Lipids

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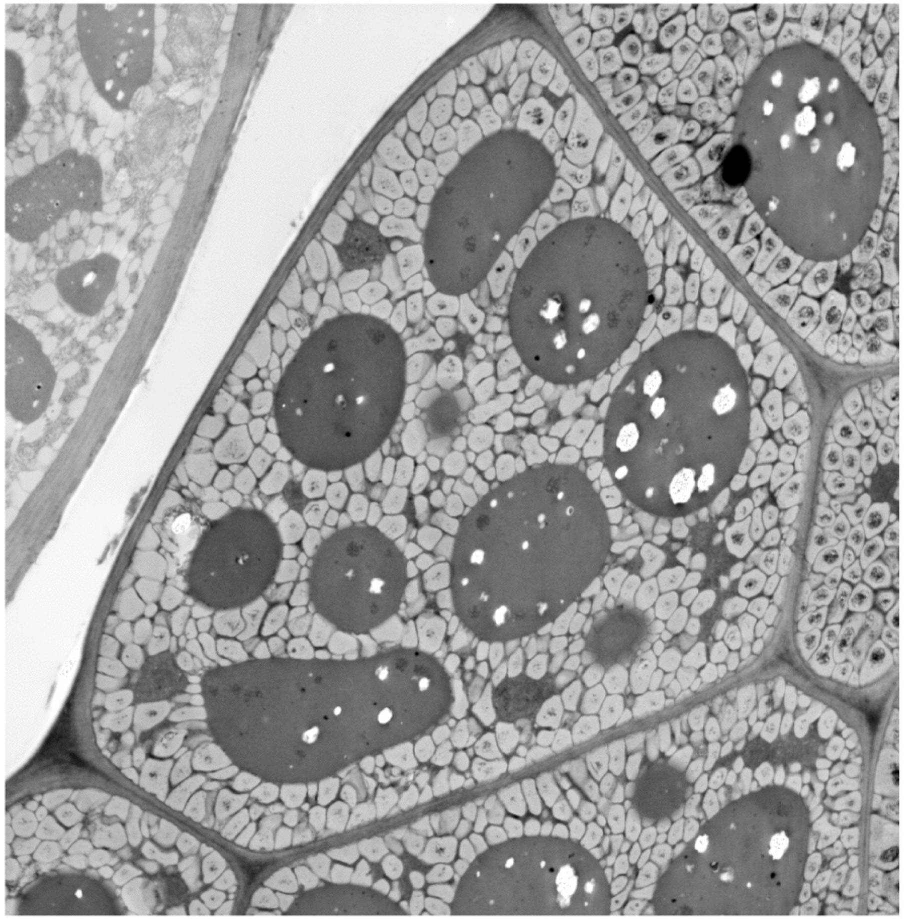
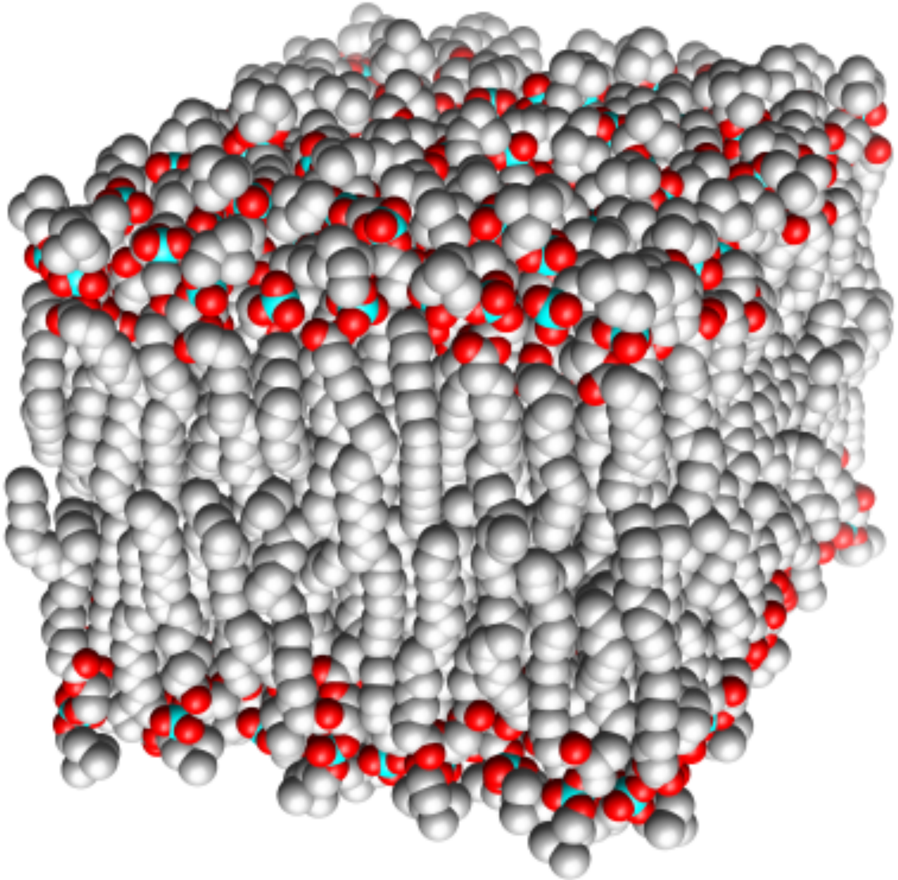
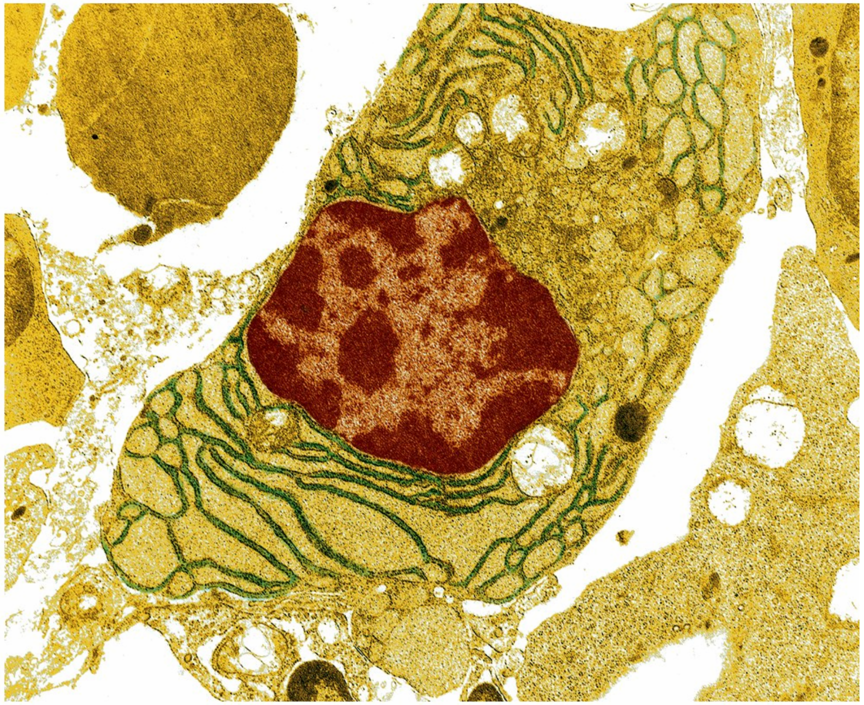




F Malatesta

Lipids

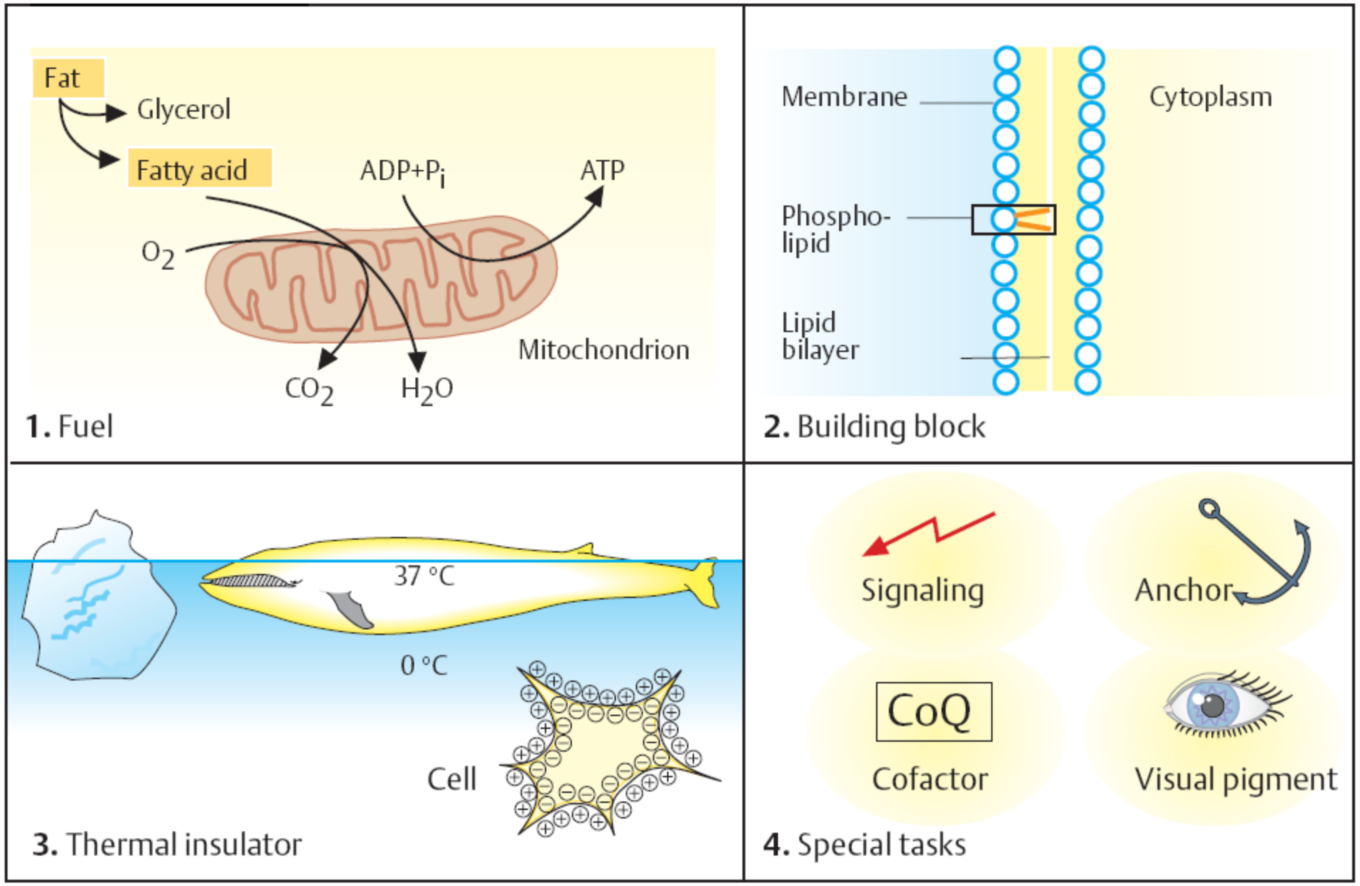


- organic compounds insoluble in H_2O with strong amphiphilic character
- extracted from animal and plant tissues by means of apolar solvents
- heterogeneous class of compounds: simple and complex
- importance: high caloric content

  fundamental for cellular compartmentalization

Functions of lipids

- Energy reserve
- Structural
- Insulating materials (thermal, electrical, mechanical)
- Special roles (hormones, enzyme cofactors, second messengers)



An heterogeneous class of compounds: simple and complex

a) fatty acids: long chain organic acids (> 7 C); free or esterified to alcohols

b) glycerides: fatty acid esters of glycerol (mono-, di- e triglycerides)

c) waxes: esters of fatty acids with monovalent alcohols with a high C number

d) phospholipids: lipids having an esterified o-phosphoric acid residue (glycerol-3-phosphate derivatives and sphingosine phosphate derivatives)

e) cerebrosides-glycolipids: esters of fatty acids with sphingosine bound to a hexose

f) sulfolipids: glycolipids in which an hexose is sulfonated

g) gangliosides: fatty acid esters with sphingosine containing hexosamine

h) prostaglandines: arachidonic acid derivatives with hormonal function

i) terpenes: high molecular weight compounds whose skeleton is made up of multiples of isoprenoid units (2-methyl-butadiene)

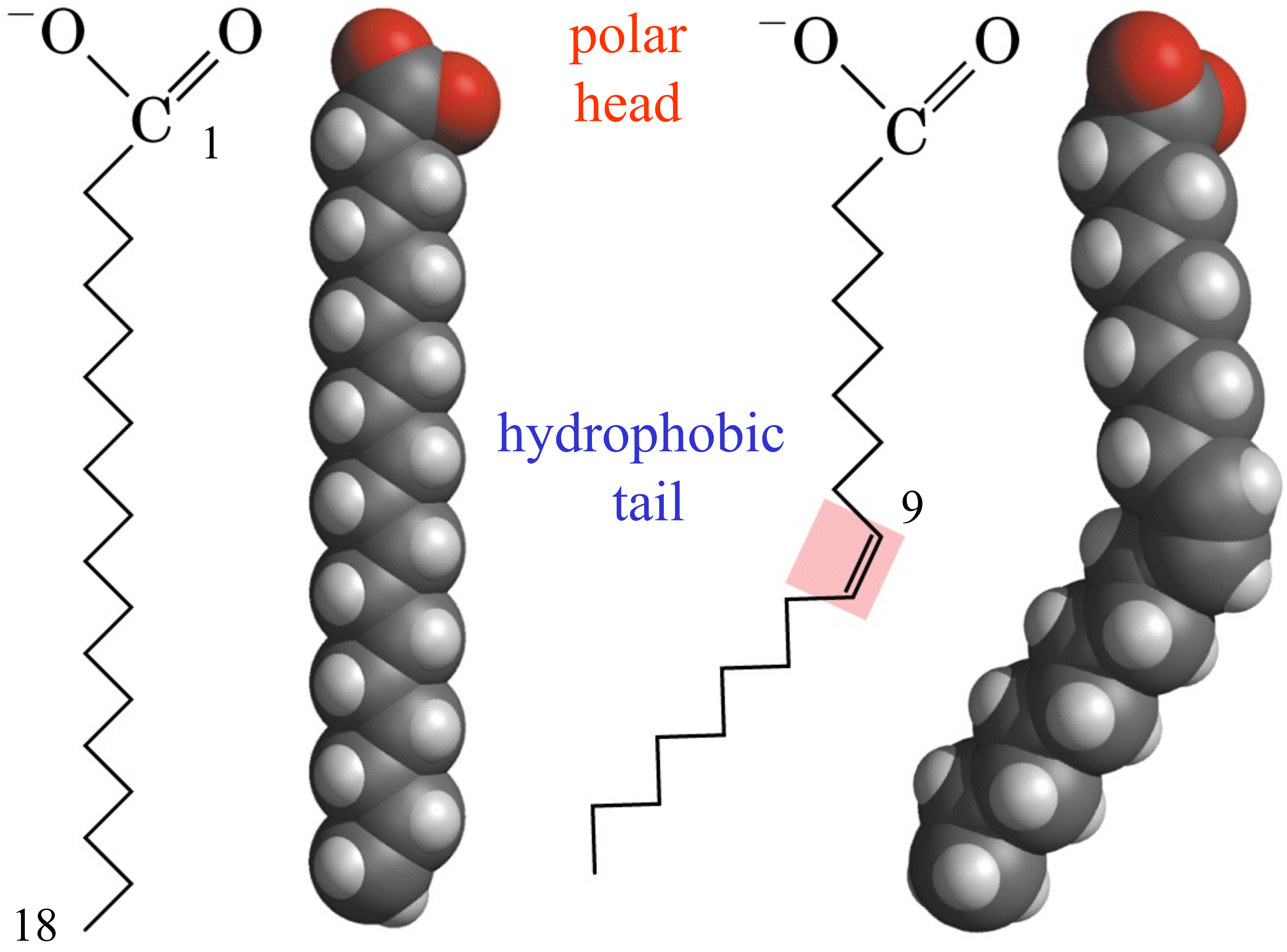
j) steroids: derivatives of cyclopentanoperihydrophenantrene (sex hormones, vitamin D, bile acids)

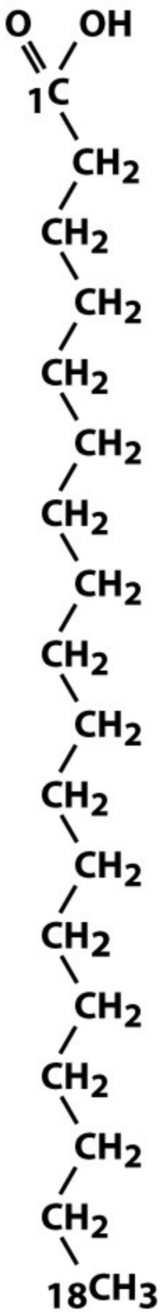
Some natural fatty acid

carbon chain	structure	systematic name	name (ethymology)	T_{fus} (°C)
12:0	$CH_3(CH_2)_{10}COOH$	*n*-dodecanoic acid	lauric (*laurus)*	44.2
14:0	$CH_3(CH_2)_{12}COOH$	*n*-tetradecanoic acid	miristic (*myristica)*	53.9
16:0	$CH_3(CH_2)_{14}COOH$	*n*-hexadecanoic acid	palmitic (*palma)*	63.1
18:0	$CH_3(CH_2)_{16}COOH$	*n*-octadecanoic acid	stearic (hard fat)	69.6
20:0	$CH_3(CH_2)_{18}COOH$	*n*-eicosanoic acid	arachidic (*arachis)*	76.5
24:0	$CH_3(CH_2)_{22}COOH$	*n*-tetracosanoic acid	lignoceric (*lignum+cera)*	86.0
16:1 (Δ^9)	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	*cis*-9-hexadecenoic acid	palmitoleic	−0.5
18:1 (Δ^9)	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	*cis*-9-octadecenoic acid	oleic (*oleum)*	13.4
18:2 ($\Delta^{9,12}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH$-$(CH_2)_7COOH$	*cis,cis*-9,12-octadecadienoic acid	linoleic	−5
18:3($\Delta^{9,12,15}$)	$CH_3CH_2CH{=}CHCH_2CH{=}CH$-$CH_2CH{=}CH(CH_2)_7COOH$	*cis,cis,cis*-9,12,15-octadecatrienoic acid	α-linolenic	−11
20:4($\Delta^{5,8,11,14}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH$-$CH_2CH{=}CHCH_2CH{=}CH$-$(CH_2)_3COOH$	*cis,cis,cis,cis*-5,8,11,14-icosatetraenoic acid	arachidonic	−49.5

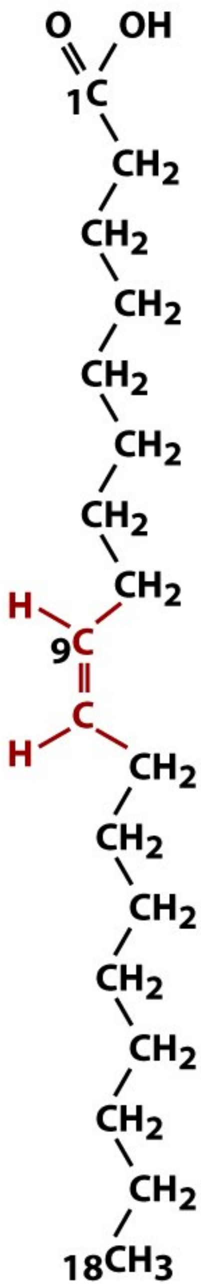
stearic acid, 18:0
octadecanoic acid

oleic acid, 18:1 (Δ^9)
cis-9-octadecenoic acid

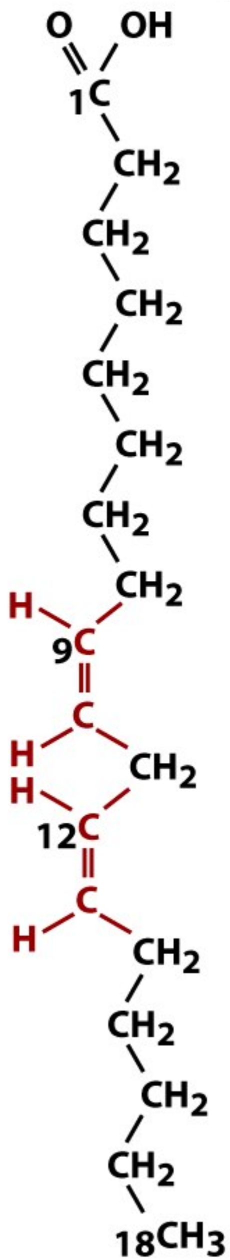




stearic acid (18:0)



oleic acid (18:1 Δ^9)



linoleic acid (18:1 $\Delta^{9,12}$) (ω-6)

Even number of carbon atoms. The double bonds are always in the *cis* configuration and are not conjugated

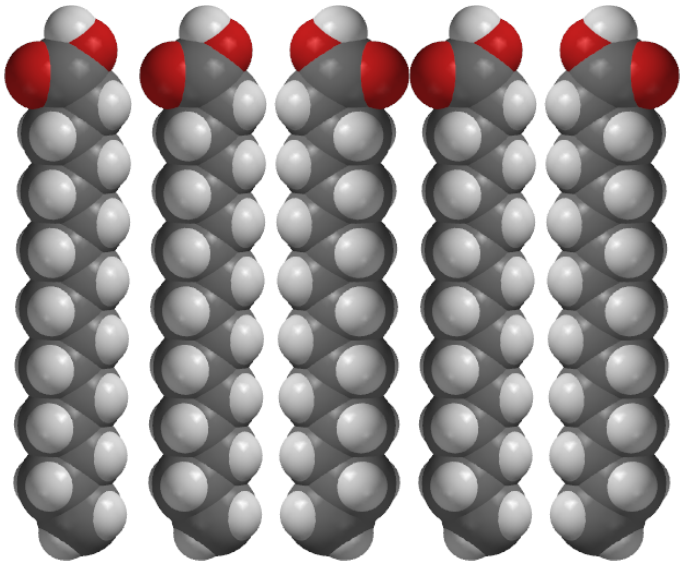
acid	melting T (°C)
lauric (12:0)	44.2
miristic (14:0)	53.9
palmitic (16:0)	63.1
stearic (18:0)	69.6
arachidic (20:0)	76.5
palmitoleic (16:1 Δ^9)	− 0.5
oleic (18:1 Δ^9)	13.4
linoleic (18:2 $\Delta^{9,12}$)	− 5

The packing of fatty acids depends on their degree of saturation (the melting point of saturated fatty acids is greater than that of the unsaturated ones)

saturated fatty acids

palmitic acid (16:0)

T_{fus} = 63.1 °C

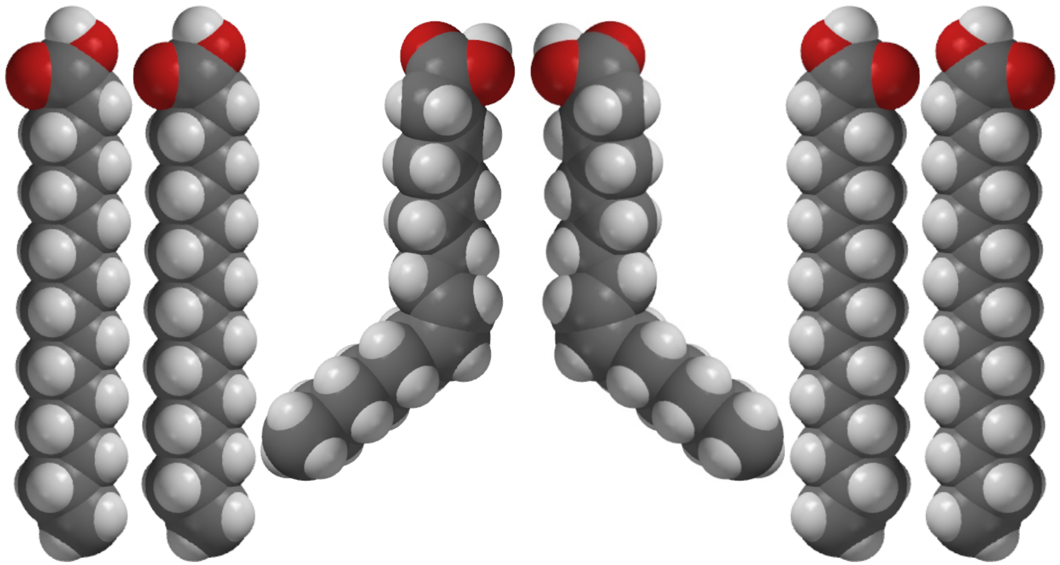


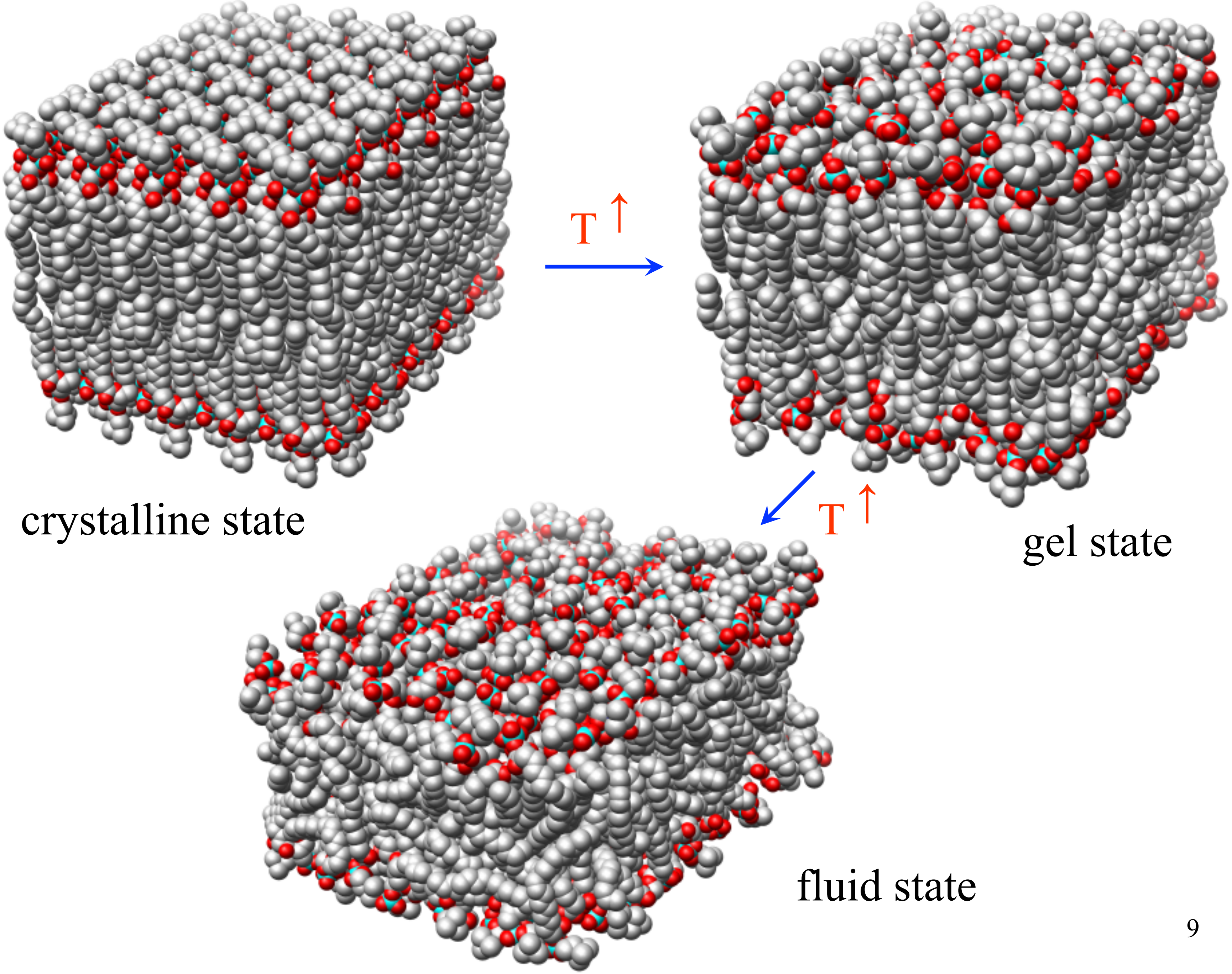
mixture of saturated and unsaturated fatty acids

palmitic acid (16:0) +

palmitoleic acid (16:1 Δ^9)

T_{fus} = −0.5 °C



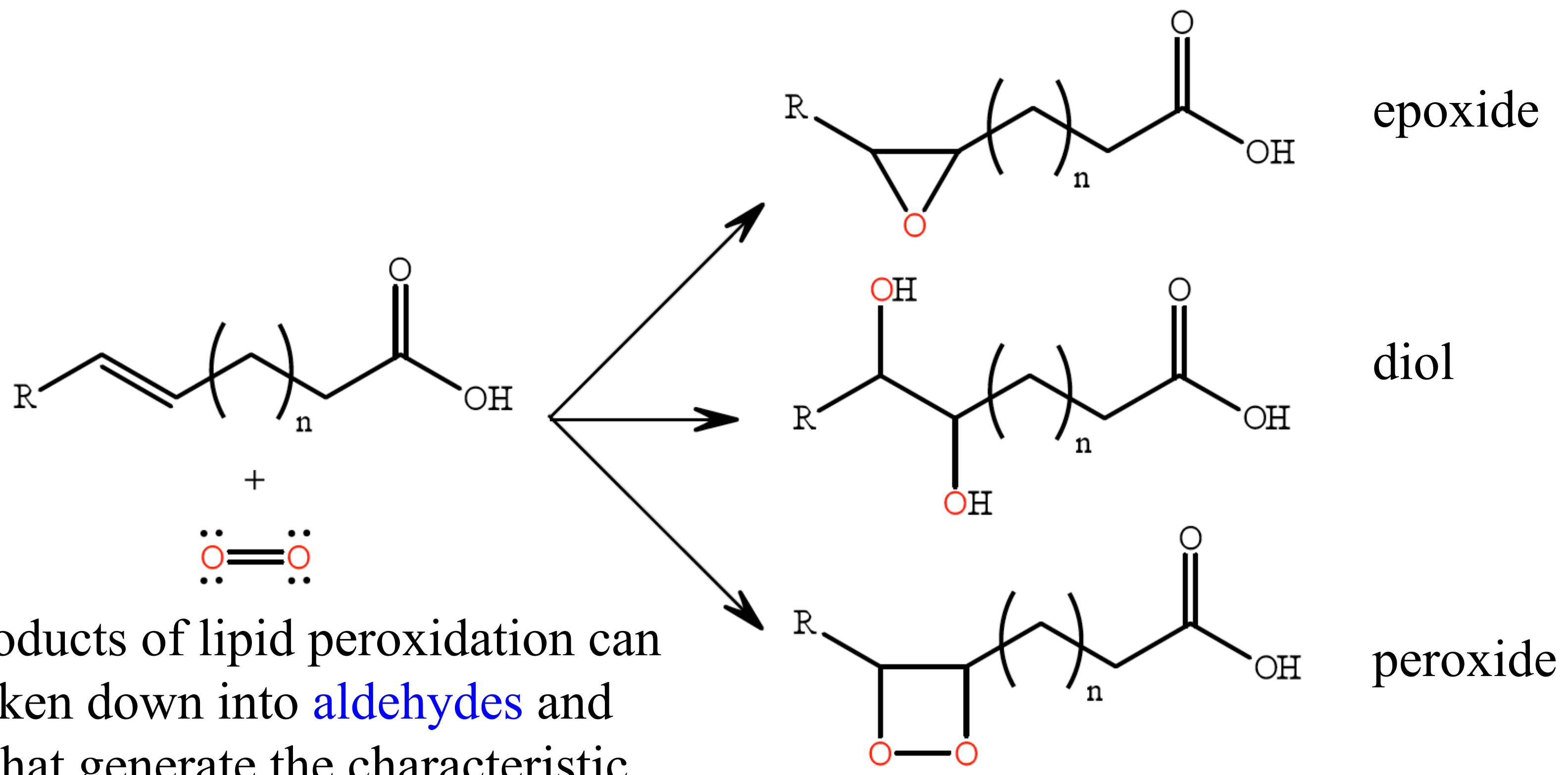

T ↑
crystalline state
T ↑
gel state
fluid state

The reactions of fatty acids

- weak acids with K_A ~10^{-5} M (tends to decrease as the chain increases)
- they react with mineral acids and alcohols to form esters
- unsaturated fatty acids undergo oxidation:

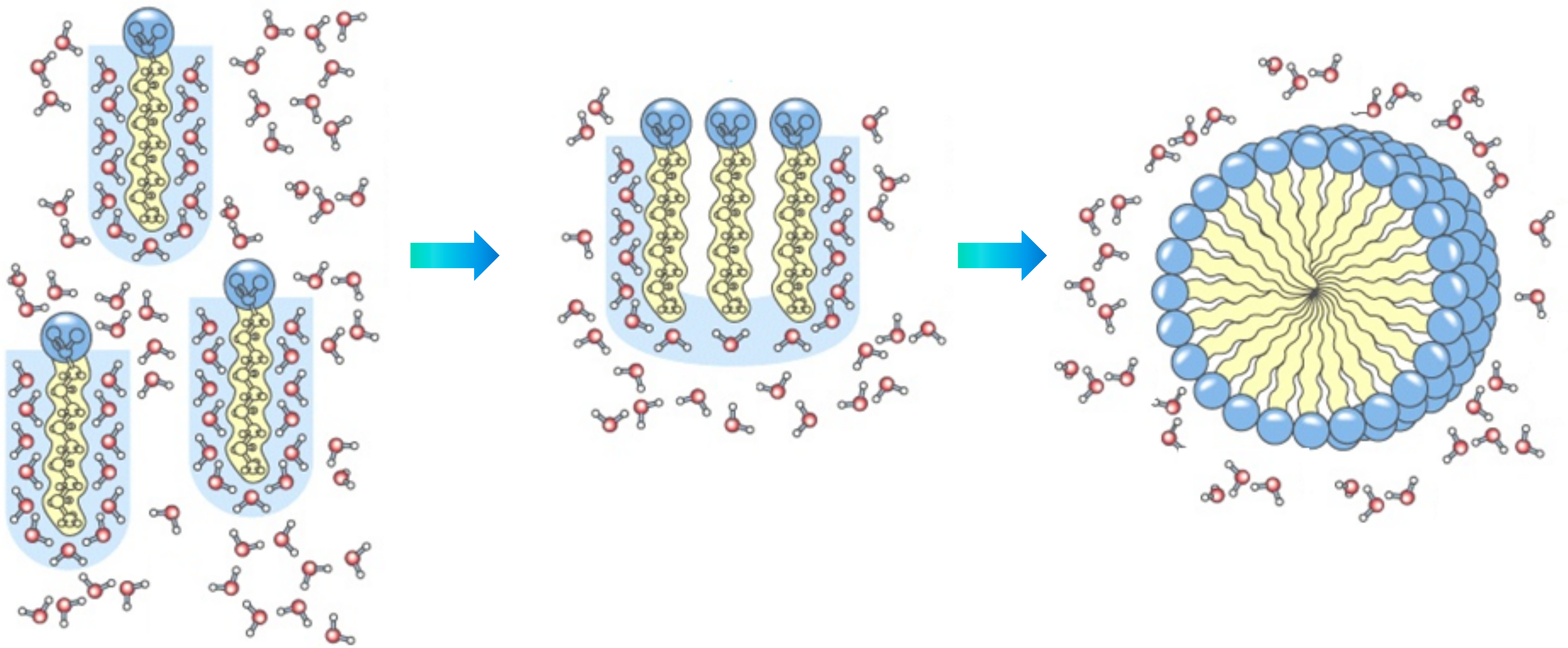
non enzimatic → lipid peroxidation

enzimatic → β-oxidation (including saturated fatty acids)



The products of lipid peroxidation can be broken down into aldehydes and acids that generate the characteristic smell and taste of rancid.

Fatty acids form micelles

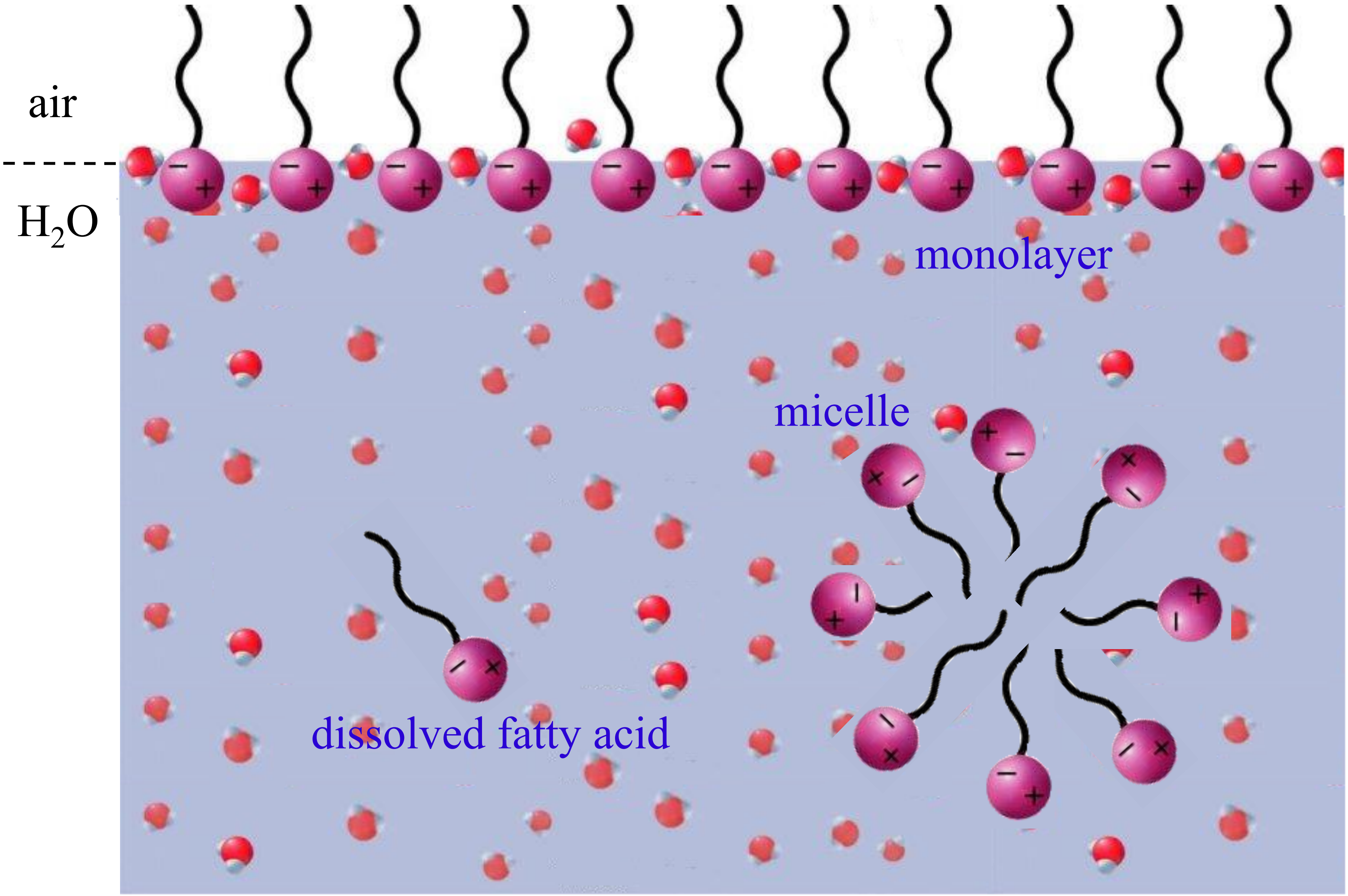


When a fatty acid is dispersed in H_2O, it forces water molecules to adopt an ordered configuration

As the concentration of fatty acid increases, it aggregates by decreasing the number of water molecules in the ordered configuration

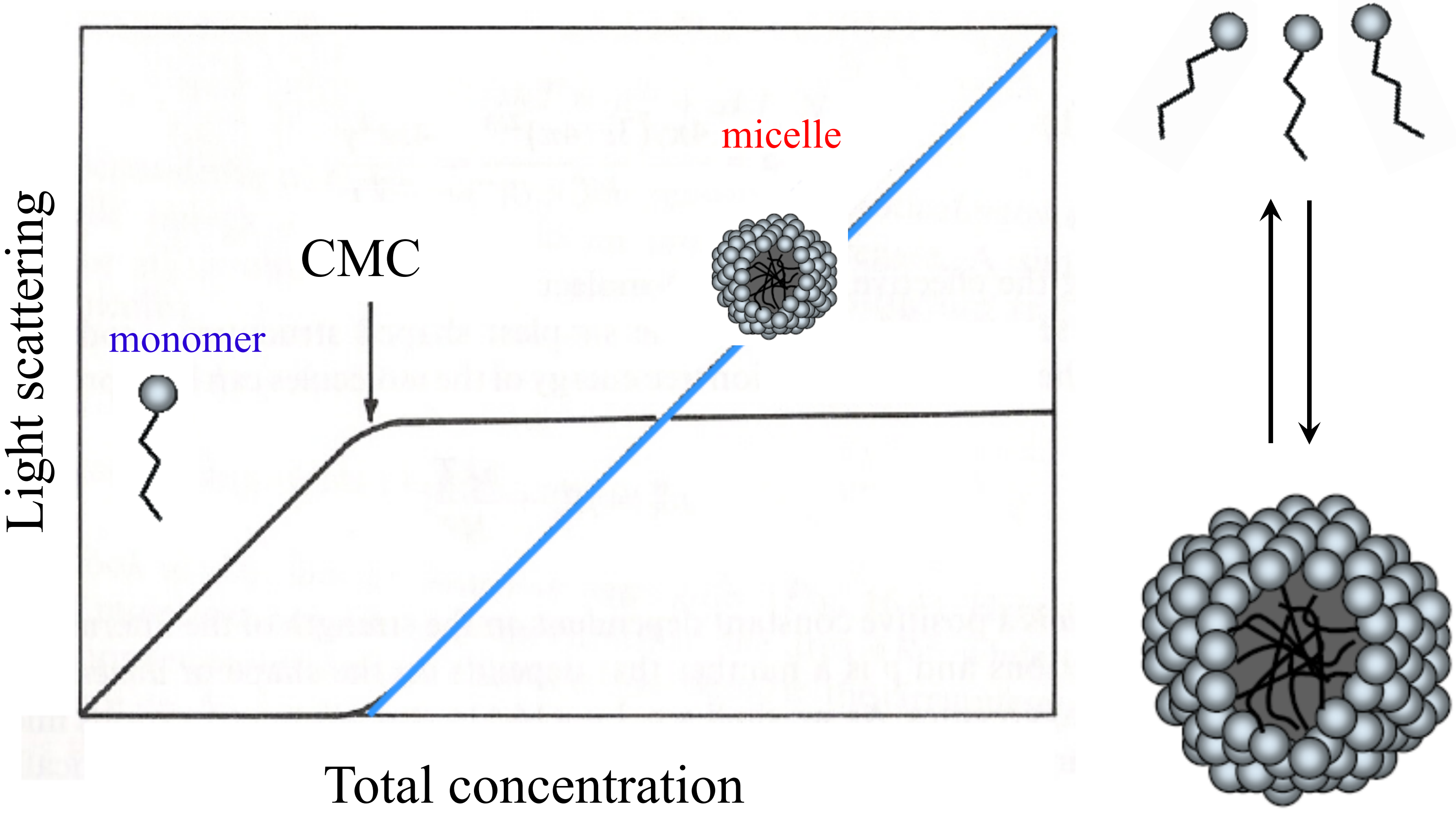
Beyond a certain concentration threshold, the fatty acids aggregate further to form the micelles

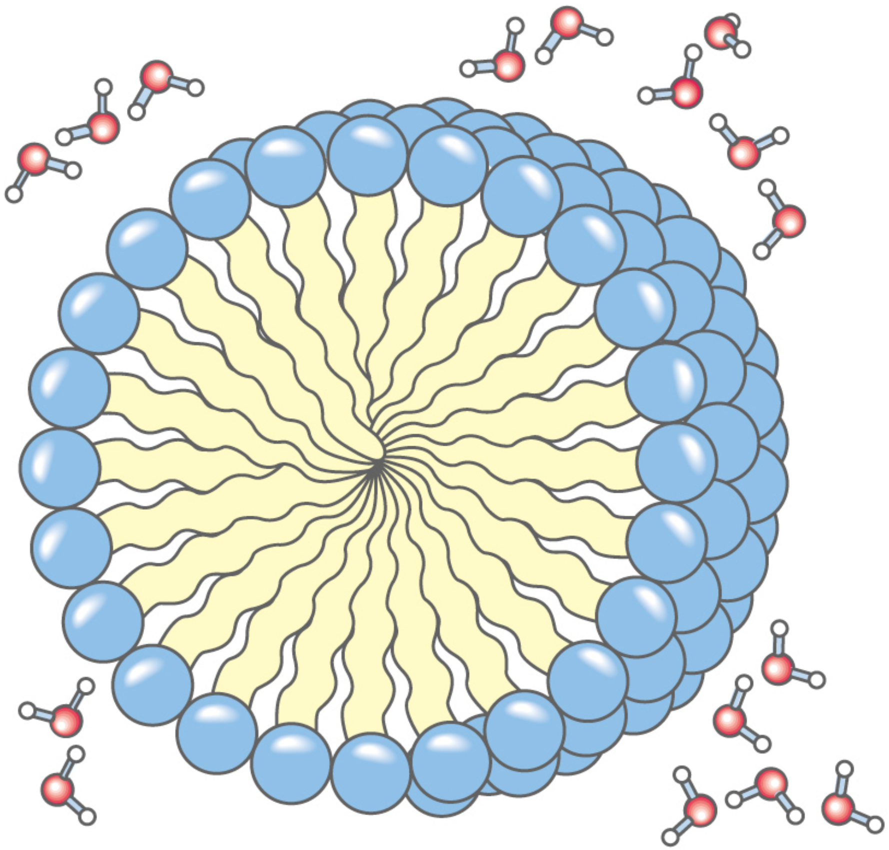
The solubilization of fatty acids in H_2O

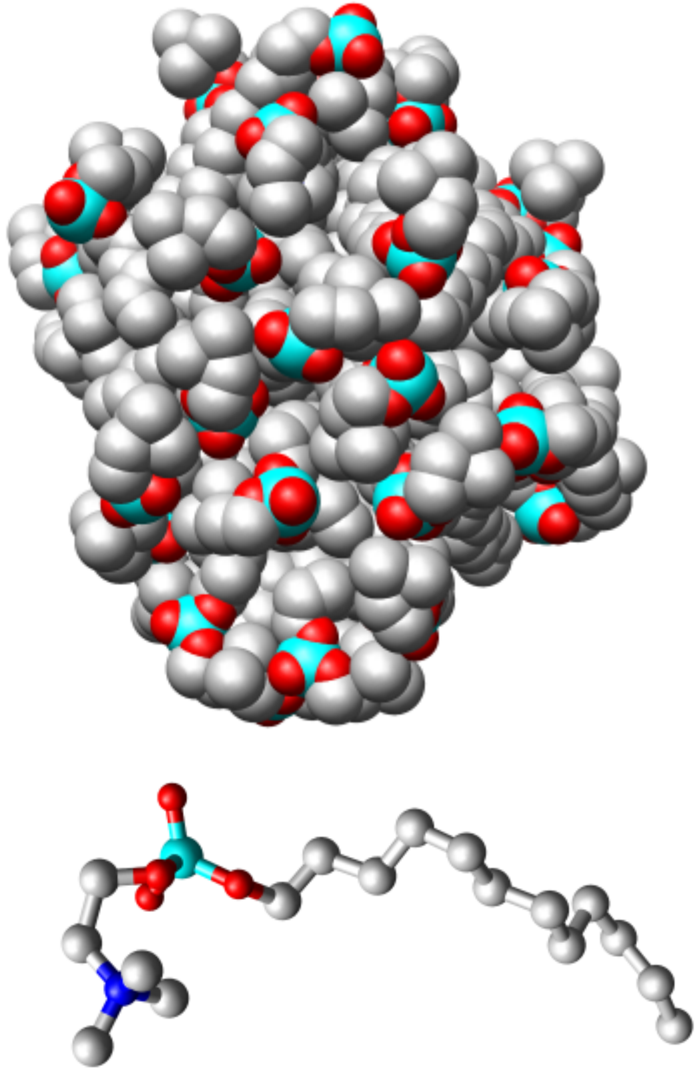


Critcal micelle concentration (CMC)

Fatty acids (but also detergents) can exist in aqueous solution in monomeric form only up to a certain concentration (CMC). Above the CMC, the lipid aggregates to form the micelles.



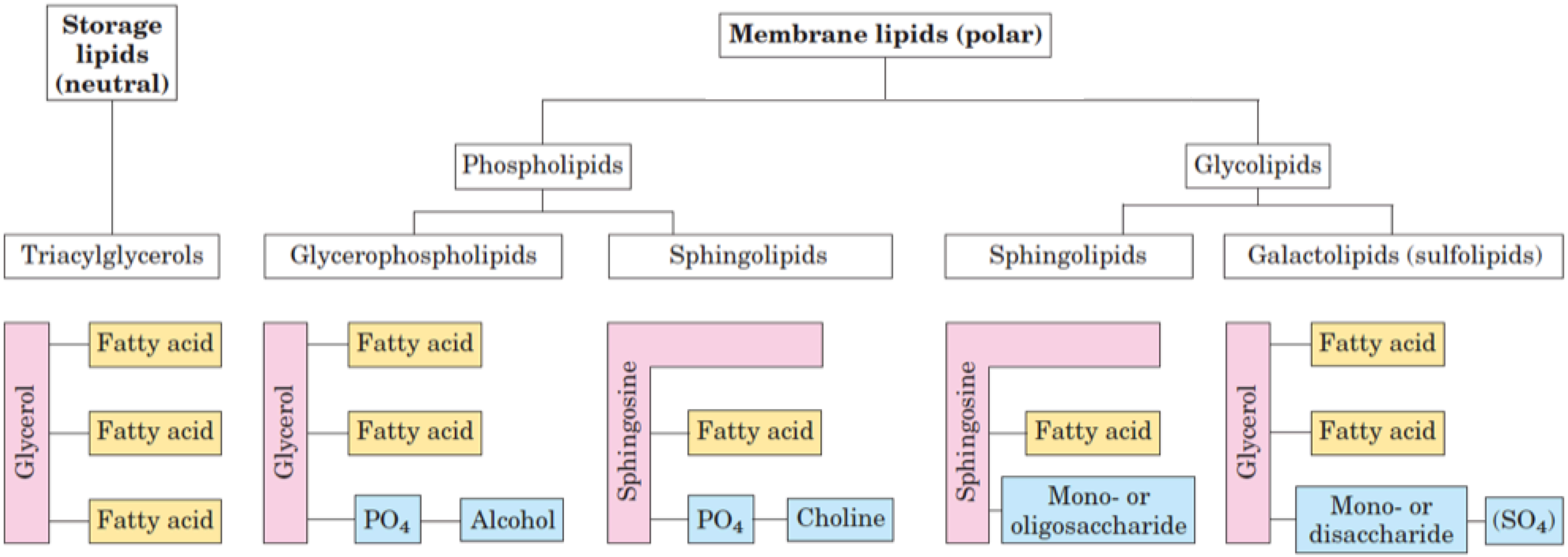




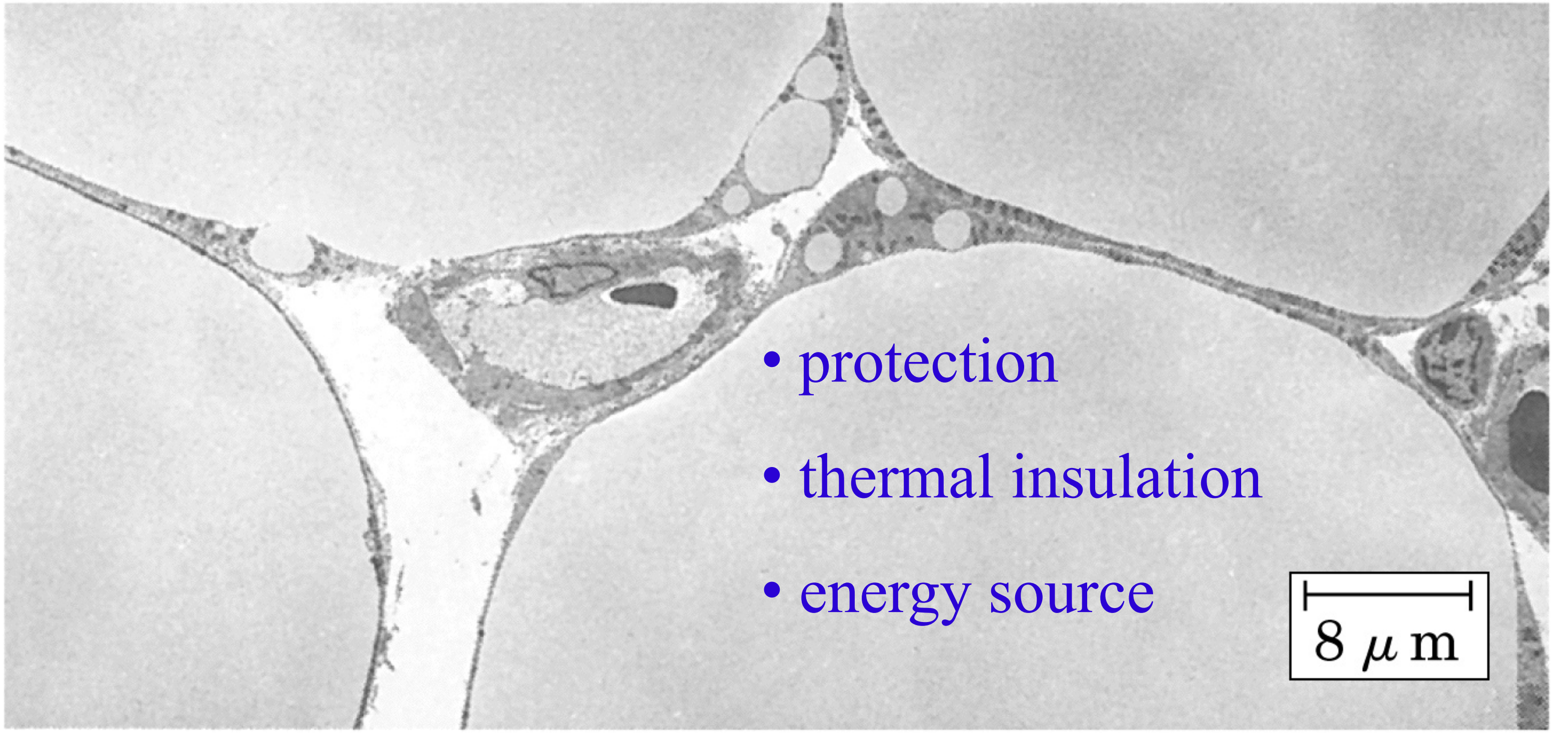
dodecylphosphocholine

Complex lipids

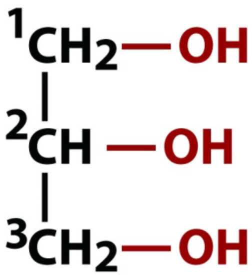
Some common types of storage and membrane lipids.

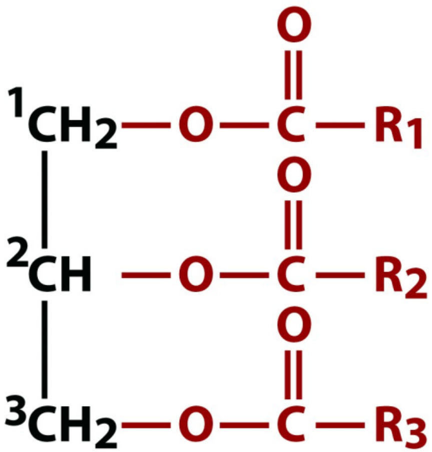


Triacylglycerols (or triglycerids)



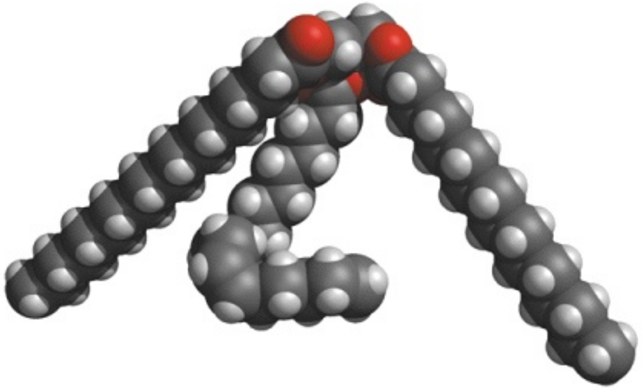
glycerol
(propane-1,2,3-triol)

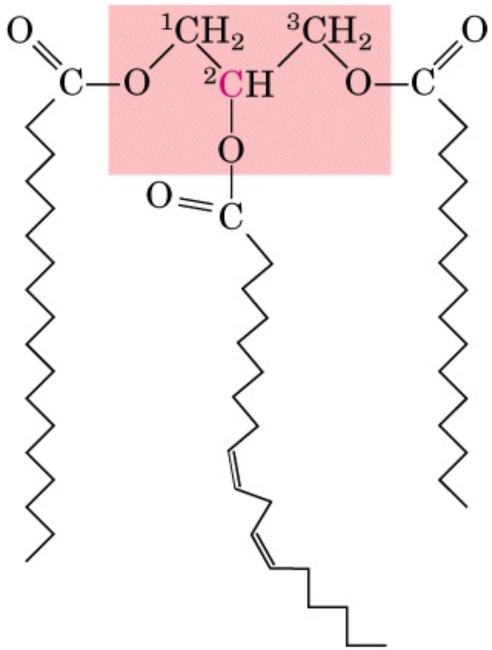




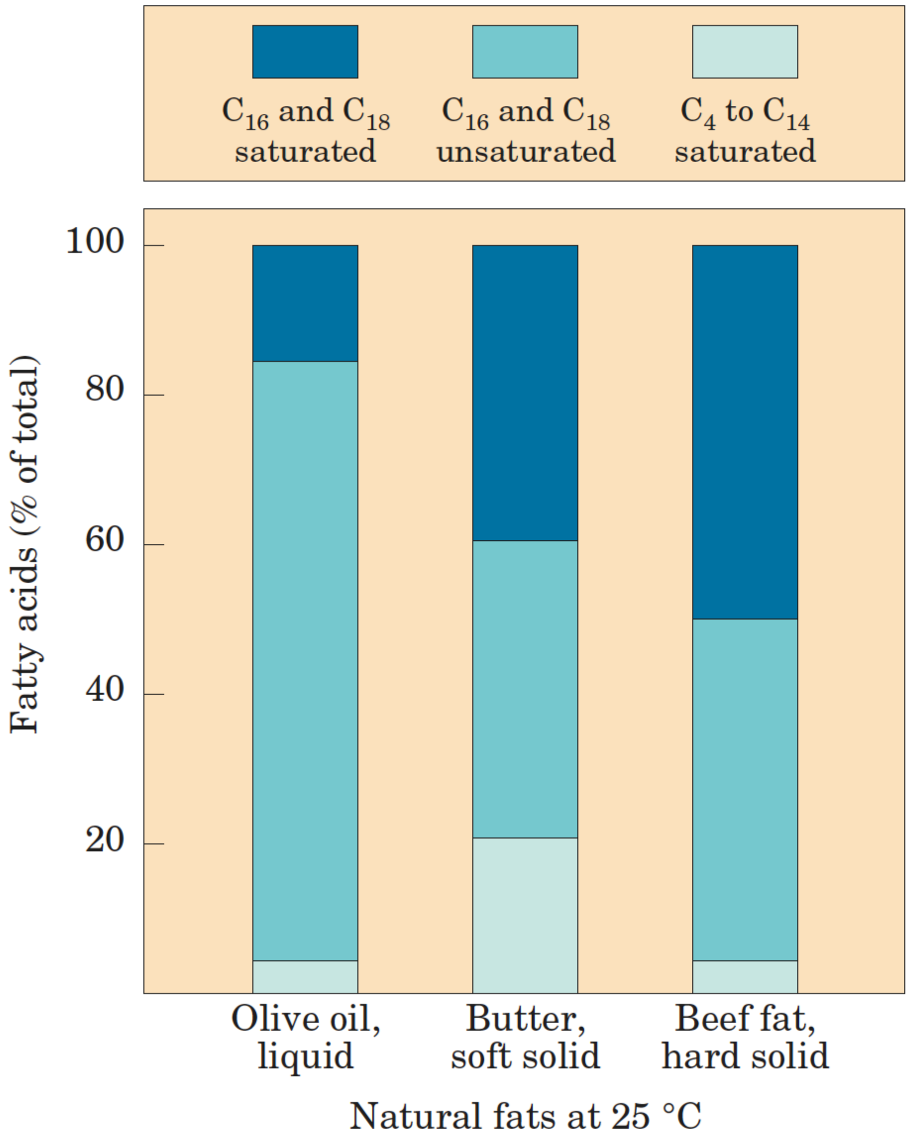
fatty acids are
esterified to glycerol

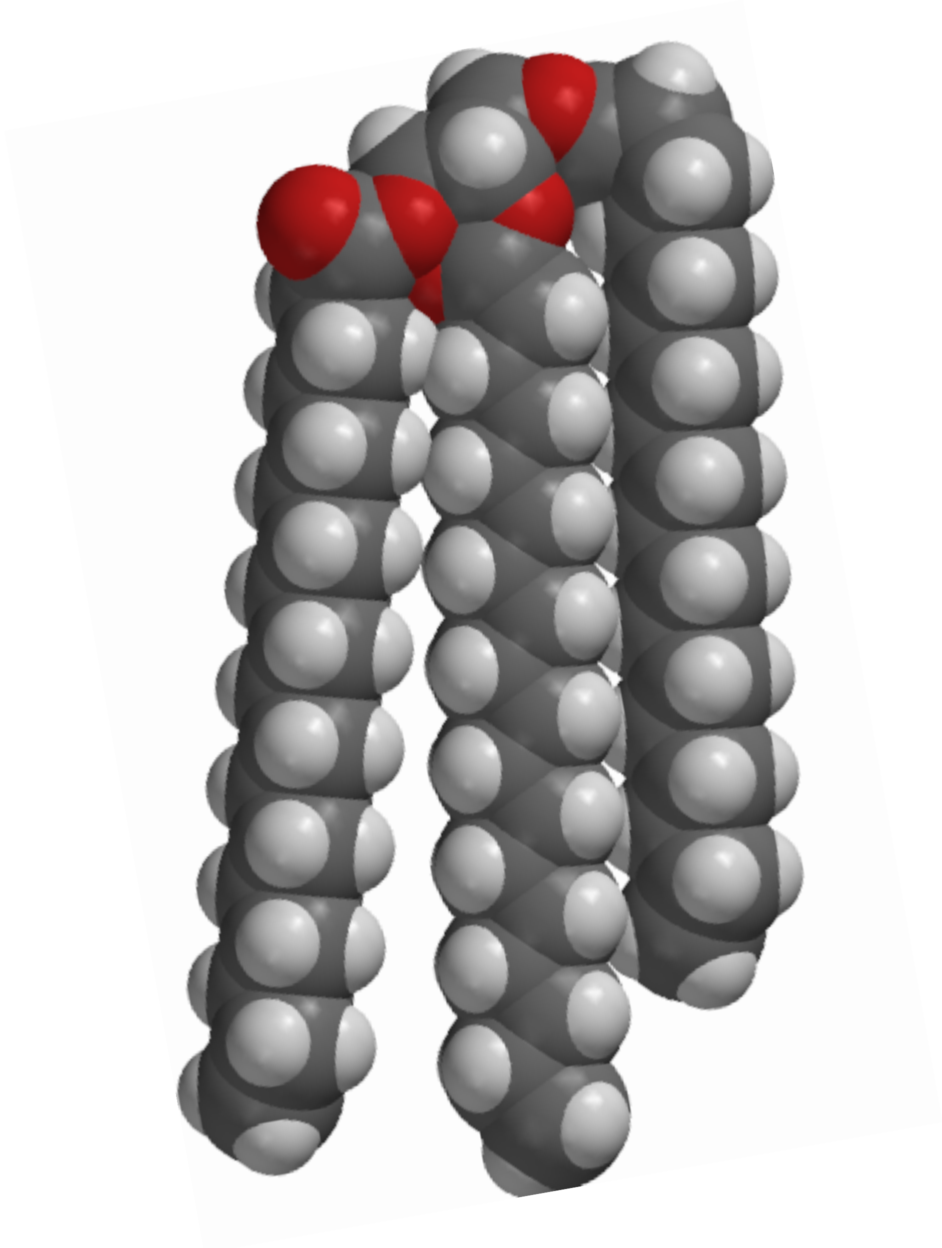
Triacylglycerols

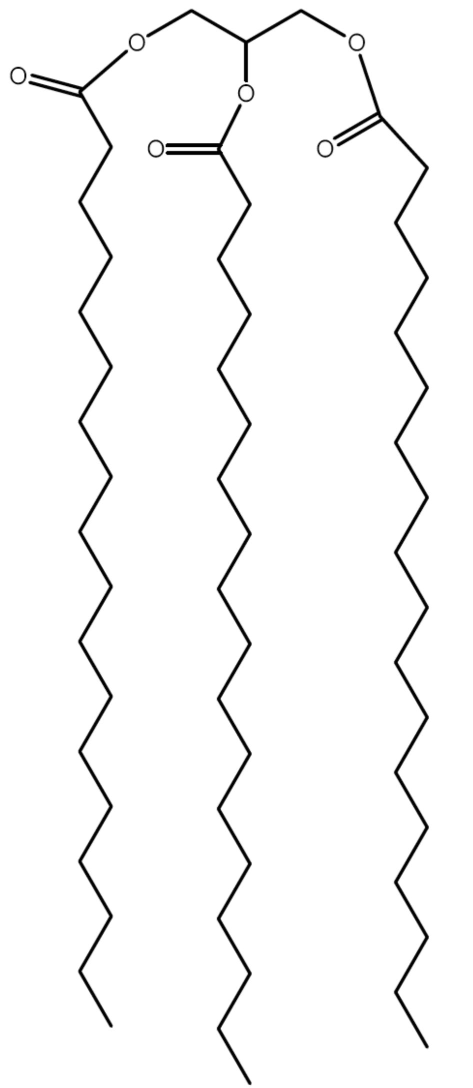




1-stearoyl-2-linoleoyl-3-palmitoyl
-glycerol (a mixed trigliceride)

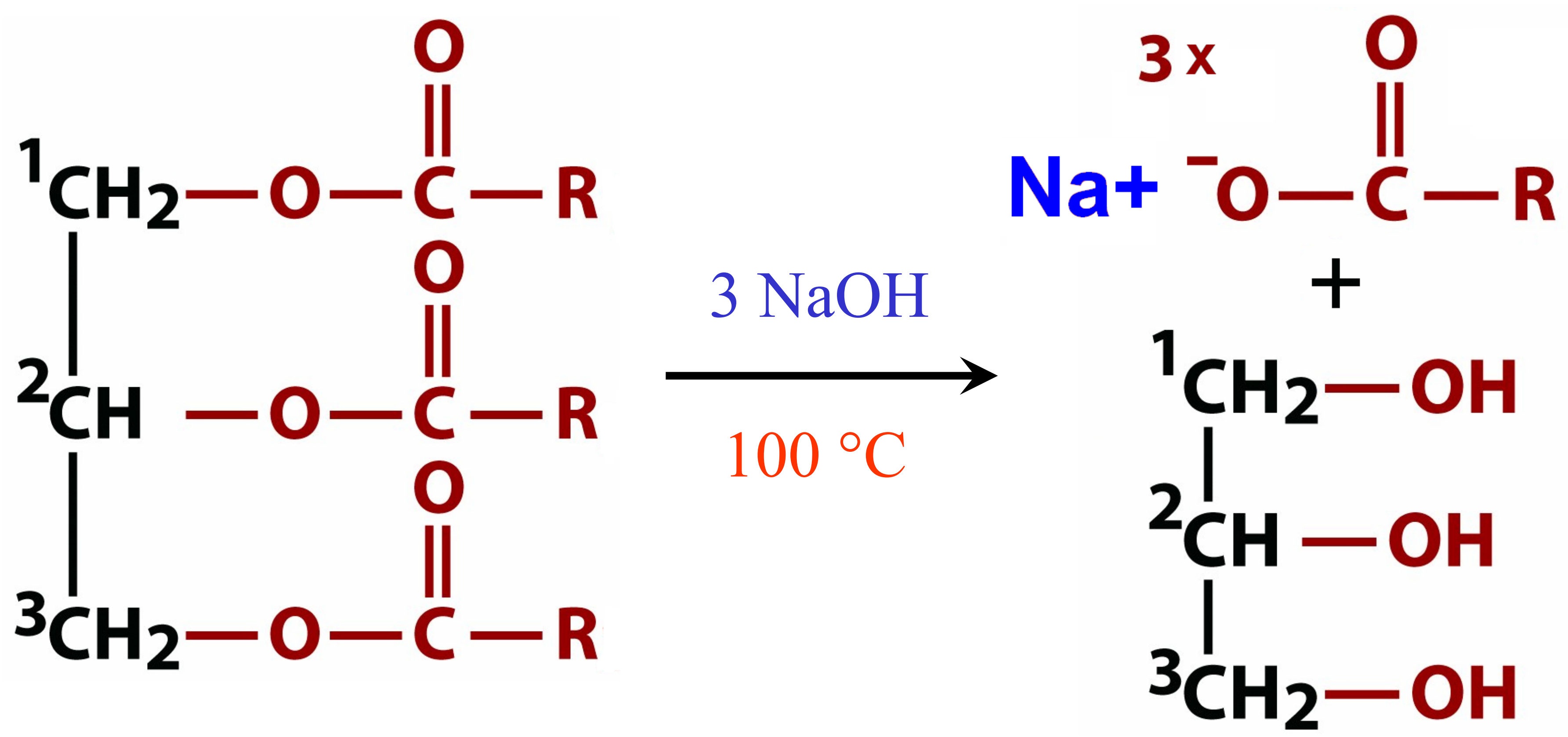






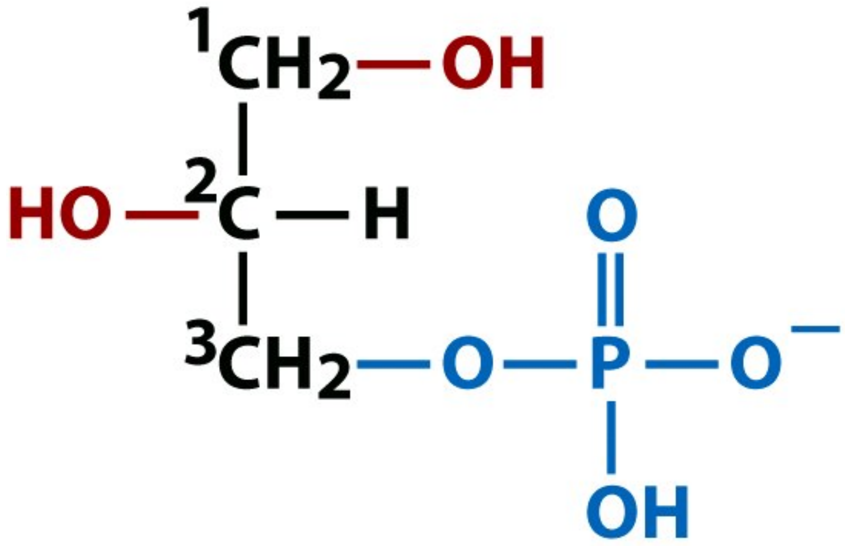
tristearoylglycerol

Saponification: soap is generally a sodium or potassium salt of a long-chain aliphatic carboxylic acid. It is prepared by alkaline hydrolysis, of animal or vegetable fats

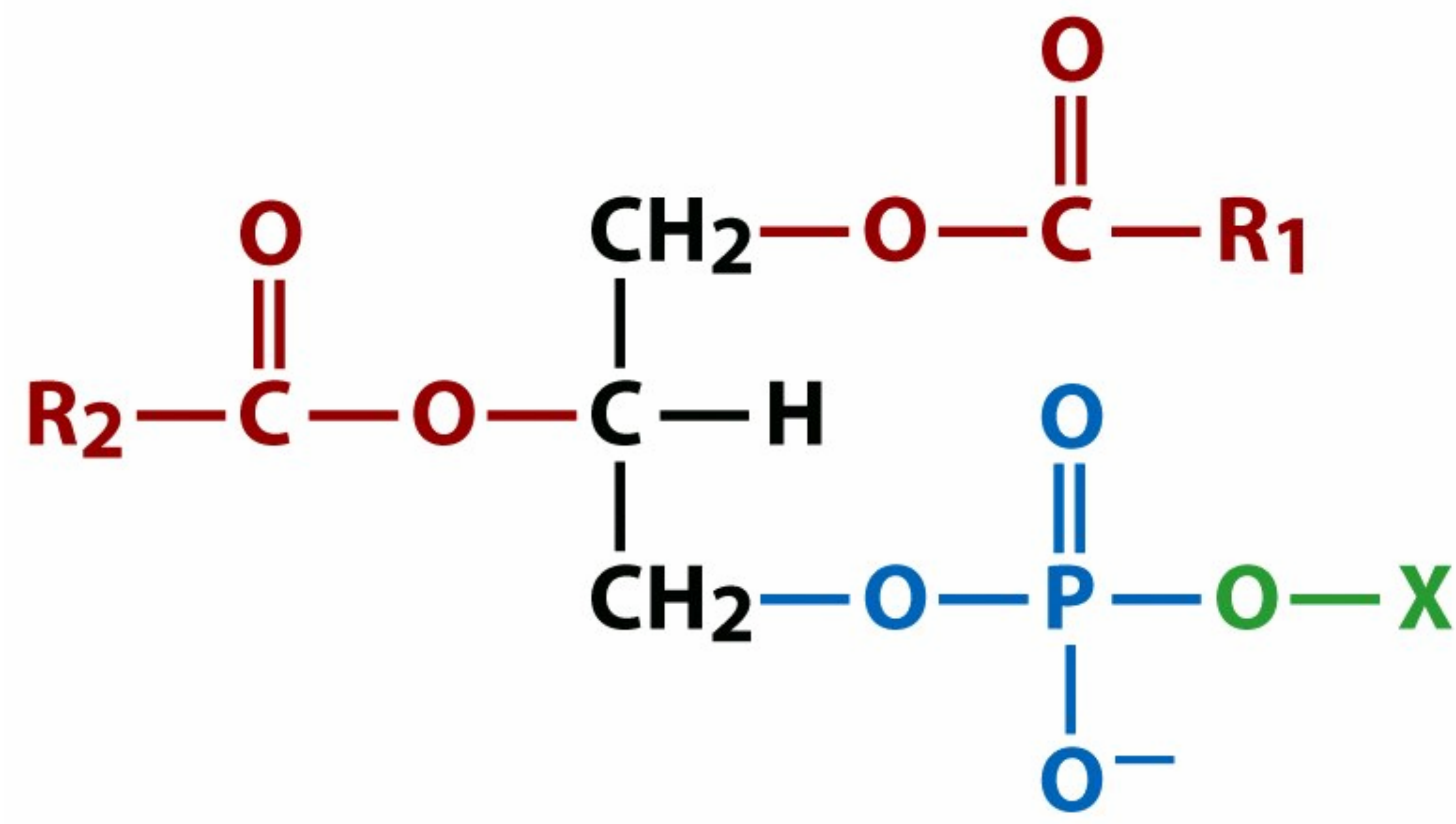


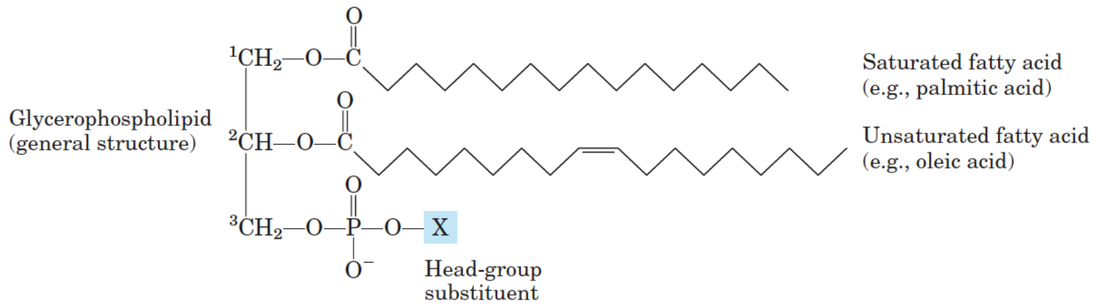
Glycerophospholipids

- main constituents of biological membrane
- they are synthesized starting from glycerol-3-phosphate (an intermediate of glucose metabolism) by esterification of C1 and C2 with fatty acids



Glycerophospholipids





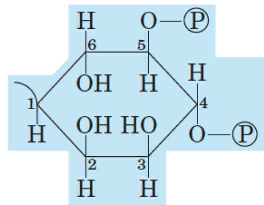
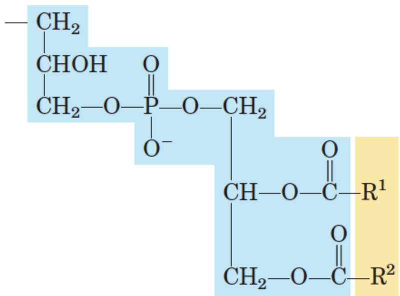
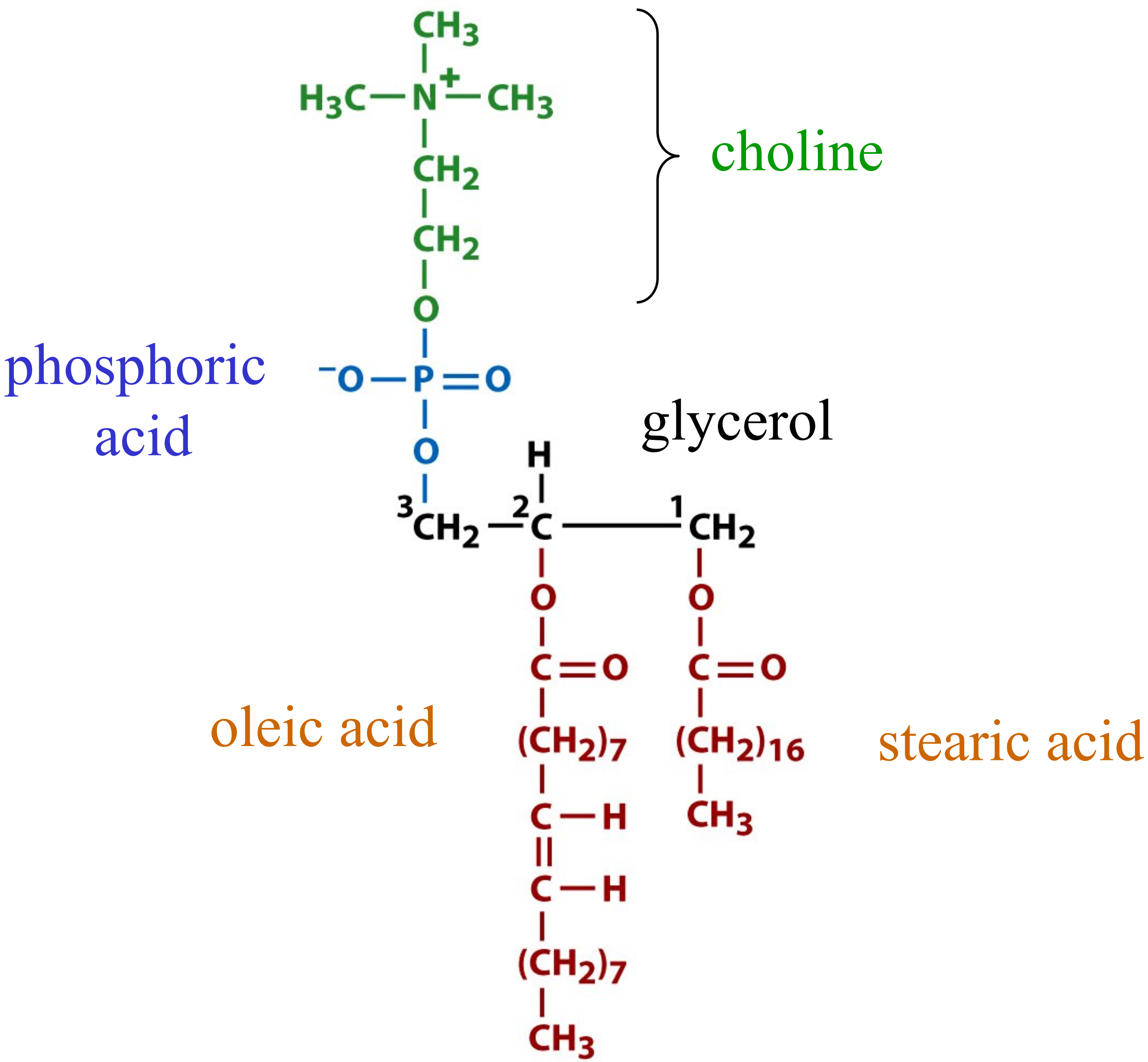
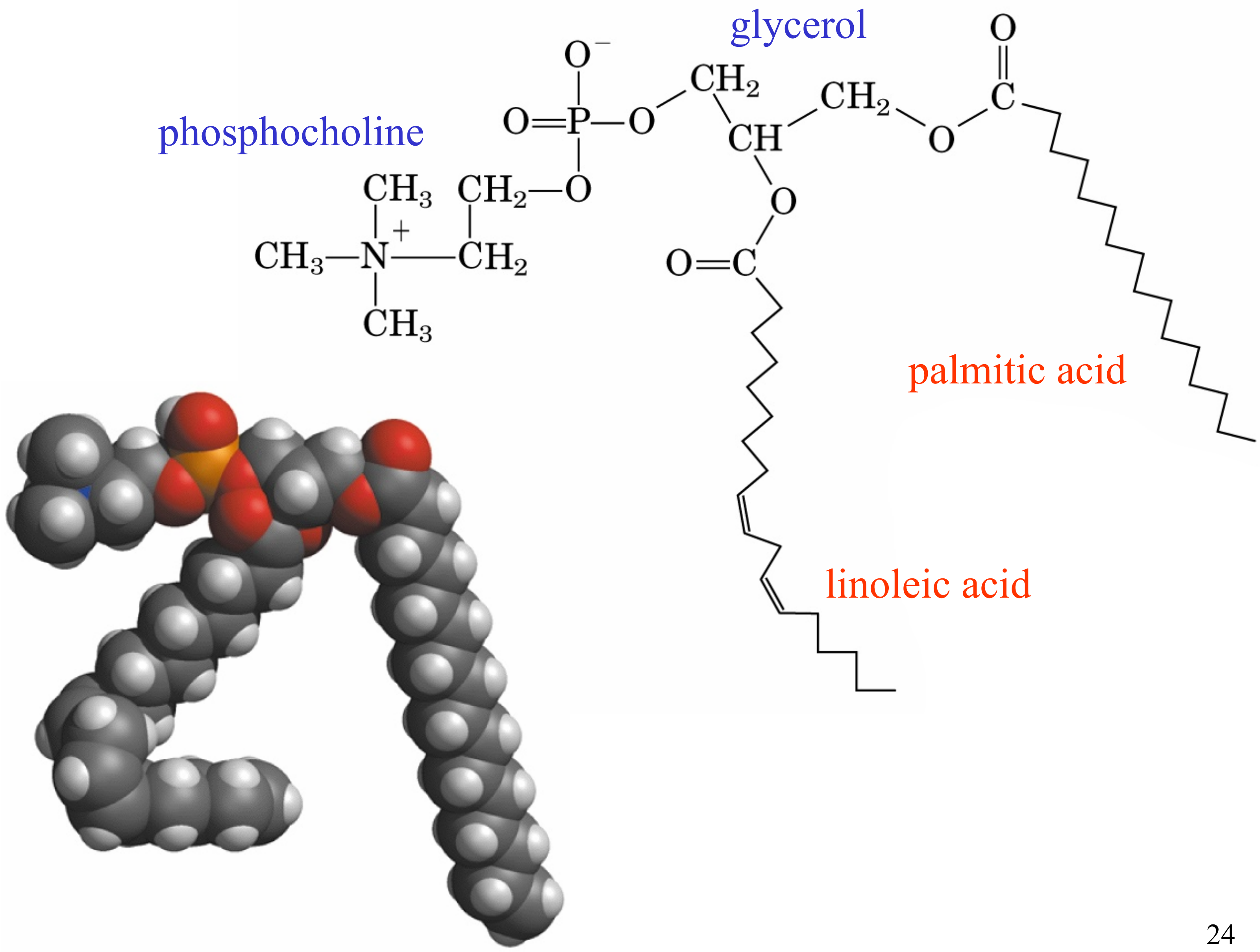
Name of glycerophospholipid	Name of X—O	Formula of X	Net charge (at pH 7)
Phosphatidic acid	—	—H	−1
Phosphatidylethanolamine	Ethanolamine	$-CH_2-CH_2-\overset{+}{N}H_3$	0
Phosphatidylcholine	Choline	$-CH_2-CH_2-\overset{+}{N}(CH_3)_3$	0
Phosphatidylserine	Serine	$-CH_2-CH(COO^-)-\overset{+}{N}H_3$	−1
Phosphatidylglycerol	Glycerol	$-CH_2-CH(OH)-CH_2-OH$	−1
Phosphatidylinositol 4,5-bisphosphate	*myo*-Inositol 4,5-bisphosphate		−4
Cardiolipin	Phosphatidyl-glycerol		−2

FIGURE 10–9 Glycerophospholipids. The common glycerophospholipids are diacylglycerols linked to head-group alcohols through a phosphodiester bond. Phosphatidic acid, a phosphomonoester, is the parent compound. Each derivative is named for the head-group alcohol (X), with the prefix "phosphatidyl-." In cardiolipin, two phosphatidic acids share a single glycerol (R^1 and R^2 are fatty acyl groups).

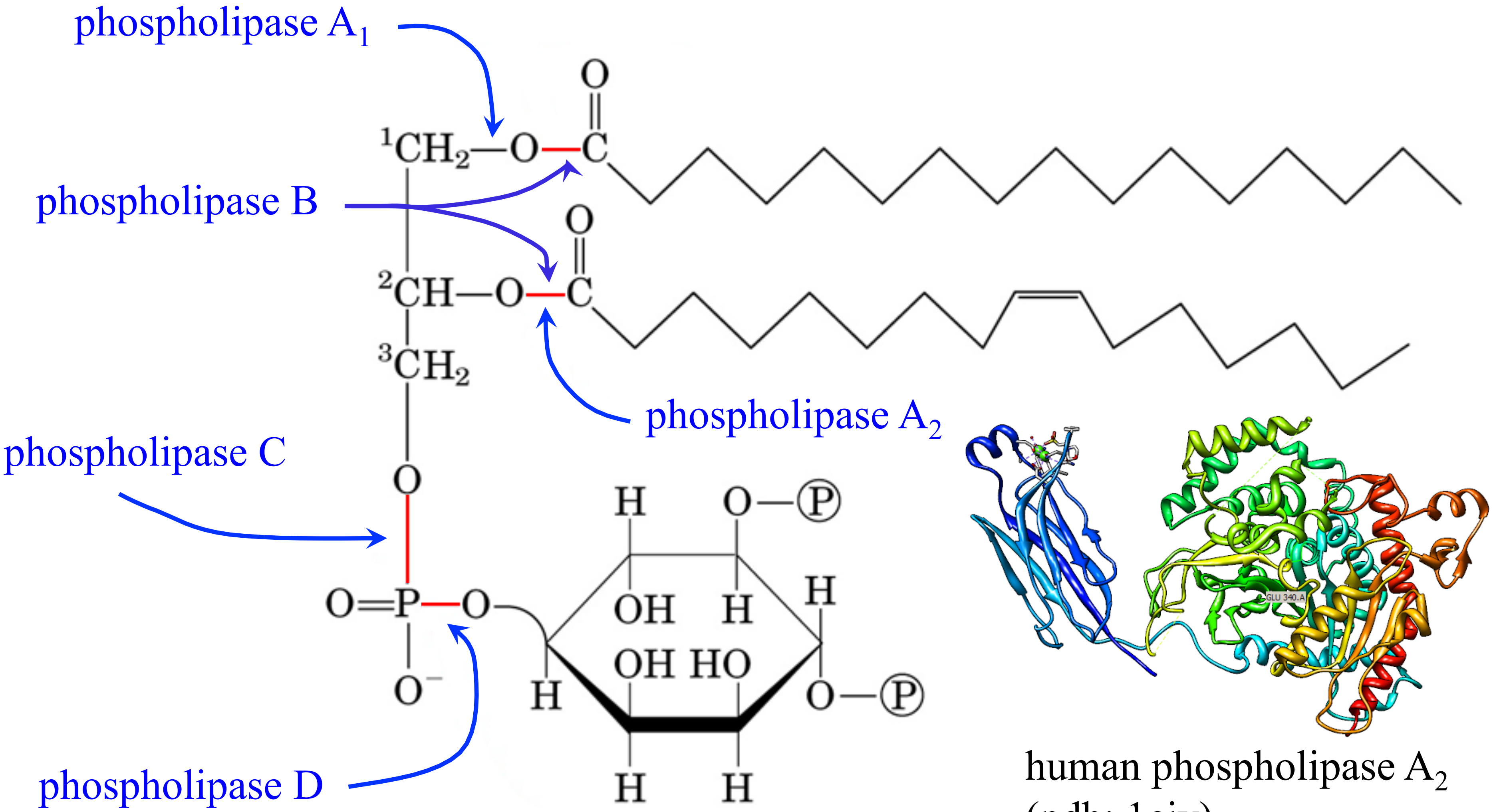
1-stearoyl-2-oleoyl-phosphaditylcholine



1-linoleyl-2-palmitoyl-phosphaditylcholine



Phospholipases hydrolyze glycerophospholipids

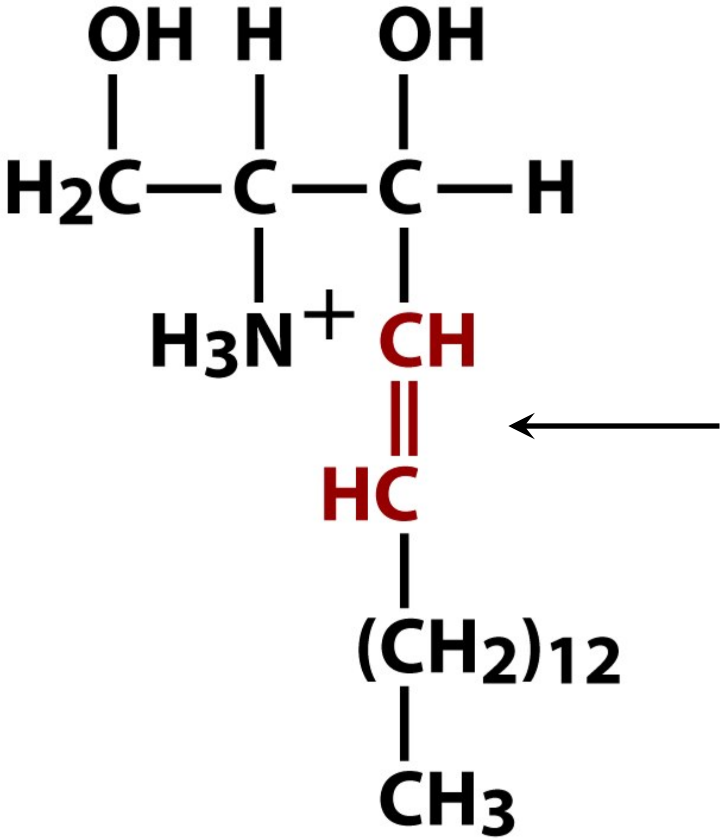


human phospholipase A_2
(pdb: 1cjy)

Sphingolipids

• they are also main components of biological membranes (20-30 mol%)

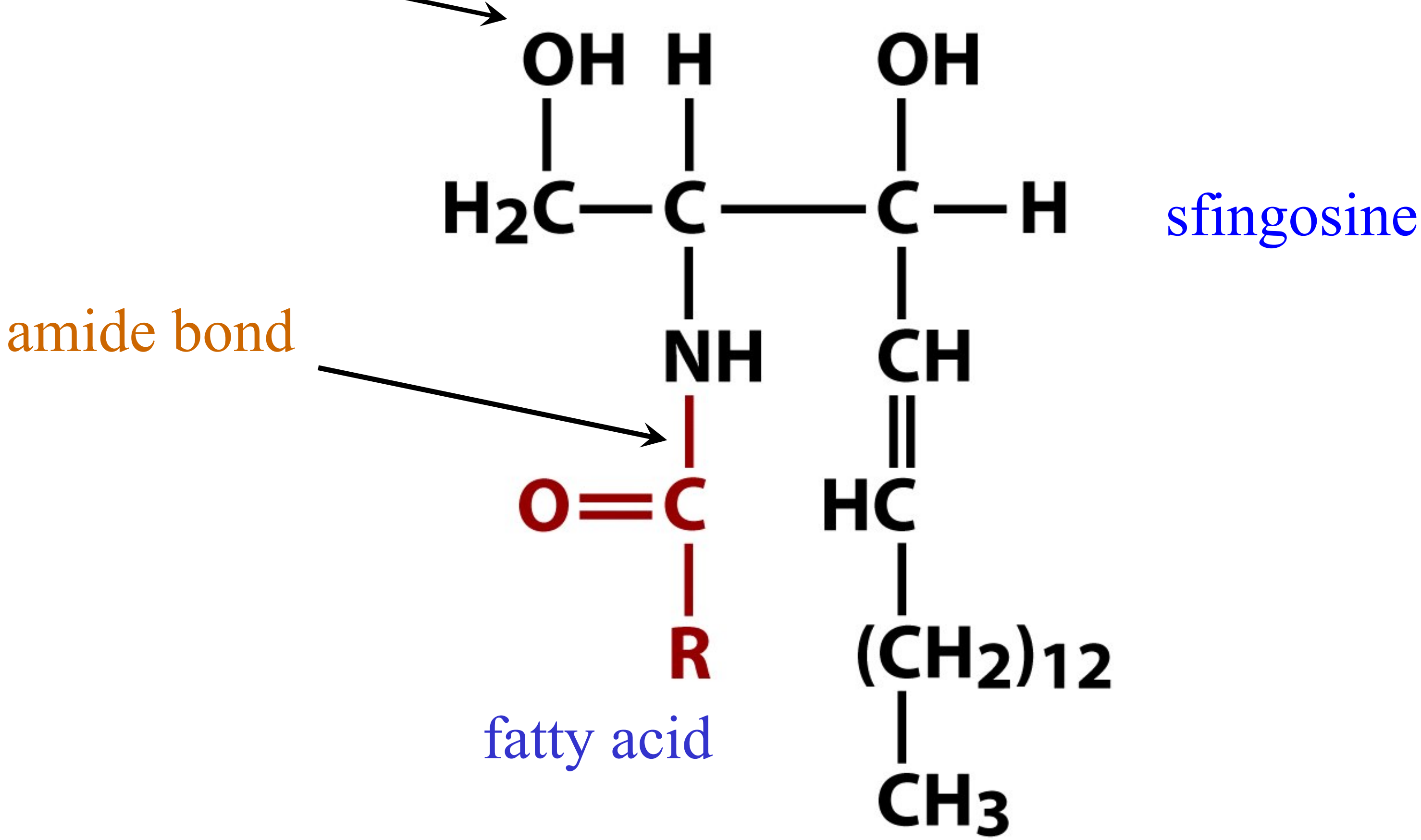
• they derive from the unsaturated amino alcohol with 18 C atoms: sphingosine



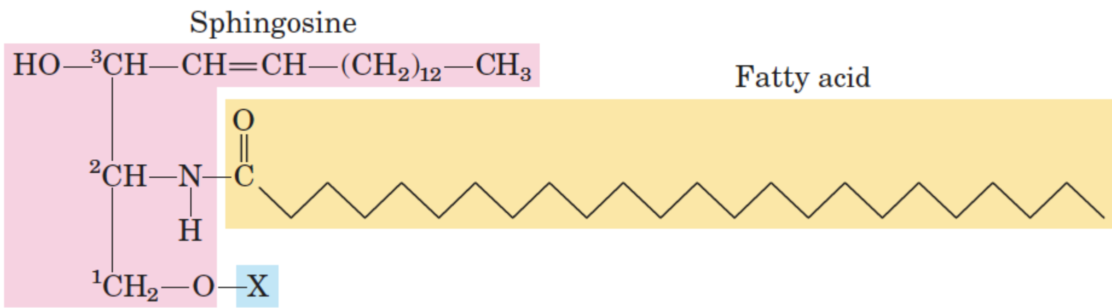
trans configuration

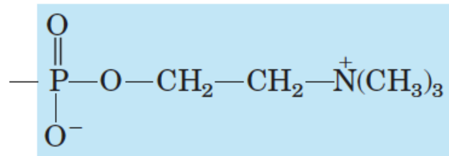
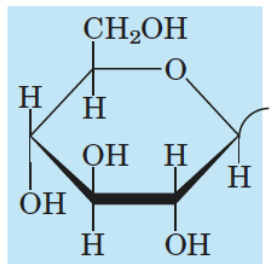
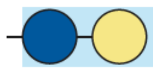
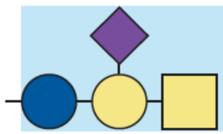
Sphingolipids

N-acyl derivatives of a fatty acid with sphingosine are known as ceramides. These are the compounds from which most of the sphingolipids originate by esterification on the hydroxyl function in poistion 3.

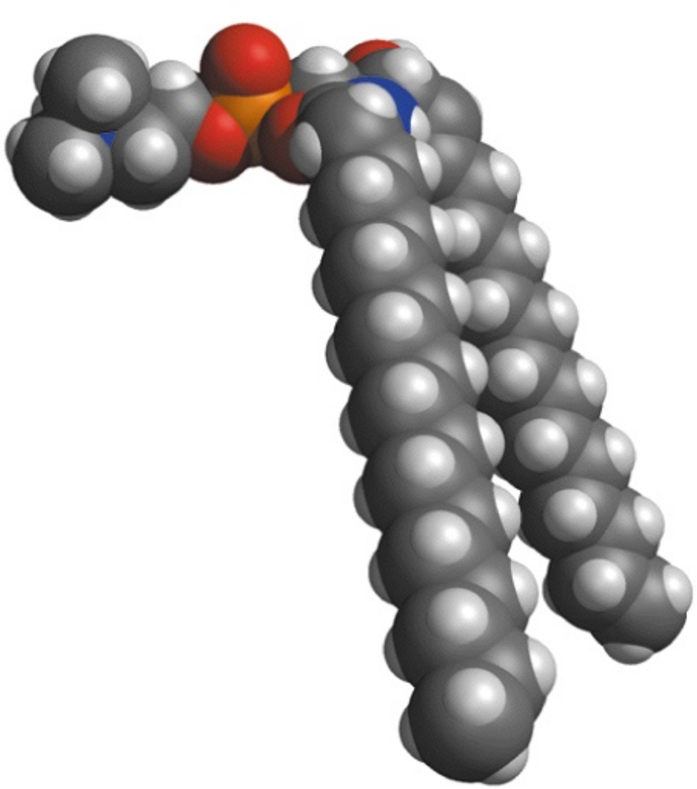


Sphingolipid (general structure)

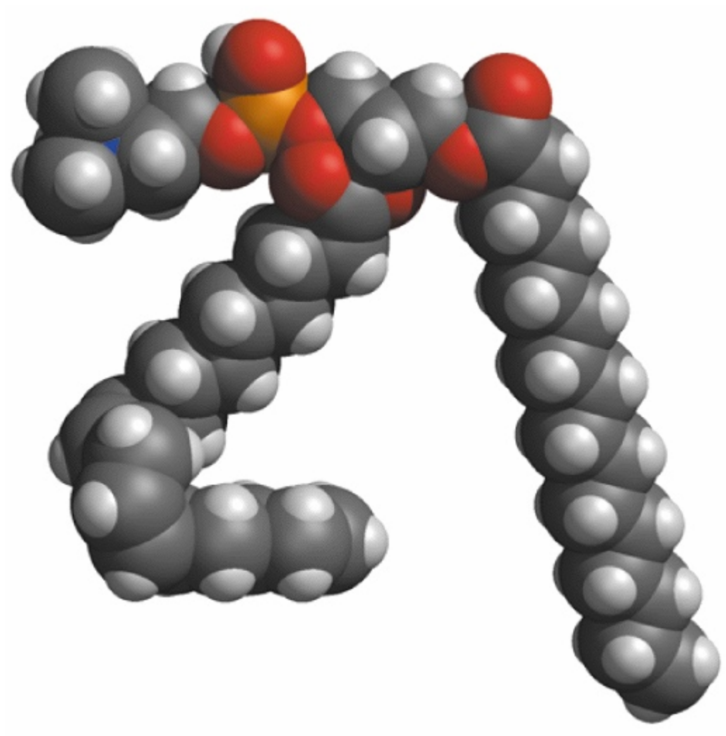


Name of sphingolipid	Name of X—O	Formula of X
Ceramide	—	—H
Sphingomyelin	Phosphocholine	
Neutral glycolipids Glucosylcerebroside	Glucose	
Lactosylceramide (a globoside)	Di-, tri-, or tetrasaccharide	
Ganglioside GM2	Complex oligosaccharide	

Although they differ chemically from glycerophospholipids, the conformations and charge distribution of sphingolipids are very similar.



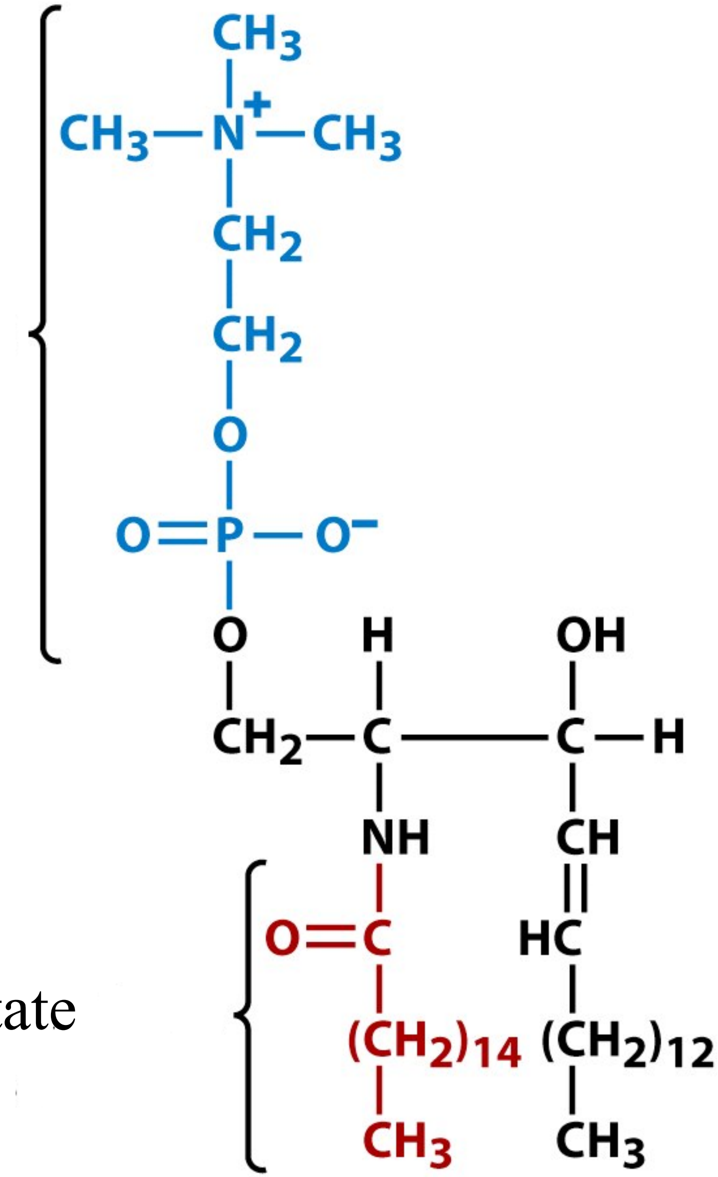
sphingomyelin



1-linoleyl-2-palmitoyl-phosphatidylcholine

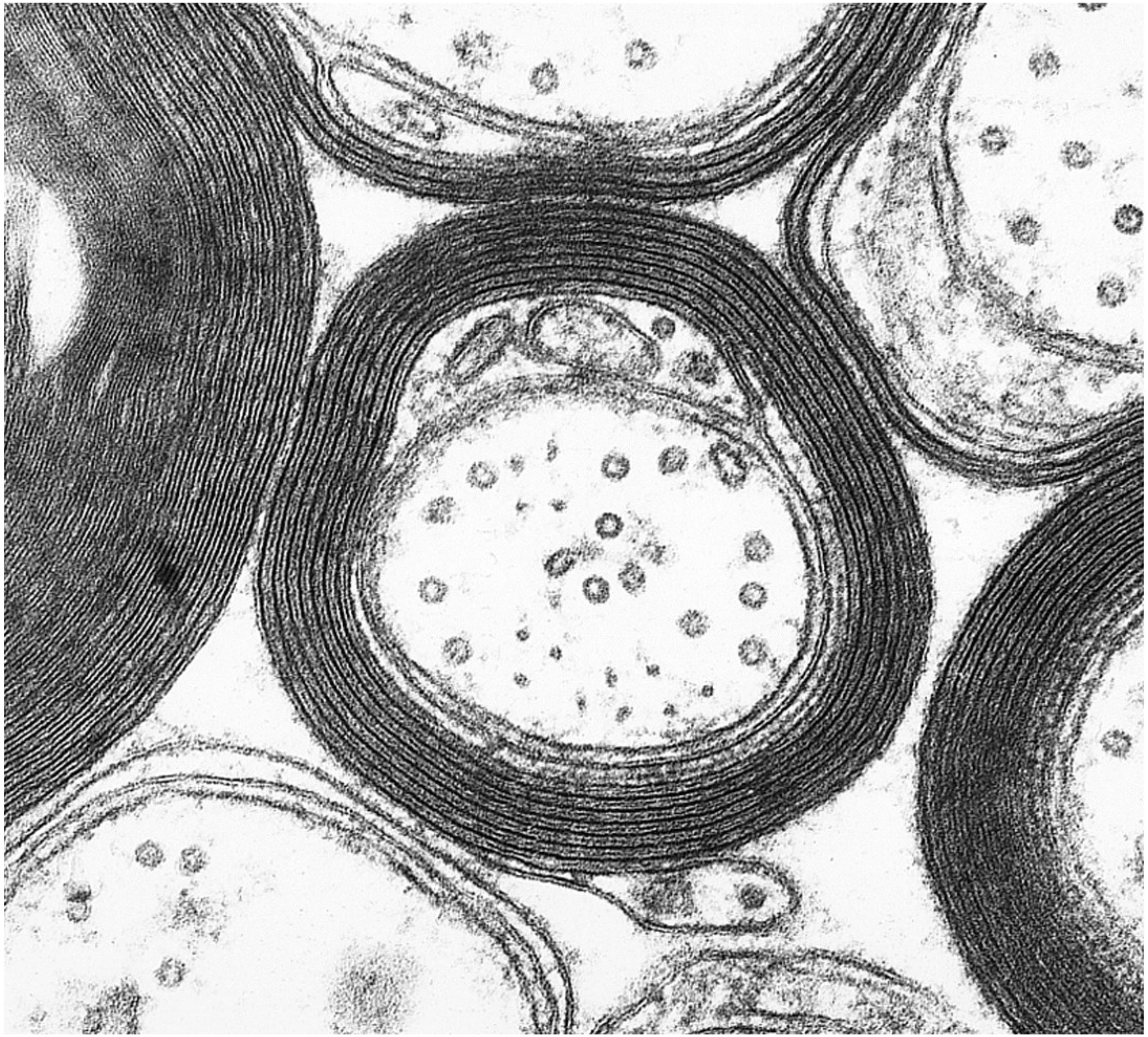
Sphingomyelin

polar head:
phosphocholine

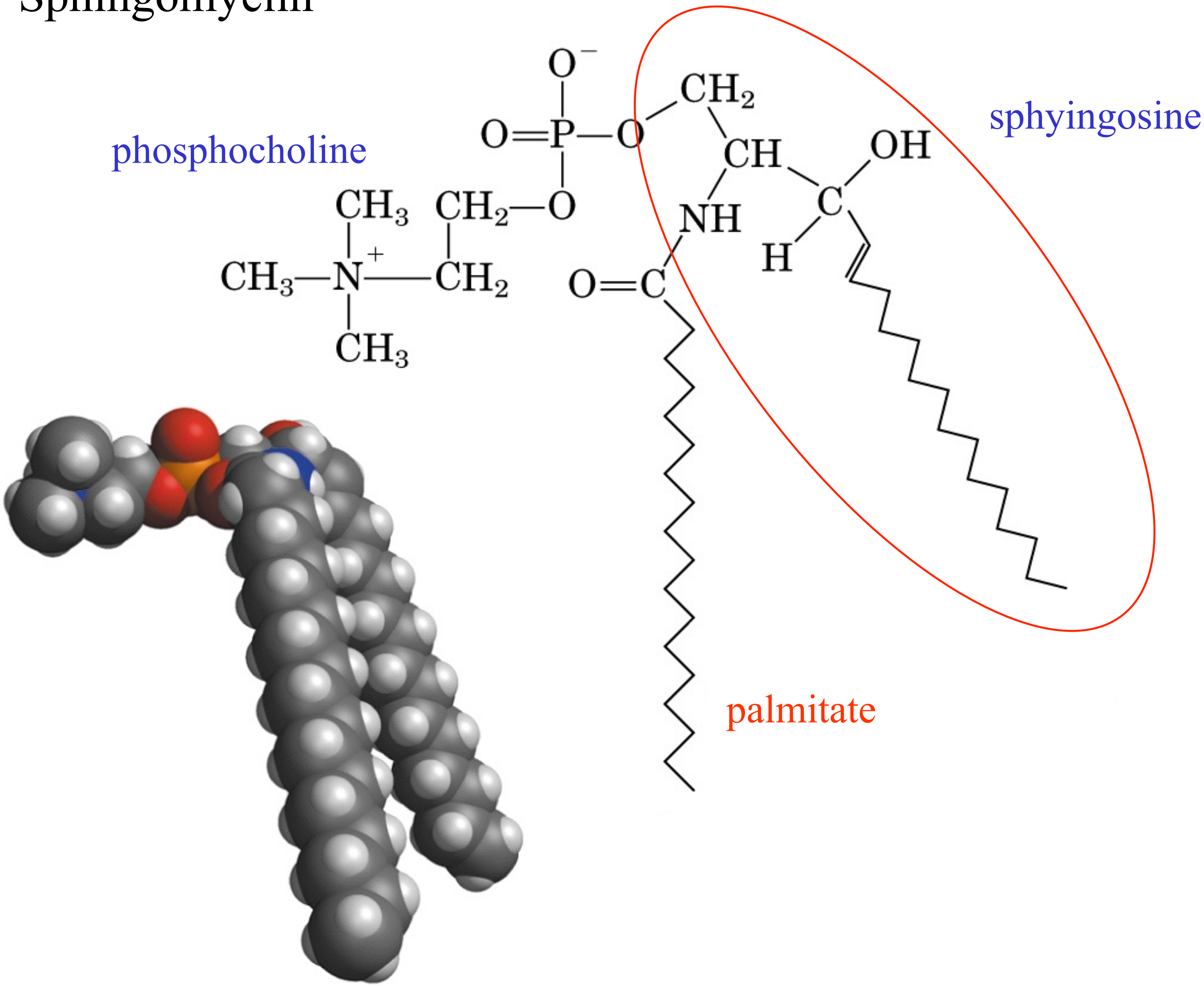


palmitate

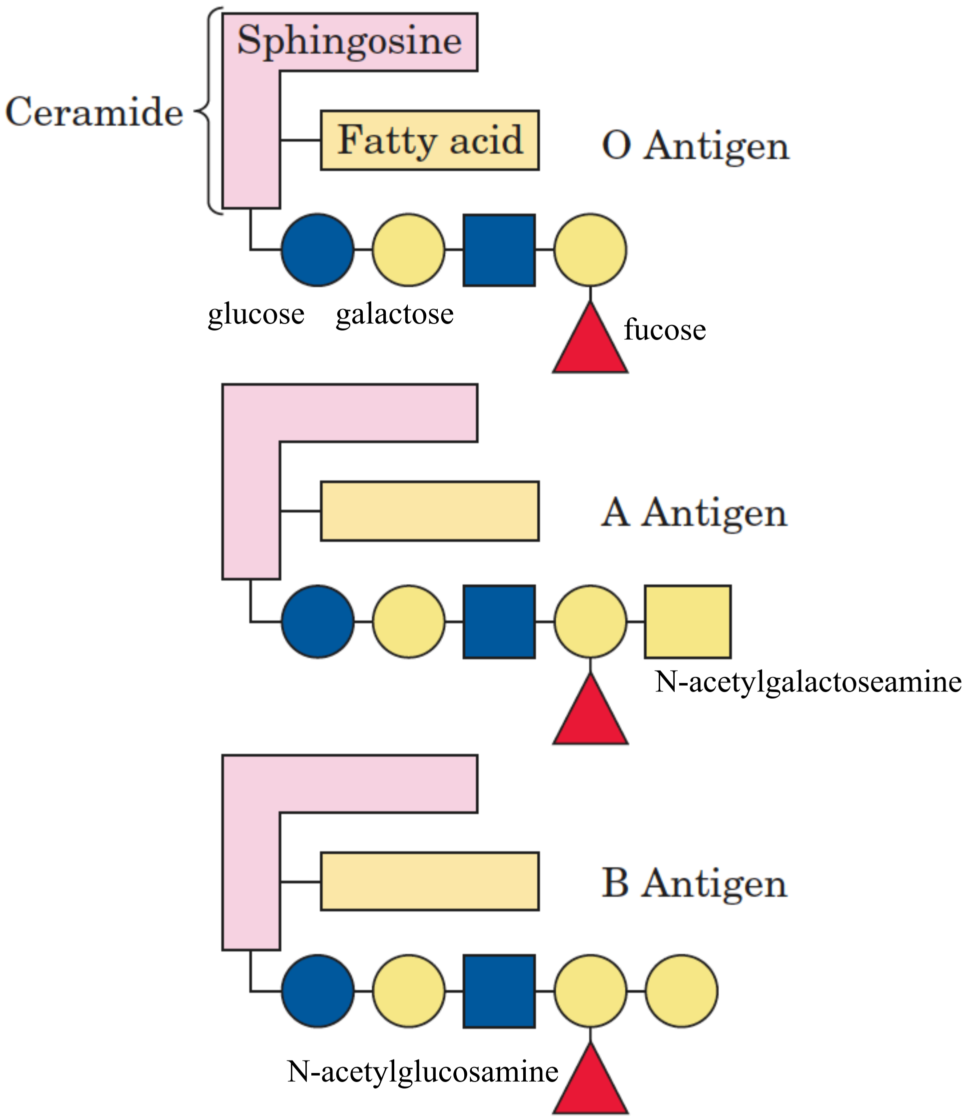
The myelin sheath of neuronal axons



Sphingomyelin



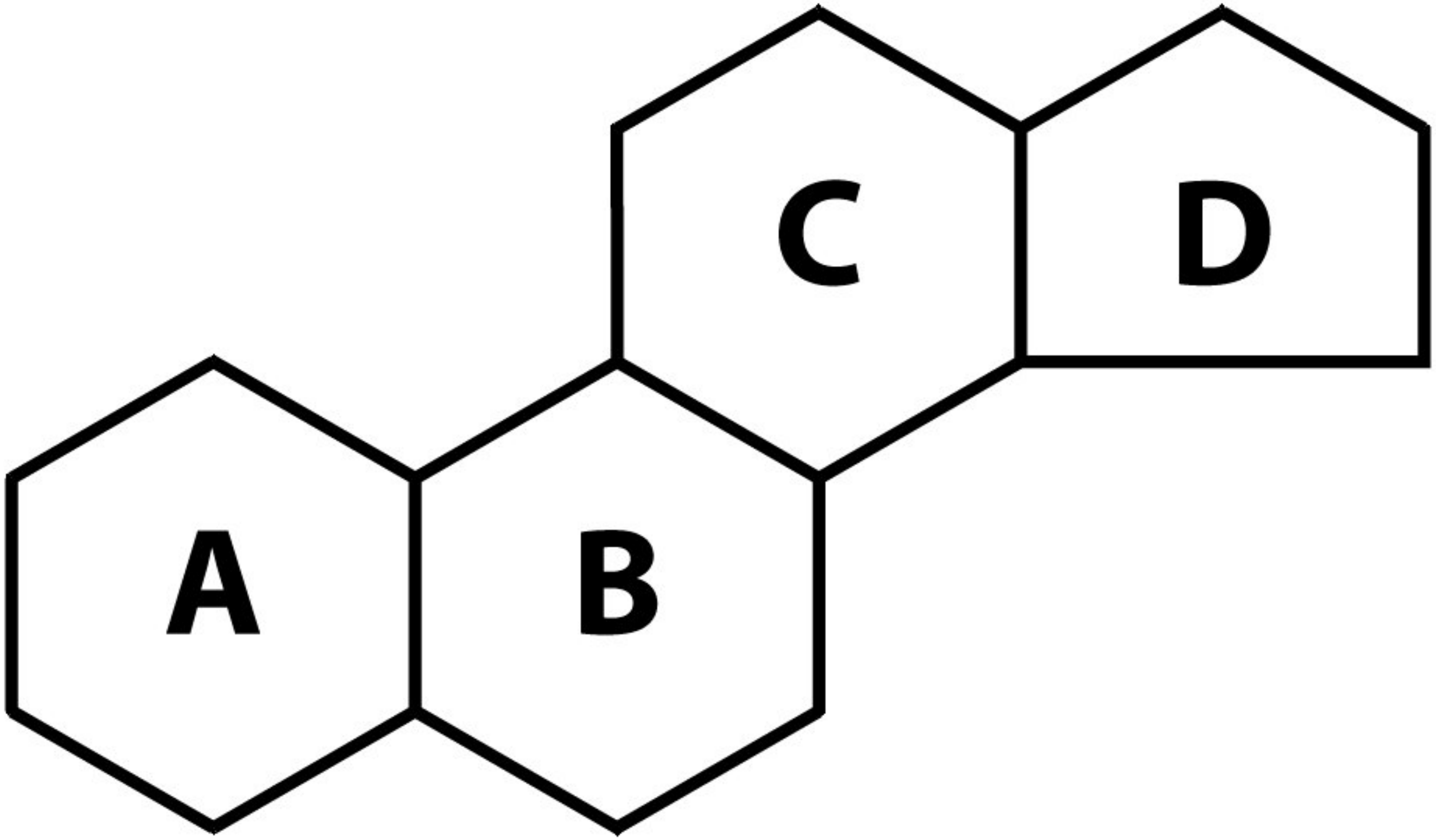
Glycosphingolipids as determinants of blood



The human blood groups (O, A, B) are determined in part by the oligosaccharide head groups of these glycosphingolipids.

Steroids

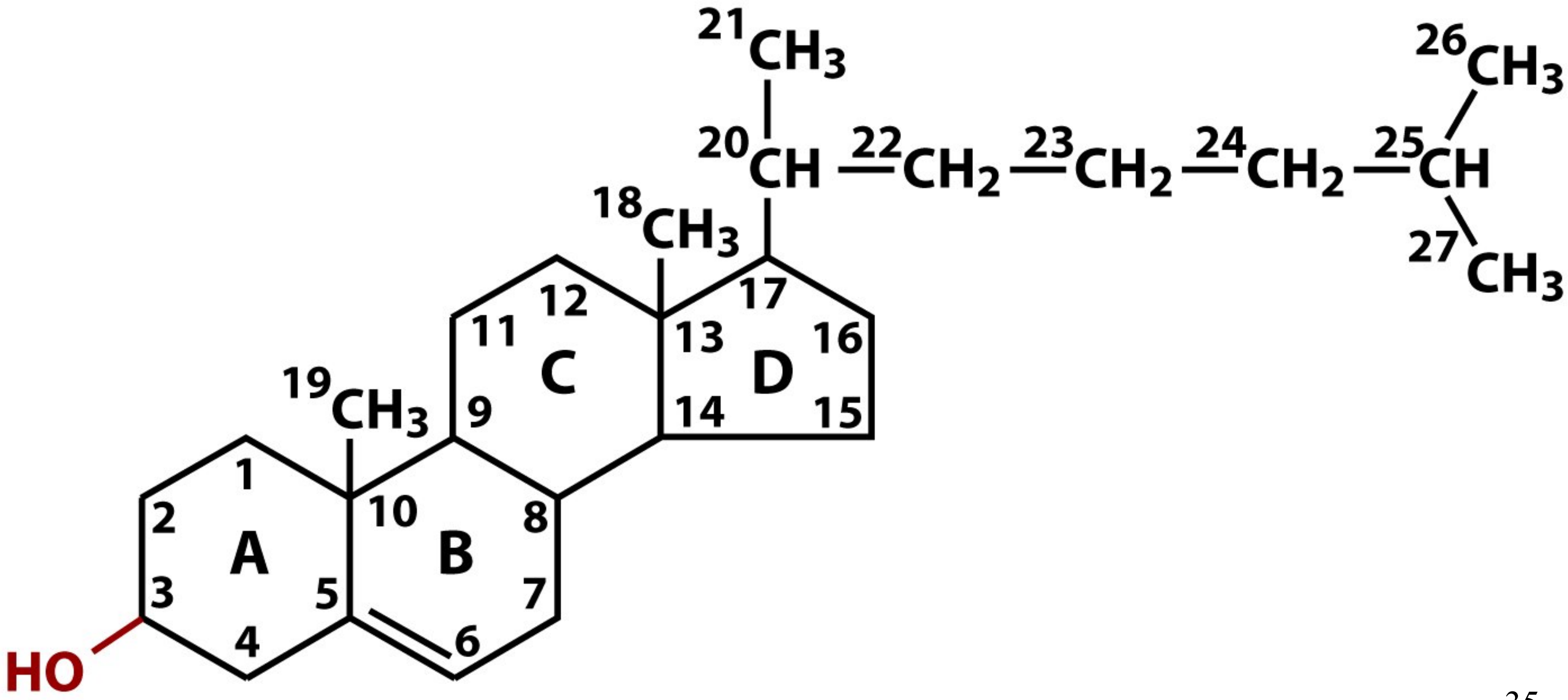
Mostly of eukaryotic origin, they derive from
cyclopentanoperihydrophenantrene



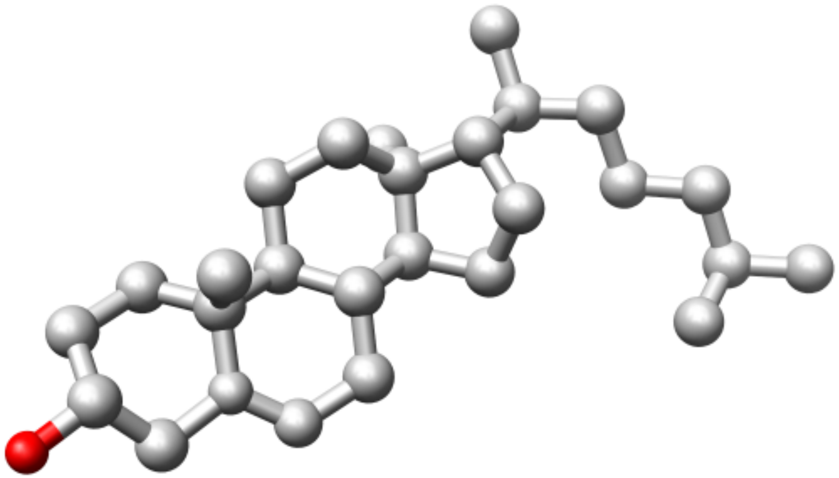
They have both structural and hormonal functions

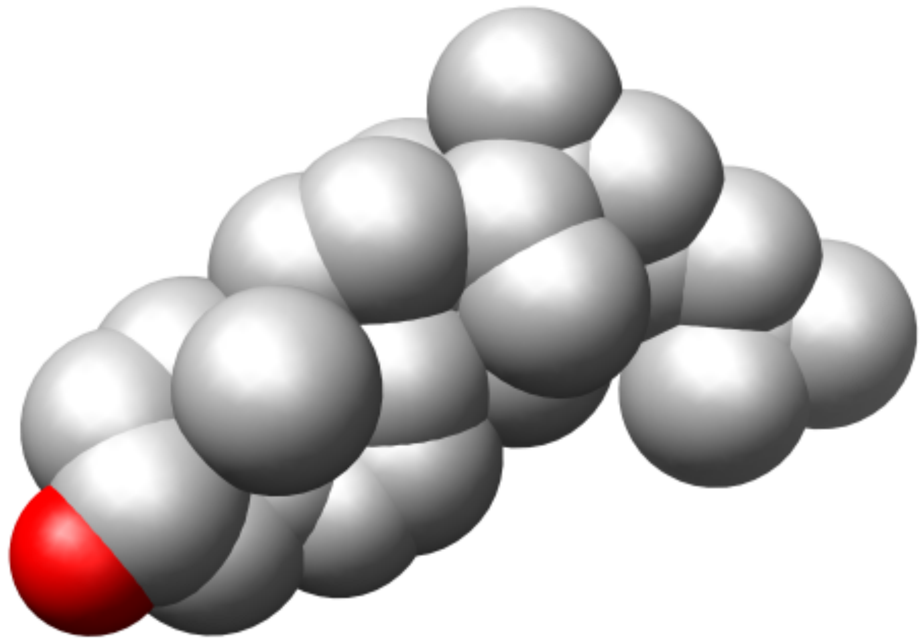
Cholesterol

The presence of the alcoholic group in position 3 confers a mild amphiphilicity. In mammals it is the metabolic precursor of steroid hormones, substances responsible for regulating a wide range of physiological functions.

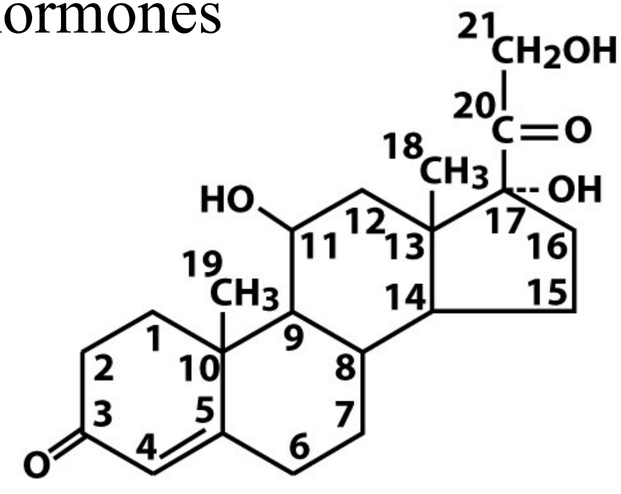


The presence of the 4 fused rings in cholesterol makes it a very rigid molecule, thus influencing the fluidity of the plasma membranes of which it is one of the main components.

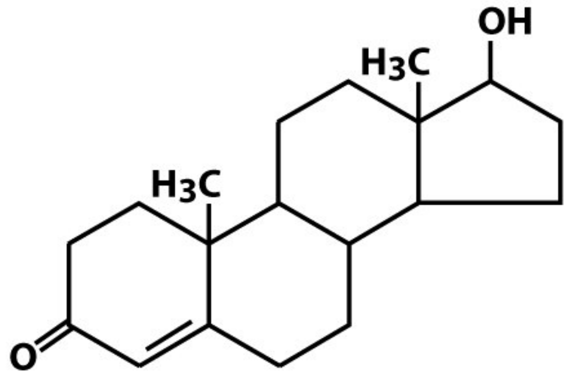




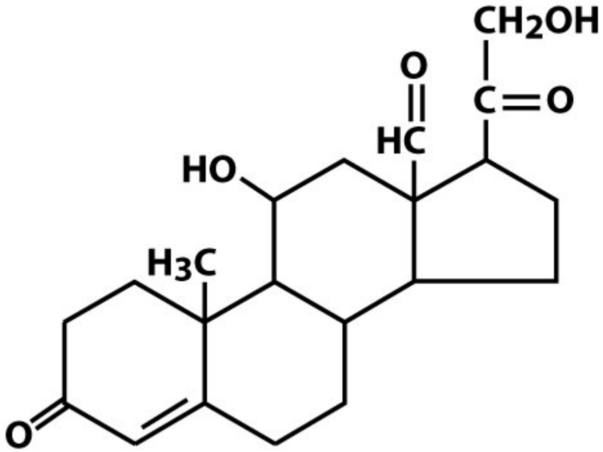
Steroid hormones



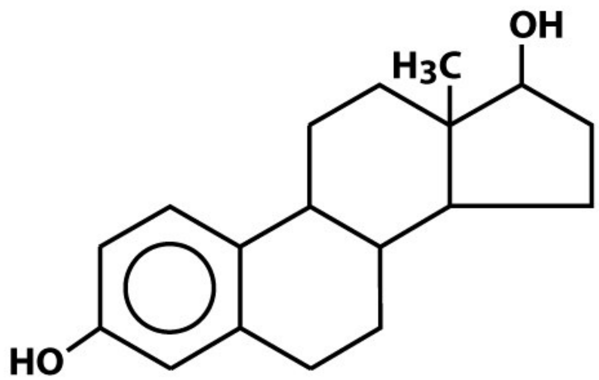
cortisol



testosterone

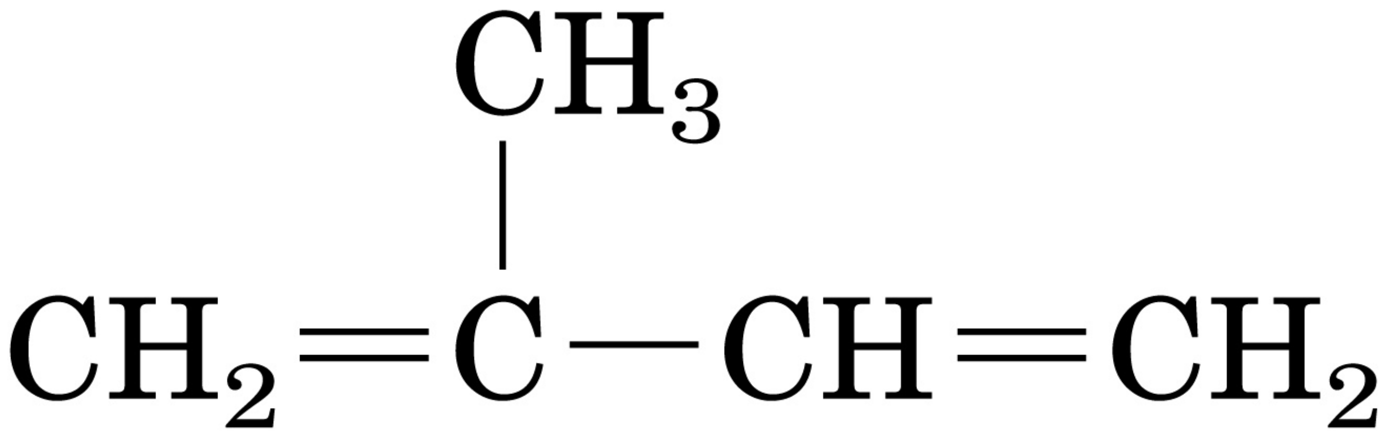


aldosterone



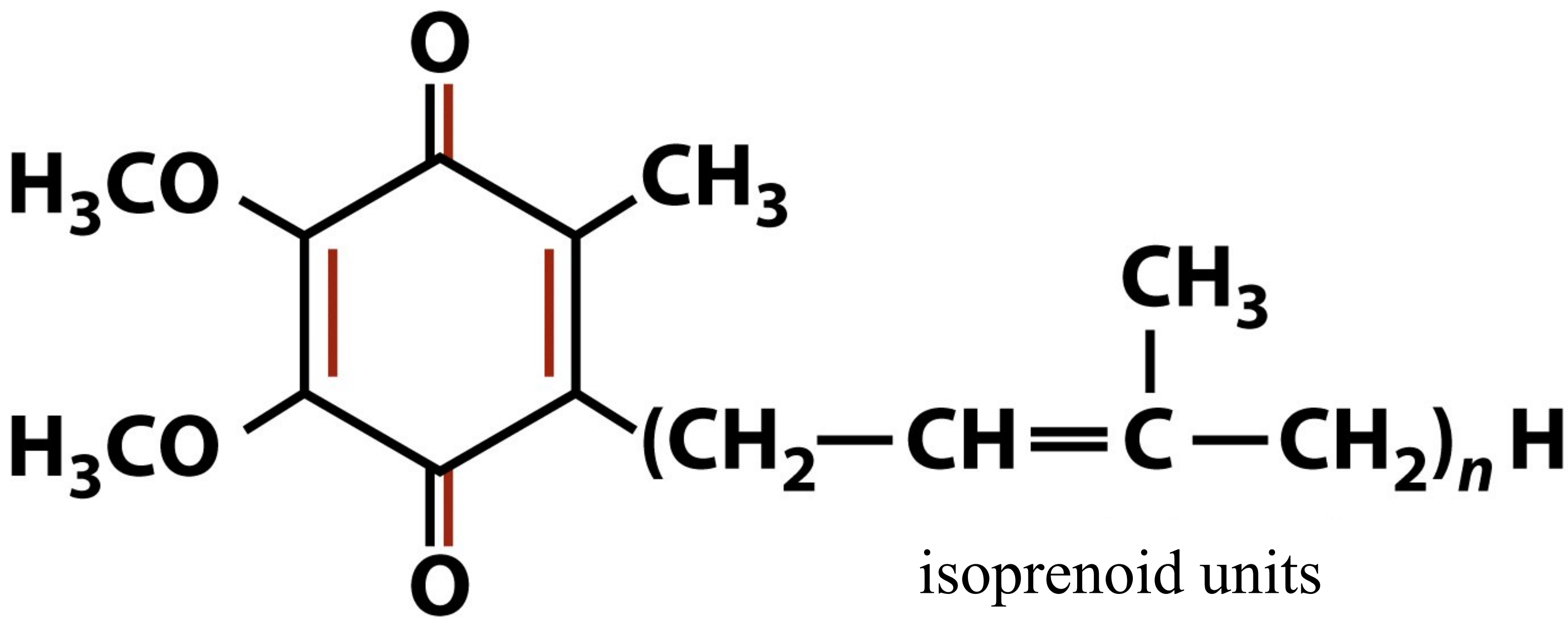
β-estradiol

Other lipids



Isoprene

Coenzyme Q or ubiquinone

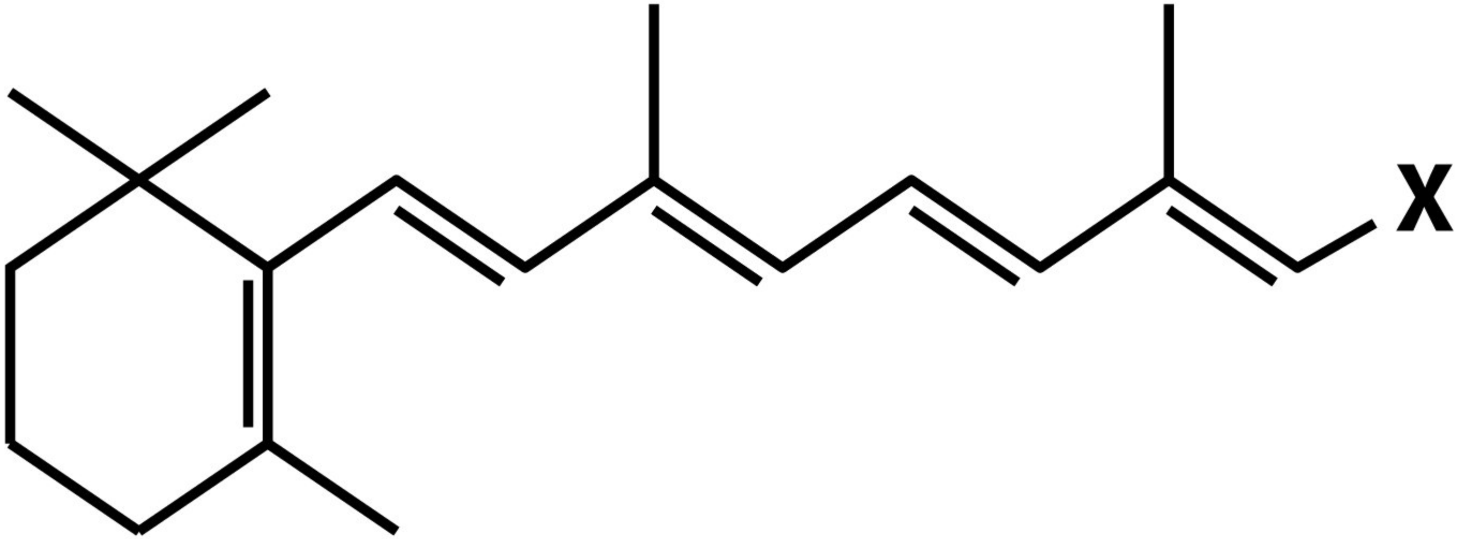


isoprenoid units

A proton-electron shuttle in electron transport chains

Vitamin A or retinol: derives form β-carotene

following oxidation to a retinal is involved in vision



$X = CH_2OH$ vitamin A or retinol

$X = CHO$ retinal

Liposomes