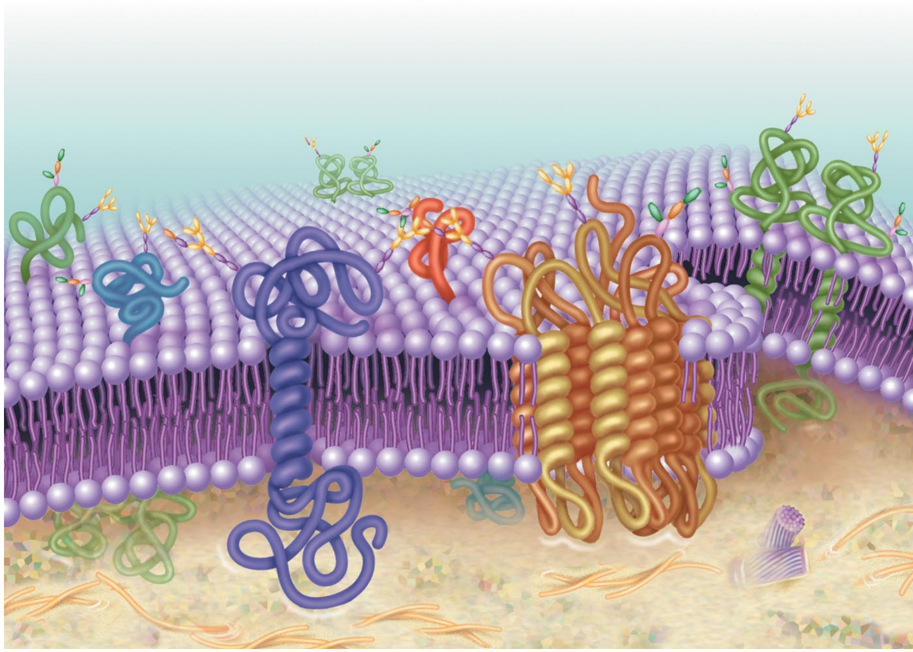
Chapter 11

Overview

- **Lipids** occur in nature
  - Substances that dissolve in non-polar solvents
    - Egg yolks, human nervous system
    - Component of plant, animal, microbial membranes



- **Functions:**
  - Energy storage – fats & oils
  - Structural - cell membranes
  - Chemical signals, vitamins, pigments
  - Protection - waterproofing

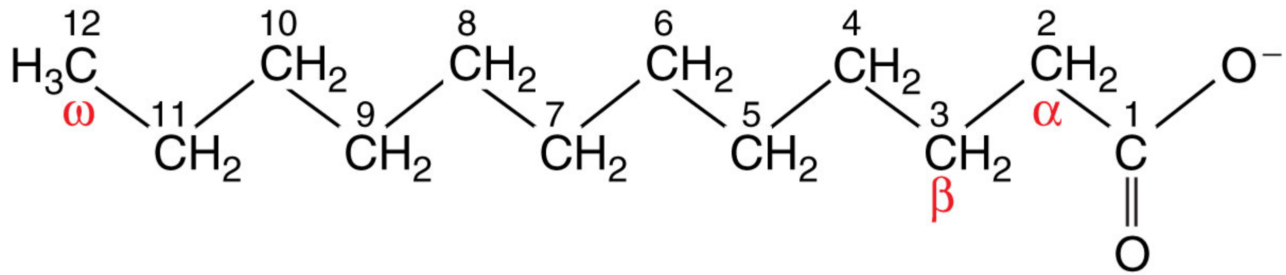
Lipids and Membranes

- Classified on basis of common solubility properties
  - soluble in organic solvents - diethyl ether, chloroform, methylene chloride, and acetone
- **Amphipathic** – polar head, non-polar tail
- **Open Chain forms**
  - fatty acids, triacylglycerols, sphingolipids, phosphoacylglycerols, glycolipids,
  - lipid-soluble vitamins
  - prostaglandins, leukotrienes, and thromboxanes
- **Cyclic forms**
  - cholesterol, steroid hormones, and bile acids

Lipids classes:

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

Figure 11.1 Fatty Acid Structure

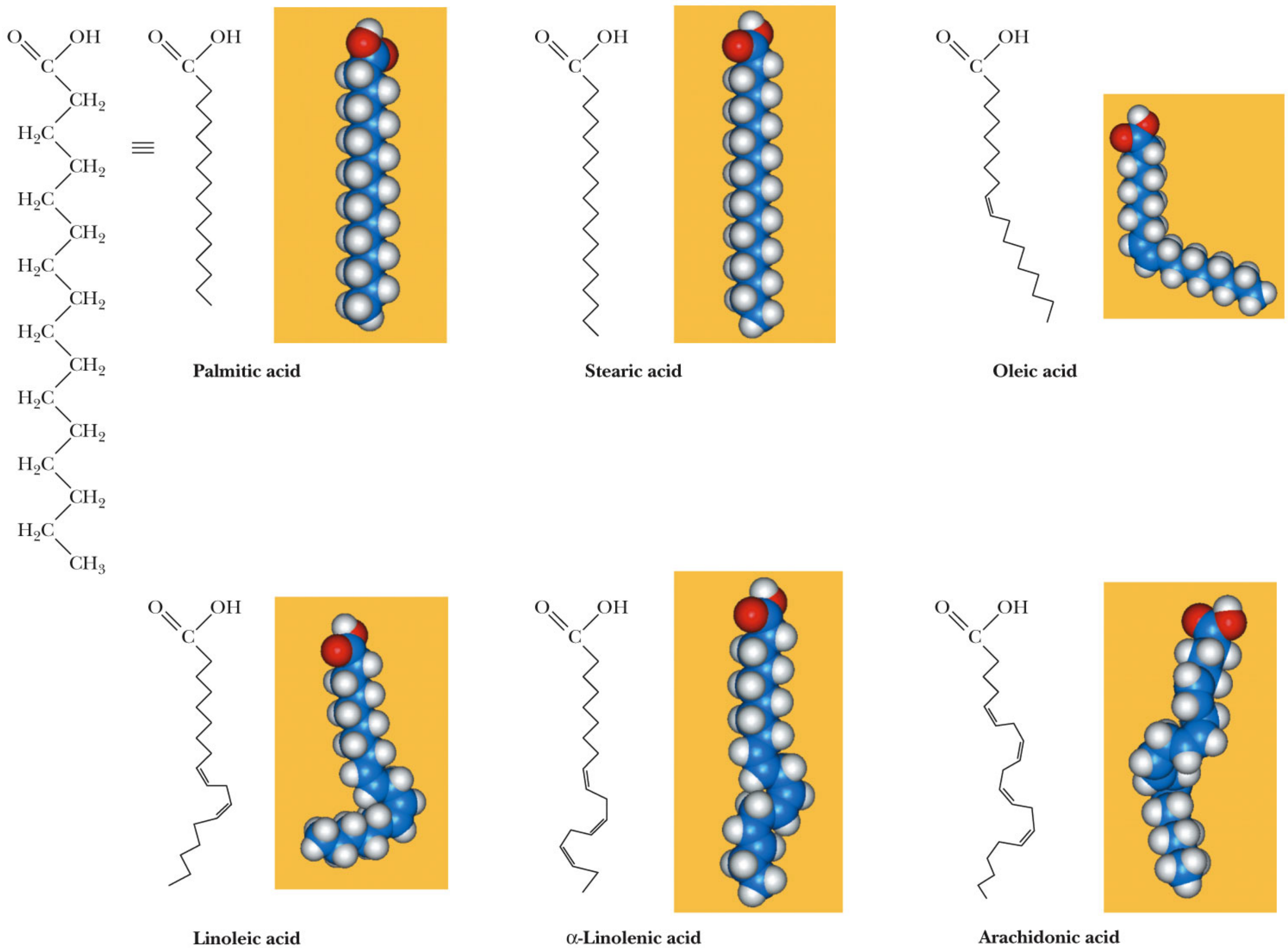


- **Fatty Acids**
  - **Monocarboxylic acids** – carboxyl head; hydrocarbon chain tail
    - Even number of carbons – 12 - 20
    - Numbered from the carboxylate end, α-carbon is adjacent to the carboxylate group
    - Terminal methyl carbon - omega (ω) carbon
    - Hydrolysis of animal fats, vegetable oils or phosphdiacylglycerols of membranes
  - **Functions:**
    - Insulation – maintain body temperature
    - Energy storage – breakdown of fatty acids for molecules for energy production
    - Water repellent – fur, feathers

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	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	$16{:}1^{\Delta 9}$
Oleic acid	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	$18{:}1^{\Delta 9}$
Linoleic acid	$CH_3(CH_2)_4CH{=}CH{-}CH_2{-}CH{=}CH(CH_2)_7COOH$	$18{:}2^{\Delta 9,12}$
α-Linolenic acid	$CH_3CH_2CH{=}CH{-}CH_2{-}CH{=}CH{-}CH_2{-}CH{=}CH(CH_2)_7COOH$	$18{:}3^{\Delta 9,12,15}$
γ-Linolenic acid	$CH_3(CH_2)_3{-}(CH_2{-}CH{=}CH)_3{-}(CH_2)_4{-}COOH$	$18{:}3^{\Delta 6,9,12}$
Arachidonic acid	$CH_3(CH_2)_3{-}(CH_2{-}CH{=}CH)_4{-}(CH_2)_3COOH$	$20{:}4^{\Delta 5,8,11,14}$

Saturated versus unsaturated Fatty acids



From McKee and McKee, *Biochemistry*, 5th Edition, © 2011 Oxford University Press

- Plants and bacteria – synthesize fatty acids from acetyl-CoA
- Animals acquire most of theirs from dietary sources
  - **Nonessential fatty acids** – mammals can synthesize saturated FA & some unsaturated ones
    - Adding 2-C units & introducing double bonds
  - **Essential fatty acids** - acquired from the diet
    - **Omega-3 fatty acids** (i.e., α-linolenic acid and its derivatives) may promote cardiovascular health
- **Acylated proteins** - fatty acids attached to protein
  - **acyl groups** help facilitate interactions with the environment
    - Myristoylation and palmitoylation

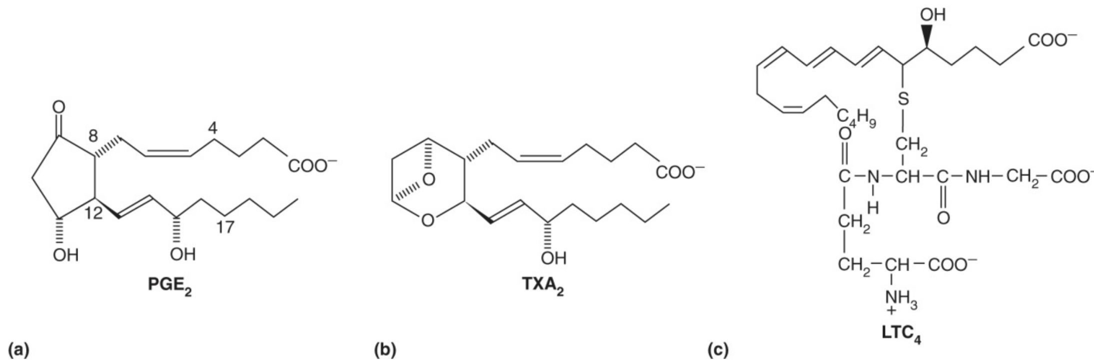


Figure 11.4a Eicosanoids

- **Eicosanoids – prostaglandins, thromboxanes, leukotrienes**
  - Mediate a wide variety of physiological processes: smooth muscle contraction, inflammation, pain perception, and blood flow regulation
  - Arachidonic acid – 20 carbon atoms, 4 double bonds
    - Precursor for all

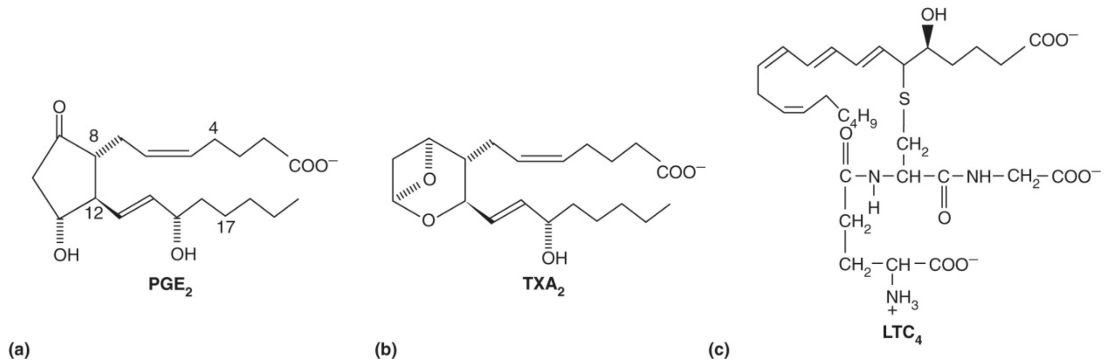
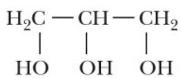


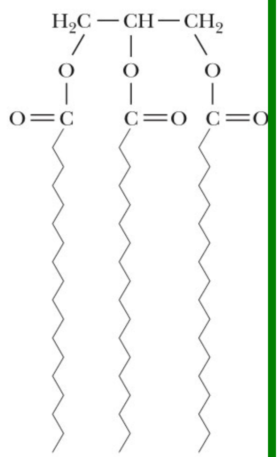
Figure 11.4a Eicosanoids

- **Prostaglandins (a)** contain a cyclopentane ring and hydroxyl groups at C-11 and C-15
  - Involved in inflammation, digestion, and reproduction
- **Thromboxanes (b)** - cyclic ether, synthesized by platets
  - Involved in platelet aggregation, vasoconstriction following tissue injury
- **Leukotrienes (c)** – linear with triene group (white blood cells)
  - **Anaphylaxis** (LTC_4, LTD_4, and LTE_4) – severe allergic reaction
  - blood vessel fluid leakage, white blood cell chemo-attractant, vasoconstriction, edema, broncho-constriction

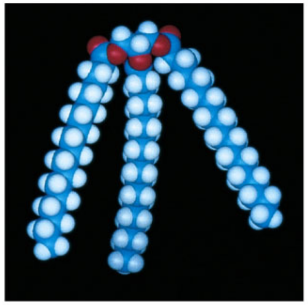
- **Triacylglycerols**
  - Esters of glycerol with three fatty acids; **neutral fats**
    - Contain fatty acids of varying lengths - mixture of saturated and unsaturated
    - Accumulate in adipose tissue – storage
      - **Lipases** – hydrolyze ester linkages
    - Solid at room temperature; high saturated fatty acid composition
    - Liquid at room temperature; high unsaturated fatty acid composition

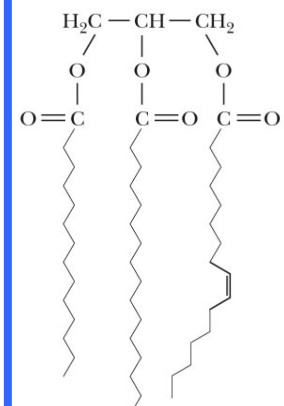


Glycerol

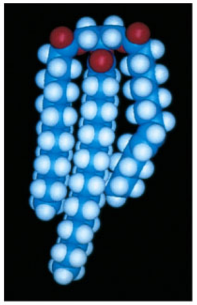


Tristearin
(a simple triacylglycerol)





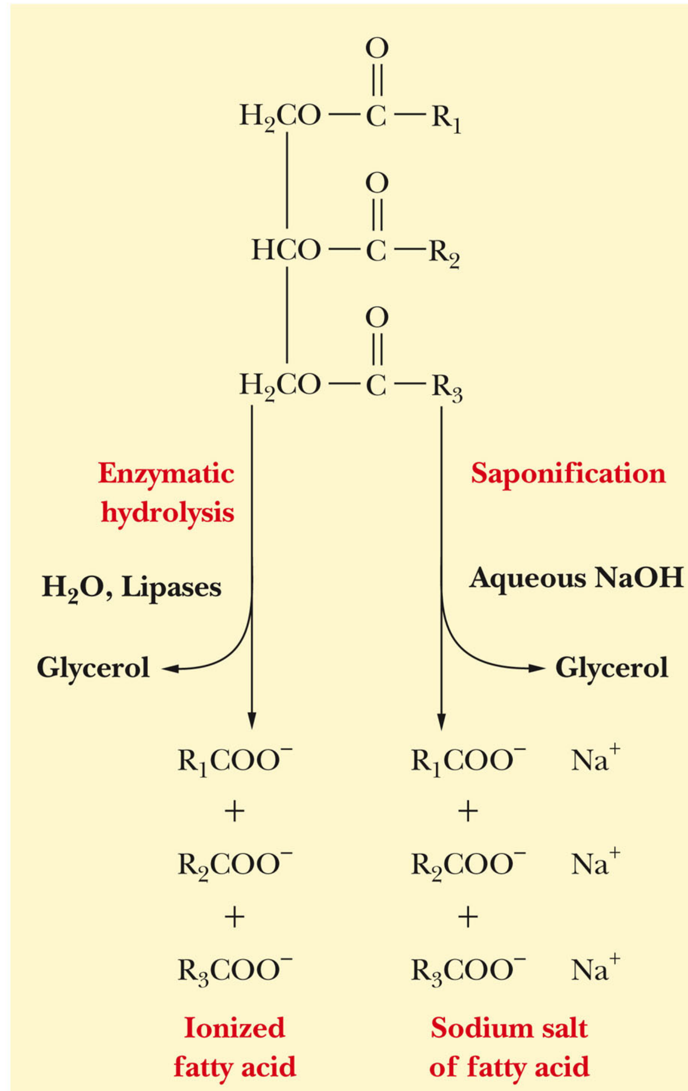
A mixed triacylglycerol



Saponification - natural soaps are prepared by boiling triglycerides (animal fats or vegetable oils) with NaOH

- Soaps form water-insoluble salts when used in water containing Ca(II), Mg(II), and Fe(III) ions (**hard water**)
  - Reactions with acids/bases as catalysts

- Glycerol – creams, lotions, nitroglycerin



- Roles in animals: energy storage (also in plants), insulation at low temperatures, water repellent for some animals' feathers and fur
  - Better energy storage form:
    1. Hydrophobic - coalesce into droplets; store an equivalent amount of energy in about one-eighth the space
    2. More reduced - can release more electrons per molecule when oxidized

- **Wax Esters**
  - Composed of long-chain fatty acids and long-chain alcohols
  - Protective coatings - leaves, stems, fruits of plants; skin and fur of animals
  - Examples include myricyl cerotate (beeswax, carnauba wax); cetyl palmitate (spermaceti)

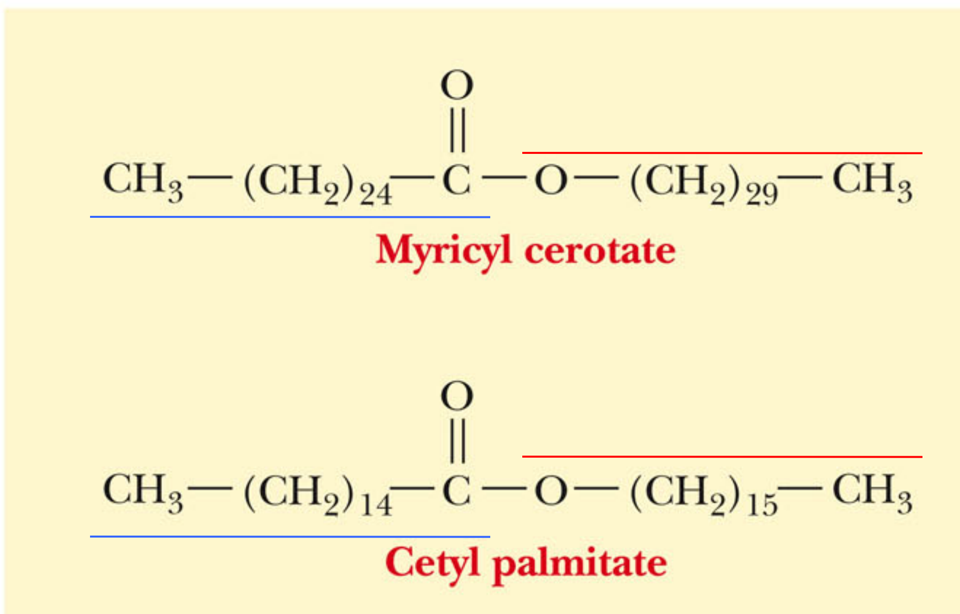
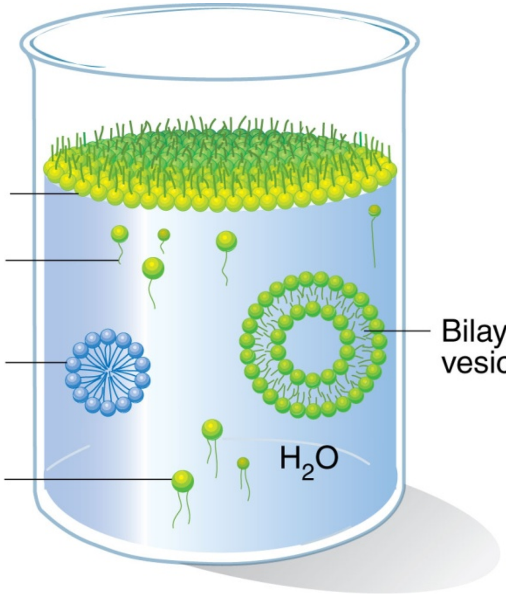


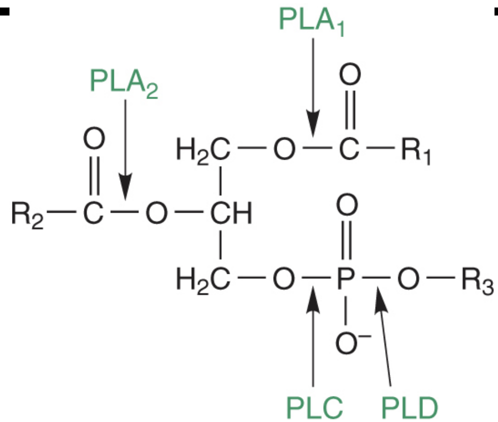
Figure 11.9 Phospholipid Molecules in Aqueous Solution



- **Phospholipids**
  - **Amphipathic - polar head** (phosphate, other polar or charged groups); hydrophobic fatty acids (nonpolar tail)
  - Act in membrane formation, emulsification, and as a surfactant
    - **Micelle** - Spontaneously rearrange into ordered structures when suspended in water

- Two types of phospholipids:
  - **Sphingomyelins** contain sphingosine instead of glycerol (also classified as sphingolipids)
    - Abundant in nervous system
  - **Phosphoglycerides** contain a glycerol, fatty acids, phosphate, an alcohol
    - Simplest - phosphatidic acid composed of glycerol-3-phosphate and two fatty acids
    - Phosphatidyl ethanolamine (cephalin) – brain & nerve tissue
    - Phosphatidylcholine (lecithin) – major part of membranes surrounding cells
    - Diphosphatidyl glycerol (cardiolipin) – inner mitochondrial membrane

Figure 11.11 Phospholipases



- **Phospholipases**- hydrolyze ester bonds in glycerophospholipid molecules
  - Three major functions
    - **Membrane remodeling**—adjust membrane flexibility or repair a damaged fatty acid
    - **Signal Transduction**—phospholipid hydrolysis initiates the signal transduction by numerous hormones
    - **Digestion**—pancreatic phospholipases degrade dietary phospholipids in the small intestine
  - **Toxic Phospholipases**—various organisms use membrane-degrading phospholipases as a means of inflicting damage
    - Bacterial α-toxin and necrosis from snake venom (PLA_2)

- **Sphingolipids** - important components of animal and plant membranes
  - **Ceramide – fatty acid linked to amino group of** sphingosine (long-chain amino alcohol)
    - Abundant in nervous system
  - Sphingomyelin – primary alcohol group esterified to phosphoric acid esterified to amino alcohol
    - Abundant in the myelin sheath of nerve cells

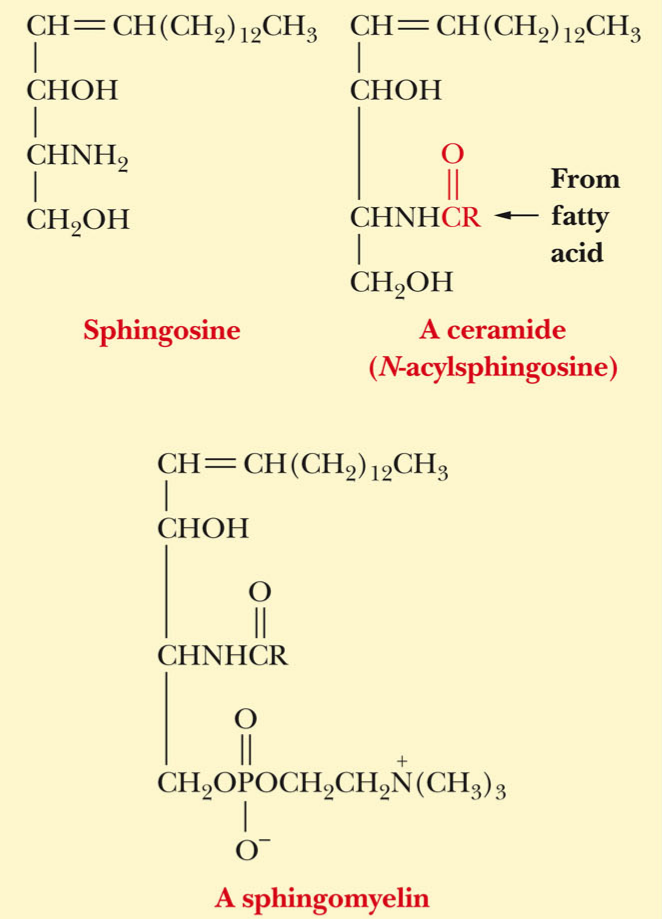
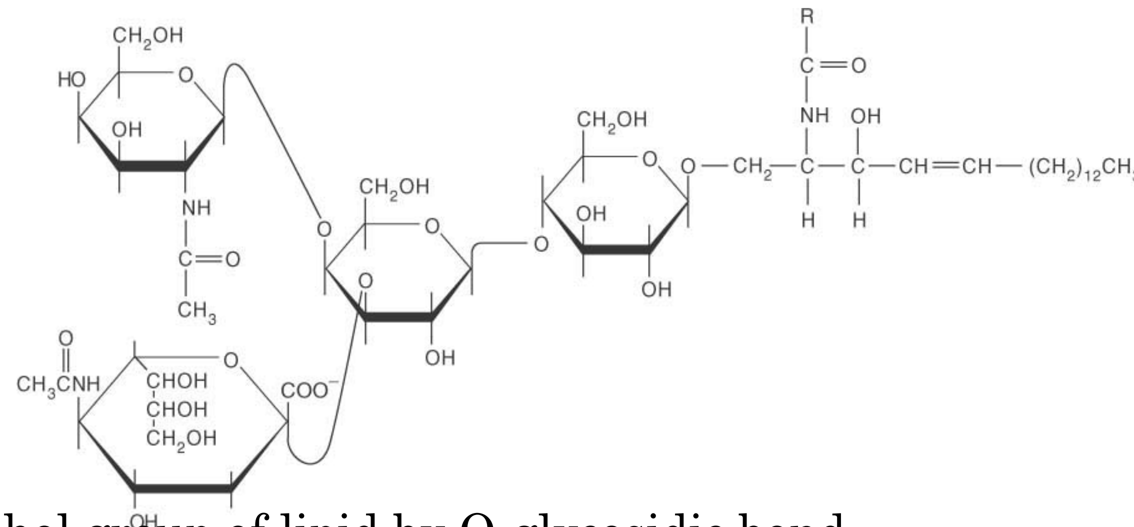


Figure 11.14a Selected Glycolipids

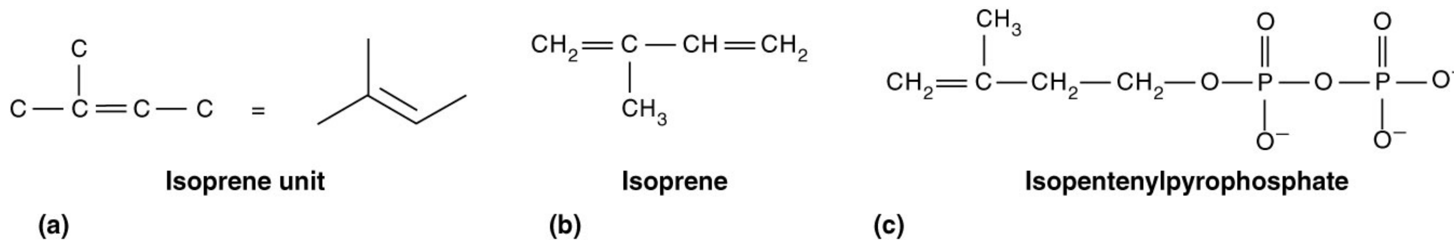


(a)

Glycolipids

- Carbohydrate bound to alcohol group of lipid by O-glycosidic bond
- **Glycosphingolipids** – ceramide without P is parent compound
- Most important classes
  - **Cerebrosides** have a monosaccharide for their head group
    - **Galactocerebroside** found in brain cell membranes
    - **Sulfatides** – sulfated cerebroside, negative charge at physiological pH
  - **Gangliosides** possess oligosaccharide groups; occur in most animal tissues and G_{M2} is involved in Tay-Sachs disease
- Found as markers on cell membranes play a large role in tissue & organ specificity

Figure 11.15 Isoprene



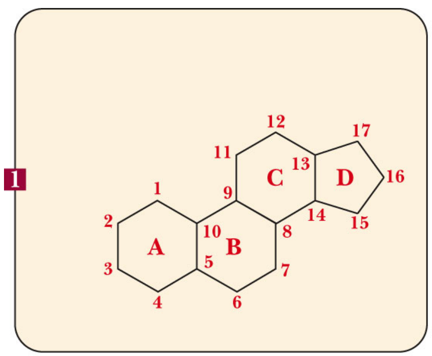
- **Isoprenoids** - repeating five-carbon structural units (isoprene units)
  - **Terpenes** - classified by the number of isoprene units
    - Monoterpenes (used in perfumes), sesquiterpines (e.g., citronella), tetraterpenes (e.g., **carotenoids**)
      - Carotenoids are the orange pigments found in plants
      - **Mixed terpenoids** consist of a nonterpene group attached to the isoprenoid group (prenyl groups)
        - Include vitamin K and vitamin E

Section 11.1: Lipid Classes

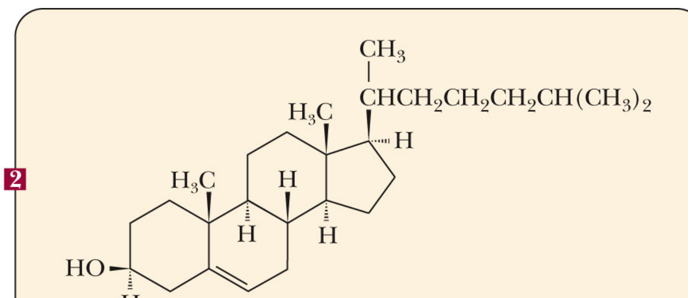
- **Steroids** – derivative of terpenes, fused-ring structure of 3 6-membered rings, 1 5-membered ring
- **Sex hormones** – regulate development of primary and secondary sex charateristics

- **Testosterone** – produced in testes, male characteristics
- **Estradiol** – produced in ovaries, female characteristics
- **Progesterone** – precursor for testosterone

1

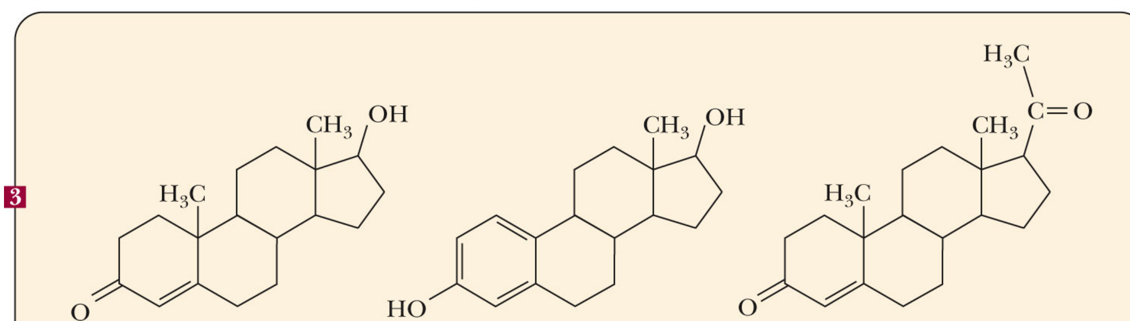


2



Cholesterol

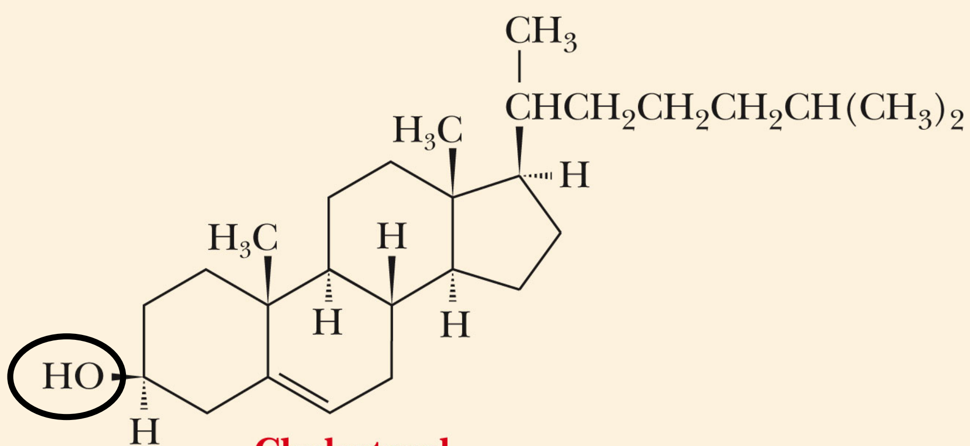
3



Testosterone Estradiol Progesterone

- **Cholesterol** - 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
  - Highly hydrophobic
  - Atherosclerosis – blocked blood vessels

2



Cholesterol

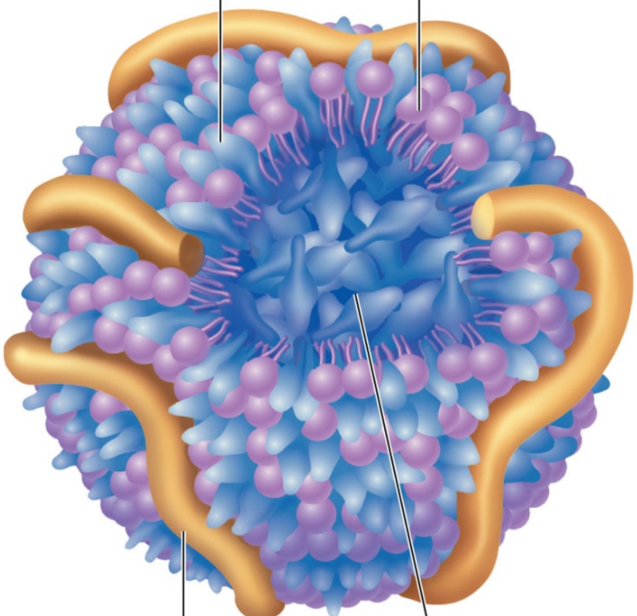


Figure 11.21 Plasma Lipoproteins

Lipoproteins – protein covalently linked to lipid groups

- Transport lipid molecules through bloodstream from organ to organ
- **Apolipoproteins** – protein component are synthesized in liver or intestine
- Five classes of apolipoproteins (A, B, C, D, and E)
  - Differentiated by types of lipoproteins with different ratios of lipid and protein components
- Four clases of plasma lipotroteins
  - Chylomicron, LDL, VLDL, HDL

Lipoproteins are classified according to their density:

- **Chylomicrons** - large lipoproteins; extremely low density; transport triacylglycerol and cholesteryl esters; synthesized in the intestines
- **Very low density lipoproteins** (VLDL) - synthesized in the liver and transport lipids to the tissues
- **Low density lipoproteins** (LDL) - principle transporters of cholesterol and cholesteryl esters to tissues
- **High density lipoprotein** (HDL) - protein-rich particle produced in the liver and intestine; may be a scavenger of excess cholesterol from membranes
  - Scavenges excess cholesteryl esters that are produced by lecithin:cholesterol acetyltransferase
  - Transports to liver converted to bile acids
  - "Good cholesterol"

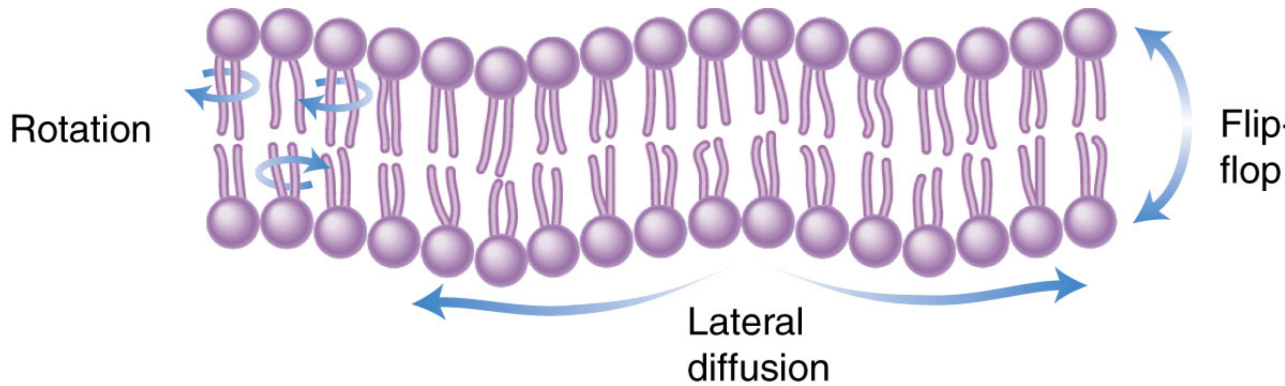
TABLE 11.5 Chemical Composition of Some Cell Membranes

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** - noncovalent heteropolymer of **lipid bilayer** and associated proteins
- **Membrane Structure**
  - Proportions of lipid, protein, and carbohydrate vary considerably among cell types and organelles

Figure 11.25 Lateral Diffusion in Biological Membranes



Fluid Mosaic Model – accepted description of biological membranes

- Phospholipids – structural component; active agents on surface
  - Largely responsible for many membrane properties
- **Fluidity** – lateral motion of components in membrane
  - Proteins 'float' & move in it's plane
- **Mosaic** – 2 components exist side by side
  - No covalent bonds between proteins & lipids

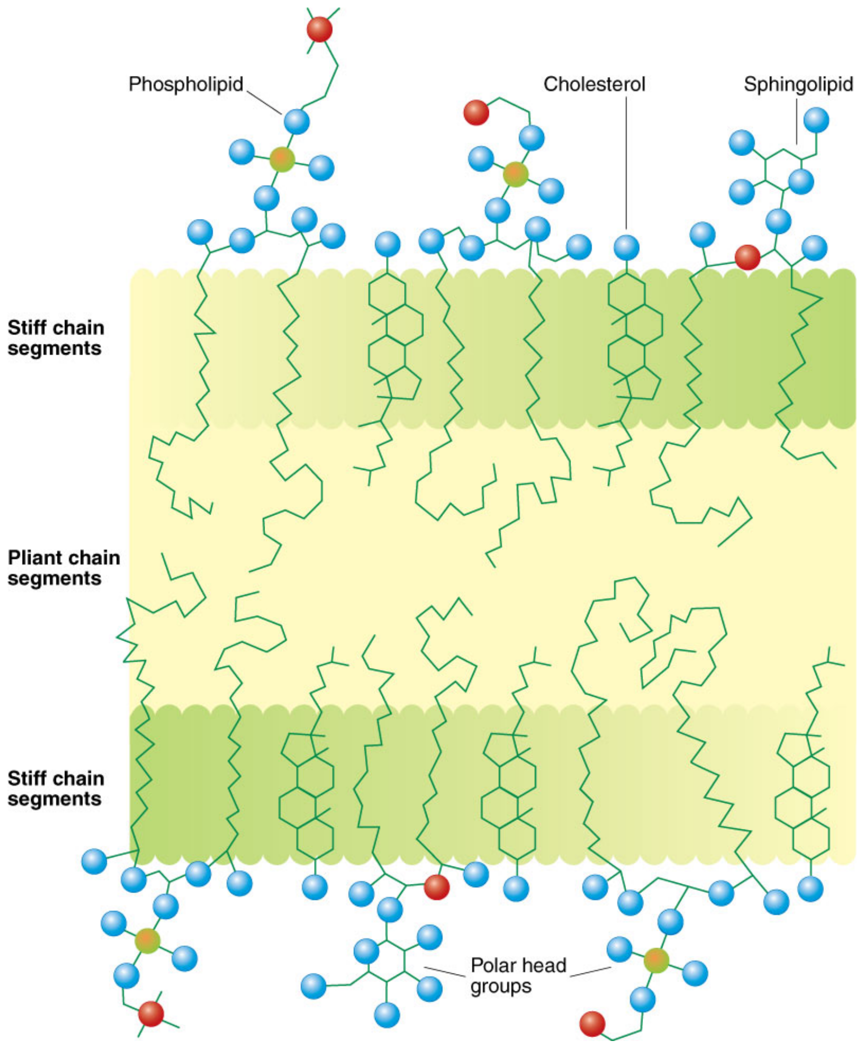
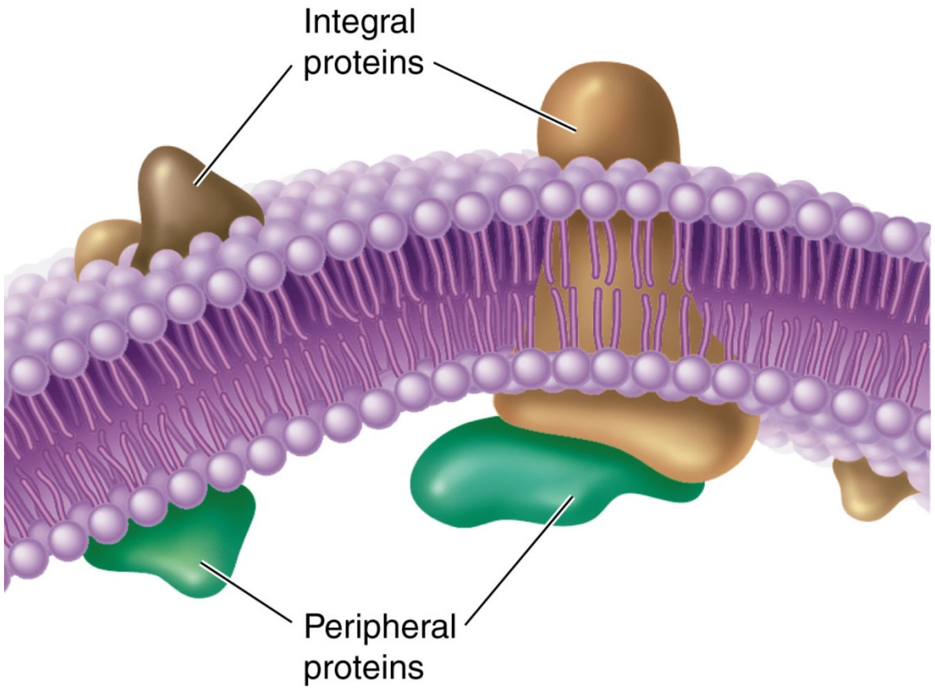


Figure 11.24 Diagrammatic View of a Lipid Bilayer

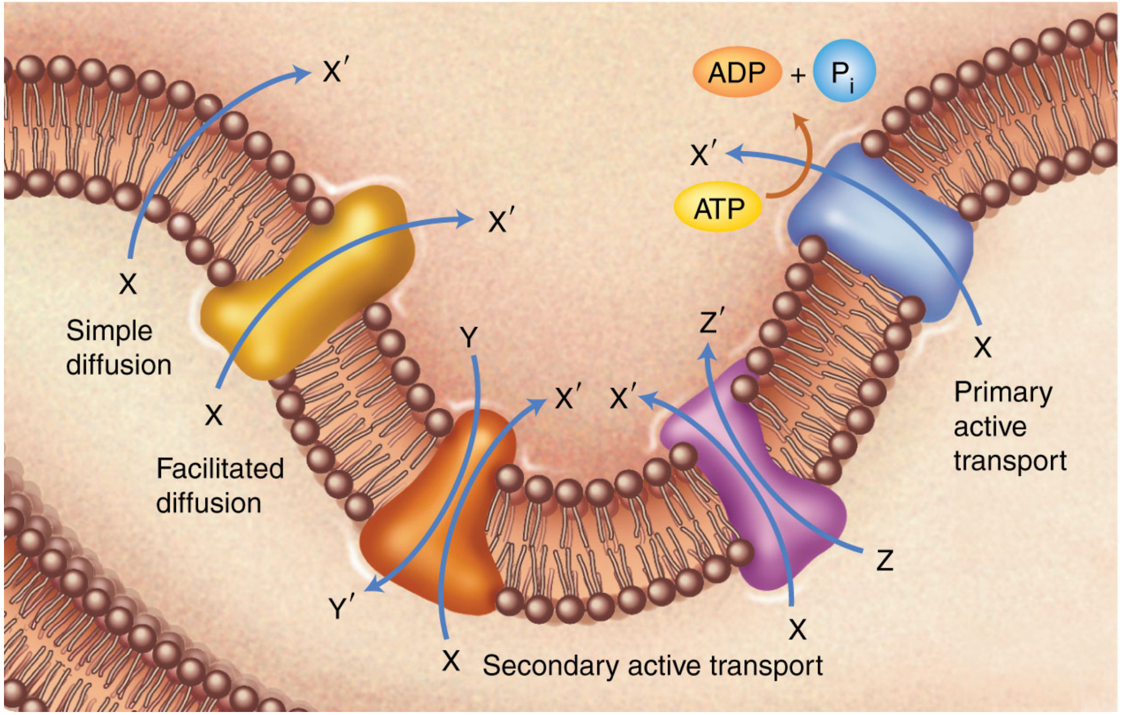
- **Flipase** - movement of phospholipids from one side of a membrane to other
- **Fluidity** - depends on unsaturated fatty acids and cholesterol
  - Higher unsaturated fat greater fluidity
  - Cholesterol contributes to stability with its rigid ring system; fluidity with its flexible hydrocarbon tail

Figure 11.26 Integral and Peripheral Membrane Proteins



- **Membrane Proteins**—facilitate movement of molecules across membrane; **peripheral** or **integral**
  - **Peripheral** – loosely bond to outer membrane
  - **Integral** – embedded in or pass through membrane

Figure 11.30 Transport across Membranes



- **Membrane Function**
  - **Membrane transport** – getting things in and out
  - **Catalysis** – reactions on membrane
  - **Receptor** – signals biochemical responses

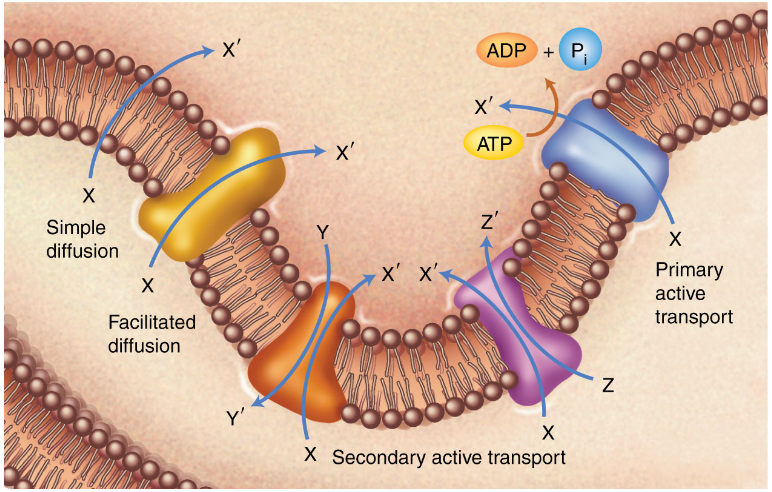
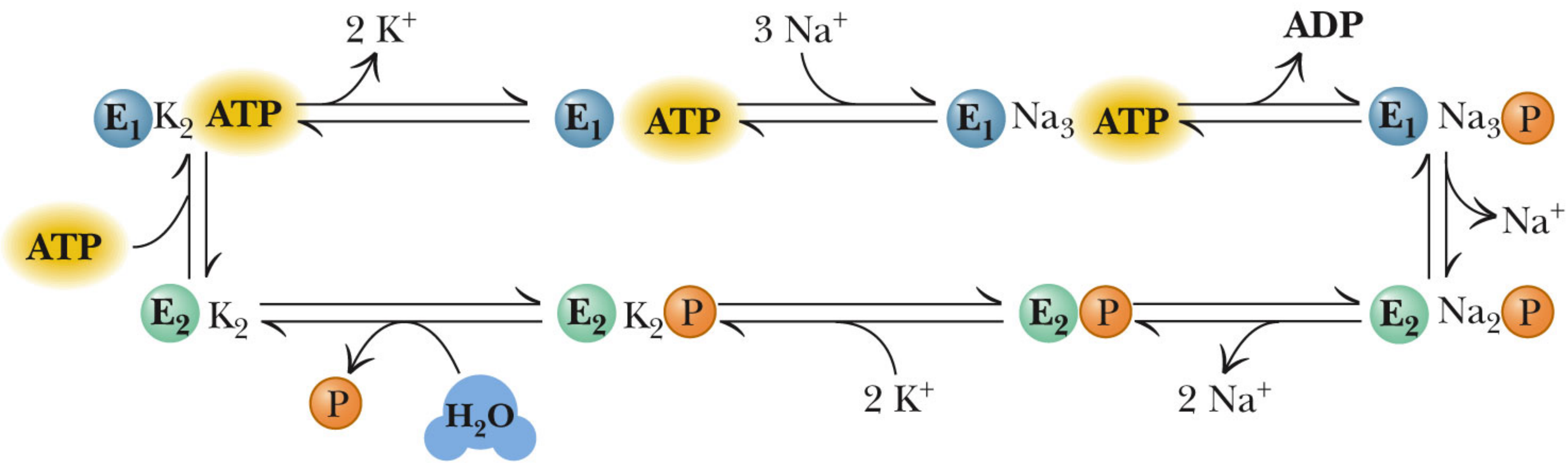


Figure 11.30 Transport across Membranes

- **Passive transport** - no energy input, down concentration gradient
  - **Simple diffusion** - small molecule or ion
  - **Facilitated diffusion** – uses carrier or channel protein
- **Active transport** - uses energy to transport molecules against a concentration gradient
  - **Primary** – linked to hydrolysis of ATP
  - **Secondary** – driven by concentration gradients generated by primary active transport

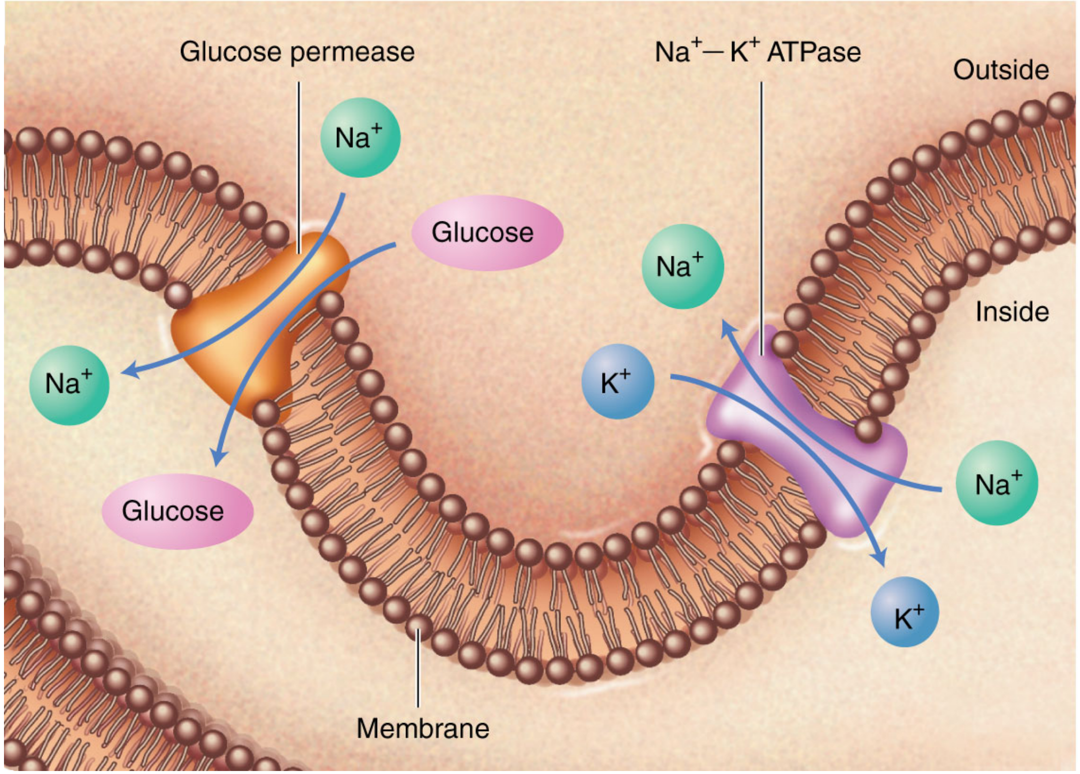
Passive diffusion

- **Simple diffusion** - propulsion of each solute by random molecular motion from high concentration to low concentration
  - Diffusion of gases O_2 and CO_2 across membranes is proportional to their concentration gradients
  - Does not require a protein channel
- **Facilitated diffusion** - channel proteins to move large or charged molecules down their concentration gradient
  - Examples include chemically gated Na^+ channel and voltage-gated K^+ channel



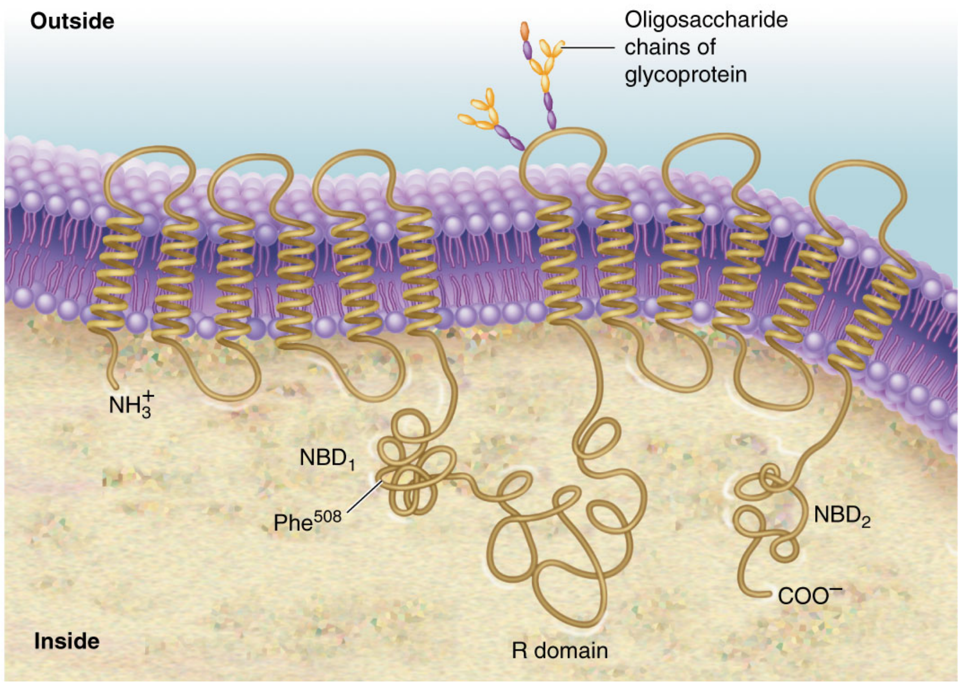
- **Primary active transport** – Na^+/K^+ ion pump
  - Sodium ions out, potassium ions in
  - Na^+-K^+ ATPase – provides energy
    - Assumes 2 conformations – E_1 and E_2

Figure 11.31 The Na^+-K^+ ATPase and Glucose Transport



- **Secondary active transport** - concentration gradients formed by primary active transport are used to move other substances across the membrane
  - Na^+-K^+ ATPase pump in the kidney drives the movement of D-glucose against its concentration gradient

Figure 11.33 The Cystic Fibrosis Transmembrane Regulator (CFTR)



- **Cystic fibrosis** - fatal autosomal recessive genetic disorder
  - **cystic fibrosis transmembrane conductance regulator** (CFTR) is missing or defective
    - Retention of Cl^- in cells
    - Missing Phe^{508} causes folding errors

- **Membrane Receptors** - mechanisms by which cells monitor and respond to changes in their environment
  - Chemical signals bind to membrane receptors in multicellular organisms for intracellular communication
    - Chemical signal molecules – hormones, neurotransmitters
  - Other receptors are involved in cell-cell recognition
    - Lymphocytes bind to cell surface of virus-infected cells
  - Binding of ligand to membrane receptor causes a conformational change and programmed response
    - Binding acetyl-choline to acetylcholine receptor opens a cation channel
  - Involved in embryonic and fetal development

- **Low-density lipoprotein receptor** - responsible for uptake of cholesterol-containing lipoproteins into cells
  - Glycoprotein found on the surface of many cells
  - Number of receptors increases in response to a need for cholesterol or steroid hormones
    - Receptor number varies from 15,000 to 70,000, depending on need
  - **Familial hypercholesterolemia** - Missing or defective receptor
    - Often caused by a failure to synthesize the receptor
    - Results in increased levels of cholesterol in the blood
      - Leads to heart attacks during childhood or early adolescence