Lipids (Greek: *lipos,* fat) are the fourth major group of molecules found in all cells. Unlike nucleic acids, proteins, and polysaccharides, lipids are not polymeric.

However, they do aggregate, and it is in this state that they perform their central function as the structural matrix of biological membranes.

Lipids exhibit greater structural variety than the other classes of biological molecules. To a certain extent, lipids constitute a catchall category of substances that are similar only in that they are largely hydrophobic and only sparingly soluble in water. In general, lipids perform three biological functions (although certain lipids serve more than one purpose in some cells):

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

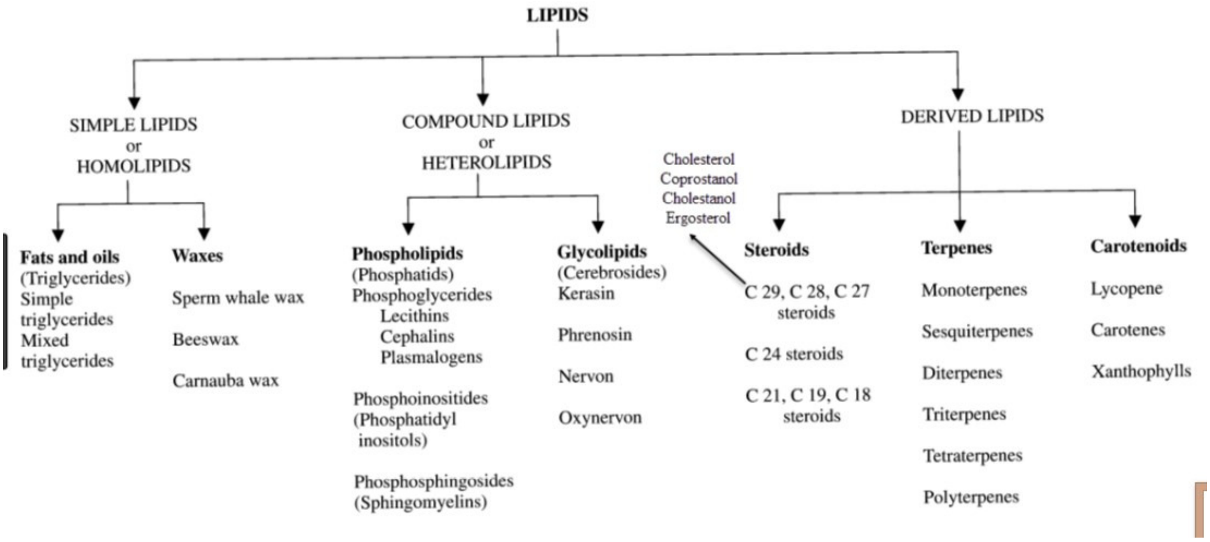
2. Lipids containing hydrocarbon chains serve as energy stores.

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

Lipids are substances of biological origin that are soluble in organic solvents such as chloroform and methanol. Hence, they are easily separated from other biological materials by extraction into organic solvents. They can then be separated chromatographically and identified by mass spectrometry according to their masses and characteristic fragmentation pattern

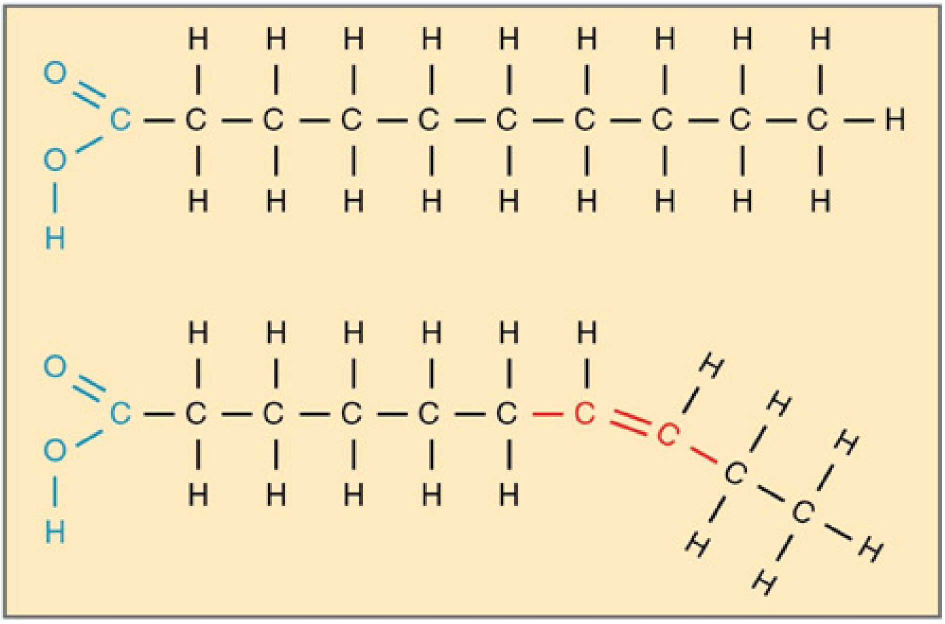
The Properties of Fatty Acids Depend on Their Hydrocarbon Chains

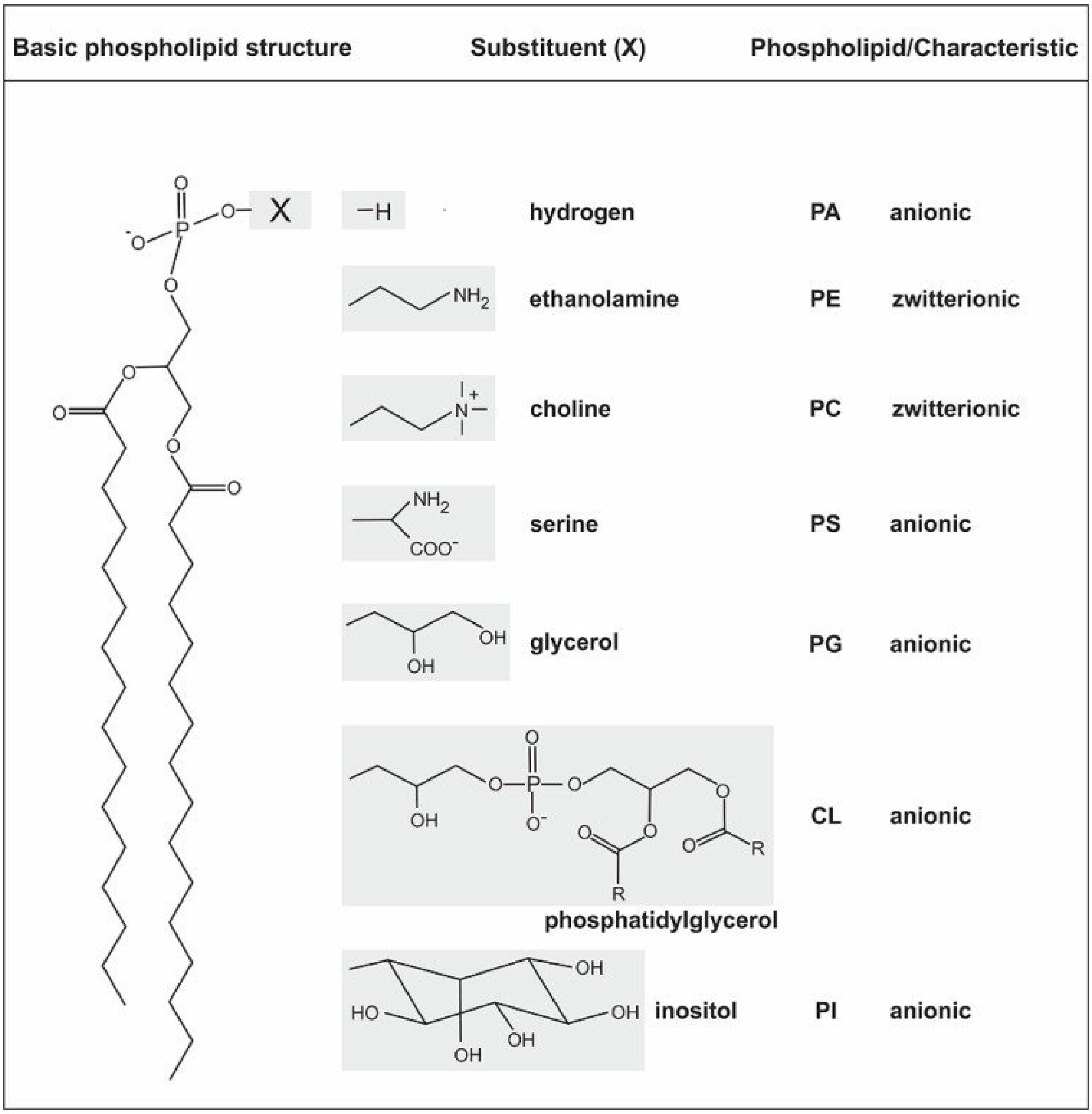
Fatty acids *are carboxylic acids with long-chain hydrocarbon side groups.* They usually occur in esterified form as major components of the various lipids In higher plants and animals, the predominant fatty acid residues are those of the C16 and C18 species: **palmitic, oleic, linoleic**, and **stearic acids**. Fatty acids with <14 or >20 carbon atoms are uncommon. Most fatty acids have an even number of carbon atoms because they are biosynthesized by the concatenation of C2 units. Fats, oils,certain vitamins and hormones, and most nonprotein membrane components are lipids.


LIPIDS
SIMPLE LIPIDS or HOMOLIPIDS
COMPOUND LIPIDS or HETEROLIPIDS
DERIVED LIPIDS
Fats and oils
(Triglycerides)
Simple triglycerides
Mixed triglycerides
Waxes
Sperm whale wax
Beeswax
Carnauba wax
Phospholipids
(Phosphatids)
Phosphoglycerides
Lecithins
Cephalins
Plasmalogens
Phosphoinositides
(Phosphatidyl inositols)
Phosphosphingosides
(Sphingomyelins)
Glycolipids
(Cerebrosides)
Kerasin
Phrenosin
Nervon
Oxynervon
Cholesterol
Coprostanol
Cholestanol
Ergosterol
Steroids
C 29, C 28, C 27 steroids
C 24 steroids
C 21, C 19, C 18 steroids
Terpenes
Monoterpenes
Sesquiterpenes
Diterpenes
Triterpenes
Tetraterpenes
Polyterpenes
Carotenoids
Lycopene
Carotenes
Xanthophylls

(a) Saturated

(b) Unsaturated





Symbols, Common Name Systematic Name Structure mp (°C)

Saturated fatty acids

12:0 Lauric acid Dodecanoic acid CH3(CH2)10COOH 44.2
14:0 Myristic acid Tetradecanoic acid CH3(CH2)12COOH 53.9
16:0 Palmitic acid Hexadecanoic acid CH3(CH2)14COOH 63.1
18:0 Stearic acid Octadecanoic acid CH3(CH2)16COOH 69.6
20:0 Arachidic acid Eicosanoic acid CH3(CH2)18COOH 77
22:0 Behenic acid Docosanoic acid CH3(CH2)20COOH 81.5
24:0 Lignoceric acid Tetracosanoic acid CH3(CH2)22COOH 88

Unsaturated fatty acids (all double bonds are cis)

16:1*n*–7 Palmitoleic acid 9-Hexadecanoic acid CH3(CH2)5CH⍰CH(CH2)7COOH −0.5
18:1*n*–9 Oleic acid 9-Octadecanoic acid CH3(CH2)7CH⍰CH(CH2)7COOH 12
18:2*n*–6 Linoleic acid 9,12-Octadecadienoic acid CH3(CH2)4(CH⍰CHCH2)2(CH2)6COOH −5
18:3*n*–3 α-Linolenic acid 9,12,15-Octadecatrienoic acid CH3CH2(CH⍰CHCH2)3(CH2)6COOH −11
18:3*n*–6 γ-Linolenic acid 6,9,12-Octadecatrienoic acid CH3(CH2)4(CH⍰CHCH2)3(CH2)3COOH −11
20:4*n*–6 Arachidonic acid 5,8,11,14-Eicosatetraenoic acid CH3(CH2)4(CH⍰CHCH2)4(CH2)2COOH −49.5
20:5*n*–3 EPA 5,8,11,14,17-Eicosapentaenoic acid CH3CH2(CH⍰CHCH2)5(CH2)2COOH −54
22:6*n*–3 DHA 4,7,10,13,16,19-Docosohexenoic acid CH3CH2(CH⍰CHCH2)6CH2COOH −44
24:1*n*–9 Nervonic acid 15-Tetracosenoic acid CH3(CH2)7CH⍰CH(CH2)13COOH 39

*a*Number of carbon atoms: Number of double bonds. For unsaturated fatty acids, the quantity “ *n*–*x* ” indicates the position of the last double bond in the fatty acid, where *n* is its number of C atoms, and *x* is the position of the last double-bonded C atom counting from the methyl-terminal (ω) end.

Over half of the fatty acid residues of plant and animal lipids are **unsaturated** (contain double bonds) and are often **polyunsaturated** (contain two or more double bonds). Bacterial fatty acids are rarely polyunsaturated but are commonly branched, hydroxylated, or contain cyclopropane rings.
Table indicates that the first double bond of an unsaturated fatty acid commonly occurs between its C9 and C10 atoms counting from the carboxyl C atom. This bond is called a Δ9- or 9-double bond. In polyunsaturated fatty acids,the double bonds tend to occur at every third carbon atom (e.g., —CH⍰CH—CH2—CH⍰CH—) and so are not conjugated (as in —CH⍰CH—CH⍰CH—).
Two important classes of polyunsaturated fatty acids are designated as ω–3 or ω–6 fatty acids, a nomenclature that identifies the last double-bonded carbon atom as counted from the methyl terminal (ω) end of the chain. **α-Linolenic acid** and linoleic acid are examples of such fatty acids.
Saturated fatty acids (which are fully reduced or “saturated” with hydrogen) are highly flexible molecules that can assume a wide range of conformations

because there is relatively free rotation around each of their C—C bonds. Nevertheless,their lowest energy conformation is the fully extended conformation,which has the least amount of steric interference between neighboringmethylenegroups. The melting points (mp) of saturated fatty acids, like those of most substances,increase with their molecular mass.
Fatty acid double bonds almost always have the cisconfiguration.
This puts a rigid 30° bend in the hydrocarbon chain. Consequently, unsaturated fatty acids pack together less efficiently than saturated fatty acids. The reducedvan der Waals interactions of unsaturated fatty acids cause their melting points todecrease with the degree of unsaturation. The fluidity of lipids containing fattyacid residues likewise increases with the degree of unsaturation of the fatty acids.
This phenomenon, as we will see, has important consequences for biological membranes.

Triacylglycerols Contain Three Esterified Fatty Acids

The fats and oils that occur in plants and animals consist largely of mixtures of **triacylglycerols**(also called **triglycerides**). These nonpolar, water-insoluble substances are fatty acid triesters of **glycerol** (*at left*). Triacylglycerols function as energy reservoirs in animals and are therefore their most abundant class of lipids even though they are not components of cellular membranes.
Triacylglycerols diff er according to the identity and placement of their three fatty acid residues. Most triacylglycerols contain two or three diff erent types of
fatty acid residues and are named according to their placement on the glycerol moiety, for example, **1-palmitoleoyl-2-linoleoyl-3-stearoylglycerol** (*at left*).
Note that the *-ate* ending of the name of the fatty acid becomes *-oyl*in the fatty
acid ester. **Fats** and **oils** (which diff er only in that fats are solid and oils are liquid
at room temperature) are complex mixtures of triacylglycerols whose fatty acid compositions vary with the organism that produced them. Plant oils are usually richer in unsaturated fatty acid residues than animal fats, as the lower melting points of oils imply.

Triacylglycerols Function as Energy Reserves.

Fats are a highly efficientforminwhich to store metabolic energy. This is because triacylglycerols are less oxidizedthan carbohydrates or proteins and hence yield significantly more energyper unit mass on complete oxidation. Furthermore, triacylglycerols, which arenonpolar, are stored in anhydrous form, whereas glycogen forexample, binds about twice its weight of water under physiological conditions.

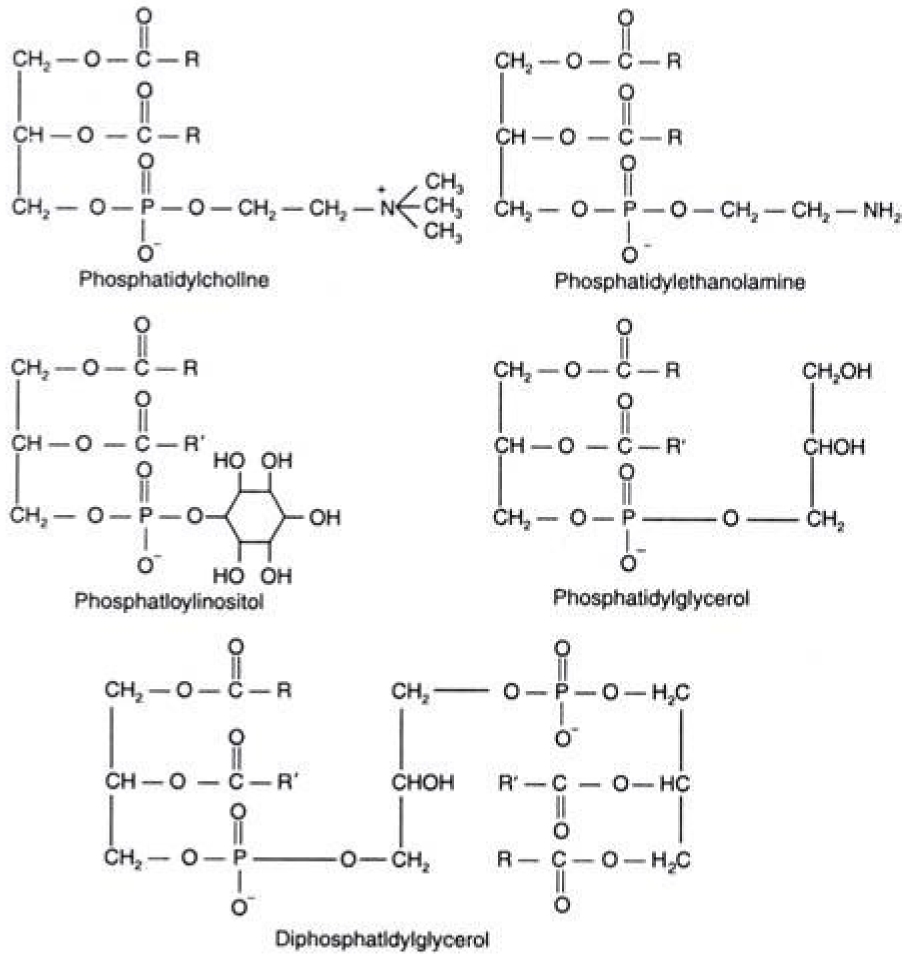
Fats therefore provide about six times the metabolic energy of an equal weight ofhydrated glycogen.

In animals, **adipocytes** are specialized for the synthesis and storage of triacylglycerols. Whereas other types of cells have only a few small droplets of fat dispersed in their cytosol, adipocytes may be almost entirelyfilled with fat globules.**Adipose tissue** is most abundant in a subcutaneous layerand in the abdominal cavity. The fat content of normal humans (21% for men,26% for women) allows them to survive starvation for 2 to 3 months. In contrast,the body's glycogen supply, which functions as a short-term energy store, canprovide for the body's energy needs for less than a day. The subcutaneous fatlayer also provides thermal insulation, which is particularly important for warmbloodedaquatic animals, such as whales, seals, geese, and penguins, which areroutinely exposed to low temperatures

Glycerophospholipids Are Amphiphilic

Glycerophospholipids(or **phosphoglycerides**) are the major lipid components of biological membranes. They consist of **glycerol-3-phosphate** whose C1 and C2 positions are esterified with fatty acids. In addition, the phosphoryl group is linked to another usually polar group, X. *Glycerophospholipids are thereforeamphiphilic molecules with nonpolar aliphatic (hydrocarbon) "tails" and polar phosphoryl-X "heads."*

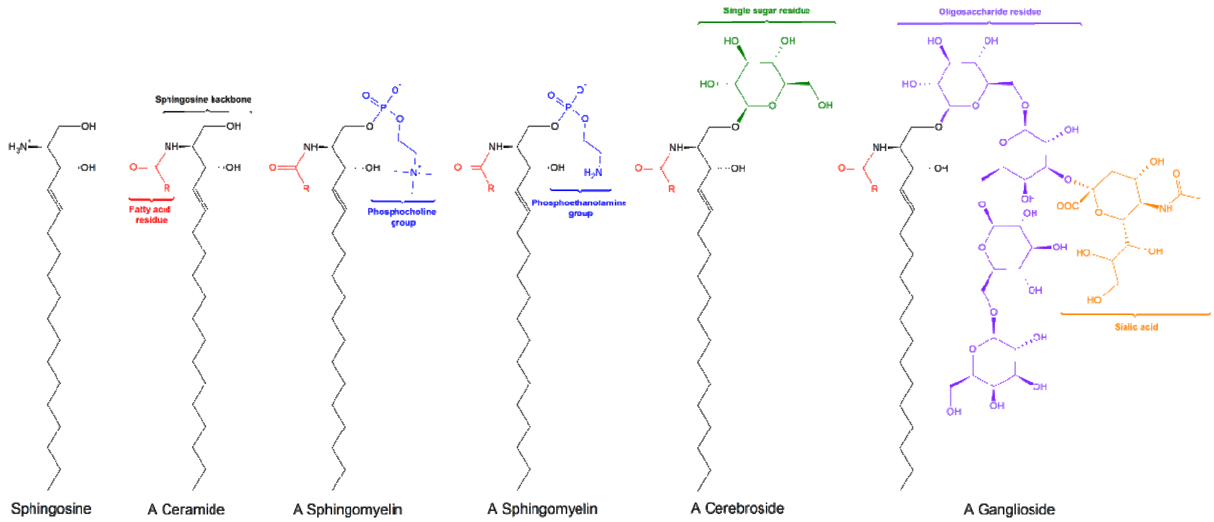
The simplest glycerophospholipids, in which X = H, are **phosphatidic acids**; they are present in only small amounts in biological membranes. In the glycerophospholipids that commonly occur in biological membranes, the head groups are derived from polar alcohol. Saturated C16 or C18 fatty acids usually occur at the C1 position of the glycerophospholipids, and the C2 position is often occupied by an unsaturated C16 to C20 fatty acid. Individual glycerophospholipids are named according to the identities of these fatty acid residues. A glycerophospholipid containing two palmitoyl chains is an important component of **lung surfactant.**



Structures of commonly occurring phospholipids (R, R′ = long chain fatty acids residues).

Plasmalogens Contain an Ether Linkage. Plasmalogens
areglycerophospholipids
in which the C1 substituent of the glycerol moiety is linked via an α,β-unsaturated ether linkage in the cisconfiguration rather than through an esterlinkage. **Ethanolamine, choline**, and serine form the most common plasmalogen head groups. The functions of most plasmalogens are not well understood. Because the vinyl ether group is easily oxidized, plasmalogens may react with oxygen free radicals, by-products of normal metabolism, thereby preventing free-radical damage to other cell constituents.

Sphingolipids Are Amino Alcohol Derivatives



Sphingolipidsare also major membrane components. They were named after the Sphinx because their function in cells was at fi rst mysterious. Most sphingolipidsare derivatives of the C18 amino alcohol **sphingosine**, whose double bond has thetransconfiguration. The *N*-acyl fatty acid derivatives of sphingosine are knownas**ceramides**:Ceramides are the parent compounds of the more abundant sphingolipid

Sphingomyelins, the most common sphingolipids, are ceramides bearing either a phosphocholine or a phosphoethanolamine head group, so they can also be classified as **sphingophospholipids.** They typically make up 10 to 20 mol % of plasma membrane lipids. *Although sphingomyelins differ chemically from phosphatidylcholine and phosphatidylethanolamine, their conformations and charge distributions are quite similar.*The membranous myelin sheath that surrounds and electrically insulates many nerve cell axons is particularly rich in sphingomyelins.

Cerebrosidesare ceramides with head groups that consist of a single sugar residue. These lipids are therefore **glycosphingolipids. Galactocerebrosides** and**glucocerebrosides**are the most prevalent. Cerebrosides, in contrast to phospholipids, lack phosphate groups and hence are nonionic.

Gangliosidesare the most complex glycosphingolipids. They are ceramides with attached oligosaccharides that include at least one sialic acid residue. The structures of **gangliosides GM1**, **GM2, and GM3**, three of the hundreds that are known. Gangliosides are primarily components of cell-surface membranes and constitute a signifi cant fraction (6%) of brain lipids.

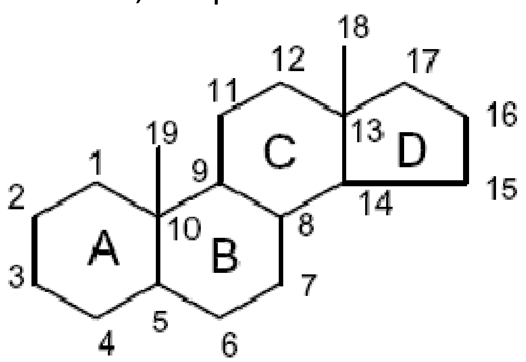
Gangliosides have considerable physiological and medical significance. Their complex carbohydrate head groups, which extend beyond the surfaces of cell membranes, act as specific receptors for certain pituitary glycoprotein hormones that regulate a number of important physiological functions. Gangliosidesare also receptors for certain bacterial protein toxins such as **cholera toxin**.

There is considerable evidence that gangliosides are specifi c determinants of cell–cell recognition, so they probably have an important role in the growth anddifferentiation of tissues as well as in carcinogenesis. Disorders of gangliosidebreakdown are responsible for several hereditary **sphingolipid storage diseases**,such as **Tay-Sachs disease**, which are characterized by an invariablyfatal neurological deterioration in early childhood.

Sphingolipids, like glycerophospholipids, are a source of smaller lipids that have discrete signaling activity. Sphingomyelin itself, as well as the ceramideportions.of more complex sphingolipids, appear to specifically modulate the activitiesof protein kinases and **protein phosphatases** (enzymes that remove phosphorylgroups from proteins) that are involved in regulating cell growth and diff erentiation.

Steroids Contain Four Fused Rings

Steroids, which are mostly of eukaryotic origin, are derivatives of **cyclopentanoperhydrophenanthrene**
, a compound that consists of four fused, nonplanar



rings (labeled A–D). Cyclopentano-perhydrophenanthrene (steroid) nucleus

The much maligned **cholesterol**, which is the most abundant steroid in animals, is further classified as a **sterol** because of its C3-OH group Cholesterol is a major component of animal plasma membranes, typically constituting 30 to 40 mol % of plasma membrane lipids. Its polar OH group gives it a weak amphiphilic character, whereas its fused ring system provides it withgreater rigidity than other membrane lipids. Cholesterol can also be esterified to longchainfatty acids to form **cholesteryl esters**, such as **cholesteryl stearate**

Plants contain little cholesterol but synthesize other sterols. Yeast and fungi alsosynthesize sterols, which diff er from cholesterol in their aliphatic side chains and number of double bonds. Prokaryotes contain little, if any, sterol. In mammals, cholesterol is the metabolic precursor of **steroid hormones**, substances that control a great variety of physiological functions through their regulation of gene expression. The structures of some steroid hormones.

Steroid hormones are classified according to the physiological responses they evoke:

1. The **glucocorticoids**, such as **cortisol** (a C21 compound), affect carbohydrate, protein, and lipid metabolism and influence a wide variety of other vital functions,
includinginflammatory reactions and the capacity to cope with stress.

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. **Testosterone**, a C19 compound, is the prototypic androgen (male sex hormone),whereas**β-estradiol**, a C18 compound, is an estrogen (female sex hormone).

Glucocorticoids and mineralocorticoids are synthesized by the cortex (outer layer) of the adrenal gland. Both androgens and estrogens are synthesized by testes and ovaries (although androgens predominate in testes and estrogenspredominate in ovaries) and, to a lesser extent, by the adrenal cortex. Because steroid hormones are water insoluble, they bind to proteins for transport through the blood to their target tissues.