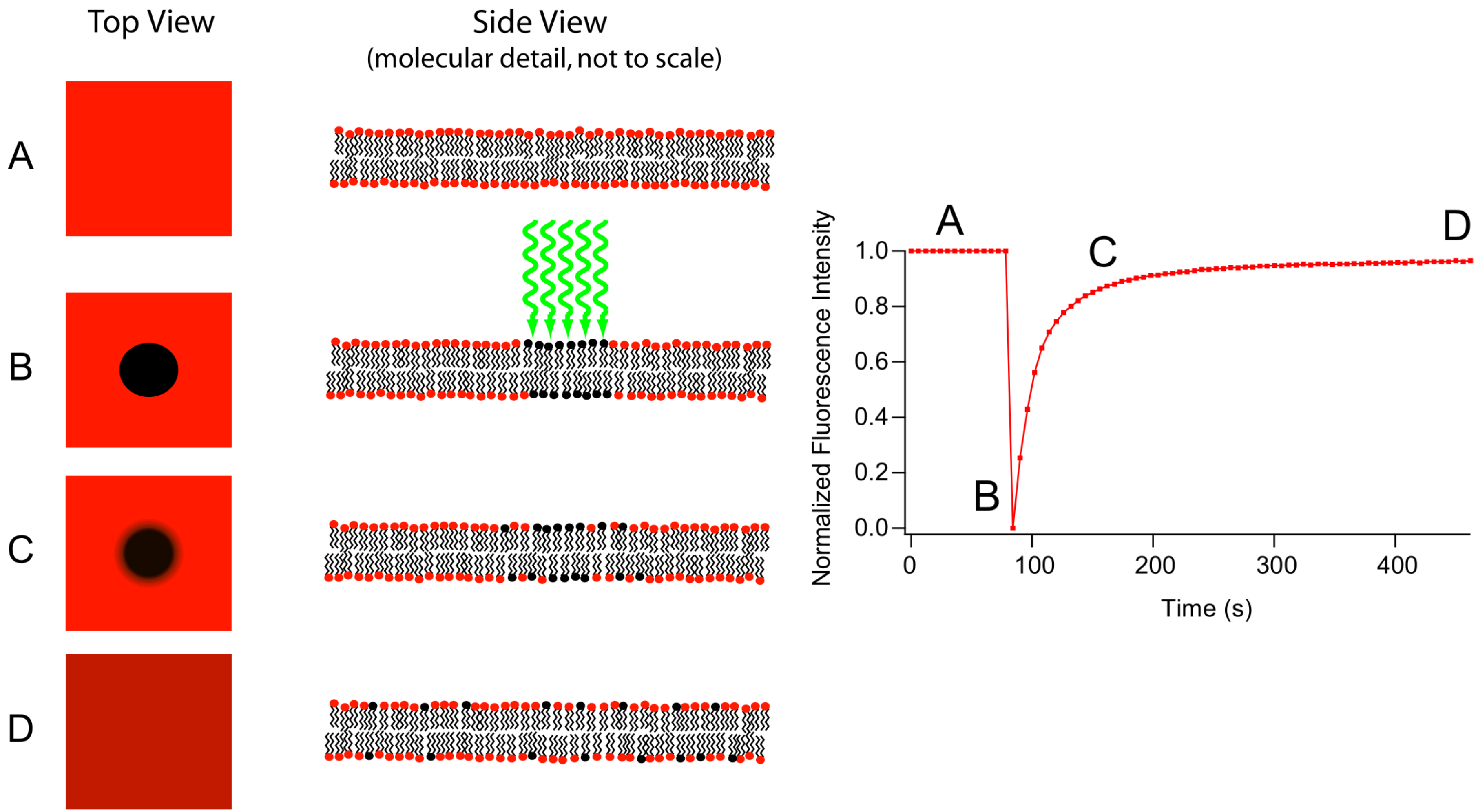
Motion of single phospholipids in a bilayer. (a) Uncatalyzed movement from one leaflet to the other is very slow, but (b) lateral diffusion within the leaflet is very rapid, requiring no catalysis.



Measurement of lateral diffusion rates of lipids by fluorescence recovery after photobleaching (FRAP).

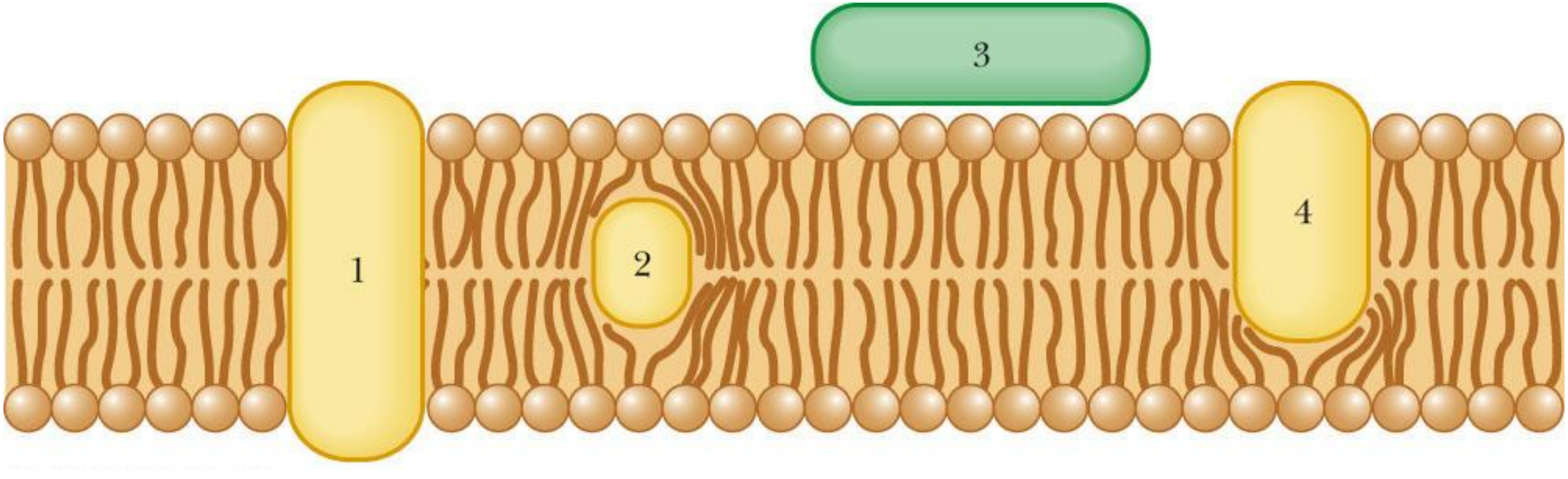
Lipids in the outer leaflet of the plasma membrane are labeled by reaction with a membrane-impermeant fluorescent probe (red), so the surface is uniformly labeled when viewed with a fluorescence microscope. A small area is bleached by irradiation with an intense laser beam and becomes nonfluorescent. With the passage of time, labeled lipid molecules diffuse into the bleached region, and it again becomes fluorescent. Researchers can track the time course of fluorescence return and determine a diffusion coefficient for the labeled lipid. The diffusion rates are typically high; a lipid moving at this speed could circumnavigate an *E. coli* cell in one second. (The FRAP method can also be used to measure lateral diffusion of membrane proteins.)

Fluorescence recovery after photobleaching is a method for determining the kinetics of diffusion through tissue or cells. It is capable of quantifying the two dimensional lateral diffusion of a molecularly thin film containing fluorescently labeled probes, or to examine single cells.



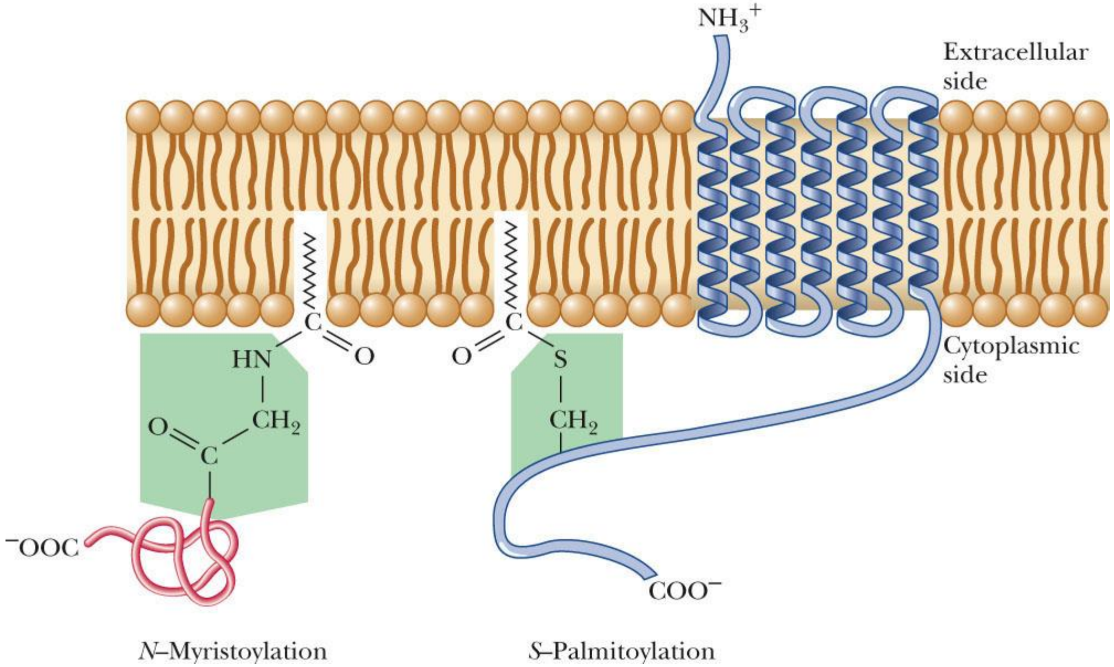
Membrane Proteins

- Functions: **transport** substances across membranes, act as receptor sites, and sites of enzyme catalysis
- Peripheral proteins (3)
  - bound by *electrostatic interactions*
  - can be removed by raising the ionic strength
- Integral proteins (1,2,4)
  - bound tightly to the interior of the membrane
  - can be removed by treatment with detergents or ultrasonification
  - removal generally denatures them



Proteins Can be Anchored to Membranes

- *N*-myristoyl- and *S*-palmitoyl anchoring motifs
- Anchors can be via *N*-terminal Gly
- Thioester linkage with Cys



Certain proteins are anchored to biological membranes by lipid anchors.
N-myristoylation and *S*-palmitoylation anchoring motifs are particularly common. *N*-myristoylation always occurs at an *N*-terminal glycine residue, whereas thioester linkages occur at cystein residues within the polypeptide chain. G-protein-coupled receptors, with seven transmembrane segments, may contain one palmitoyl anchors in thioester linkage to cystein residue in the C-terminal segment of the protein.

Fluid Mosaic Model

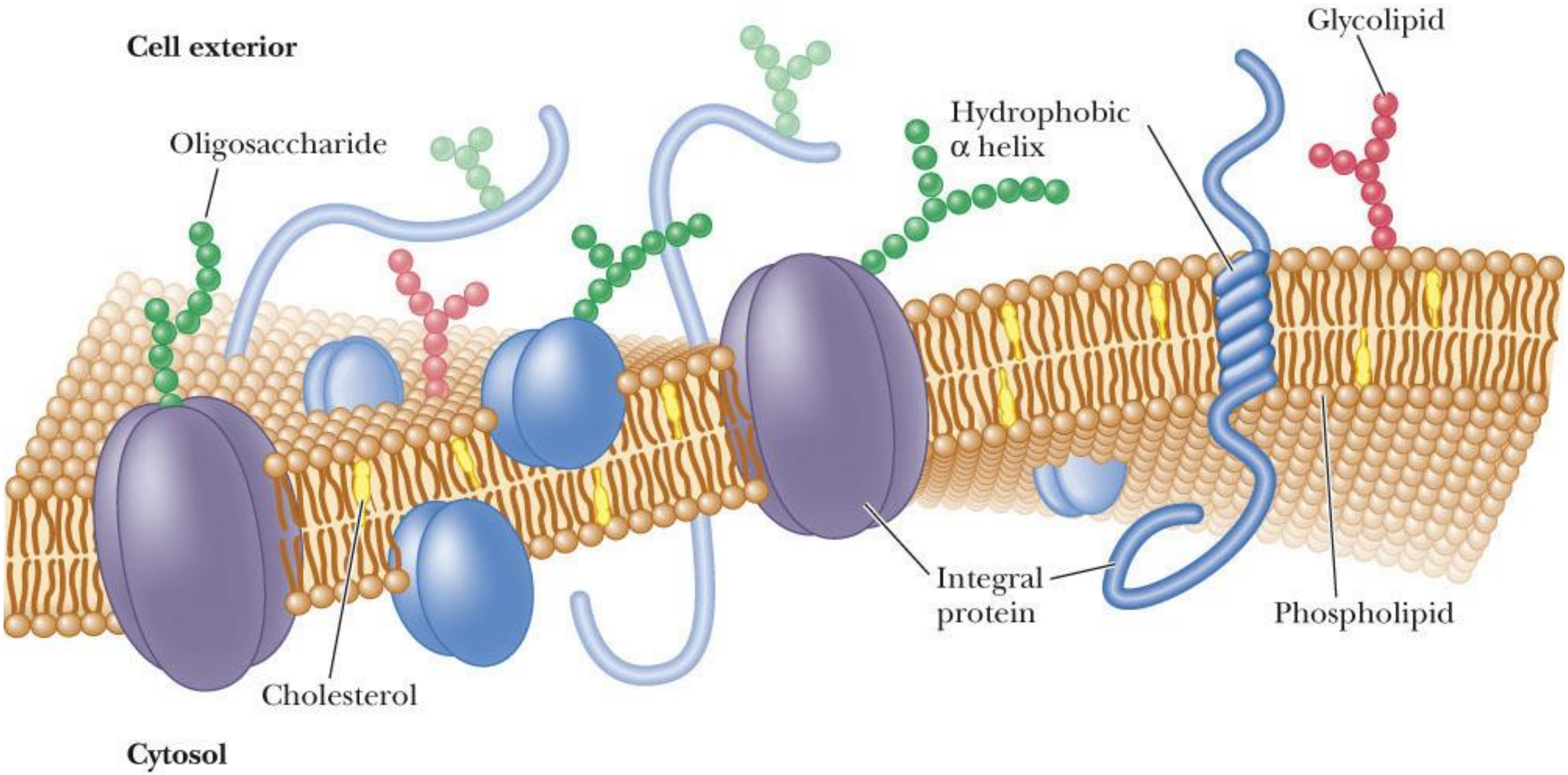
Fluid: There is lateral motion of components in the membrane;

- Proteins, for example, "***float***" in the membrane and can move along its plane

Mosaic: Components in the membrane exist *side-by-side* as separate entities

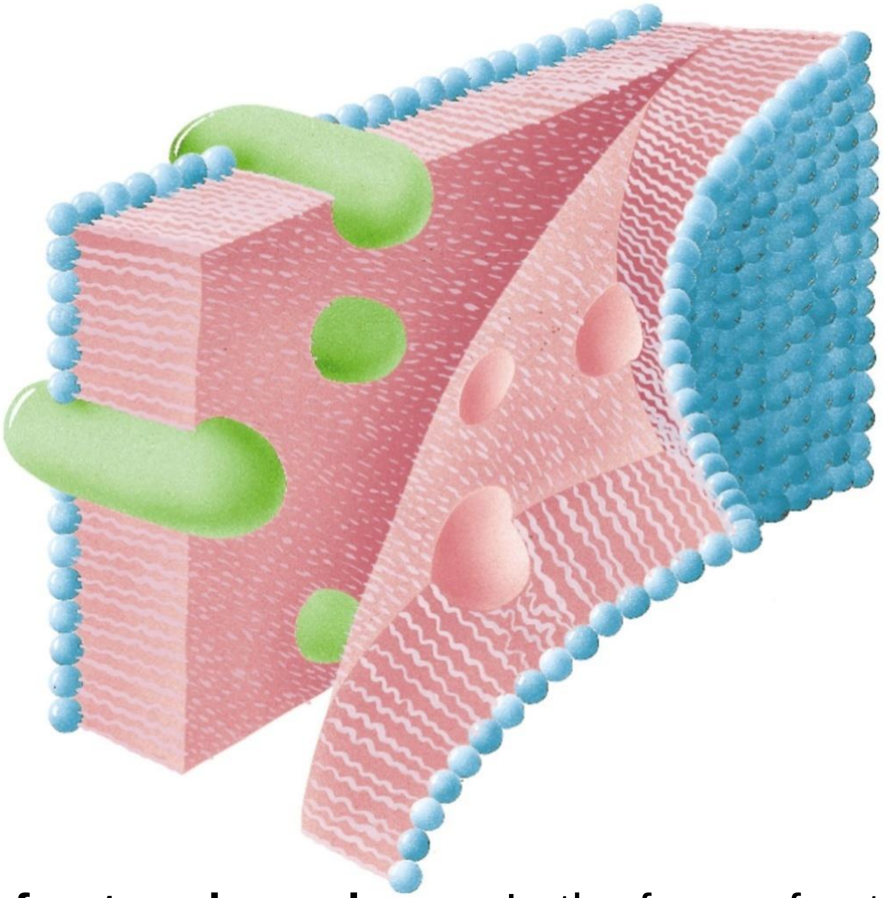
- The structure is that of a lipid bilayer with proteins, glycolipids, and steroids such as cholesterol embedded in it.
- No complexes, as for example, lipid-protein complexes, are formed.

Fluid Mosaic Model of Membrane Structure



The fatty acyl chains in the interior of the membrane form a fluid, hydrophobic region. Integral proteins float in the **sea of lipid**, held by hydrophobic interactions with their nonpolar amino acid chains. Both proteins and lipids are **free to move laterally** in the plane of the bilayer, but movement of either from one leaflet of the bilayer to the other is restricted.

Fluid Mosaic Model of Membrane Structure



Replica of a freeze-fractured membrane. In the freeze-fracture technique, the lipid bilayer is split parallel to the surface of the membrane. The hydrocarbon tails of the two layers are separated from each other, and the proteins can be seen as "*hills*" in the replica. In the other layer, seen edge on, there are "*valleys*", where the proteins were.

- **Membrane Microdomains—**lipids and proteins in membranes are not uniformly distributed.
- **Lipid rafts** are specialized microdomains and can be found in the external leaflet of the plasma membrane.
- Lipid rafts often include cholesterol, sphingolipids, and certain proteins.
- Lipid molecules are more ordered (less fluid) than non-raft regions.
- Lipid rafts have been implicated in a number of processes: exocytosis, endocytosis, and signal transduction.

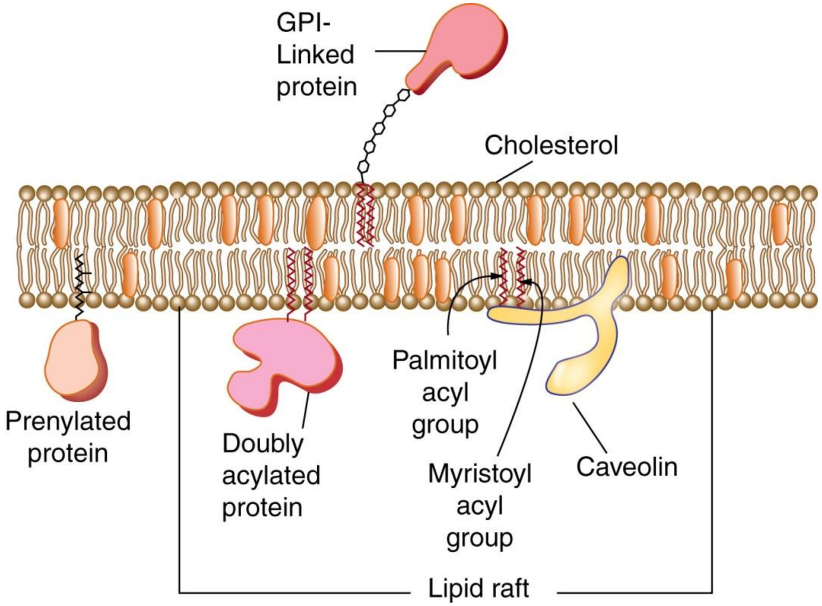


Figure 11.28 Lipid Rafts

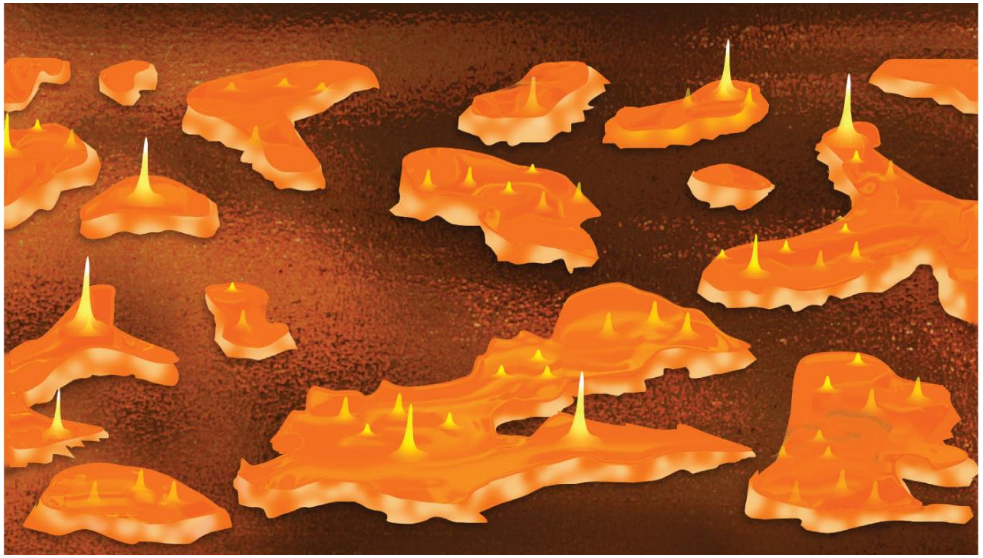


Figure 11.29 The Lipid Raft Environment

Membrane Function

There are a vast array of membrane functions, including transport of polar and charged substances and the relay of signals.

Membrane Transport : the mechanisms are vital to living organisms

- Ions and molecules constantly move across the plasma membrane and membranes of organelles.
    - Important for nutrient intake, waste excretion, and the regulation of ion concentration
- Biological transport mechanisms are classified according to whether they require energy,

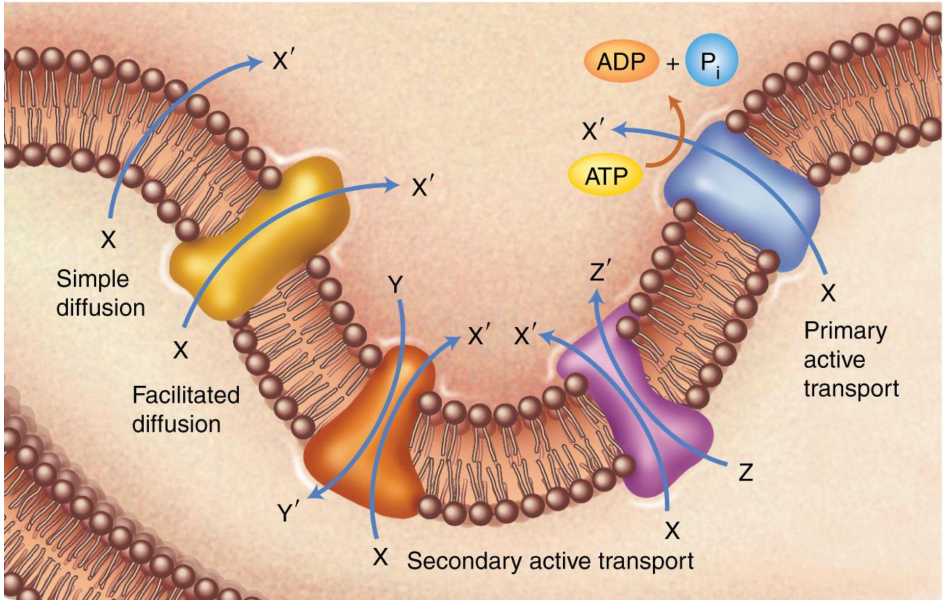


Figure 11.30 Transport across Membranes

Membrane Function: Membrane Transport

Passive transport

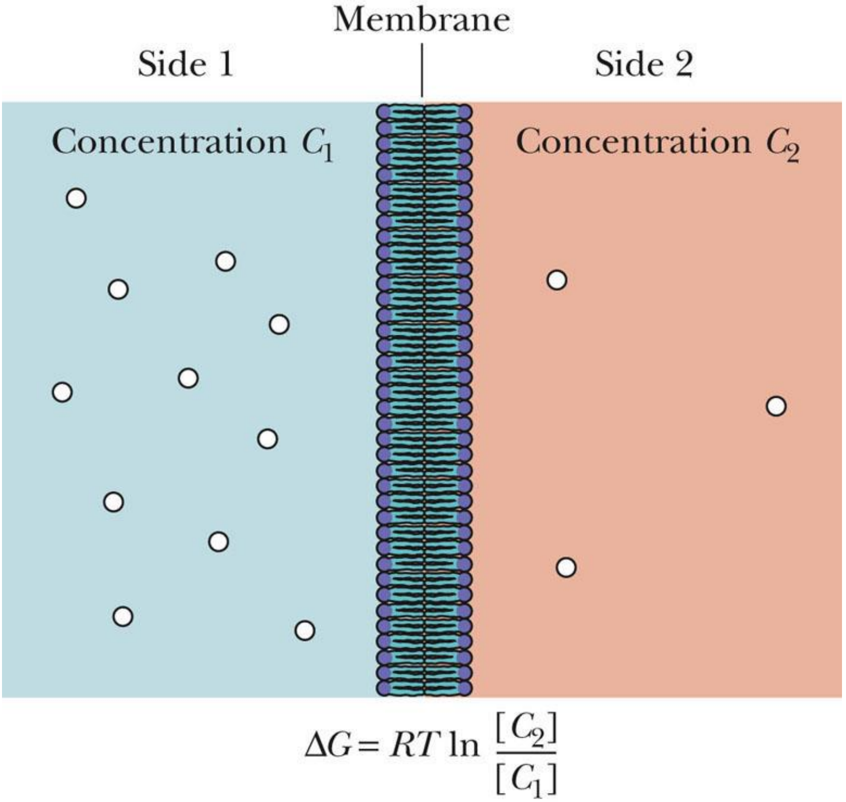
- Driven by a concentration gradient
- **Simple diffusion**: a molecule or ion moves through an opening
- **Facilitated diffusion**: a molecule or ion is carried across a membrane by a carrier/channel protein

Active transport

- A substance is moved against a concentration gradient
- **Primary active transport**: transport is linked to the hydrolysis of ATP or other high-energy molecule; for example, the Na^+/K^+ ion pump
- **Secondary active transport**: driven by H^+ gradient

Passive Transport

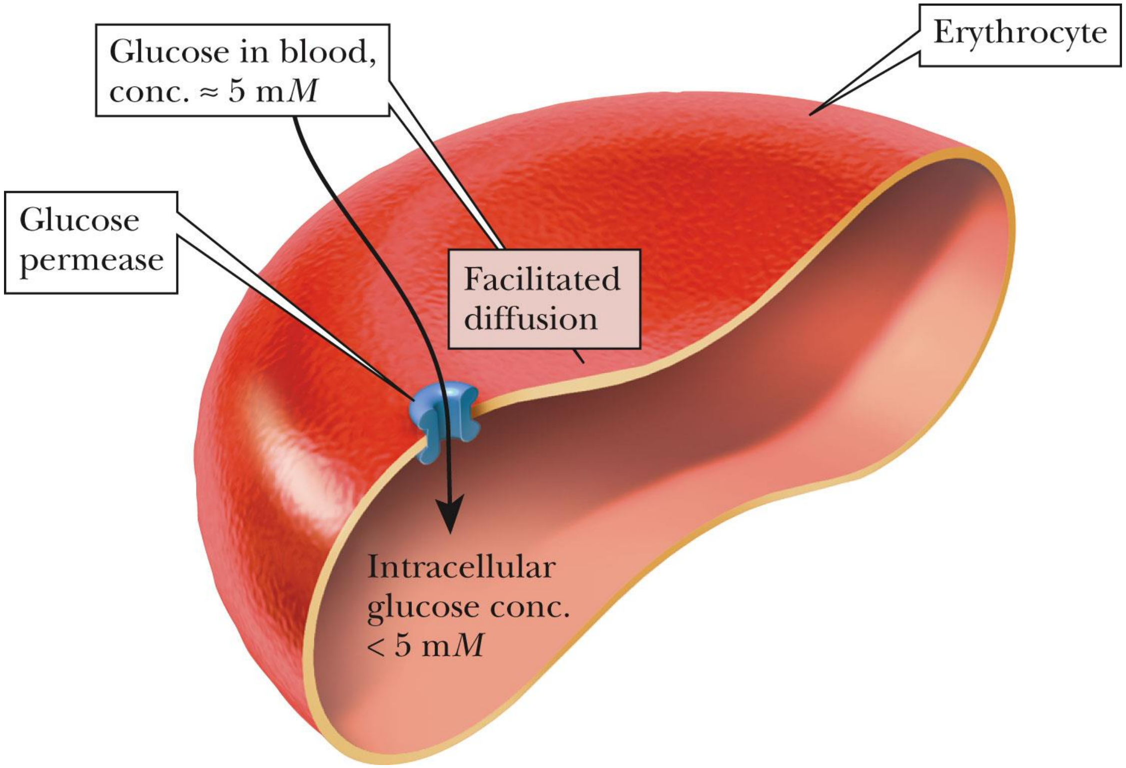
Passive diffusion of species (uncharged) across membrane dependent on **concentration**, presence of **carrier protein**



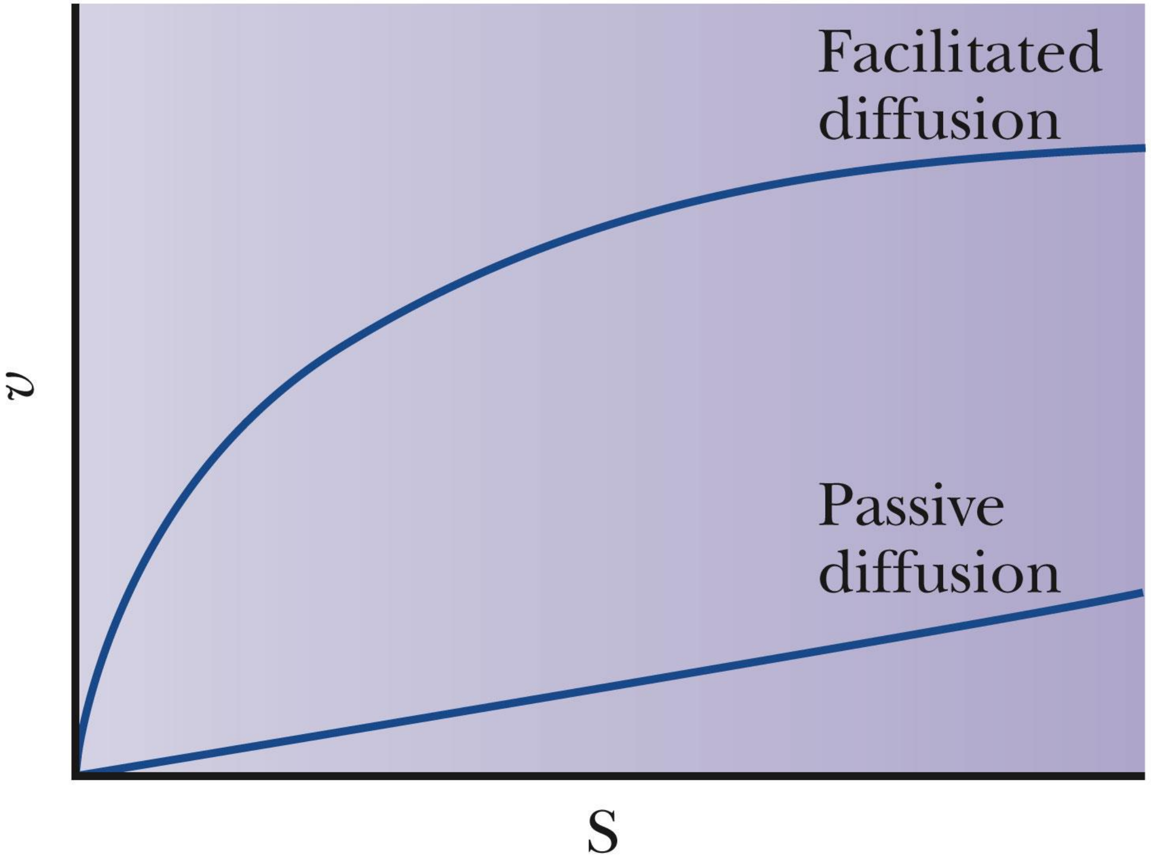
Passive diffusion. Passive diffusion of an uncharged species across a membrane depends only the concentrations (C_1 and C_2) on the two sides of the membrane.

Passive Transport

- Passive diffusion of species (uncharged) across membrane dependent on **concentration**, presence of **carrier protein.**



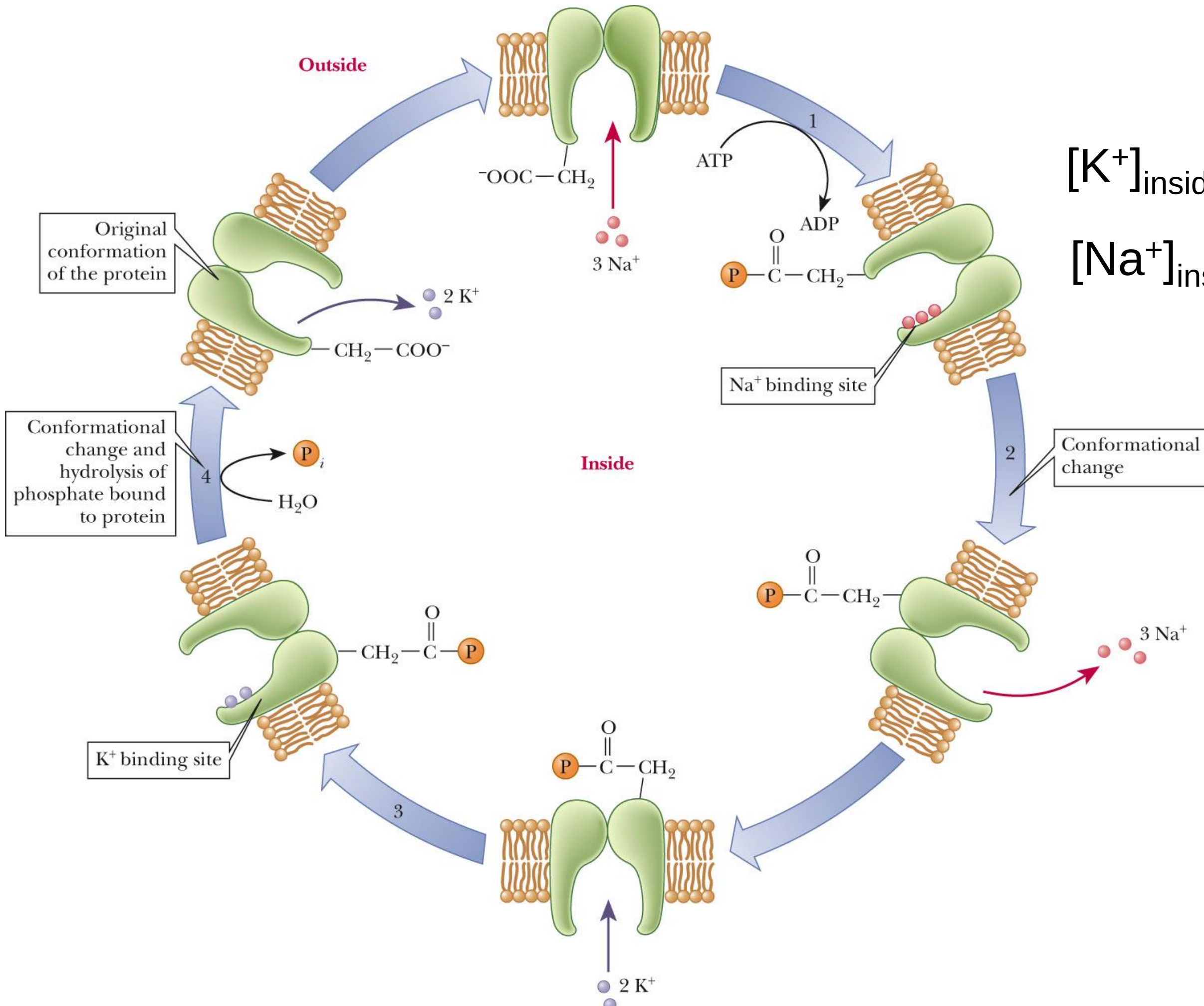
Facilitated diffusion. Glucose passes into an erythrocytes *via* glucose permease by facilitated diffusion. Glucose flows using its concentration gradient *via* passive transport.



Passive diffusion and facilitated diffusion may be distinguished graphically. The plots for facilitated diffusion are similar to plots of enzyme-catalyzed reactions and they display saturation behavior. The value ***v*** stands for velocity of transport. ***S*** is the concentration of the substance being transported.

1° Active transport

Movement of molecules against a gradient directly linked to hydrolysis of high-energy yielding molecule (e.g. ATP)



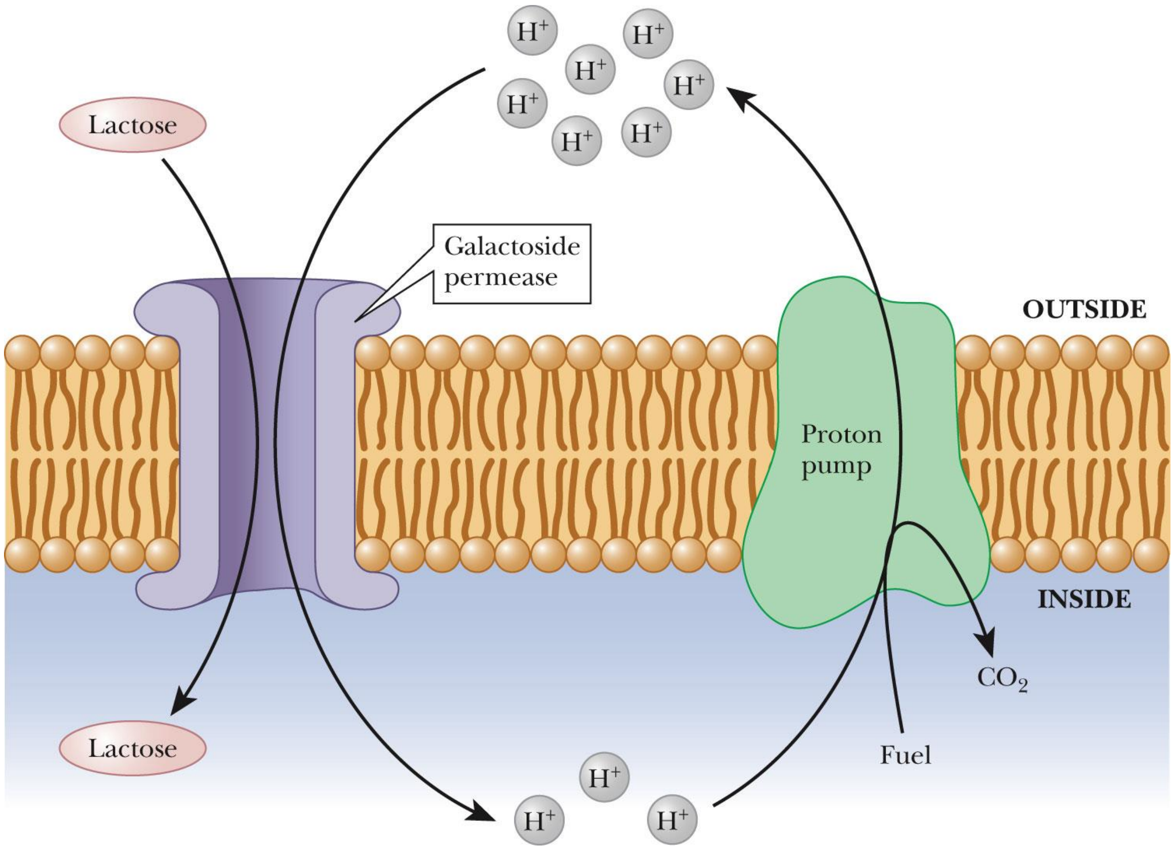
$[K^+]_{inside} > [K^+]_{outside}$

$[Na^+]_{inside} < [Na^+]_{outside}$

The sodium-potassium ion pump

2˚ Active transport

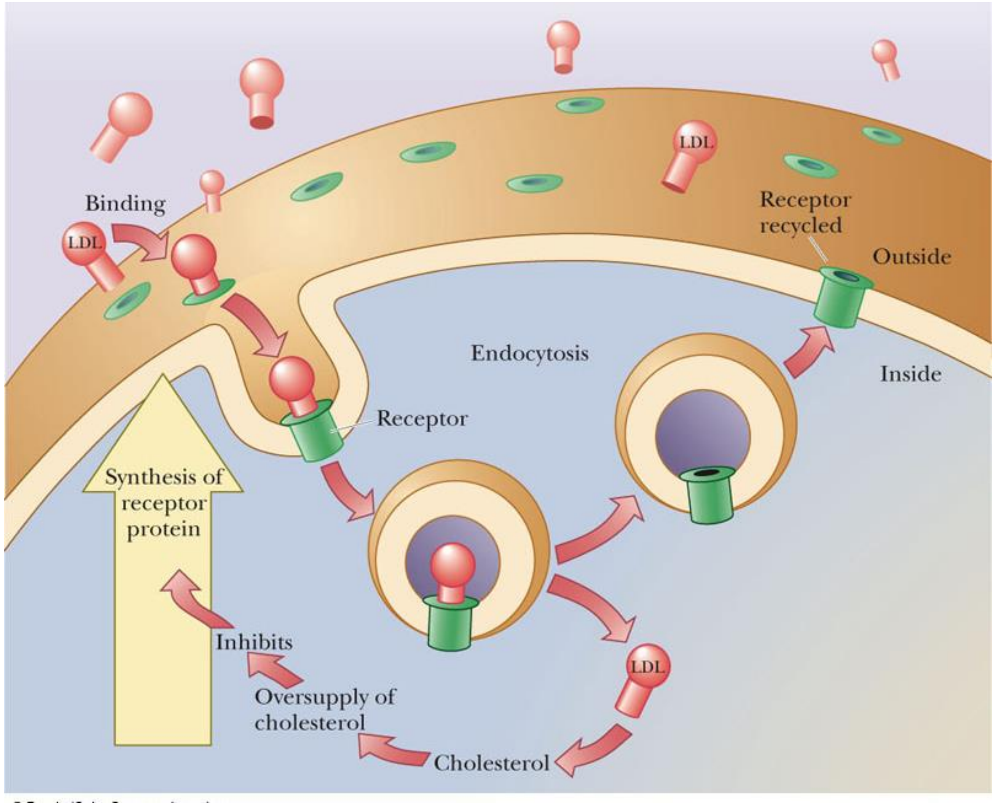
ATP is not hydrolyzed to produce energy.



An example of secondary active transport. In bacteria, galactoside permease uses the higher concentration of **H^+** outside the cell to drive the concentration of lactose inside the cell.

Membrane Receptors

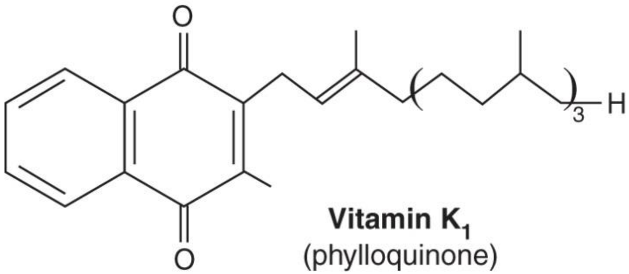
- Generally oligomeric proteins
- Binding of a biologically active substance to a receptor initiates an action within the cell



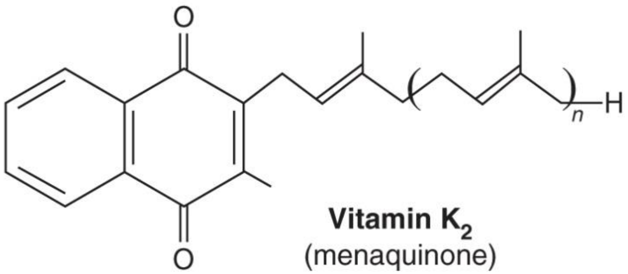
The mode of actions of the LDL. A portion of the membrane with LDL receptor and bound LDL is taken into the cell as a vesicle. The receptor protein releases LDL and is returned to the cell surface when the vesicle fuses to the membrane. LDL releases cholesterol in the cell. An oversupply of cholesterol inhibits synthesis of the LDL receptor protein. An insufficient number of receptors leads to elevated levels of LDL and cholesterol in the blood stream. This situation increases the risk of heart attack.

Lipid-Soluble Vitamins

Vitamins are divided into two classes: lipid-soluble and water-soluble



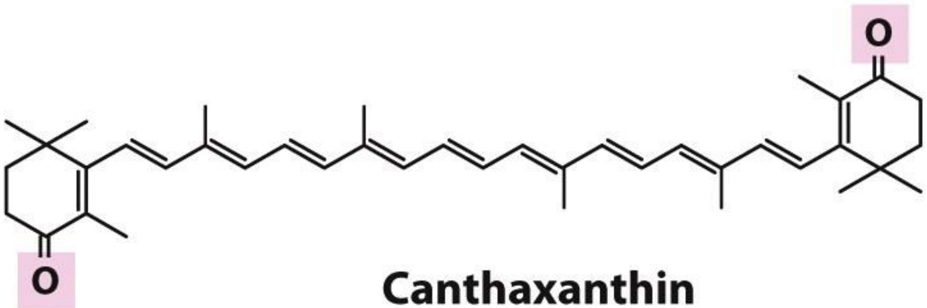
Vitamin K_1
(phylloquinone)



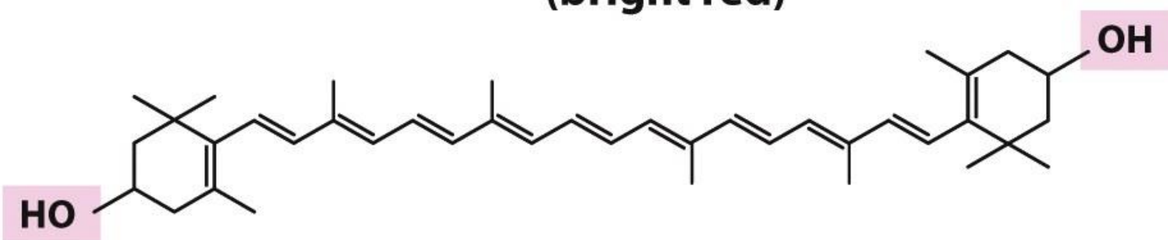
Vitamin K_2
(menaquinone)

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



Canthaxanthin
(bright red)



Zeaxanthin
(bright yellow)

Lipids as pigments in plants and bird feathers. Compounds with long conjugated systems absorb light in the visible region of the spectrum. Subtle differences in the chemistry of these compounds produce pigments of strikingly different colors. Birds acquire the pigments that color their feathers red or yellow by eating plant materials that contain carotenoid pigments, such as canthaxanthin and zeaxanthin. The differences in pigmentation between male and female birds are the result of differences in intestinal uptake and processing of carotenoids.