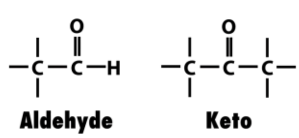
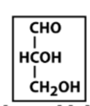
POLYSACCHARIDES AND LIPIS

Monosaccharides joined by glycosidic bonds from linear and branched polysaccharides

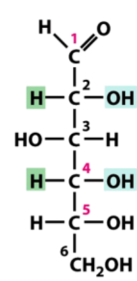
The building blocks of the polysaccharides are the simple sugar, or monosaccharides, *which are aldehyde or ketone derivatives of straight-chain polyhydroxy alcohols containing at least three carbon atoms*. They are classified according to the chemical nature of their carbonyl group and the number of their C atoms. Hexoses and pentoses are the most common monosaccharides.





D-Glyceraldehyde

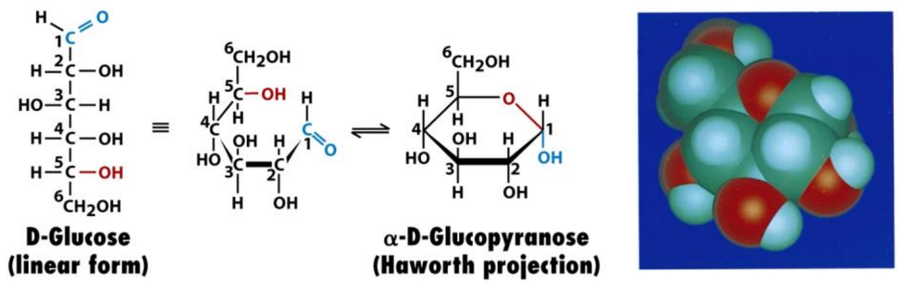
The aldohexose D-Glucose has the formula ($C_6H_{12}O_6$), two of its six C atoms are chiral centers, so D-glucose is one of 16 possible stereoisomers. D-glucose is the principal external source of energy for most cells in higher organisms and can exist in three different forms: *a linear structure and two different hemiacetal ring structures.*



D-Glucose

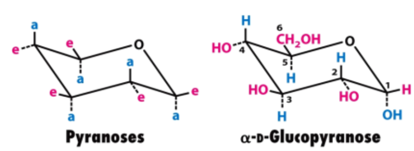
Configuration and conformation: alcohols react with the carbonyl groups of aldehydes and ketones to form hemiacetals and hemiketals.

The hydroxyl and either the aldehyde or ketone functions of *monosaccharides can likewise react intramolecularly to form cyclic hemiacetals and hemiketals*. The configurations of the substituents of each C atom are represented by their Haworth projections. When a monosaccharide cyclizes, the carbonyl C, called the anomeric carbon, becomes a chiral center with two possible configurations (anomers).

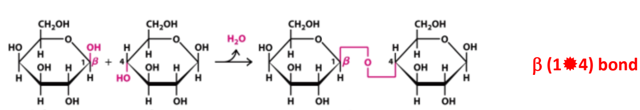


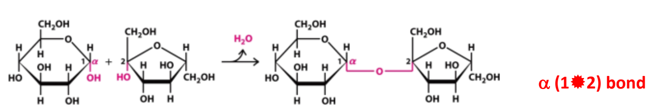
α- OH of the anomeric C is on the opposite side of the sugar ring from the CH_2OH group at the chiral center that designates the D configuration

Sugars are conformationally variable. The most stable conformation for the pyranose ring has a nonplanar, chairlike shape. In this conformation, each bond from a ring carbon to a nonring atom is either axial (nearly perpendicular) or equatorial (nearly in the plane).



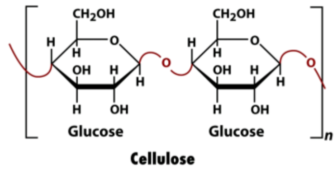
Polysaccharides, which are also known as ***glycans***, *consist of monosaccharides linked together by glycosidic bonds*. They are classified as homopolysaccharides or heteropolysaccharides if they consist of one type or more than one type of monosaccharide. *Polysaccharide, in contrast to proteins and nucleic acids, form branched as well as linear polymers*. **Disaccharides**, formed from two monosaccharides, are the simplest polysaccharides. Lactose contains a β (1✹4) bond, and sucrose contains an α (1✹2) bond.



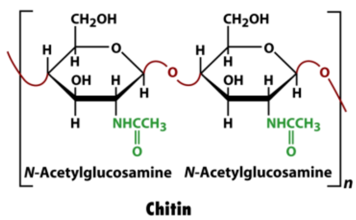


Structural Polysaccharides: Cellulose and Chitin.

Cellulose, the major component of plant cell walls, *is an unbranched polymer of up to 15,000 D-glucose residues linked by β (1→4) bonds.* The cellulose fibers are embedded in and cross-linked by a matrix containing other polysaccharides and lignin.

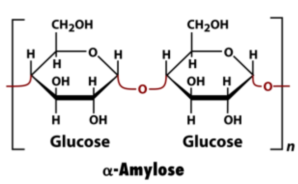


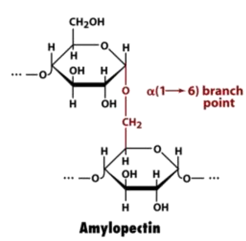
Chitin is the principal component of the exoskeletons of invertebrates such as crustaceans, insects, and spiders and is also present in the cell walls of most fungi and many algae. *It is a homopolymer of β (1→4) linked N-acetyl-D-glucosamine residues.*

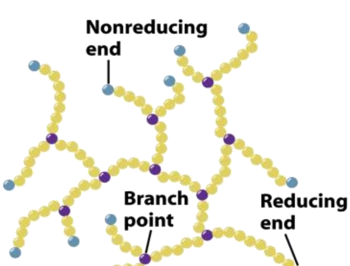


Storage Polysaccharides: Starch and Glycogen

Starch is a mixture of glycans that plants synthesize as their principal energy reserve. It is deposited in the chloroplasts of plant cells as insoluble granules *composed of α-amylose* (linear polymer of several thousand glucose residues) *and amylopectin* (branched molecule with α(1→6) branch points every 24 to 30 residues on average).



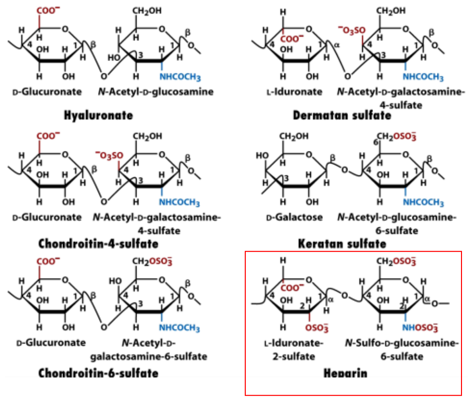




Schematic diagram of glycogen's branched structure

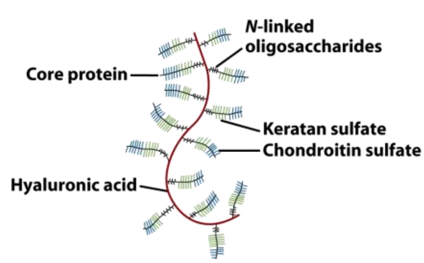
Glycogen, the storage polysaccharide of animals, is present in all cells but is most prevalent in skeletal muscle and in liver, where it occurs as cytoplasmic granules. *It is a very long, highly branched polymer of glucose, which has many nonreducing ends that permit the rapid mobilization of glucose in times of metabolic need.*

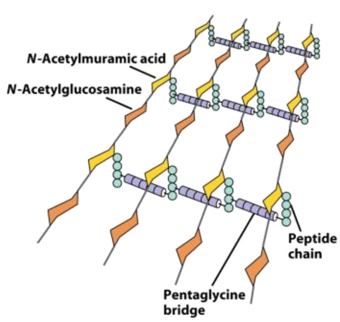
Glycosaminoglycans (GAGs) are *unbranched polysaccharides containing uronic acid and amino sugars that are often sulfated.* The gel-like matrix of the ECM is composed largely by GAGs.



Glycoproteins occur in all forms of life and have functions that span the entire spectrum of protein activities. The polypeptide chains of glycoproteins are synthesized under genetic control. *Their carbohydrate chains*, in contrast, *are enzymatically generated and covalently linked to the polypeptide without the rigid guidance of nucleic acid templates*. For this reason, glycoproteins tend to have variable carbohydrate composition (**microheterogeneity**).

Proteoglycans are enormous molecules *consisting of hyaluronic acid with attached core proteins that bear numerous glycosaminoglycans and oligosaccharides*. The extended brushlike structure of proteoglycans, together with the polyanionic character of their GAGs components, cause these complexes to be highly hydrated.



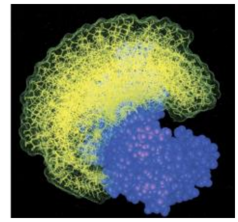


Bacterial cell walls *consist of covalently linked polysaccharide and polypeptide chains*, which form a baglike macromolecule that completely encases the cell (*peptidoglycan*).

Glycosylated proteins may contain *N*-linked oligosaccharides (attached to Asn) or *O*-linked oligosaccharides (attached to Ser or Thr) or both. Different molecules of a glycoprotein may contain different sequences and locations of oligosaccharides.

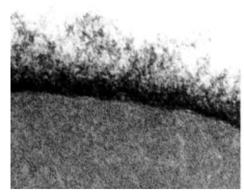
Functions of oligosaccharides

Oligosaccharides play important roles in protein processing and in cell-surface recognition phenomena.



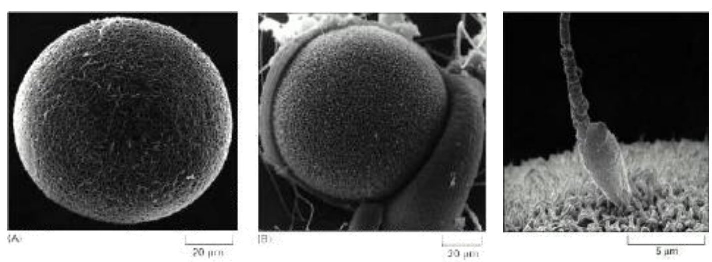
1. Structural effects of oligosaccharides. Oligosaccharides are usually attached to proteins at sequences that form surface loops or turns. Since sugars are hydrophilic, the oligosaccharide tend to project away from the protein surface and can occupy time-averaged volumes of considerable size. In addition, some oligosaccharides may play structural roles by limiting the conformational freedom of their attached polypeptide chains, and may also help to identify proteins nearing the end of their life span.

glycocalyx

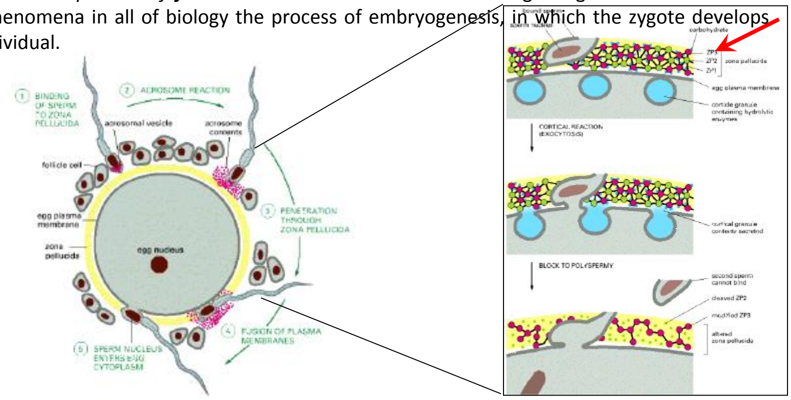


2. Oligosaccharides mediate recognition events. All cells are coated by with sugars in the form of *glycoconjugates* such as *glycoproteins and glycolipids*. *Lectins* are proteins that bind carbohydrates, which are ubiquitous in nature and frequently appear on the surfaces of cells. Proteins known as *selectins* mediate the attachment between leukocytes and the surfaces of endothelial cells.

Fertilization



Once released, egg and sperm alike are destined to die within minutes or hours unless they find each other and fuse in the process of ***fertilization***. Fertilization marks the beginning of one of the most remarkable phenomena in all of biology the process of embryogenesis, in which the zygote develops into a new individual.



Oligosaccharides are antigenic determinants. The carbohydrates on cell surfaces are some of the best known immunochemical markers. The ABO blood group antigens *are oligosaccharide components of glycoproteins and glycolipids on the surfaces of an individual's cells.*

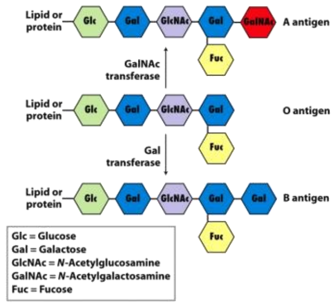


TABLE 10-2 ABO Blood Groups

BLOOD GROUP	ANTIGENS ON RBCS*	SERUM ANTIBODIES	CAN RECEIVE BLOOD TYPES
A	A	Anti-B	A and O
B	B	Anti-A	B and O
AB	A and B	None	All
O	O	Anti-A and anti-B	O

In mammals other than human and some monkeys, *cell-surface carbohydrates include a terminal galactosyl-α(1→3)-galactose disaccharide. Humans*, who lack the enzyme required for its synthesis, *produce antibodies against the disaccharide*. This innate immunoreactivity is the primary reason for the rapid *rejection* of animal tissues that have been transplanted into humans. Genetic engineering has produced ***"transplant-friendly" pigs*** that lack the gene for 1,3-galactosyltransferase and hence cannot add the terminal galactose to their cell-surface oligosaccharides.

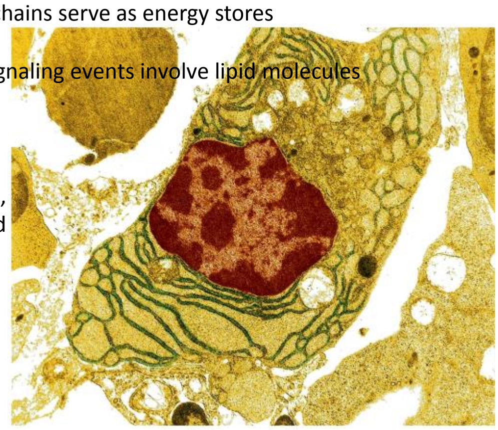
Lipids and biological membranes

Lipids are a diverse group of molecules that are soluble in organic solvents and, in contrast to other major types of biomolecules, do not form polymers. In general, lipids perform three biological functions:

1. lipid molecules in the form of lipid bilayers are essential components of biological membranes

2. lipids containing hydrocarbon chains serve as energy stores

3. many intra- and intercellular signaling events involve lipid molecules



Lipids classification

fatty acids, triacylglycerols, glycerophospholipids, sphingolipids, and steroids

Lipid bilayers

why bilayers form, lipid mobility

Structure and physical properties of the major classes of lipids

Fatty acids are *carboxylic acids whose chain lengths and degrees of unsaturation vary.* In higher plants and animals, the predominant fatty acids residues are those of the C_{16} and C_{18} species.

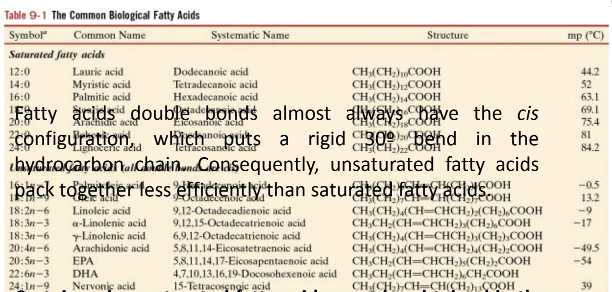
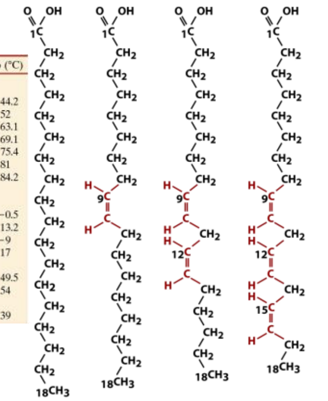


Table 9-1 The Common Biological Fatty Acids

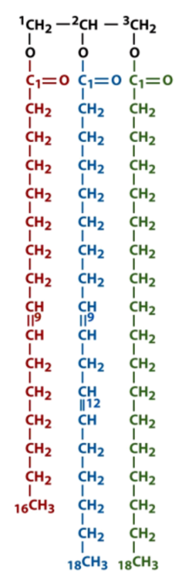
Symbol[a]	Common Name	Systematic Name	Structure	mp (°C)
Saturated fatty acids				
12:0	Lauric acid	Dodecanoic acid	$CH_3(CH_2)_{10}COOH$	44.2
14:0	Myristic acid	Tetradecanoic acid	$CH_3(CH_2)_{12}COOH$	52
16:0	Palmitic acid	Hexadecanoic acid	$CH_3(CH_2)_{14}COOH$	63.1
18:0	Stearic acid	Octadecanoic acid	$CH_3(CH_2)_{16}COOH$	69.1
20:0	Arachidic acid	Eicosanoic acid	$CH_3(CH_2)_{18}COOH$	75.4
22:0	Behenic acid	Docosanoic acid	$CH_3(CH_2)_{20}COOH$	81
24:0	Lignoceric acid	Tetracosanoic acid	$CH_3(CH_2)_{22}COOH$	84.2
Unsaturated fatty acids (all double bonds are cis)				
16:1n−7	Palmitoleic acid	9-Hexadecenoic acid	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	−0.5
18:1n−9	Oleic acid	9-Octadecenoic acid	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	13.2
18:2n−6	Linoleic acid	9,12-Octadecadienoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_2(CH_2)_6COOH$	−9
18:3n−3	α-Linolenic acid	9,12,15-Octadecatrienoic acid	$CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6COOH$	−17
18:3n−6	γ-Linolenic acid	6,9,12-Octadecatrienoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_3(CH_2)_3COOH$	
20:4n−6	Arachidonic acid	5,8,11,14-Eicosatetraenoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2COOH$	−49.5
20:5n−3	EPA	5,8,11,14,17-Eicosapentaenoic acid	$CH_3CH_2(CH{=}CHCH_2)_5(CH_2)_2COOH$	−54
22:6n−3	DHA	4,7,10,13,16,19-Docosohexenoic acid	$CH_3CH_2(CH{=}CHCH_2)_6CH_2COOH$	
24:1n−9	Nervonic acid	15-Tetracosenoic acid	$CH_3(CH_2)_7CH{=}CH(CH_2)_{13}COOH$	39

Fatty acids double bonds almost always have the *cis* configuration, which puts a rigid 30º bend in the hydrocarbon chain. Consequently, unsaturated fatty acids pack together less efficiently than saturated fatty acids.

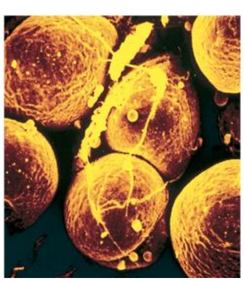
Certain polyunsaturated fatty acids must be obtained in the diet. *Linoleic acid must be obtained* in the diet and is therefore an *essential fatty acid*. It is also an important constituent of epidermal sphingolipids that function as the skin's water permeability barrier.

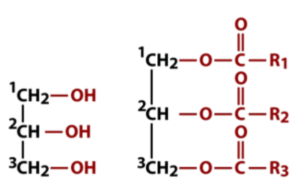


Triacylglycerols are nonpolar, water insoluble substances which consist of three fatty acids esterified to glycerol. Their function as energy reservoirs in animals and are therefore their most abundant class of lipids even though they are not components of cellular membranes.

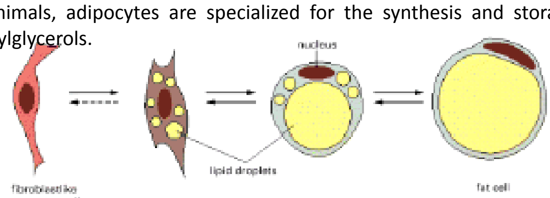


1-Palmitoleoyl-2-linoleoyl-3-stearoyl-glycerol



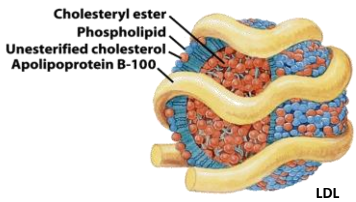


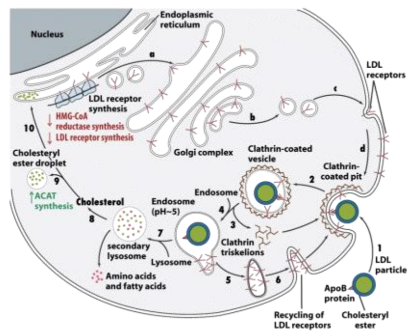
In animals, adipocytes are specialized for the synthesis and storage of triacylglycerols.



Since triacylglycerols are water insoluble, whereas digestive enzymes are water soluble, triacylglycerols digestion takes place at lipid-water interfaces. The digestion depends on the emulsifying activity of bile acids and the activation of lipases at the lipid-water interface. *The bile acids are amphipathic detergent-like molecules that act to solubilize fat globules.*

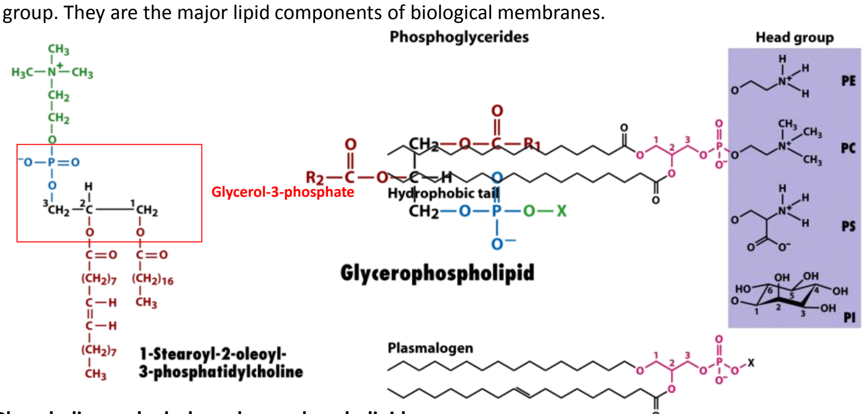
Lipids are transported by the circulation in complex with proteins. *Lipoproteins are globular micelle-like particles that consist of a nonpolar core of triacylglycerols and cholesteryl esters surrounded by an amphiphilic coating of protein, phospholipids, and cholesterol.*



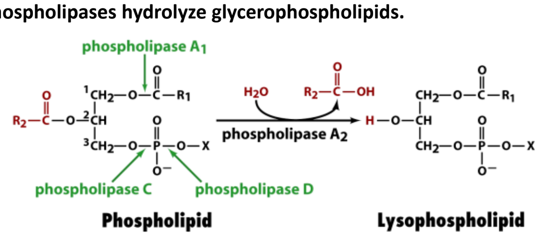


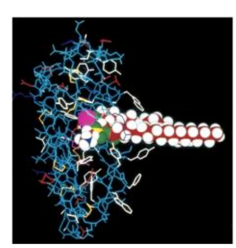
Receptor-mediated endocytosis is a general mechanism whereby cells take up large molecules, each through a corresponding specific receptor. Cells take up cholesterol and other lipids by the receptor-mediated endocytosis of LDL.

Glycerophospholipids are amphipathic molecules that contain two fatty acid chains and a polar head group. They are the major lipid components of biological membranes.



Phospholipases hydrolyze glycerophospholipids.

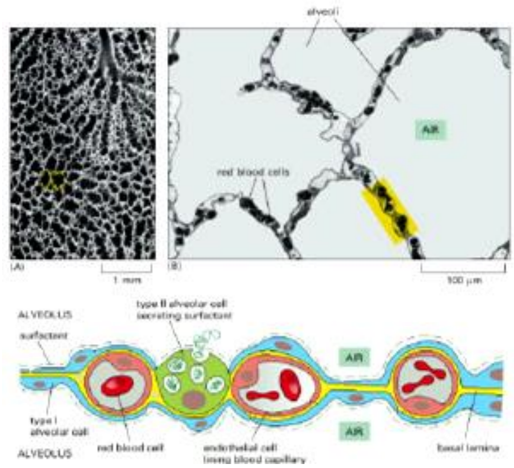




Lung surfactant

Dipalmitoyl phosphatidylcholine (DPPC) is the major lipid of lung surfactant, the protein-lipid mixture that is essential for normal pulmonary function. The surfaces of the cells that form the alveoli are coated with surfactant, which decreases the alveolar surface tension.

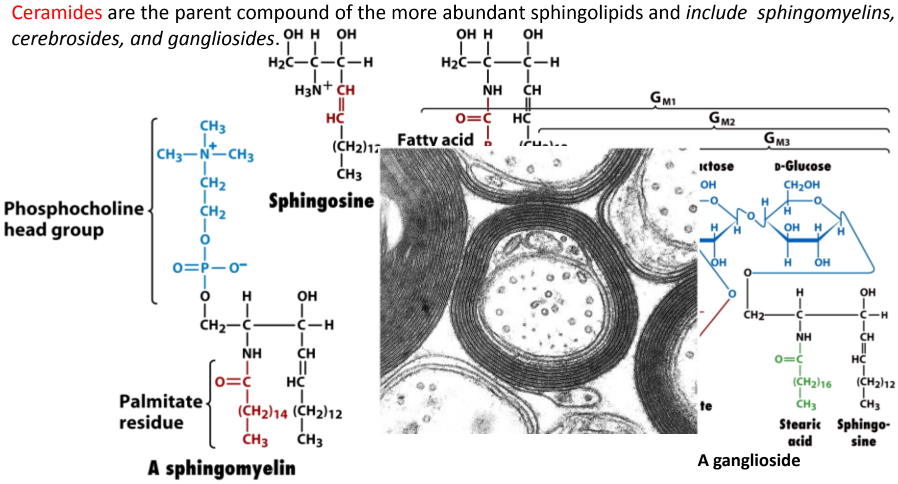
The chains of DPPC are saturated and tend to extent straight out without bending. This allows close packing of DPPC molecules, which are oriented in a single layer with their nonpolar tails toward the air and their polar heads toward the alveolar cells.



Respiratory distress syndrome.

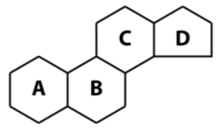
Sphingolipids are also major membrane components. Most sphingolipids are *derivates of the C18 amino alcohol sphingosine whose double bond has the trans configuration*. The *N*-acyl fatty acid derivatives of sphingosine are known as *ceramides*.

Ceramides are the parent compound of the more abundant sphingolipids and *include sphingomyelins, cerebrosides, and gangliosides*.



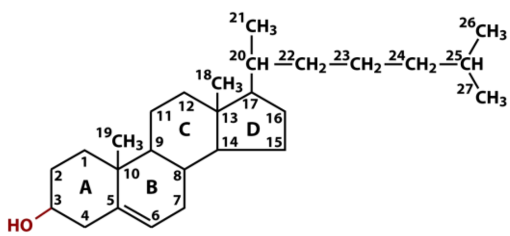
Son receptores de la toxina colerica de bacterias.

Steroids which are mostly of eukaryotic origin, are derivates of a compound that consists of four fused, nonplanar rings (cyclopentanoperhydrophenanthrene).



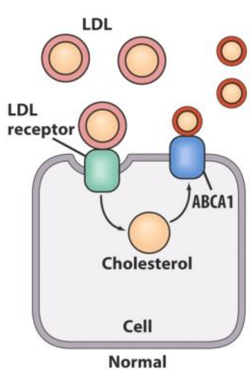
Cyclopentanoperhydrophenanthrene

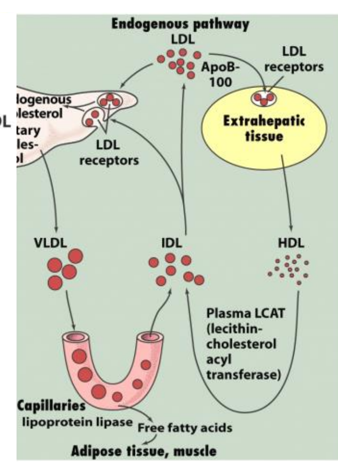
Cholesterol, which is the most abundant steroid in animals, is further classified as a sterol because of its C3-OH group. Its polar OH group gives it a weak amphiphilic character, whereas its fused ring system provides it with greater rigidity than other lipids.

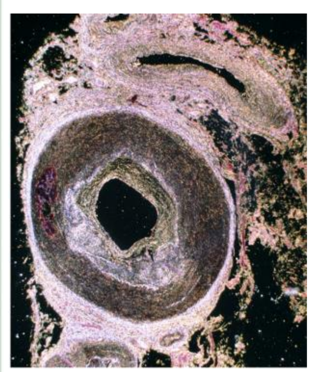


Cholesterol

Cholesterol is a vital constituent of cell membranes and the precursor of steroid hormones and bile acids. It is clearly essential to life, yet its deposition in arteries is associated with cardiovascular disease and stroke, two leading causes of death in humans.



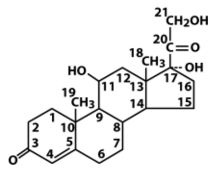




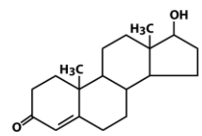
Atherosclerosis results from accumulation of lipid in vessel walls. Hypercholesterolemia, associated with certain genetic defects or a high-cholesterol diet, contributes to the development of atherosclerosis.

In mammals, *cholesterol is the metabolic precursor of* ***steroid hormones***, substances that regulate a great variety of physiological functions, and bile acids. Because steroid hormones are water-insoluble, they bind to proteins for transport through the blood to their target tissue.

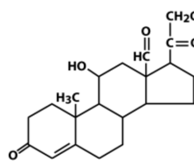
1. The glucocorticoids, such as cortisol, affect the carbohydrate, protein, and lipid metabolism and influence a wide variety of other vital functions.
2. Aldosterone and other mineralocorticoids regulate the excretion of salt and water by the kidneys.
3. The androgens and estrogens affect sexual development and function.



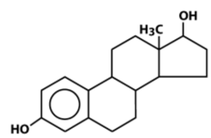
Cortisol (hydrocortisone)
(a glucocorticoid)



Testosterone
(an androgen)

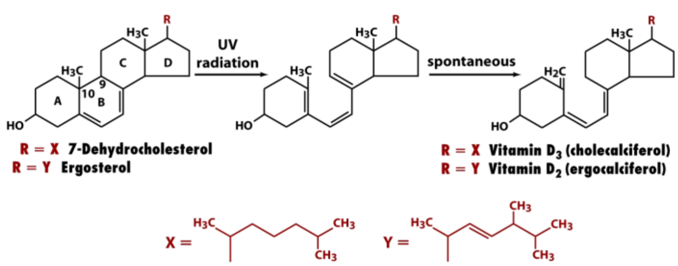


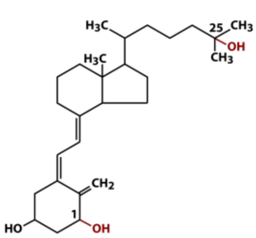
Aldosterone
(a mineralocorticoid)



β-Estradiol
(an estrogen)

Cholesterol, steroid hormones, and vitamin D are all based on a four-ring structure. Vitamin D regulates Ca^{2+} metabolism. The various form of vitamin D are sterol derivatives in which the steroid B ring is disrupted between C9 and C10.



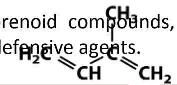


1α,25-Dihydroxycholecalciferol

The ***active forms*** of vitamin D_2 and D_3 are produced through their enzymatic *hydroxylation* carried out by the liver and by the kidney. Since vitamin D is water insoluble, it can accumulate in fatty tissue. Excessive intake of vitamin D over long periods result in vitamin D intoxication.

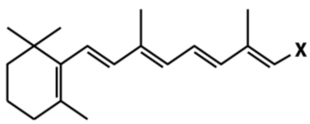
Other lipids. Among the compounds that are not structural components of membranes (soluble in lipid membrane) are the isoprenoid, *which are built from five-carbon units with the same carbon skeleton as isoprene.*

The plant kingdom is rich in isoprenoid compounds, which serve as pigments, molecular signals (hormones and pheromones), and defensive agents.



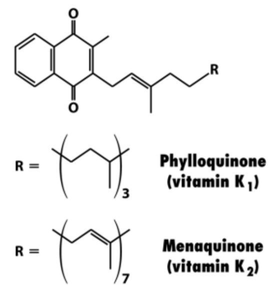
Isoprene

Vitamin A or **retinol** is derived mainly from plant products such as β-carotene.

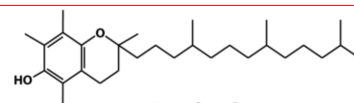


X = CH_2OH **Retinol (vitamin A)**
X = CHO **Retinal**

Vitamin K is a lipid synthesized in plants and bacteria.

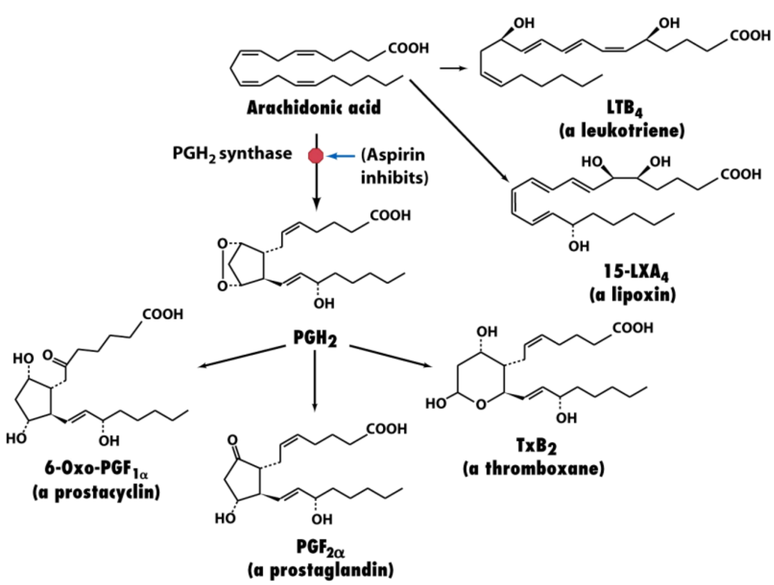


Vitamin E is a group of compounds whose most abundant member is α-tocopherol.

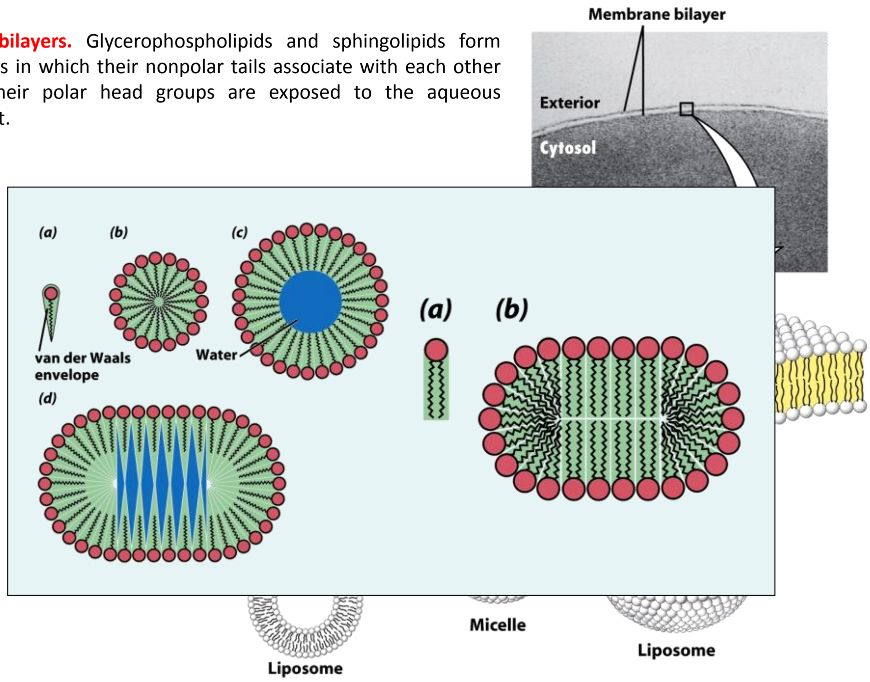


α-Tocopherol (vitamin E)

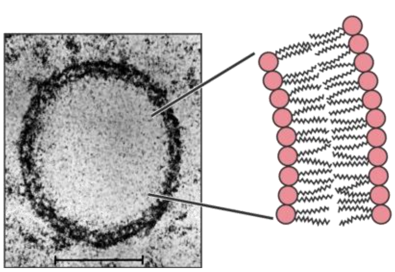
Other less common lipids are derived form relatively abundant membrane lipids. The **arachidonic acid derivates** *prostaglandins, prostacyclins, thromboxanes, leukotrienes, and lipoxins are signaling molecules that have diverse physiological roles.*

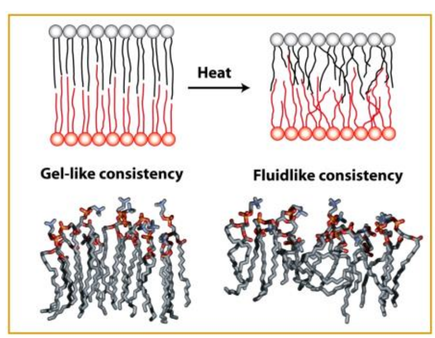


Lipid bilayers. Glycerophospholipids and sphingolipids form bilayers in which their nonpolar tails associate with each other and their polar head groups are exposed to the aqueous solvent.



Although the transverse diffusion of a lipid across a bilayer is extremely slow, lipids rapidly diffuse in the plane of the bilayer. Bilayer fluidity varies with temperature and with the chain lengths and degree of unsaturation of its component fatty acid residues.

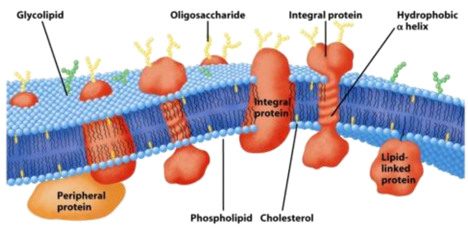




Cholesterol, which by itself does not form a bilayer, decreases membrane fluidity because its rigid ring system interferes with the motions of the fatty acid side chains in other membrane lipids.

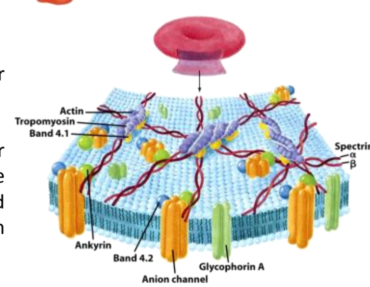
Membrane structure and assembly

Biological membranes contain proteins as well as lipid. The exact lipid and protein components and the ratio of protein to lipid varies with the identity of the membranes. The proteins of biological membranes include integral (*intrinsic*) proteins and membrane-associated proteins which may be anchored to the membrane via isoprenoid, fatty acid, or glycosylphosphatidylinositol groups. Peripheral (*extrinsic*) proteins are loosely associated with the membrane surface.



The fluid mosaic model of membrane structure accounts for the lateral diffusion of membrane proteins and lipids.

The arrangements of membrane proteins may depend on their interactions with an underlying protein skeleton, as in the erythrocyte. Membrane proteins and lipids are distributed asymmetrically in the two leaflets and may form domains such as lipid rafts.



SUMMARY

➢ Three major biopolymers formed by polymerization reactions (net dehydration) of basic chemical blocks are present in cells: proteins, composed of amino acids linked by peptide bonds; nucleic acids, composed of nucleotides linked by phophodiester bonds; and **polysaccharides, composed of monosaccharides linked by glycosidic bonds. Phospholipids, the fourth major chemical building block, assemble noncovalently into biomebranes.**

➢Many molecules in cells contain at least one asymmetric carbon atom, which bonded to four dissimilar atoms. Such molecules can exist as optical isomers, designated D and L, which have different biological activities. In biological systems, nearly all sugars are D isomers, whereas nearly all amino acids are L isomers.

➢Glucose and other hexoses can exist in three forms: an open-chain linear structure, a six-member ring, and a five-member ring. In biological systems, the pyranose form of D-glucose predominates.

➢ Phospholipids are amphipathic molecules with a hydrophobic tail connected by a small organic molecule to a hydrophilic head. The long hydrocarbon chain of a fatty acid may contain no carbon-carbon double bond or one or more double bonds; a *cis* double bond bends the chain.