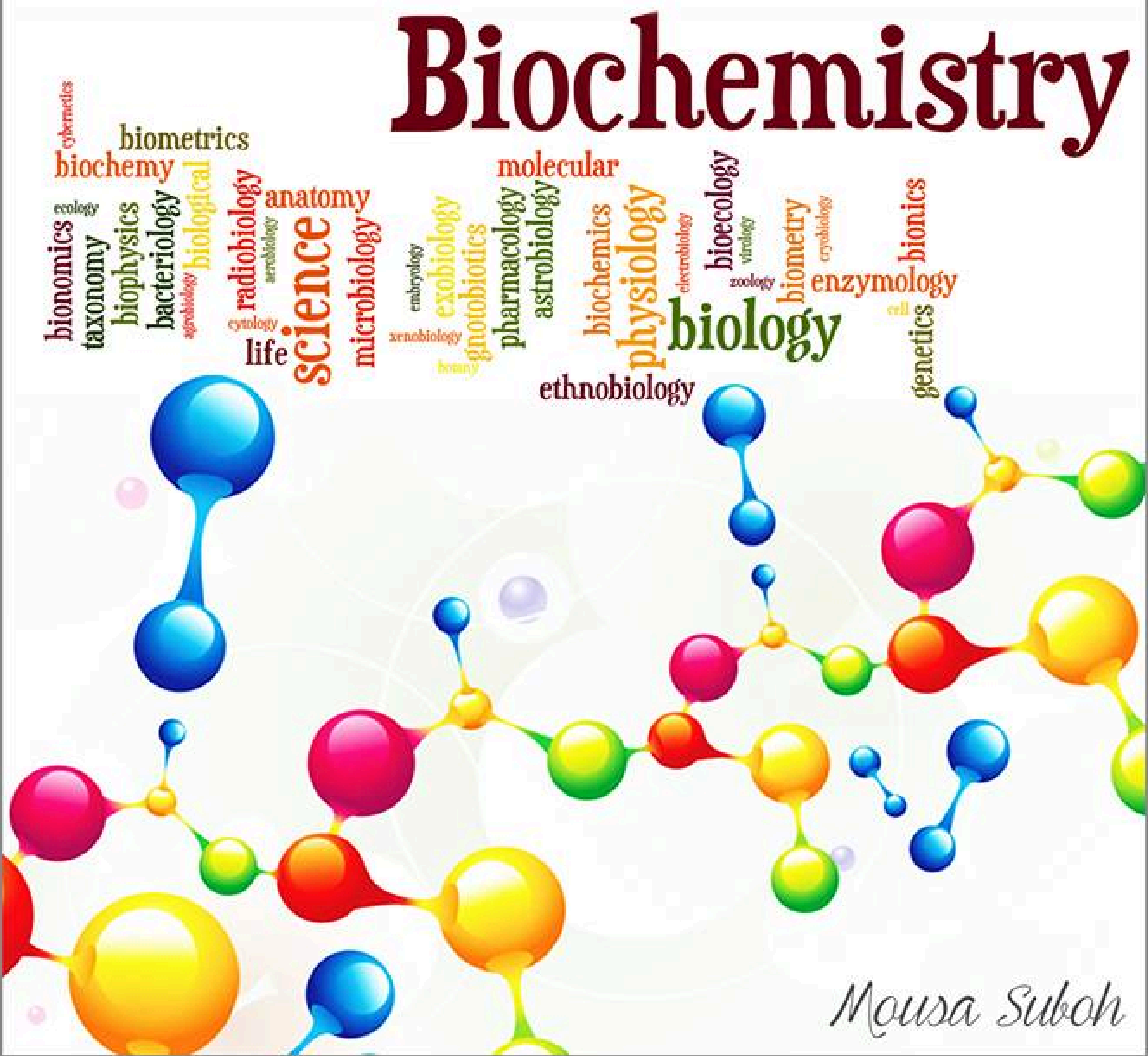
Slide : 2

Dr. Name : Mamoun Ahram

Sections : 1 , 2 , 3

■ Slide □ Sheet

Medical Committee
The University of Jordan



Lipids

Dr. Mamoun Ahram
Lecture 7
Summer 2013-2014

Resources

- This lecture
- Campbell and Farrell's Biochemistry, Chapter 8

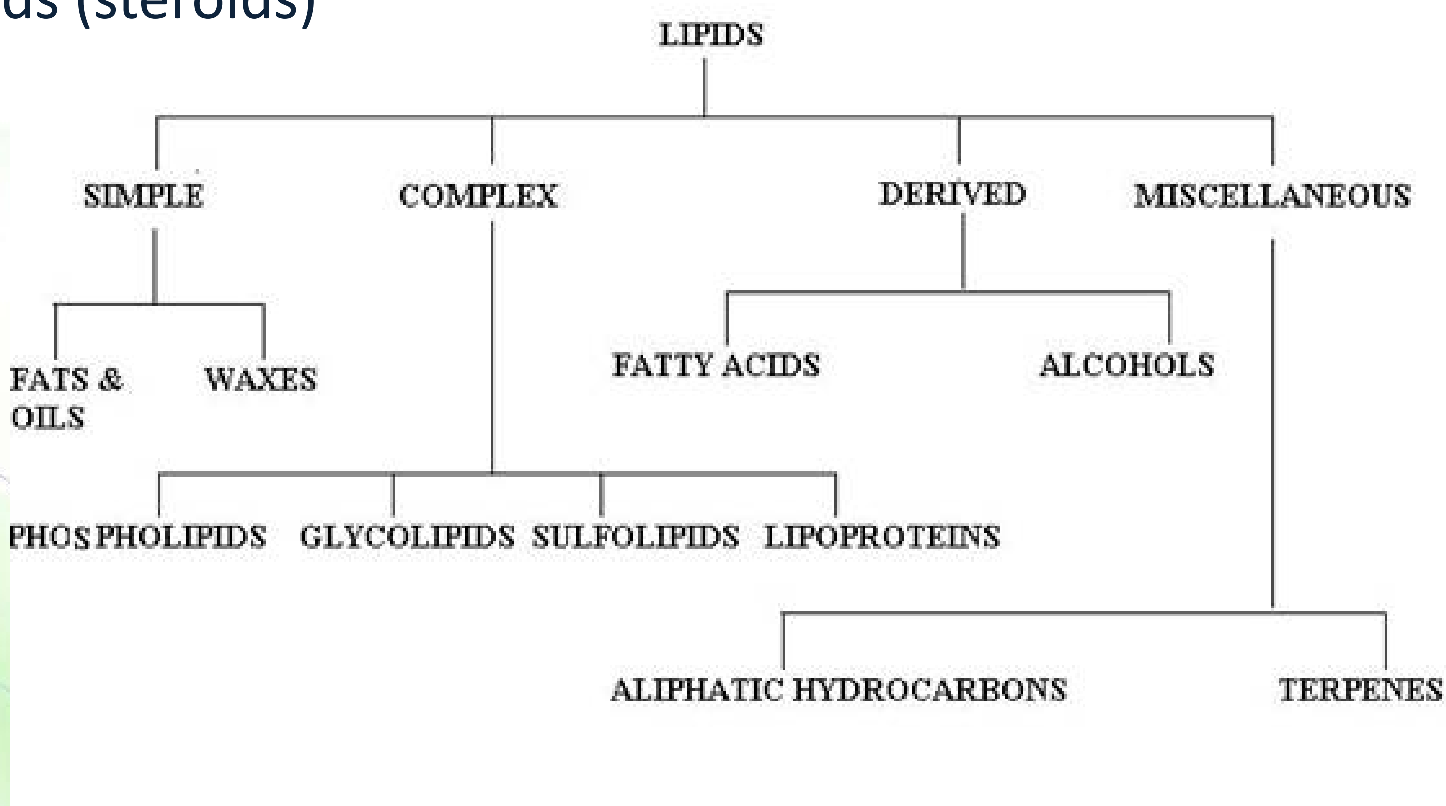
Lipids

- Lipids are a heterogeneous class of naturally occurring organic compounds that share some properties based on structural similarities, mainly a dominance of nonpolar groups.

- They are Amphipathic in nature.
- They are insoluble in water, but soluble in fat or organic solvents (ether, chloroform, benzene, acetone).
- They are widely distributed in plants & animals.

Classes

- Simple lipids (fats, oils, and waxes)
- Complex lipids (glycerides , glycerophospholipids, sphingolipids, glycolipids, lipoproteins)
- Derived lipids (fatty acids, alcohols, eicosanoids)
- Cyclic lipids (steroids)



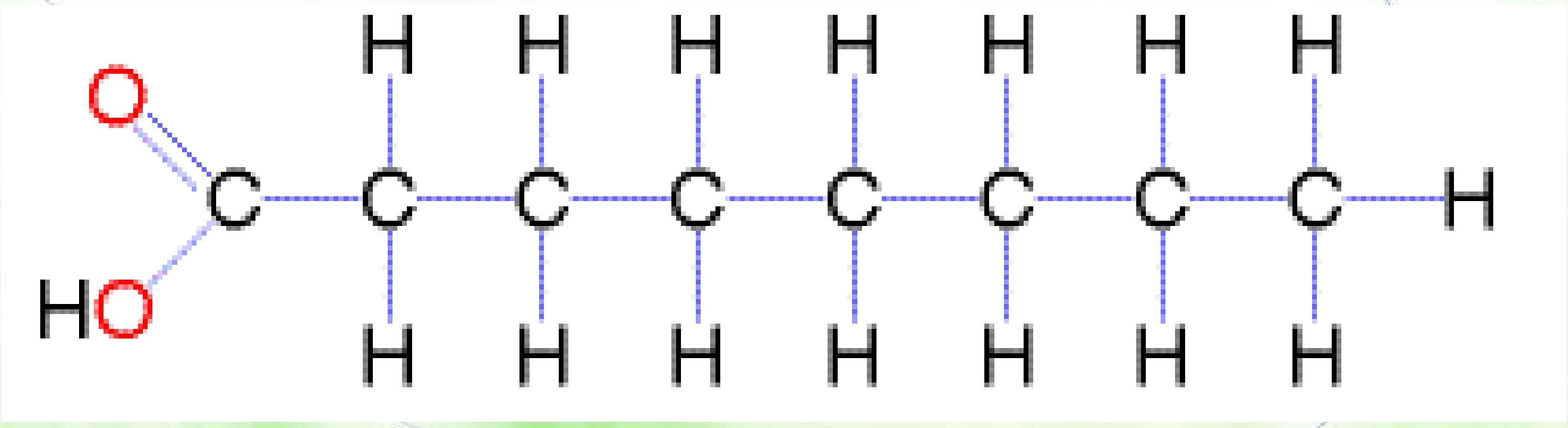
Lipid Functions

- Lipids include:
  - Storage Lipids
  - Structural Lipids in Membranes
  - Lipids as Signals, Cofactors & Pigments
- Source of energy
  - They are storable to <u>unlimited amount</u> (vs. carbohydrates)
  - They provide considerable amount of <u>energy</u> to the body (25% of body needs) & provide a high-energy value (more energy per gram vs. carbohydrates & proteins)
- Structural components (cell membranes)
- Precursors of hormone and vitamins
- Shock absorbers thermal insulator

Fatty acids

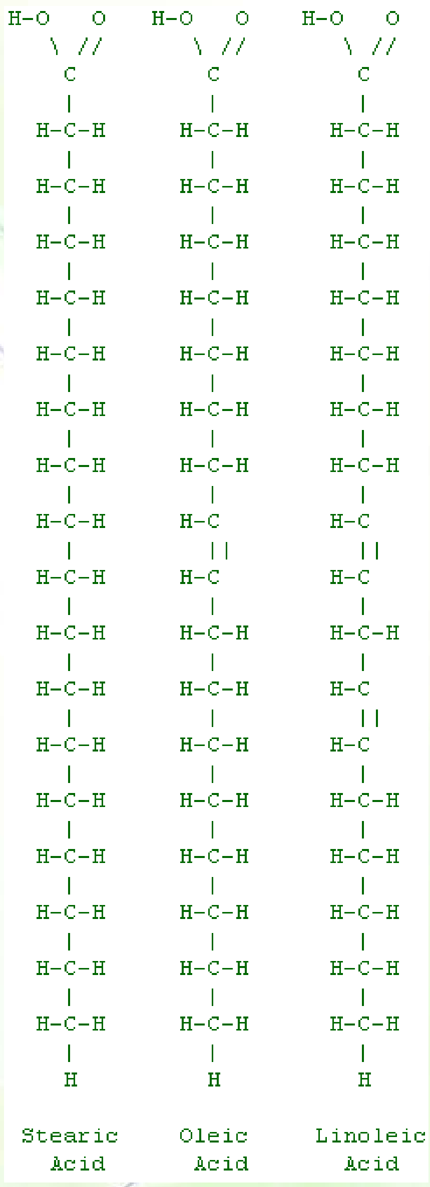
- Aliphatic mono-carboxylic acids
- Formula: **$R\text{-}(CH_2)_n\text{-}COOH$**
- Lengths
  - Physiological (12-24)
  - Abundant (16 and 18)
- Degree of unsaturation
- Amphipathic molecules

Function:
- **Building blocks of other lipids**
- **Modification of many proteins (lipoproteins)**
- **Important fuel molecules**
- **Derivatives of important cellular molecules**

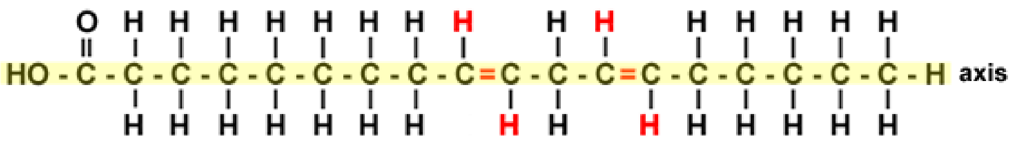


Types of fatty acids

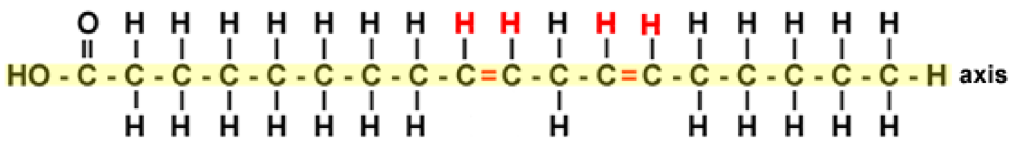
- Saturated fatty acids
  - Short chain F.A. (1-6 carbons)
  - Medium-chain F.A. (7-10 carbons)
  - Long chain F.A.(more the 10 carbon)
- Unsaturated fatty acids
  - Monounsaturated
  - Polyunsaturated



Cis vs. trans bonds



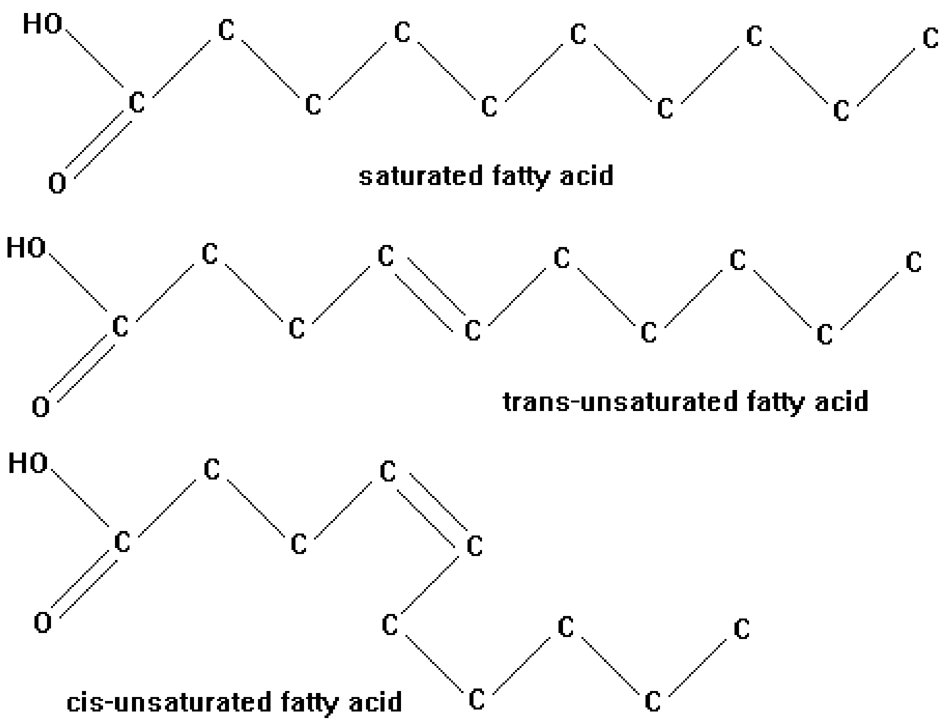
linoleic acid: *trans* configuration (*trans* isomer)



linoleic acid: *cis* configuration (*cis* isomer)

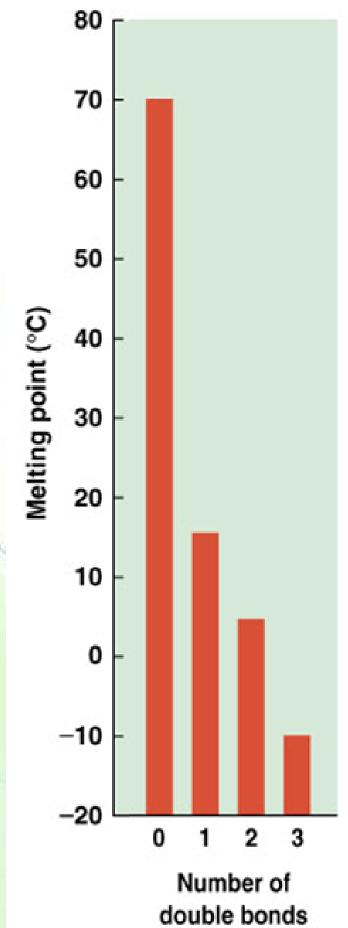
cis isomer predominates; trans is rare

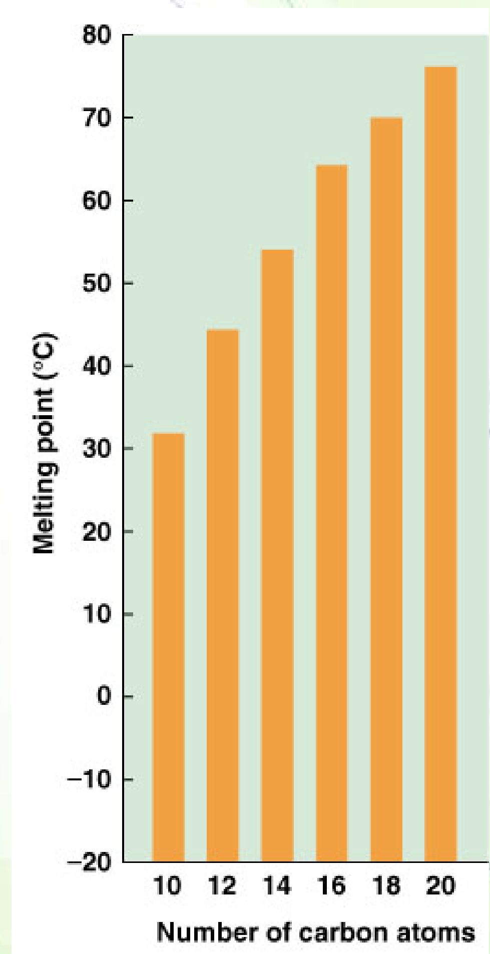
cis- vs. trans-fatty acids



Properties of fatty acids

- The properties of fatty acids (melting point and solubility) are dependent on chain length and degree of saturation





Properties of fatty acids

Short chain F.A.	Medium-chain F.A.	Long chain F.A.
They are liquid in nature	Solids at room temperature	Solids at room temperature
Water-soluble	Water-soluble	Water-insoluble
Volatile ar room temperature	Non-volatile at room temperature	Non-volatile &
acetic, butyric, & caproic acids	Examples: caprylic & capric F.A.	Examples: palmitic, stearic, & lignoceric F.A
		Occur in hydrogenated oils, animal fats, butter & coconut & palm oils

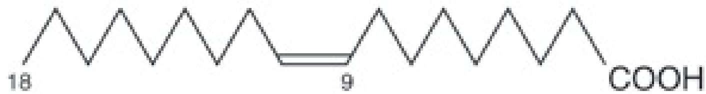
Greek number prefix

Number	prefix	Number	prefix	Number	prefix
1	Mono-	5	Penta-	9	Nona-
2	Di-	6	Hexa-	10	Deca-
3	Tri-	7	Hepta-	20	Eico-
4	Tetra-	8	Octa-		

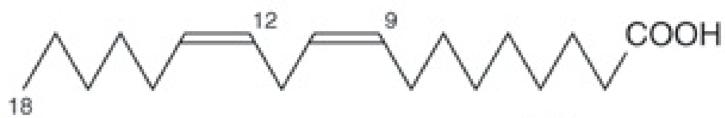
Naming of a fatty acid

- Alkane to oic
  - Octadecane (octa and deca) is octadecanoic acid
    - One double bond = octadecenoic acid
    - Two double bonds = octadecadienoic acid
    - Three double bonds = octadecatrienoic acid
- Designation of carbons and bonds
  - 18:0 = a C18 fatty acid with no double bonds
    - stearic acid (18:0); palmitic acid (16:0)
  - 18:2 = two double bonds (linoleic acid)
- Designation of location of bonds
  - Δ^n: The position of a double bond
    - cis-Δ^9 :a cis double bond between C 9 and 10
    - trans-Δ^2:a trans double bond between C 2 and 3

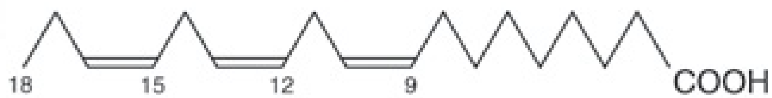
Palmitoleic acid (ω7, 16:1, Δ^{9})



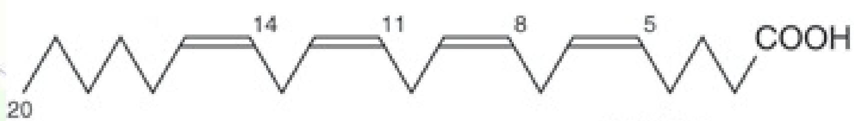
Oleic acid (ω9, 18:1, Δ^{9})



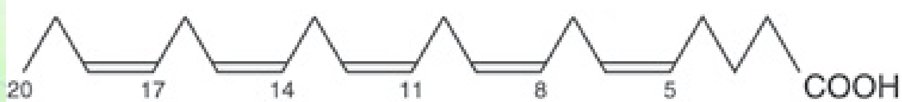
***Linoleic acid (ω6, 18:2, $\Delta^{9,12}$)**



***α-Linolenic acid (ω3, 18:3, $\Delta^{9,12,15}$)**



***Arachidonic acid (ω6, 20:4, $\Delta^{5,8,11,14}$)**

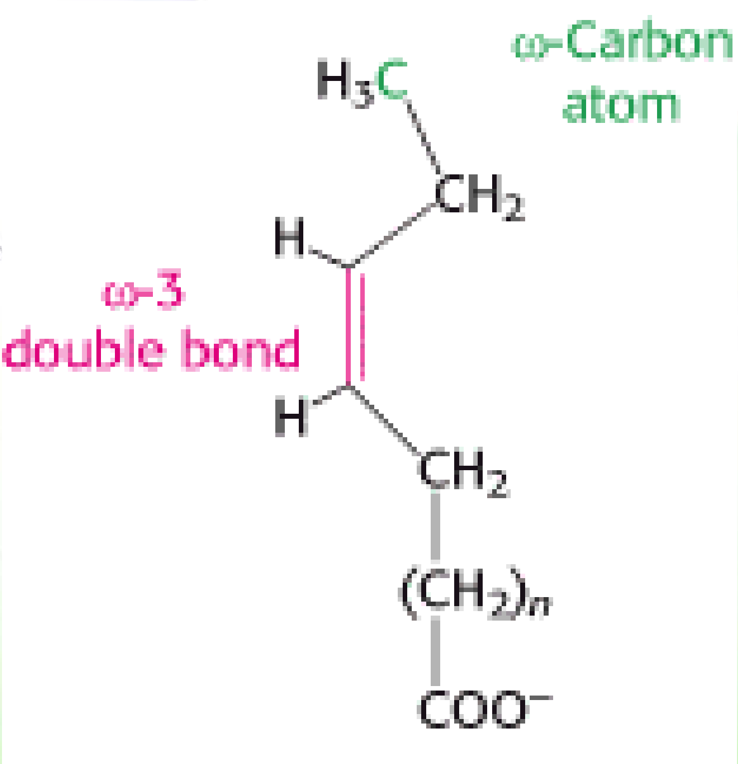


Eicosapentaenoic acid (ω3, 20:5, $\Delta^{5,8,11,14,17}$)

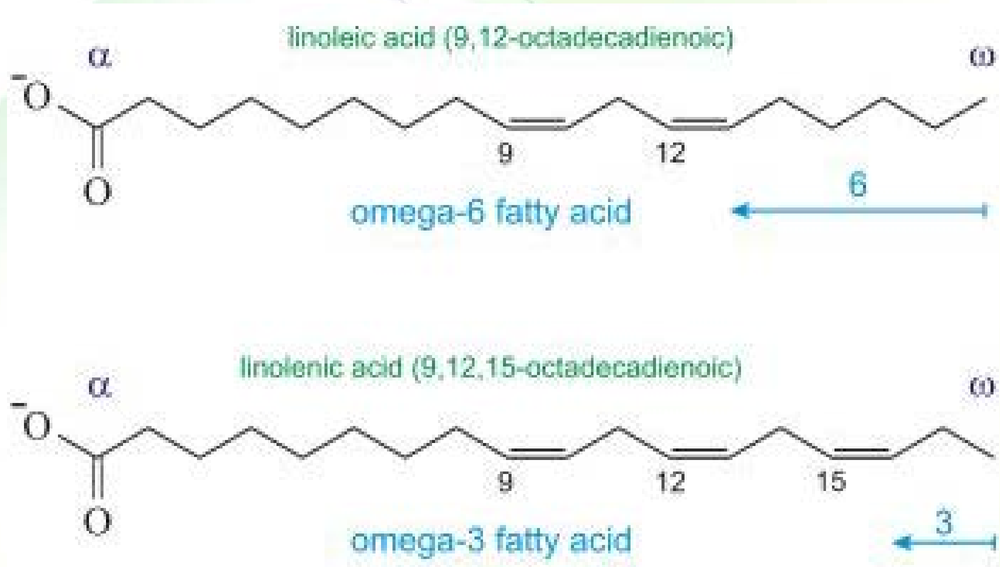
Number of carbons	Number of double bonds	Common name	Systematic name	Formula
14	0	Myristate	n-Tetradecanoate	$CH_3(CH_2)_{12}COO^-$
16	0	Palmitate	n-Hexadecanoate	$CH_3\ (CH_2)\ _{14}COO$-
18	0	Stearate	n-Octadecanoate	CH_3(CH2) $_{16}COO$-
18	1	Oleate	cis-Δ^9-Octadecenoate	$CH_3(CH_2)\ _7CH{=}CH(CH_2)\ _7COO$-
18	2	Linoleate	cis,cis-Δ^9,Δ^{12}-Octadecadienoate	$CH_3(CH_2)\ _2(CH{=}CHCH_2)\ _2(CH_2)\ _6COO$-
18	3	Linolenate	all-cis-$\Delta^9,\Delta^{12},\Delta^{15}$-Octadecatrienoate	$CH_3CH_2(CH{=}CHCH_2)\ _3(CH_2)\ _6COO$-
20	4	Arachidonate	all-cis-$\Delta^5,\Delta^8,\Delta^{11},\Delta^{14}$-Eicosatetraenoate	$CH_3\ _(CH_2)\ _4(CH{=}CHCH_2)\ _4(CH_2)\ _2COO$-

Another way of naming

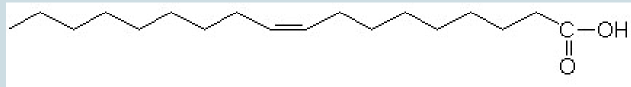
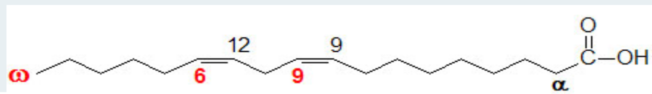
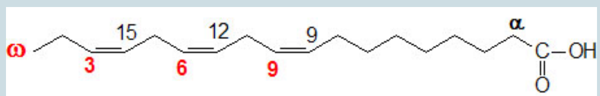
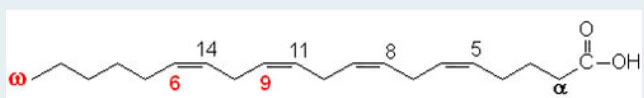
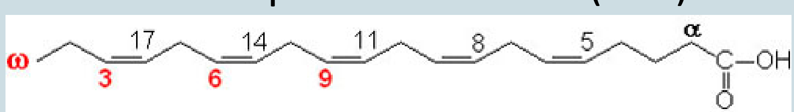
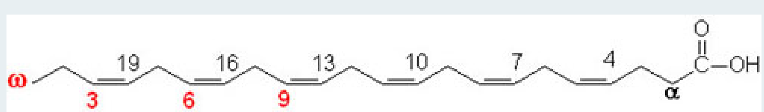
- (ω)-C: distal methyl C as #1



An ω-3 fatty acid



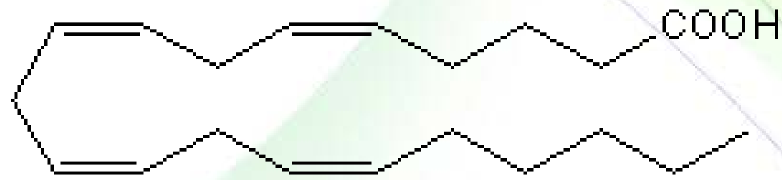
- **Linoleic acid: precursor of arachidonates**
- **Linolenic acid: precursor of EPA and DHA**

Numerical Symbol	Common Name and Structure	Comments
$18{:}1^{\Delta 9}$	Oleic acid 	Omega-9 monounsaturated
$18{:}2^{\Delta 9,12}$	Linoleic acid 	Omega-6 polyunsaturated
$18{:}3^{\Delta 9,12,15}$	α-Linolenic acid (ALA) 	Omega-3 polyunsaturated
$20{:}4^{\Delta 5,8,11,14}$	Arachidonic acid 	Omega-6 polyunsaturated
$20{:}5^{\Delta 5,8,11,14,17}$	Eicosapentaenoic acid (EPA) 	Omega-3 polyunsaturated (fish oils)
$22{:}6^{\Delta 4,7,10,13,16,19}$	Docosahexaenoic acid (DHA) 	Omega-3 polyunsaturated (fish oils)

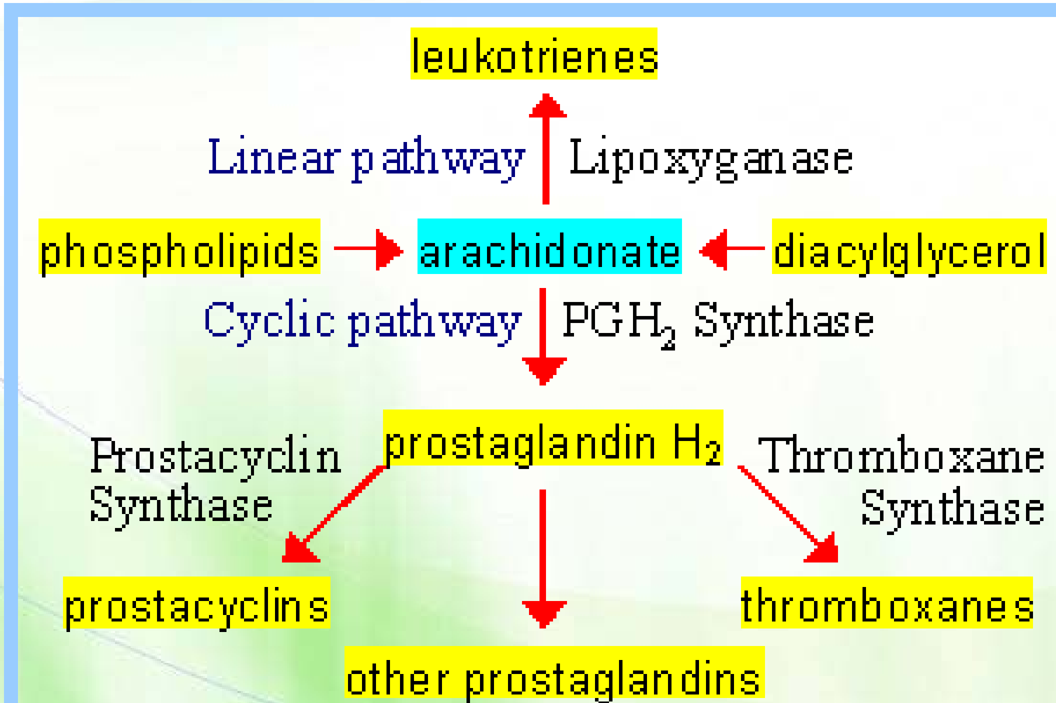
Derived fatty acids: Eicosanoids

Arachidonate

- all *cis*-$\Delta^5,\Delta^8,\Delta^{11},\Delta^{14}$-eicosatetraenoate, $CH_3(CH_2)_4(CH=CHCH_2)_4(CH_2)_2COO^-$

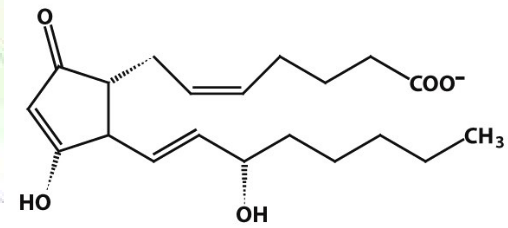


Arachidonic acid

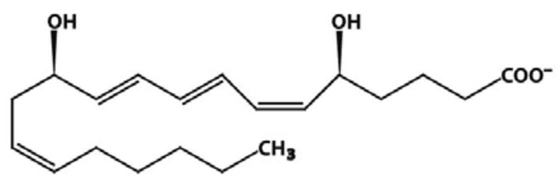


Eicosanoids and their functions

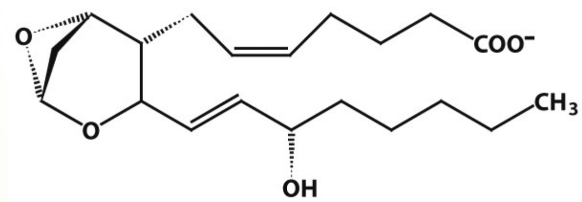
- Prostaglandins
  - Inhibition of platelet aggregation
    - Blood clotting
- Leukotrienes
  - Constriction of smooth muscles
    - Asthma
- Thromboxanes
  - Constriction of smooth muscles
  - Platelet aggregation
- Prostacyclins
  - An inhibitor of platelet aggregation
  - A vasodilator



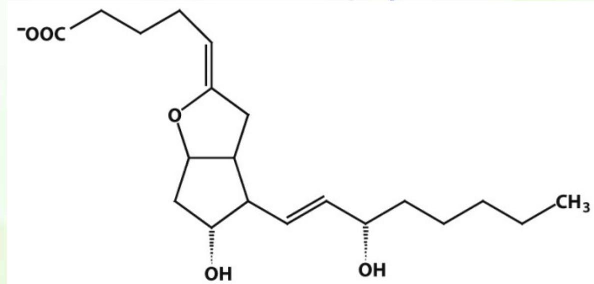
Prostaglandin E_2



Leukotriene B_4



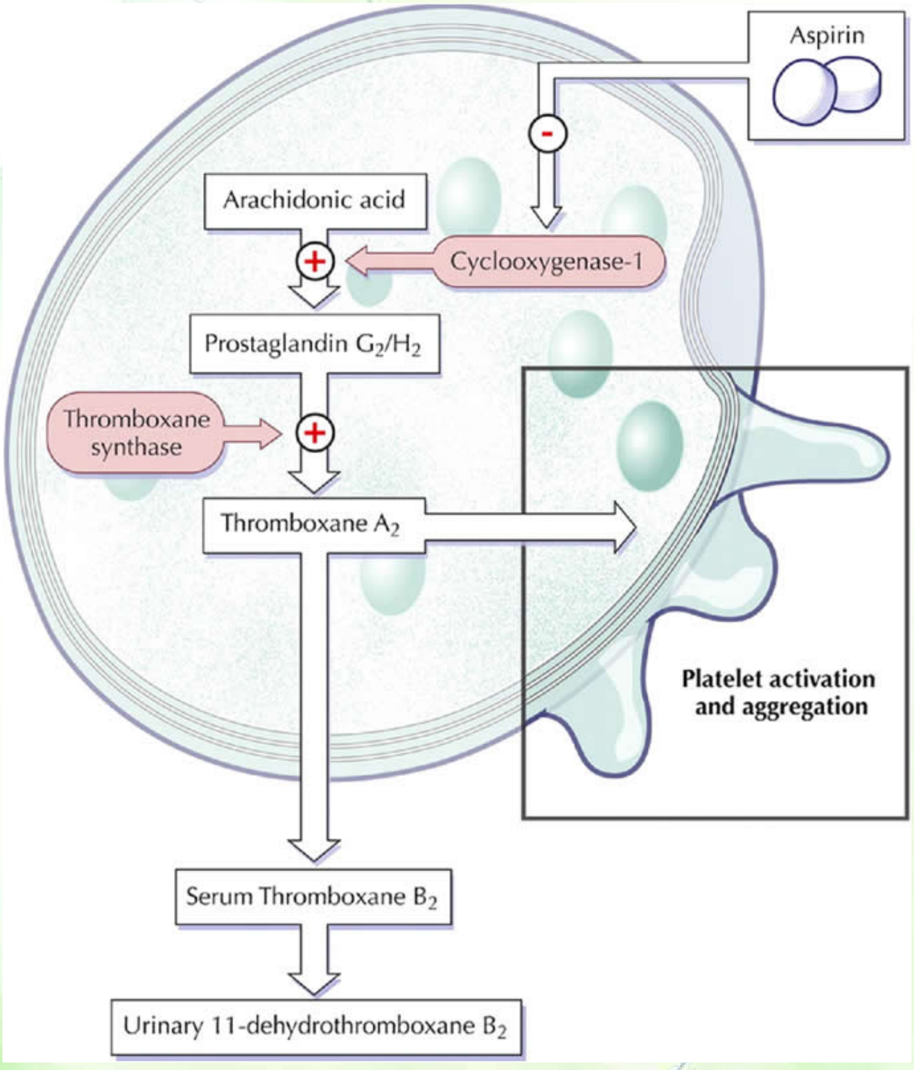
Thromboxane A_2 (TXA_2)



Prostacyclin (PGI_2)

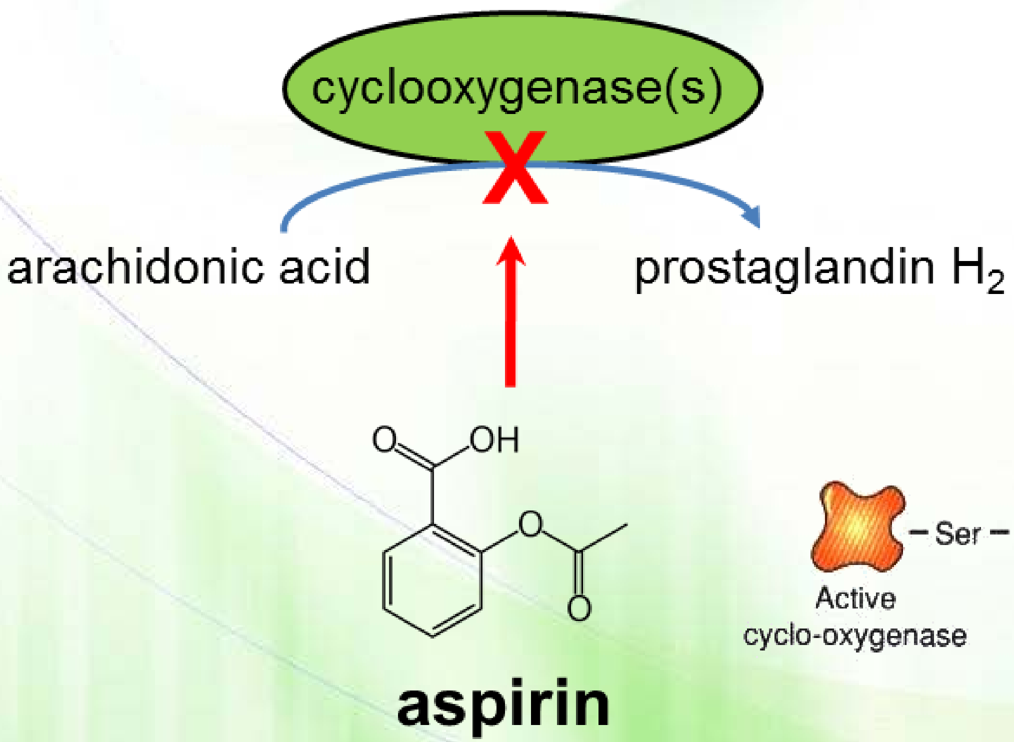
Aspirin and the heart

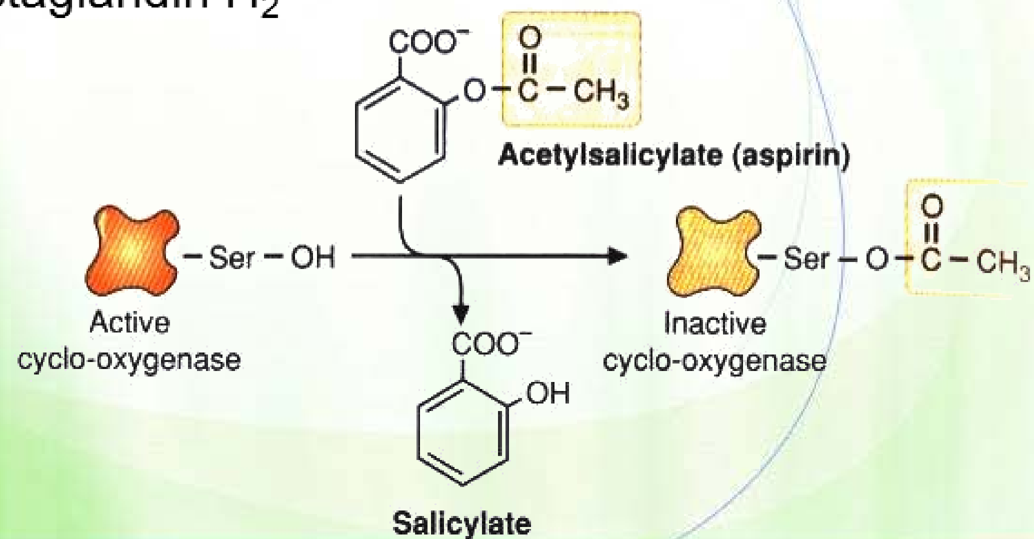
- Thromboxane A2 leads to platelet activation and aggregation.
- Aspirin acts as a potent antiplatelet agent by inhibiting cyclooxygenase preventing thromboxane A2 (TXA2) generation.



Aspirin

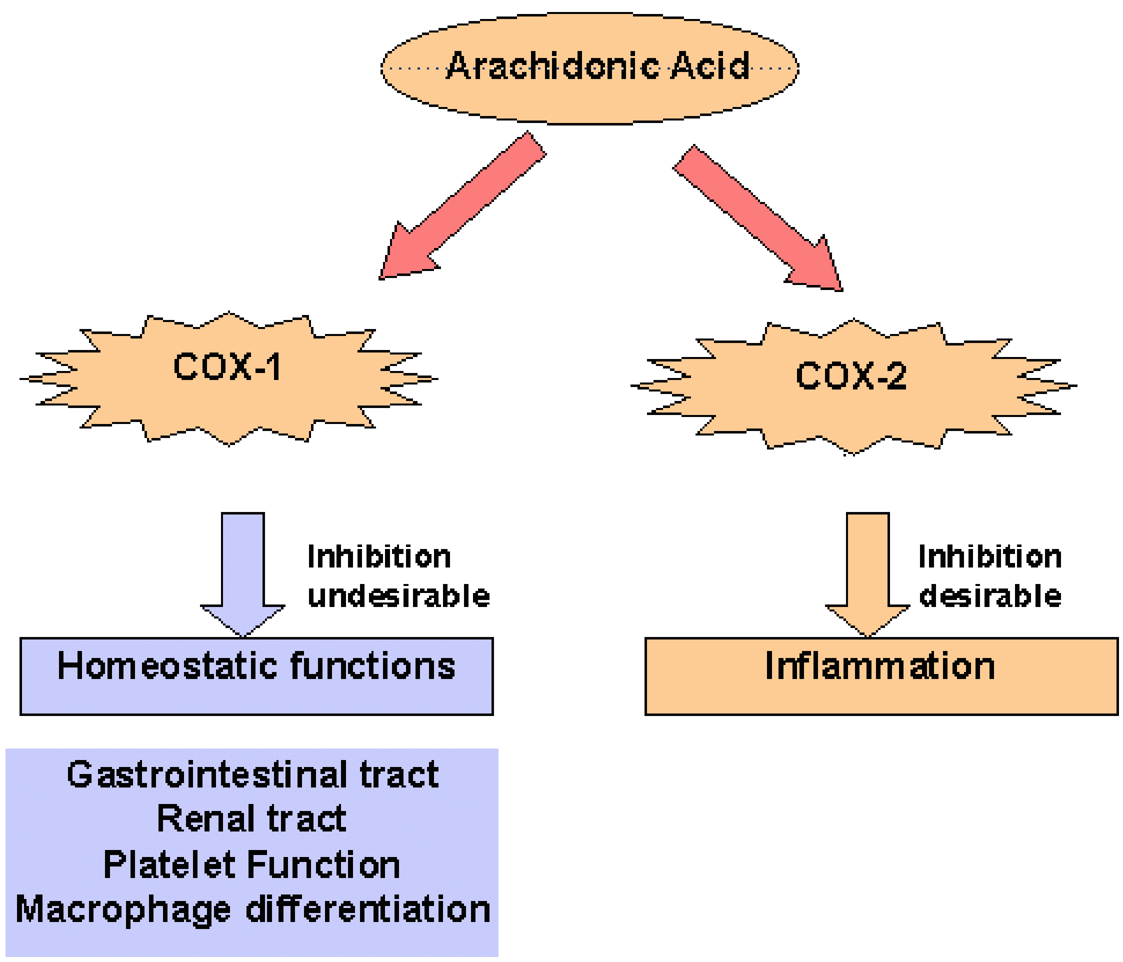
- Aspirin is anti-inflammatory and fever-reducing (antipyretic).
- It irreversibly inhibits cyclooxygenase (COX), the enzyme that catalyzes conversion of arachidonic acid to prostaglandins.





Targets of Aspirin

- Cyclooxygenase is present in two forms in cells, COX-1 and COX-2.
- Aspirin targets both, but COX-2 should only be the target.



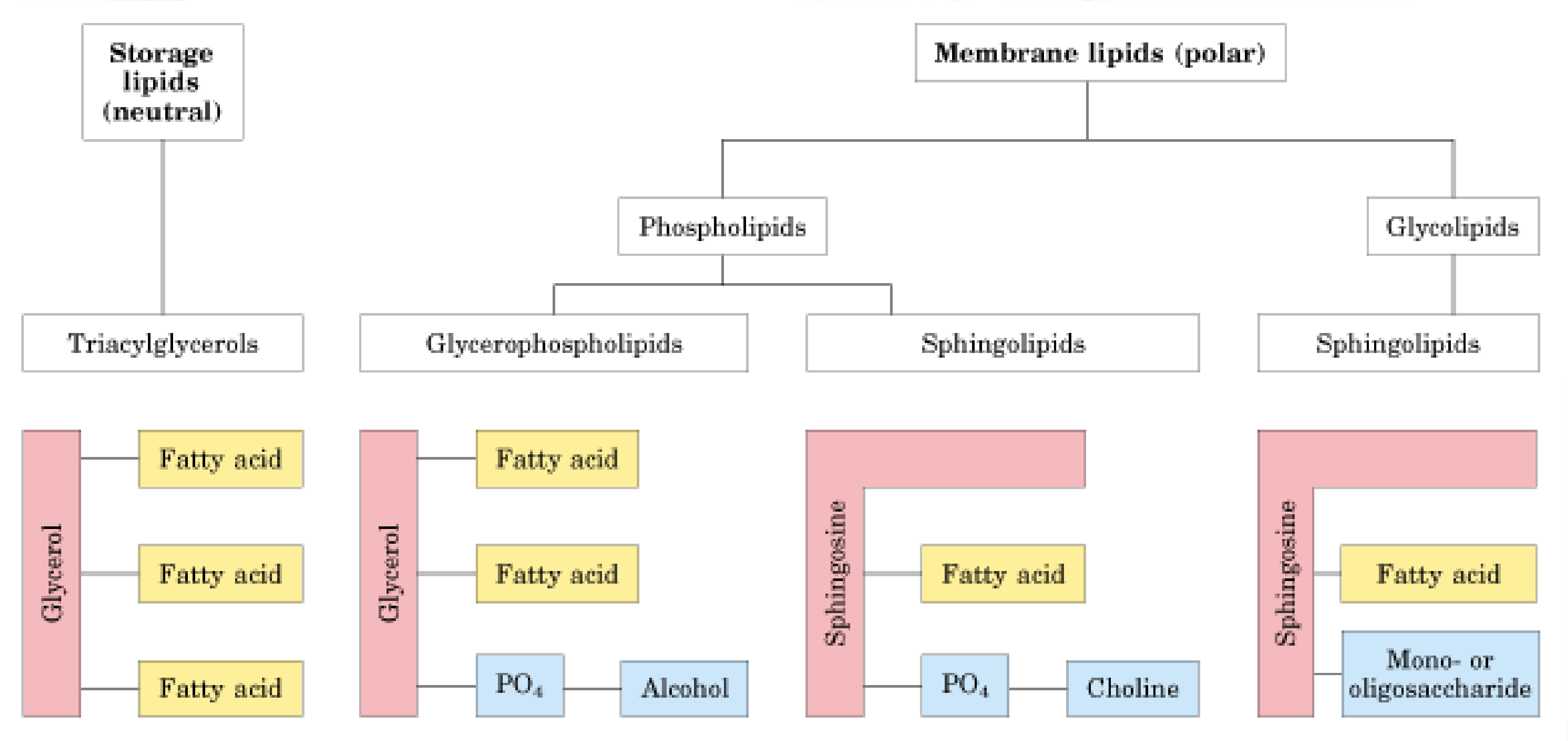
Celebrex

- A new generation drug, Celebrex, targets COX2, but is prescribed with a strong warning of side effects on the label.

Omega fatty acids

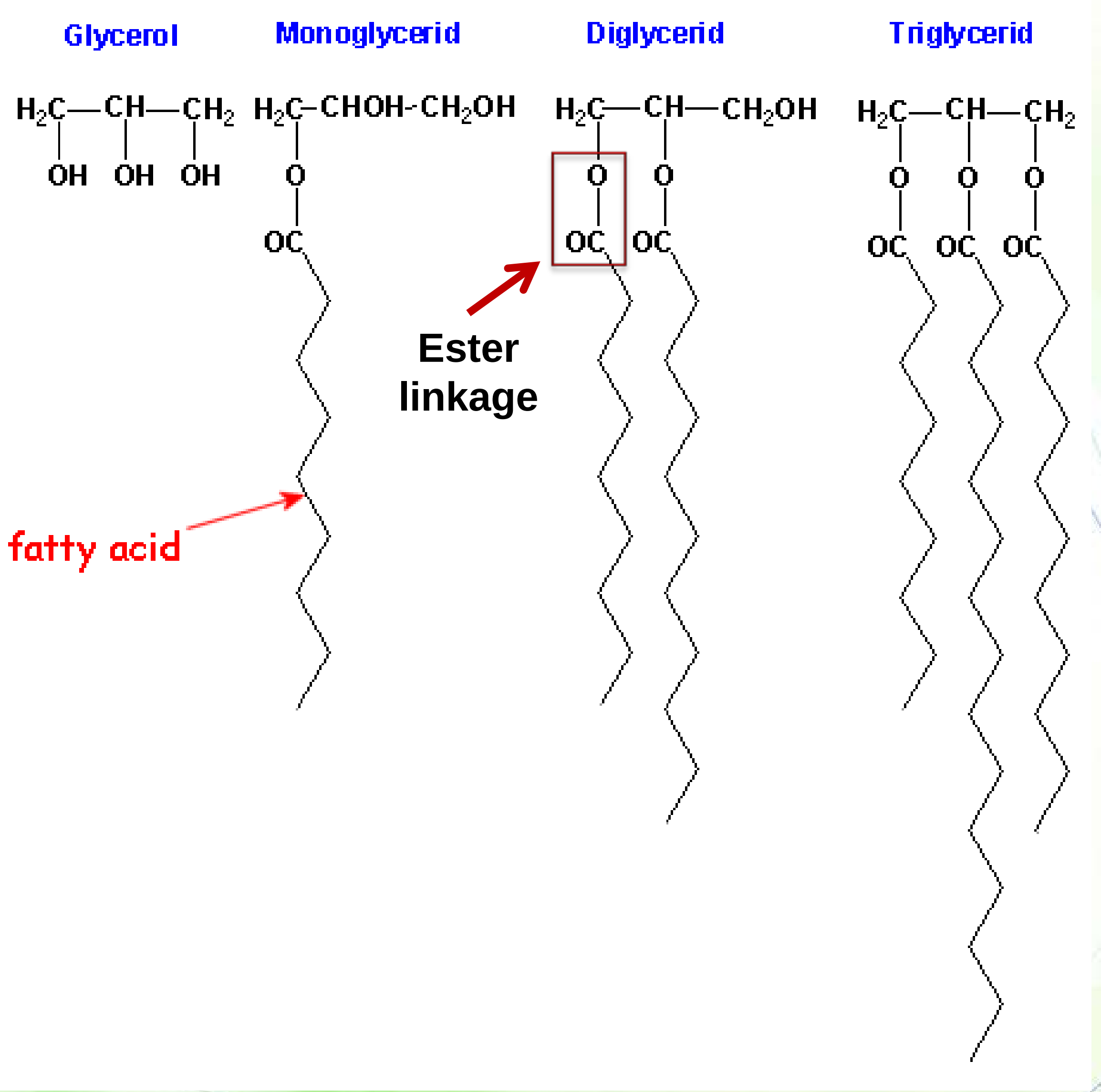
- Omega-3 fatty acids
  - α-linolenic acid → eicosapentaenoic acid (EPA) → docosahexaenoic acid (DHA)
    - They reduce inflammatory reactions by:
      - Reducing conversion of arachidonic acid into eicosanoids
      - Promoting synthesis of anti-inflammatory molecules
- Omega-6 fatty acids:
  - Arachidonic acid
    - stimulates platelet and leukocyte activation,
    - signals pain,
    - Induces bronchoconstriction,
    - regulates gastric secretion
- Omega-9 fatty acids
  - Oleic acid
    - Reduces cholesterol in the circulation

Complex lipids

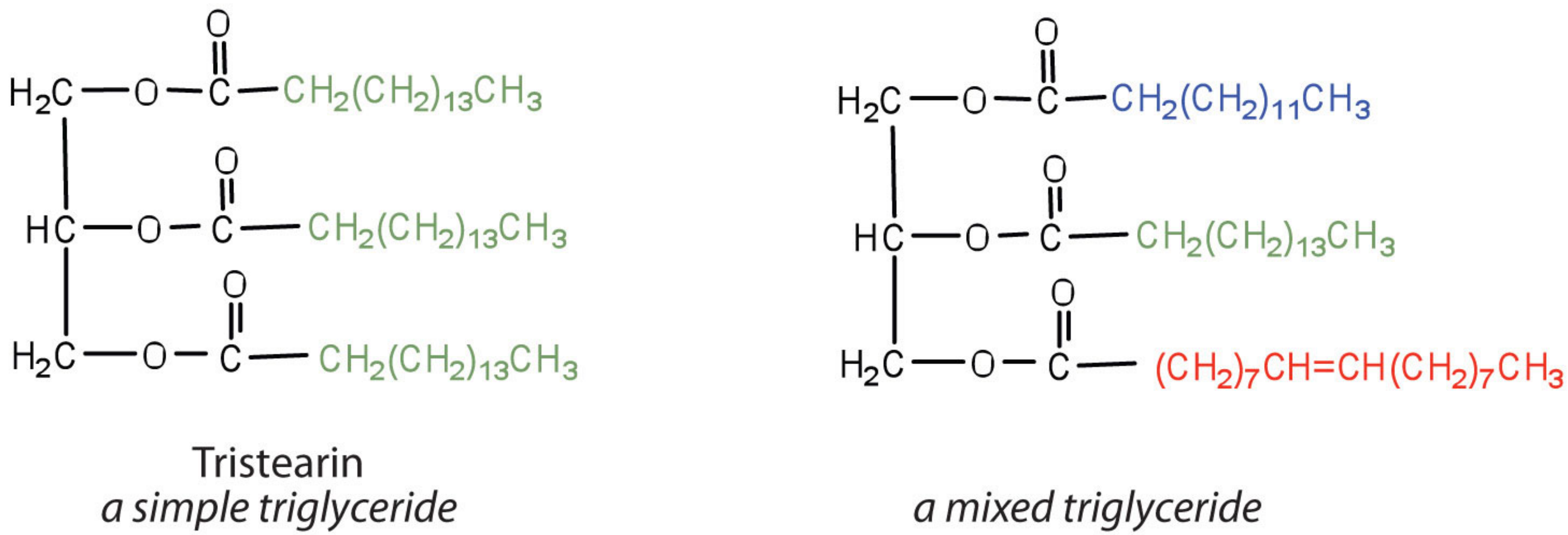


Storage lipids (neutral)
Membrane lipids (polar)
Phospholipids
Glycolipids
Triacylglycerols
Glycerophospholipids
Sphingolipids
Sphingolipids
Glycerol
Fatty acid
Fatty acid
Fatty acid
Glycerol
Fatty acid
Fatty acid
PO4
Alcohol
Sphingosine
Fatty acid
PO4
Choline
Sphingosine
Fatty acid
Mono- or oligosaccharide

Triglycerides



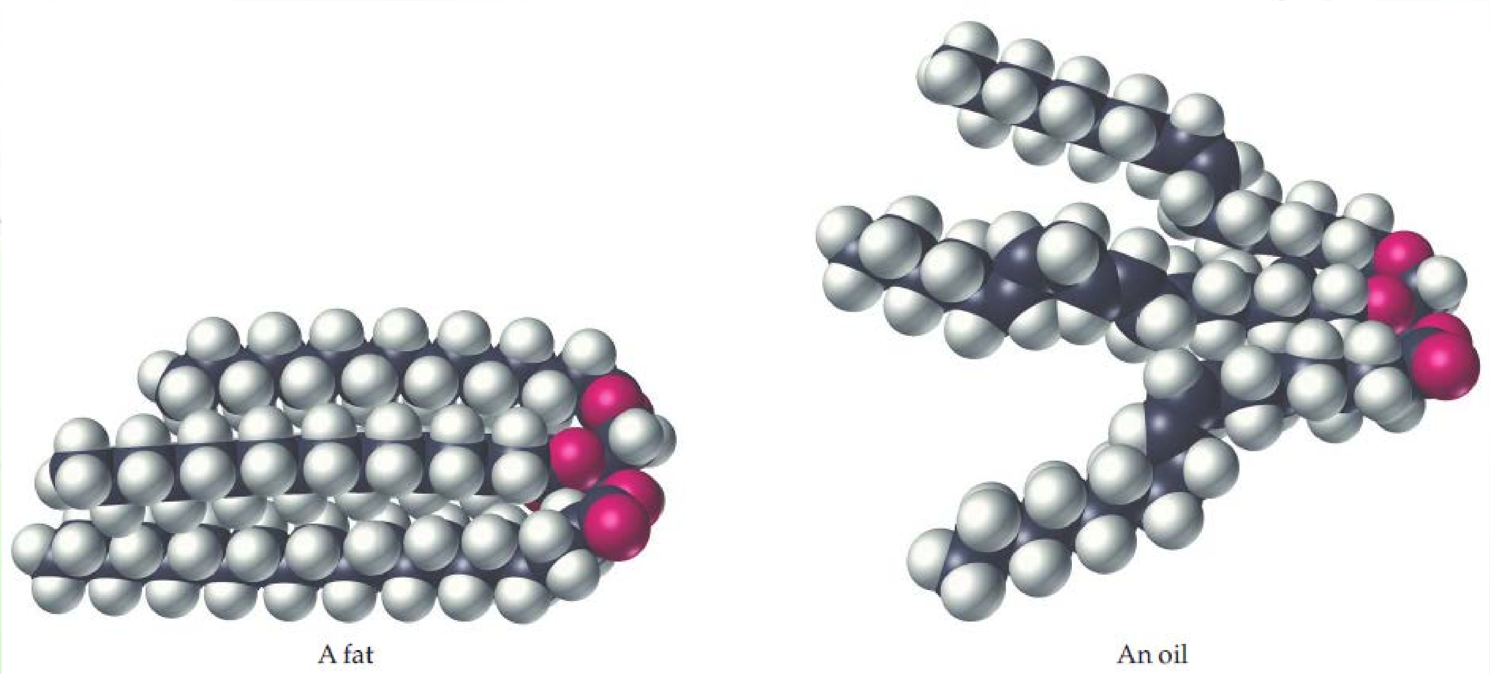
Types of glycerides



How soluble will a triglyceride be if fatty acids are unsaturated?

Solid vs. liquid fats

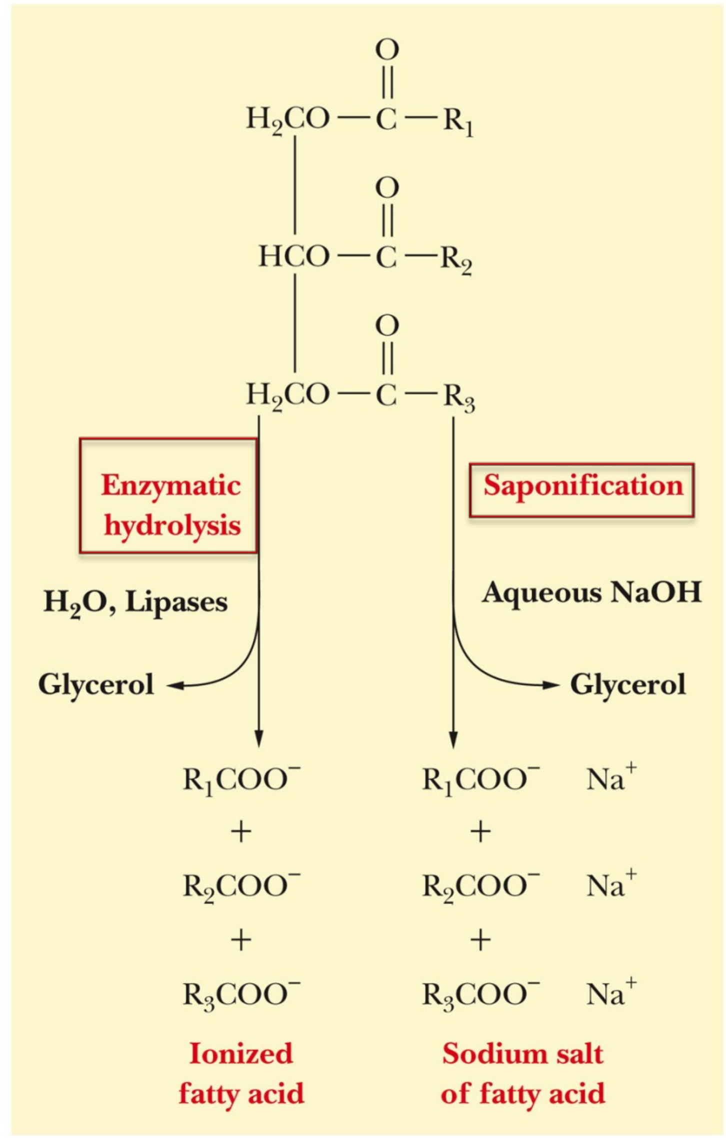
- Vegetable oils consist almost entirely of unsaturated fatty acids, whereas animal fats contain a much larger percentage of saturated fatty acids.
  - This is the primary reason for the different melting points of fats and oils



Saponification

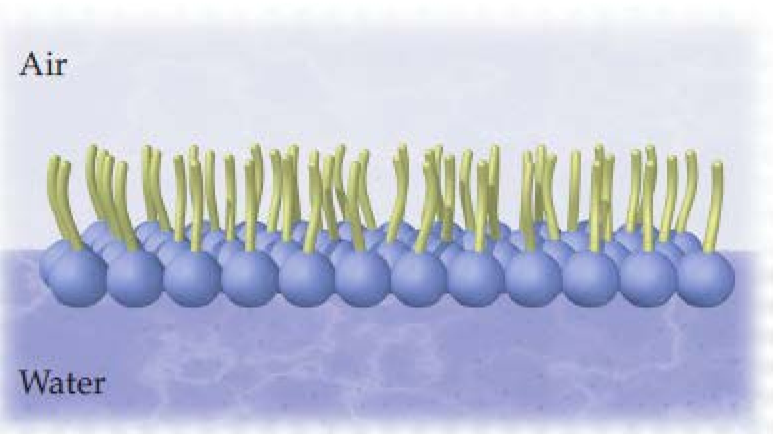
- Hydrolysis : steam, acid, enzyme (e.g., lipase of pancreas)

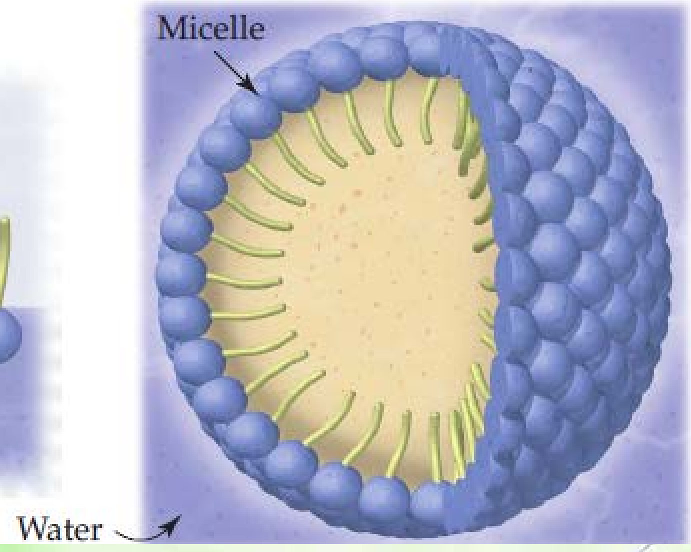
- Saponification: Alkaline hydrolysis produces salts of fatty acids (soaps). Soaps cause emulsification of oily material



How does soap work?

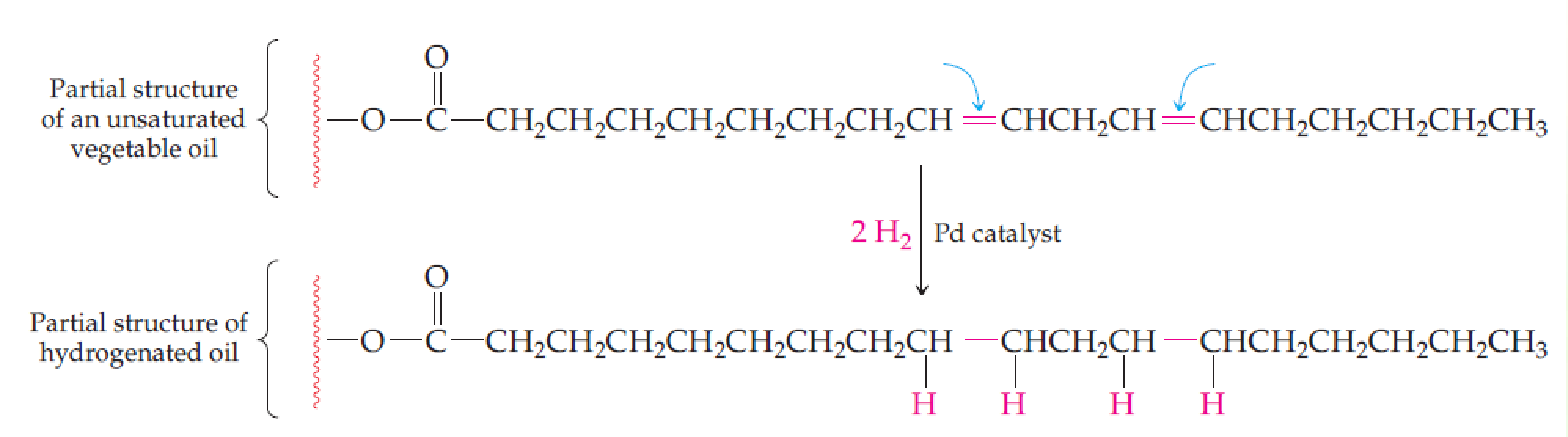
- When mixed with water, the hydrophobic hydrocarbon tails cluster together to create a nonpolar microenvironment and the hydrophilic ionic heads interact with water.
- The resulting spherical clusters are called **micelles.**
- Grease and dirt are trapped inside micelles and the complex can be rinsed away.





Hydrogenation

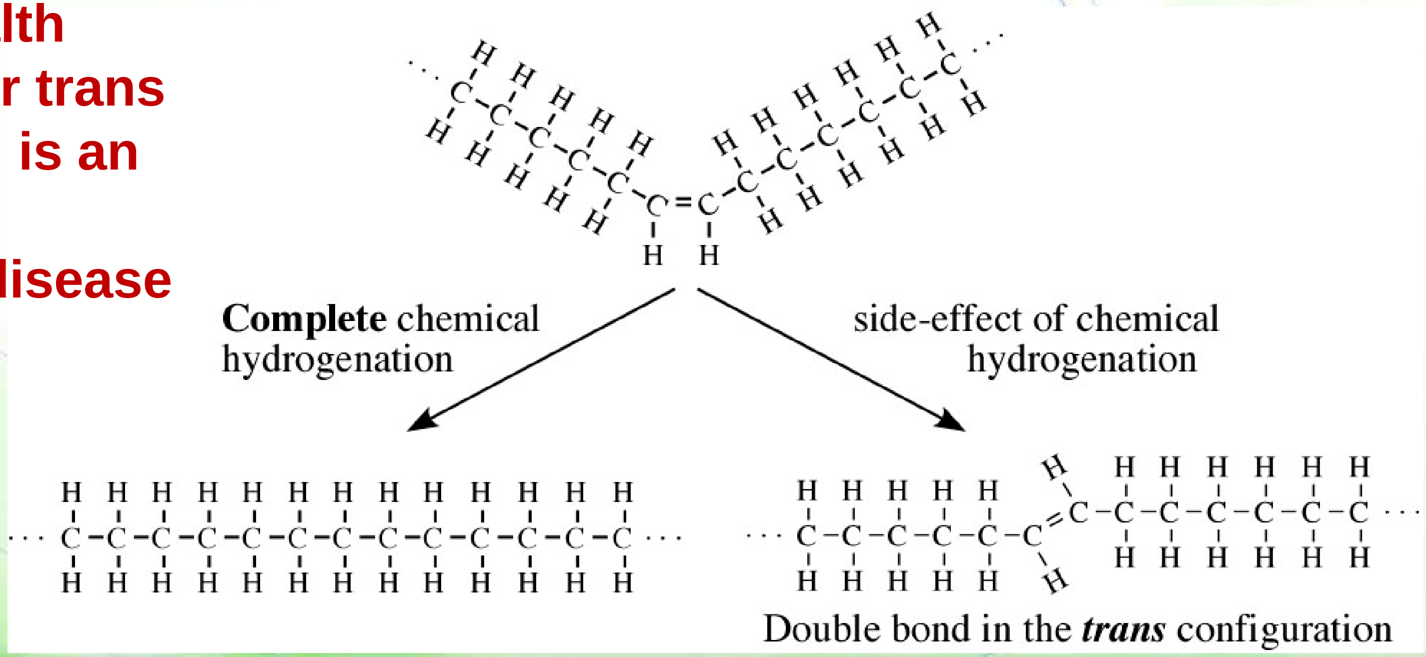
- The carbon-carbon double bonds in vegetable oils can be hydrogenated to yield saturated fats in the same way that any alkene can react with hydrogen to yield an alkane.



Trans fat

- Although the animal fat is unhealthy, it has better cooking properties and better taste.
- Therefore, chemists invented a method of converting unsaturated fat into solid form by partially hydrogenating it.
- Partial hydrogenation converts some, but not all, double bonds into single bonds generating (trans fats).

The primary health risk identified for trans fat consumption is an elevated risk of coronary heart disease (CHD).



Example: margarine

- In margarine, only about two-thirds of the double bonds present in the starting vegetable oil are hydrogenated, so that the margarine remains soft in the refrigerator and melt on warm toast.

Nutrition Facts
Serv Size 1 Tbsp (14g)
Servings: About 24
Calories 80
Calories from Fat 80

Amount/Serving	% DV*	Amount/Serving	% DV*
Total Fat 8g	**12%**	**Cholesterol** 0mg	**0%**
Sat Fat 2.5g	**13%**	**Sodium** 85mg	**4%**
Trans Fat 0g		**Total Carb** 0g	**0%**
Polyunsat Fat 3g		Sugars 0g	
Monounsat Fat 2.5g		**Protein** 0g	

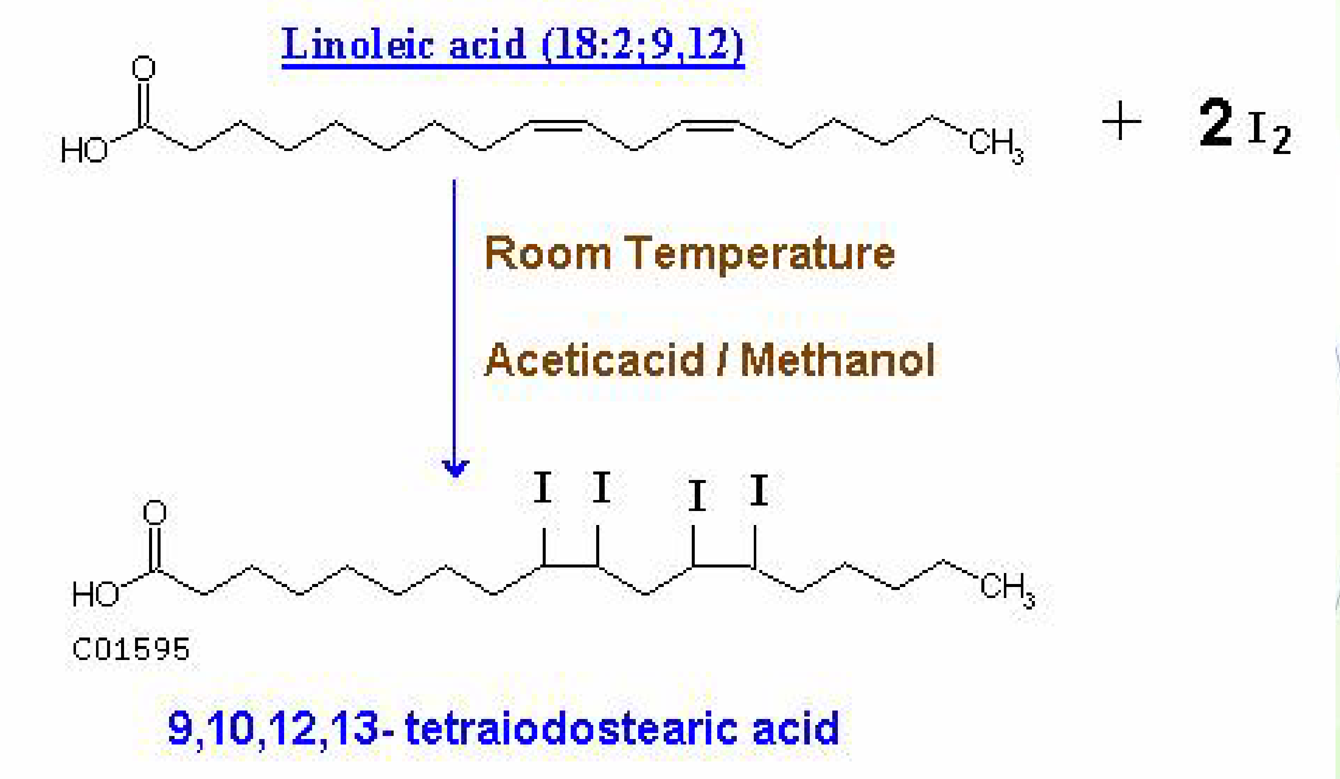
Vitamin A 15% • Vitamin D 15%
Vitamin B6 35% • Vitamin B12 20% • Vitamin E 15%
Not a significant source of dietary fiber, Vitamin C, Calcium and Iron

*Percent Daily Values (DV) are based on a 2,000 calorie diet.

INGREDIENTS: Natural Oil Blend (palm fruit, soybean, fish, canola and olive oils), water, plant sterols; contains less than 2% of salt, sorbitan esters of fatty acids, monoglycerides of vegetable fatty acids, natural and artificial flavors, TBHQ (to preserve freshness), potassium sorbate, lactic acid, soy lecithin, vitamin B12, vitamin E acetate,vitamin B6, beta carotene (color), vitamin A palmitate, calcium disodium EDTA, Vitamin D3.

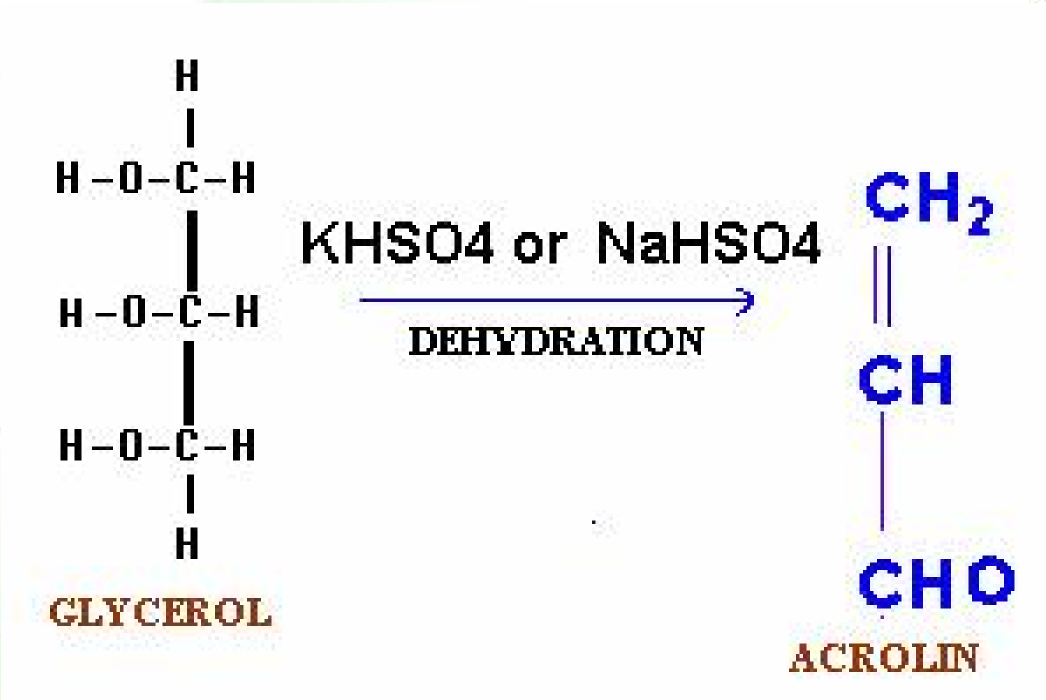
Chemical Properties of fats & oils

- Halogenation: added to unsaturated F.A (e.g., iodination)
  - Used to determine the degree of unsaturation of the fat or oil that determines its biological value



Acrolin test

- When fats are heated in the presence of a dehydrating agent, NaHSO4 or KHSO4, they produce unsaturated aldehydes called acrolin from the glycerol moiety.
- Acrolin easily recognized by its strong odour and thus forms the basis of the test for the presence of glycerol in fat molecule.



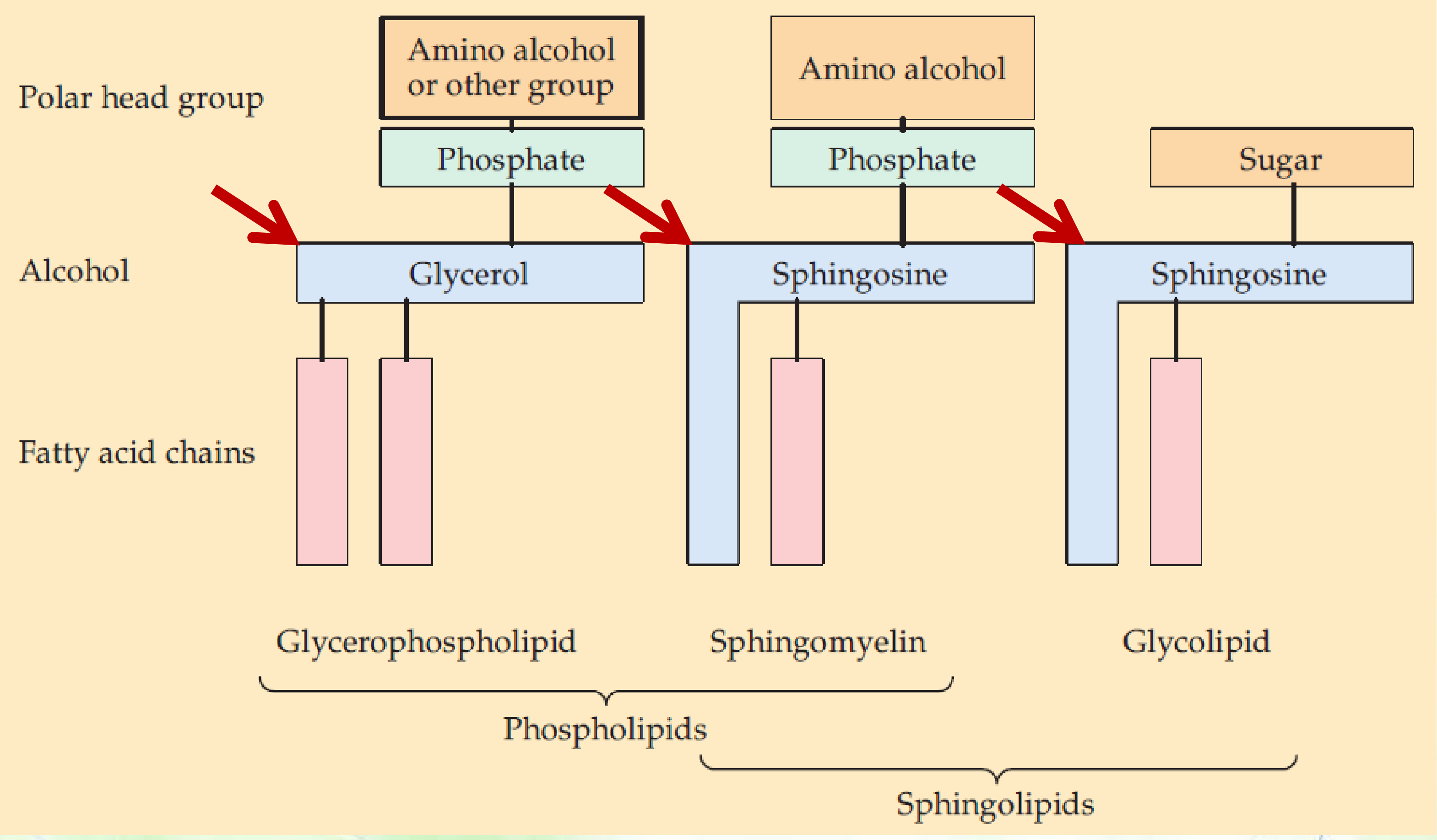
Waxes

$$\underbrace{CH_3(CH_2)_{14}-\overset{\overset{\displaystyle O}{\|}}{C}}_{\text{Palmitic acid}}-\underbrace{O-CH_2-(CH_2)_{28}-CH_3}_{\text{Triacontanol}}$$

- Solid simple lipids containing a monohydric alcohol (C16 ~ C30, higher molecular weight than glycerol) esterified to long-chain fatty acids (C14 ~ C36). Examples: palmitoyl alcohol
- Insoluble in water & Negative to acrolein test
- Are not easily hydrolyzed (fats) & are indigestible by lipases
- Are very resistant to rancidity
- Are of no nutritional value
- Coatings that prevent loss of water by leaves of plants

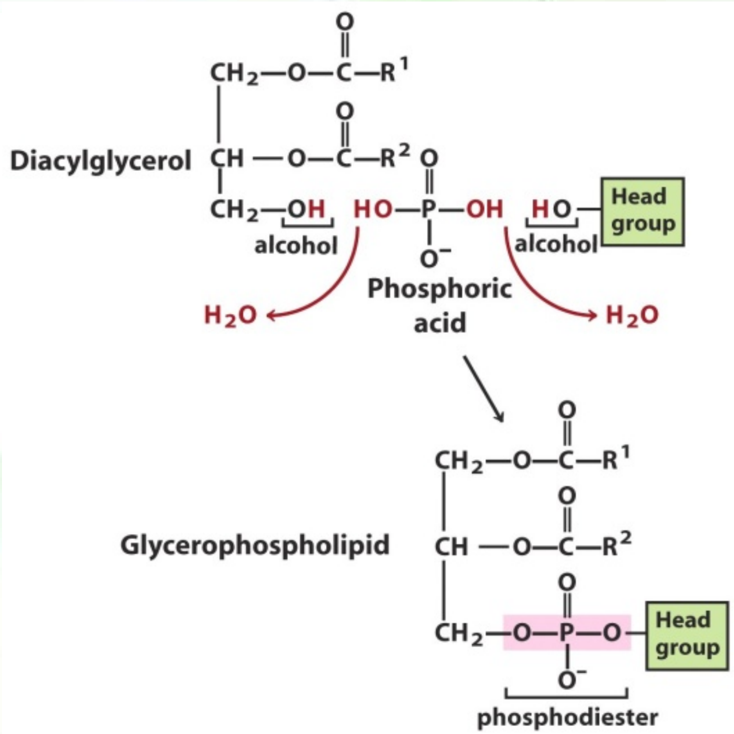
Type	Structural Formula	Source	Uses
Beeswax	$CH_3(CH_2)_{14}-\overset{\overset{O}{\|}}{C}-O-(CH_2)_{29}CH_3$	Honeycomb	Candles, shoe polish, wax paper
Carnauba wax	$CH_3(CH_2)_{24}-\overset{\overset{O}{\|}}{C}-O-(CH_2)_{29}CH_3$	Brazilian palm tree	Waxes for furniture, cars, floors, shoes
Jojoba wax	$CH_3(CH_2)_{18}-\overset{\overset{O}{\|}}{C}-O-(CH_2)_{19}CH_3$	Jojoba	Candles, soaps, cosmetics

Membrane lipids



The most prevalent class of lipids in membranes is the <u>glycerophospholipids</u>

Phospholipids (phosphoacylglycerols)



Phosphatidic acid	**—**	$-H$
Phosphatidylethanolamine	**Ethanolamine**	$-CH_2-CH_2-\overset{+}{N}H_3$
Phosphatidylcholine	**Choline**	$-CH_2-CH_2-\overset{+}{N}(CH_3)_3$
Phosphatidylserine	**Serine**	$-CH_2-\underset{COO^-}{CH}-\overset{+}{N}H_3$

Classification of Glycerophospholipids

- Phosphatidic acids
- Phosphatidylcholine (lecithins)
  - Most abundant membrane lipid
- Cephalins
  - Phosphatidylethanolamine
  - Phosphatidylserine
    - abundant in brain
- Phosphatidylinositol
  - sends messages across cell membranes
- Cardiolipin
- Plasmalogens

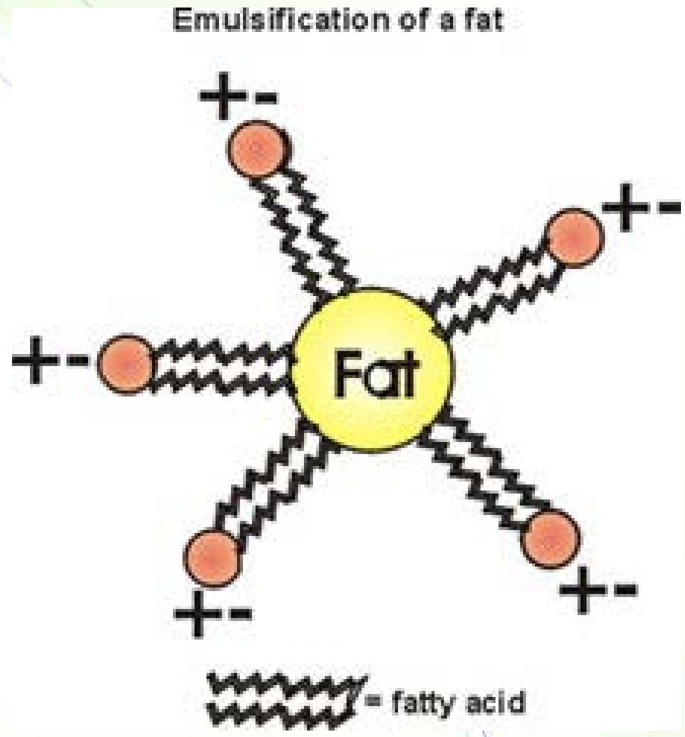
Glycerophospholipids - Lecithins

Phosphatidylcholine	Choline	$-CH_2-CH_2-\overset{+}{N}(CH_3)_3$

- Snake venom contain lecithinase, which hydrolyzes polyunsaturated fatty acids and converting lecithin into lysolecithin
  - hemolysis of RBCs

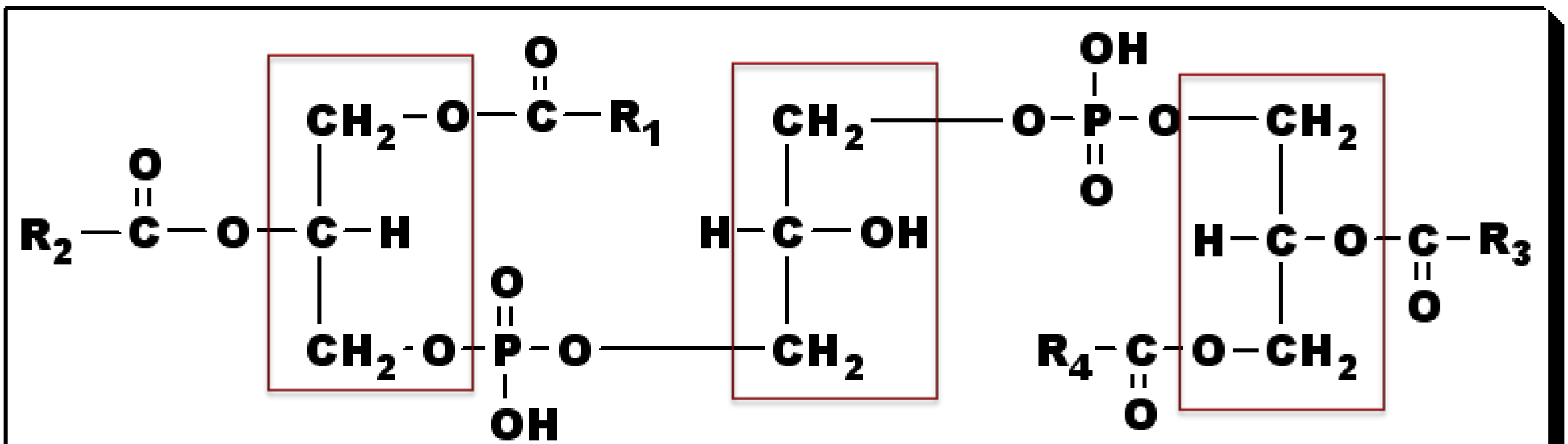
Emulsification

- Because of their amphipathic nature, they act as emulsifying agents, that is substances that can surround nonpolar molecules and keep them in suspension in water



Glycerophospholipids - Cardiolipins

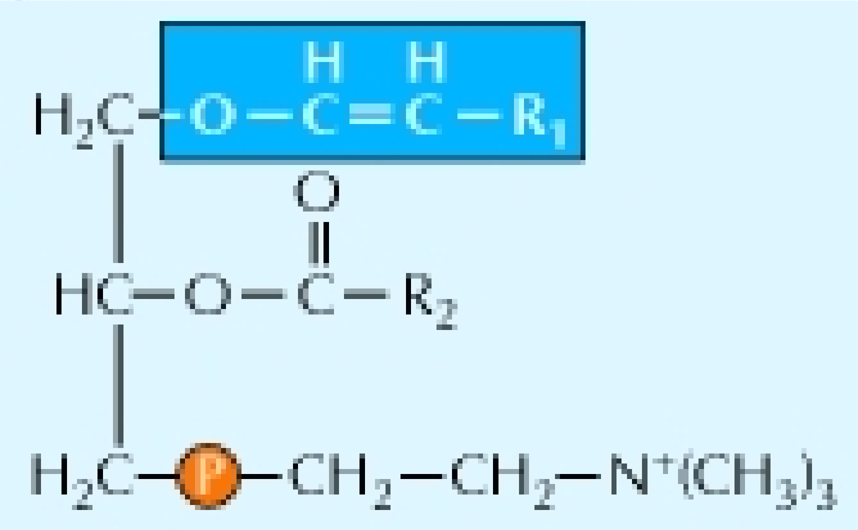
- Diphosphatidyl-glycerol
- Found in the inner membrane of mitochondria
- Initially isolated from heart muscle (cardio)
- Structure: 3 molecules of glycerol, 4 fatty acids & 2 phosphate groups

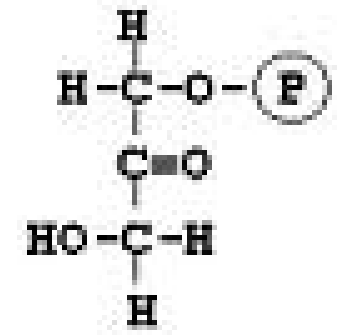


Cardiolipin

Plasmalogens

- They are found in the cell membrane phospholipids fraction of brain & muscle, liver, and semen.
- They have a protective role against reactive oxygen species
- Structure:
  - Precursor: Dihydroxyacetone phosphate
  - Unsaturated fatty alcohol at C1 connected by ether bond
  - In mammals: at C3; phosphate + ethanolamine or choline

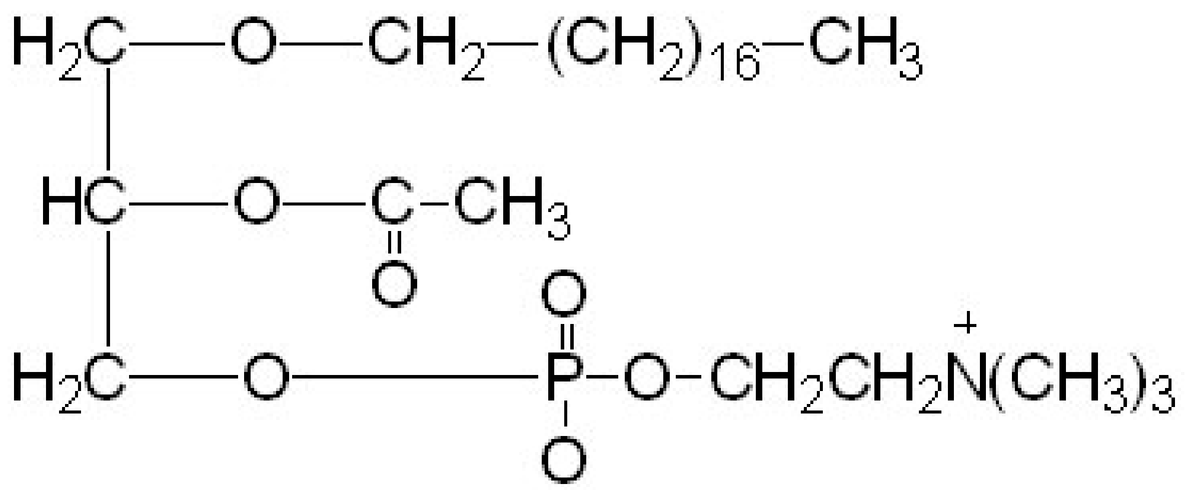




Dihydroxyacetone phosphate

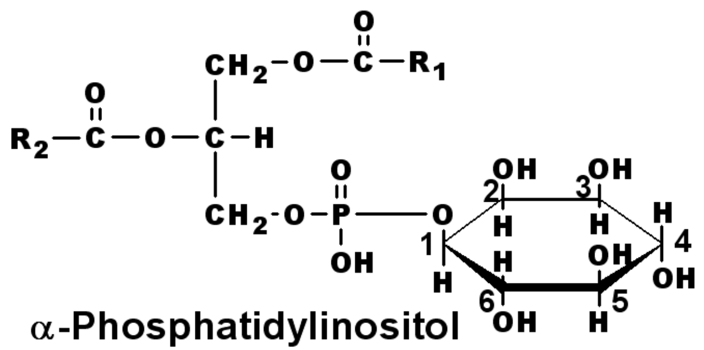
Major classes of plasmalogens

- Ethanolamine plasmalogen (myelin-nervous tissues)
- Choline plasmalogen (cardiac tissue)
  - Platelet activating factor
- Serine plasmalogens



Glycerophospholipids - Inositides

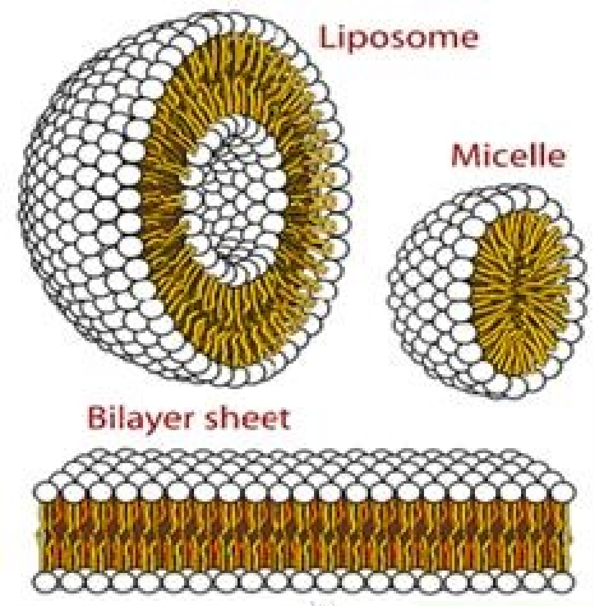
- Phosphatidyl inositol
- Nitrogenous base: cyclic sugar alcohol (inositol)
- Structure: glycerol, saturated FA, unsaturated FA, phosphoric acid, & inositol
- Source: Brain tissues



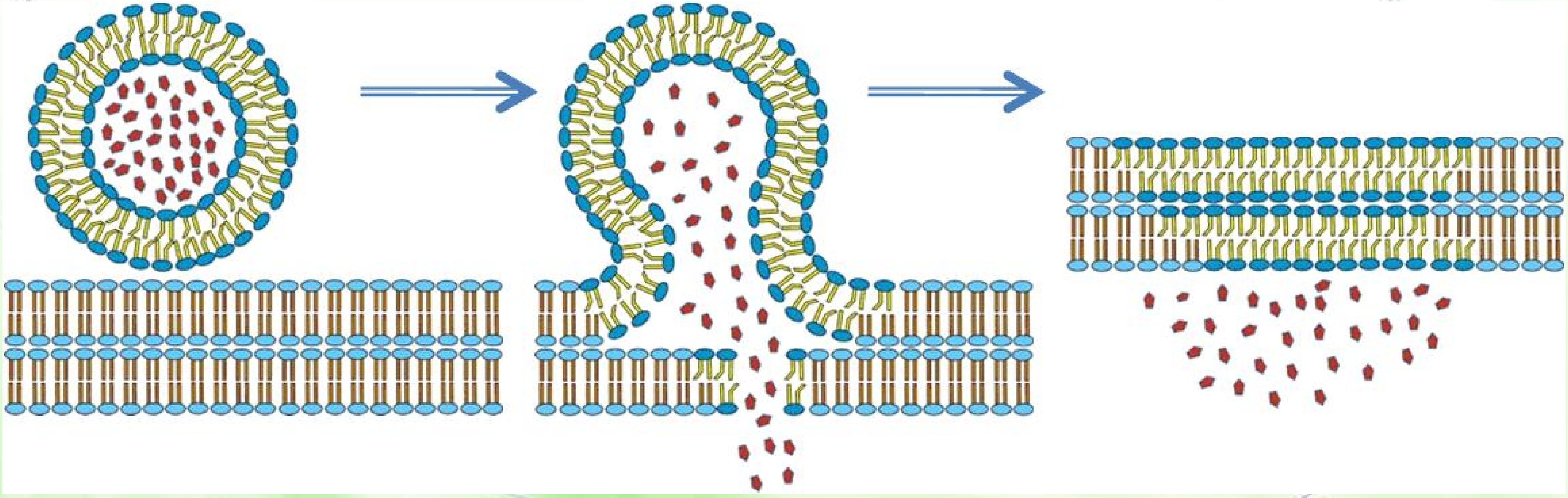
α-Phosphatidylinositol

- Functions:
  - Major component of cell membrane
  - Second messenger during signal transduction
  - On hydrolysis by phospholipase C, phosphatidyl-inositol-4,5-diphosphate produces diacyl-glycerol (DAG) & inositol-triphosphate (IP3); which liberates calcium

The different structures of phospholipids

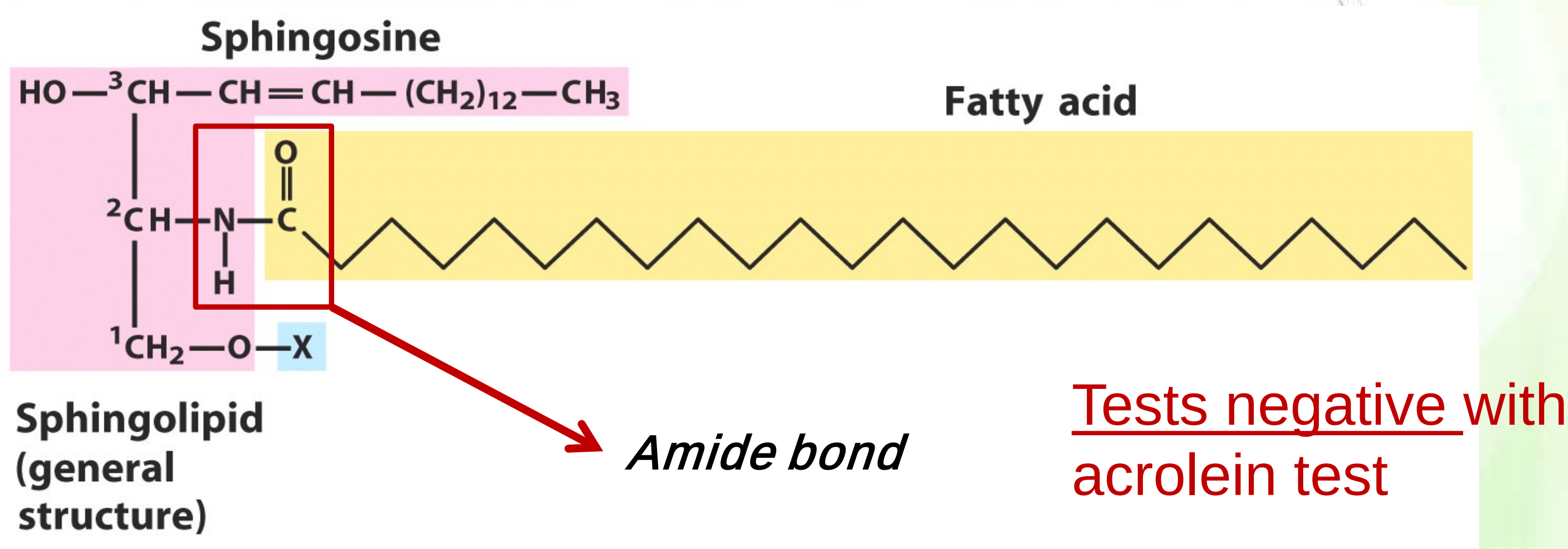


Uses of liposomes: delivery

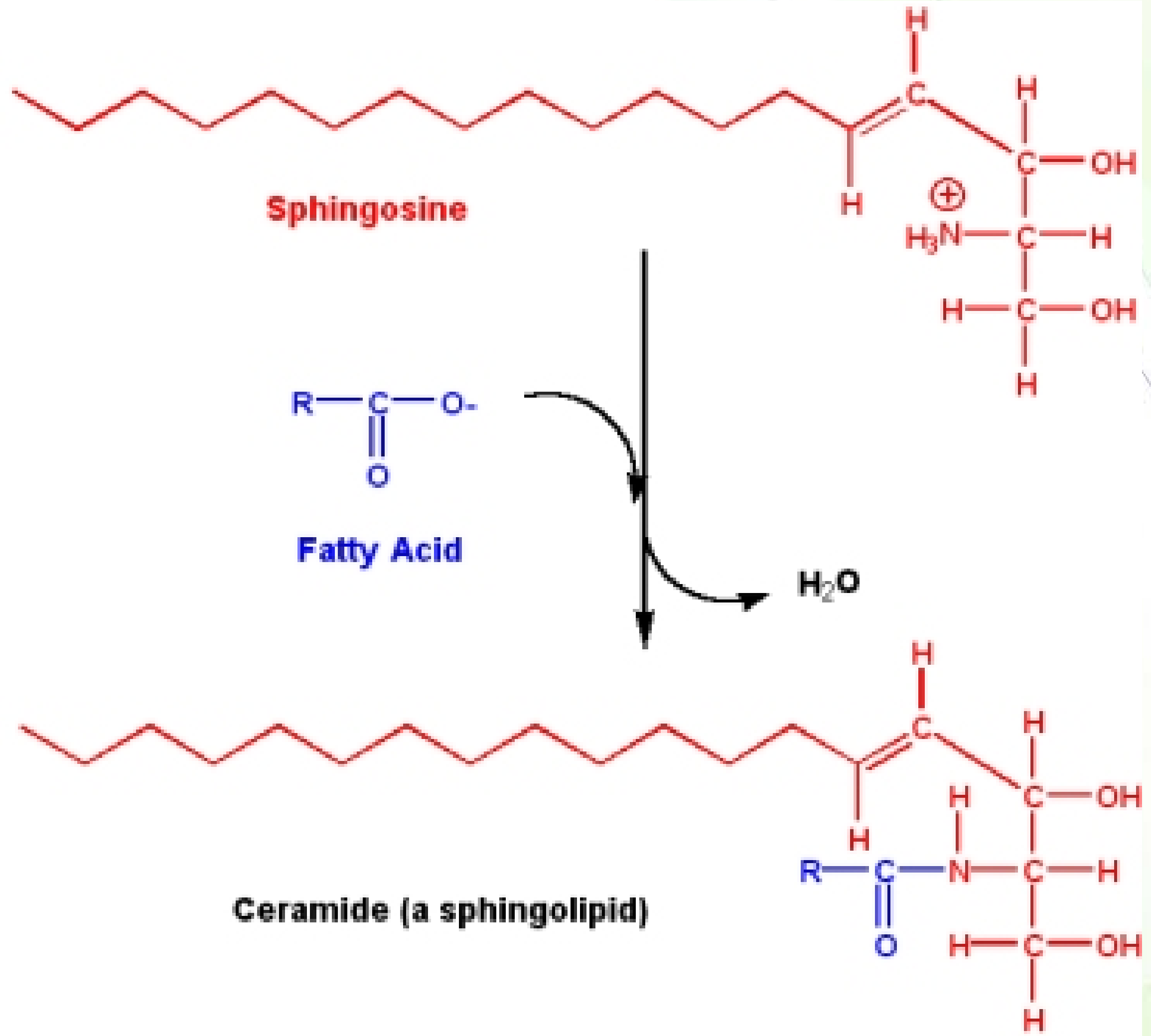


Sphingolipids

- Sphingolipids are found in the plasma membranes of all eukaryotic cells and is highest in the cells of the central nervous system
- The core of sphingolipids is the long-chain amino alcohol, sphingosine



Ceramide

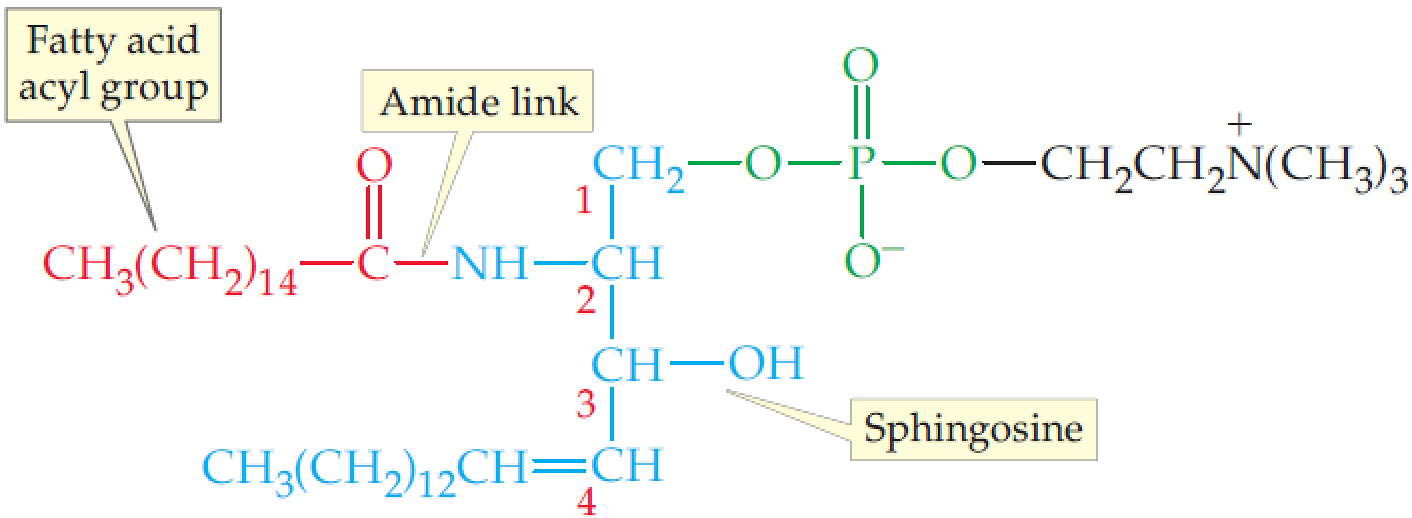


Types of sphingolipids

- The sphingolipids are divided into the two subcategories:
  - Sphingomyelins
  - Glycosphingolipid (or glycolipids)

Sphoingomyelin

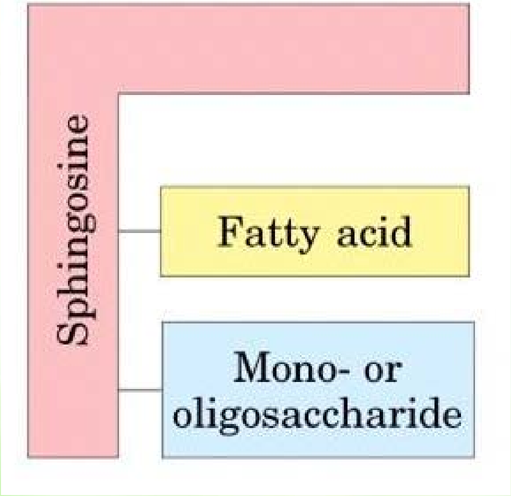
- Sphoingomyelin is a sphinglolipid that is a major component of the coating around nerve fibers
- The group attached to C1 is a phosphocholine



A sphingomyelin (a sphingolipid)

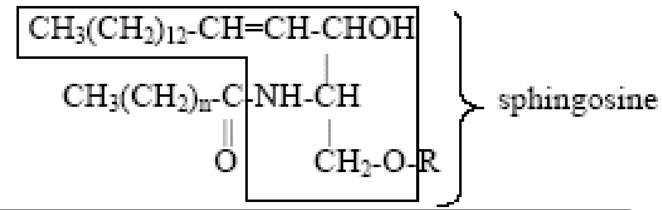
Glycolipids

- Sphingolipids can also contain carbohydrates attached at C-1 and these are known as glycolipids
- Glycolipids are present on cell membranes and act as cell surface receptors that can function in cell recognition (e.g., pathogens) and chemical messengers
- There are three types of glycolipids
  - Cerebrosides
  - Globosides
  - Gangliosides



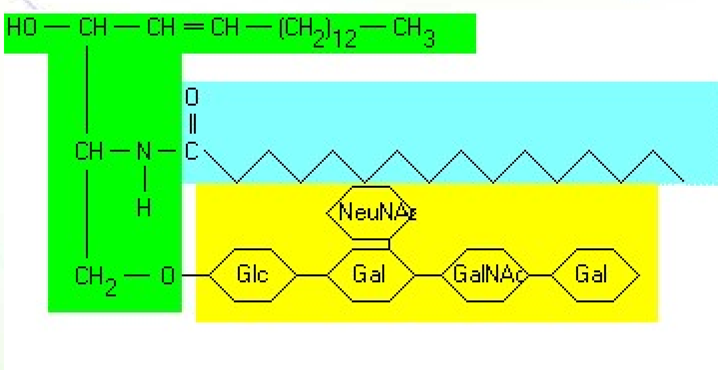
Glycolipids

- **Cerebrosides: the simplest glycolipids, contain a single hexose (galactose or glucose).**
- **Globosides and gangliosides are more complex glycolipids.**
- **Both contain glucose, galactose, and N-acetylgalactosamine, but gangliosides must also contain sialic acid.**

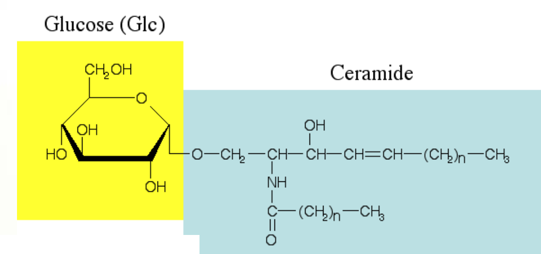


glycolipids

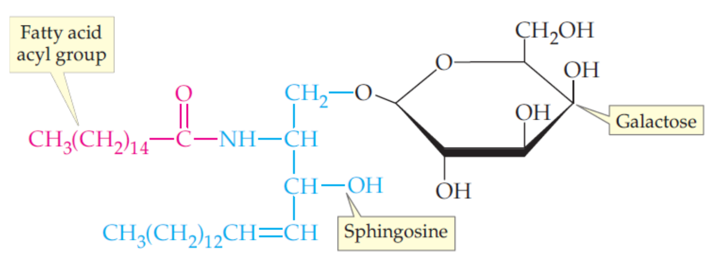
Sphingolipid type	R group
Ceramide	H
Sphingomyelin	phosphocholine
Cerebroside	monosaccharide (galactose or glucose)
Globoside	two or more sugars (galactose, glucose, N-acetylglucosamine
Ganglioside	three or more sugars including at least one sialic acid



Glucocerebroside



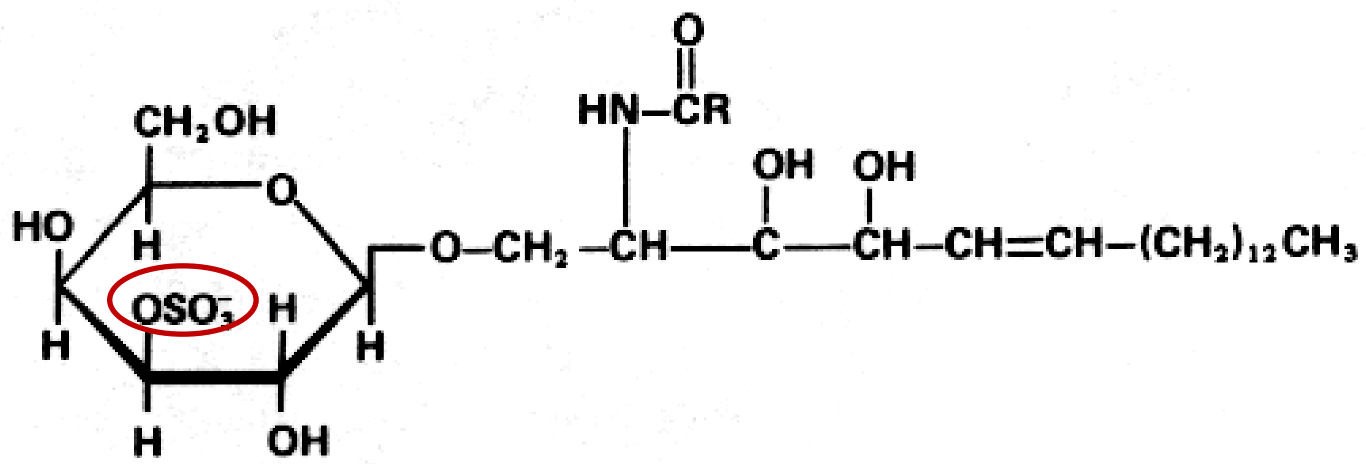
Gangliosides are targeted by cholera toxin in the human intestine.

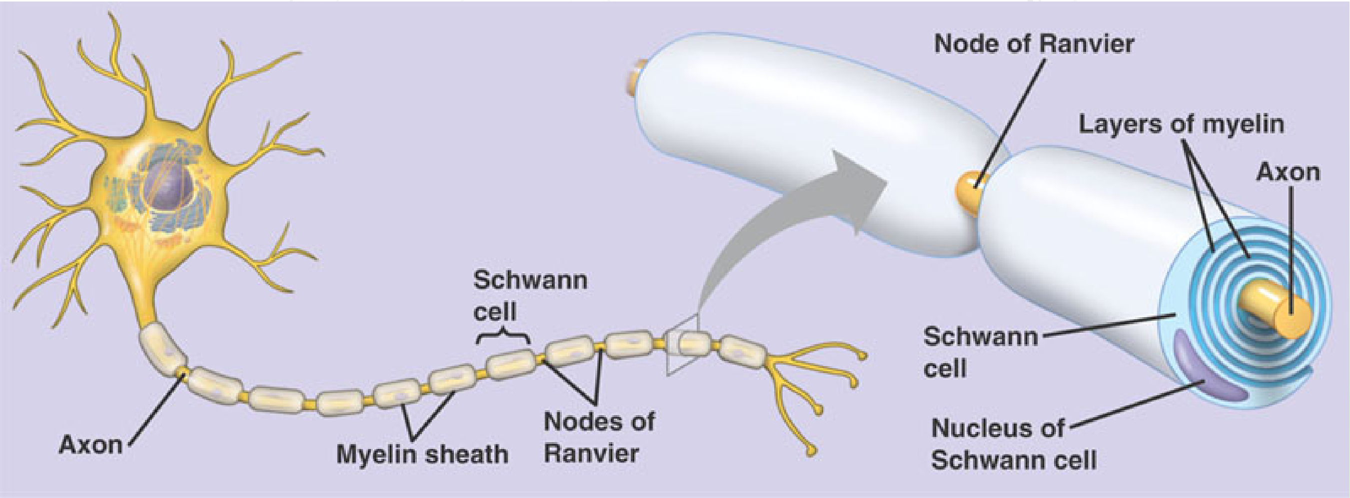


A glycolipid
(A cerebroside)

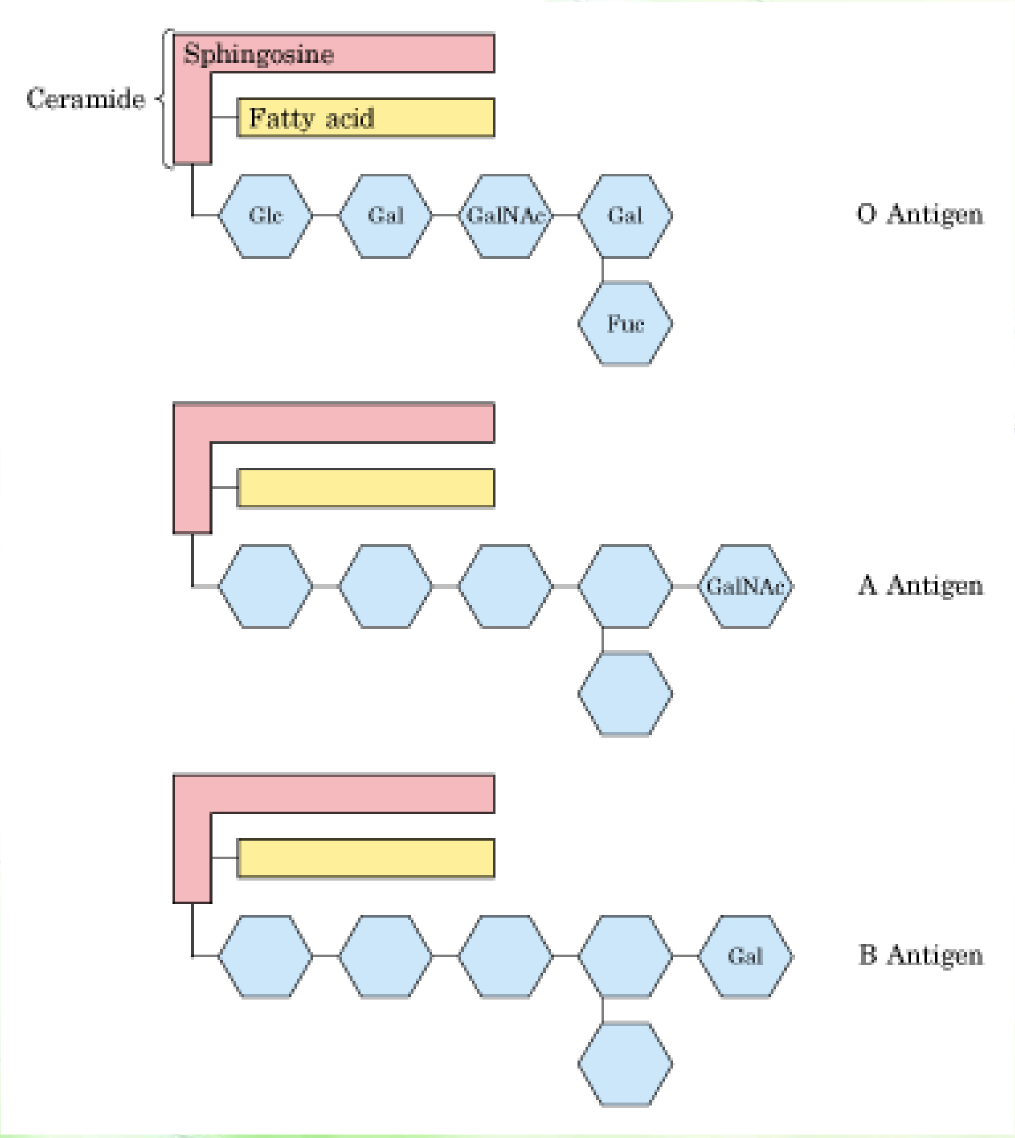
Sulfatides

- Synthesized from galactocerebroside
- Abundant in brain myelin

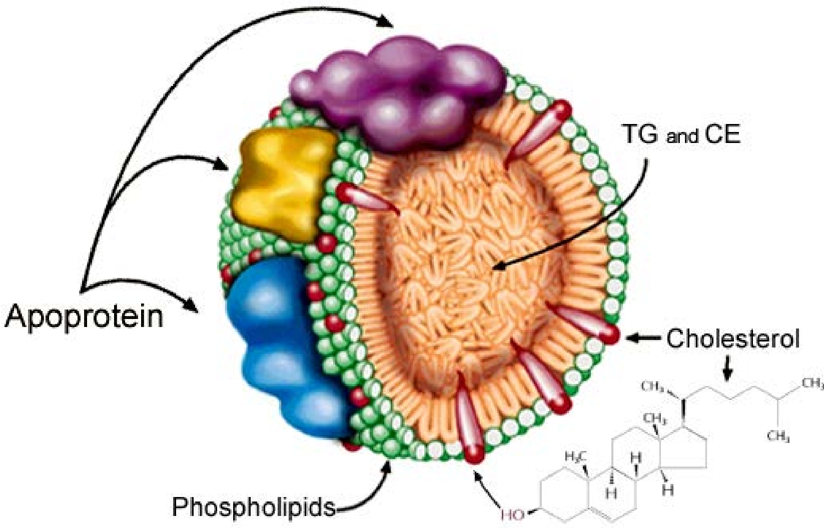




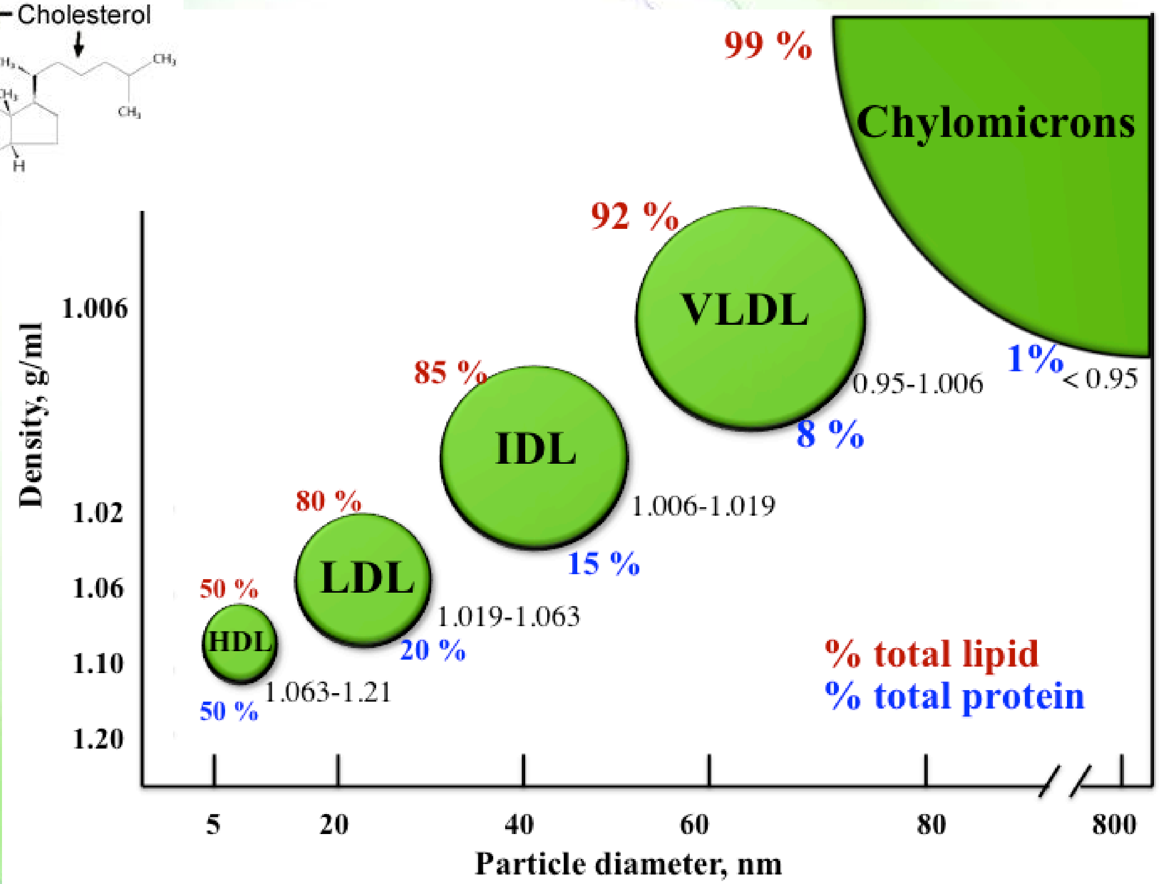
Sphingolipids and blood groups



Lipoproteins



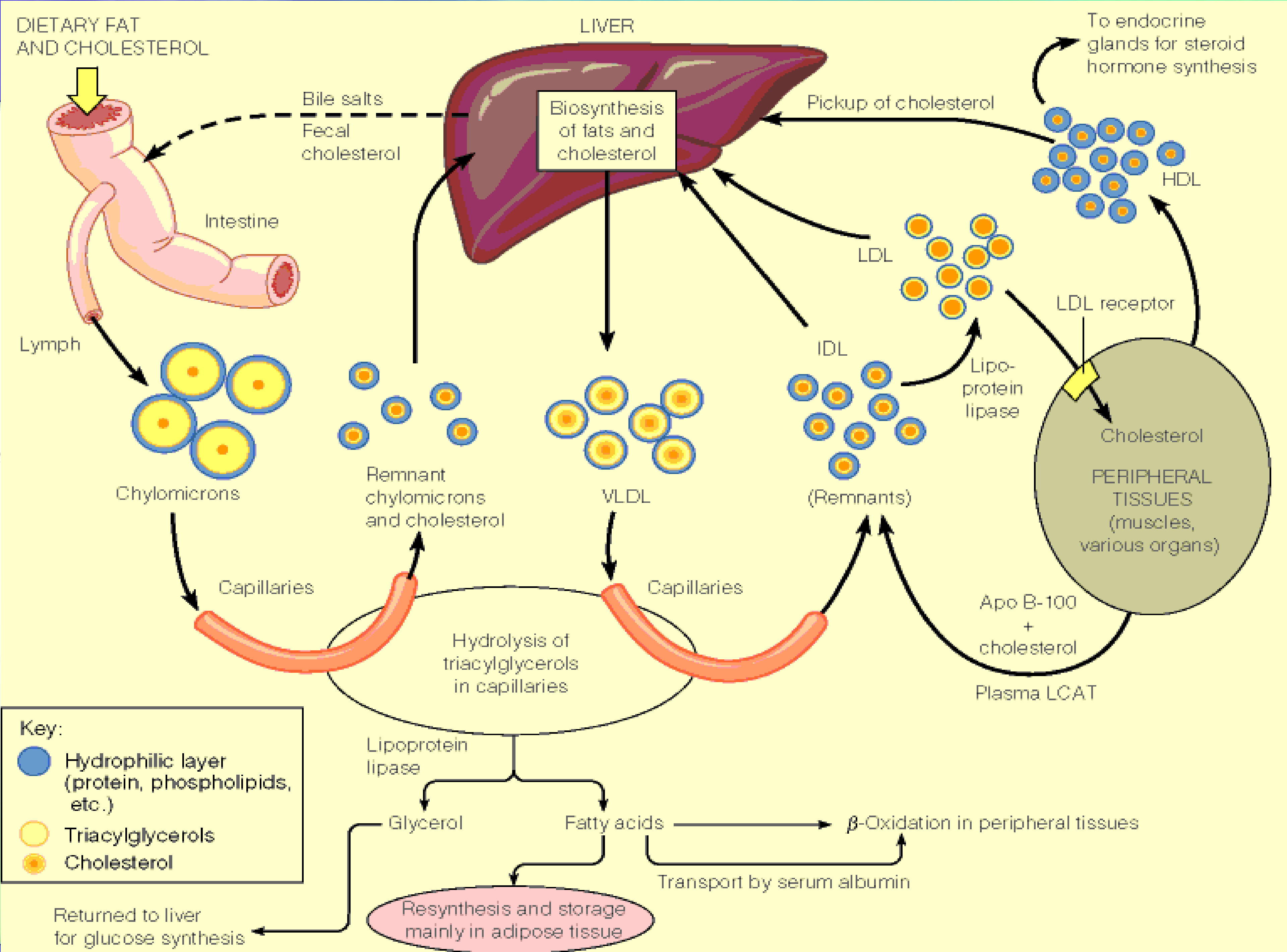
Function: transport of different types of lipids (cholesterol, cholesterol esters, phospholipids & triacylglycerols) in blood plasma.



As lipid content increases, the density decreases

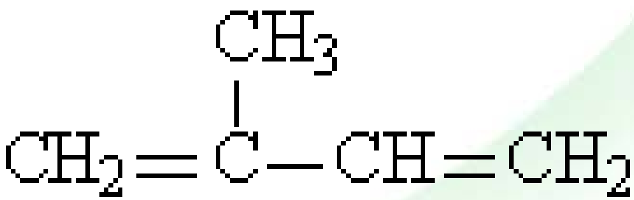
Features of lipoproteins

	Chylomicrons	VLDL	LDL	HDL
Density (g/ml)	< 0.94	0.94-1.006	1.006-1.063	1.063-1.210
Diameter (Å)	6000-2000	600	250	70-120
Total lipid (wt%) *	99	91	80	44
Triacylglycerols	85	55 Liver	10	6
Cholesterol esters	3	18	50 (bad)	40 (good)
Function	Transport of <u>dietary</u> TG	Transport of liver TG	Transport of cholesterol to peripheral tissues	Transport of cholesterol from peripheral tissues (cholesterol scavengers)


DIETARY FAT
AND CHOLESTEROL
LIVER
To endocrine
glands for steroid
hormone synthesis
Bile salts
Biosynthesis
of fats and
cholesterol
Pickup of cholesterol
Fecal
cholesterol
HDL
Intestine
LDL
LDL receptor
Lymph
IDL
Lipo-
protein
lipase
Cholesterol
PERIPHERAL
TISSUES
(muscles,
various organs)
Chylomicrons
Remnant
chylomicrons
and cholesterol
VLDL
(Remnants)
Capillaries
Capillaries
Apo B-100
+
cholesterol
Hydrolysis of
triacylglycerols
in capillaries
Plasma LCAT
Key:
Hydrophilic layer
(protein, phospholipids,
etc.)
Triacylglycerols
Cholesterol
Lipoprotein
lipase
Glycerol
Fatty acids
β-Oxidation in peripheral tissues
Transport by serum albumin
Returned to liver
for glucose synthesis
Resynthesis and storage
mainly in adipose tissue

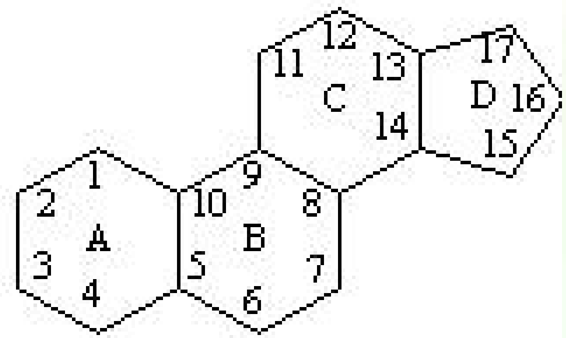
Steroids

The precursor



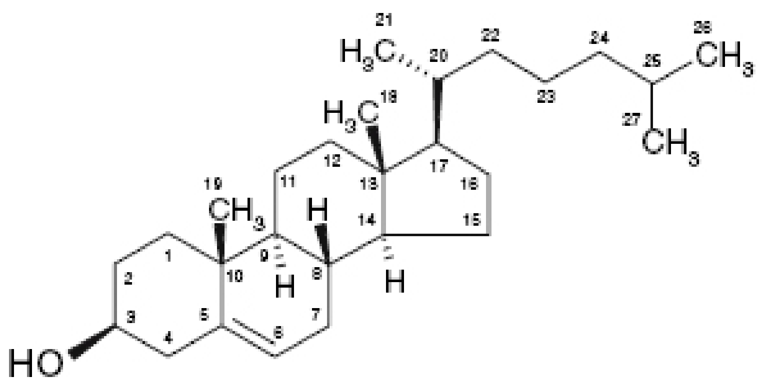
Isoprene

The nucleus

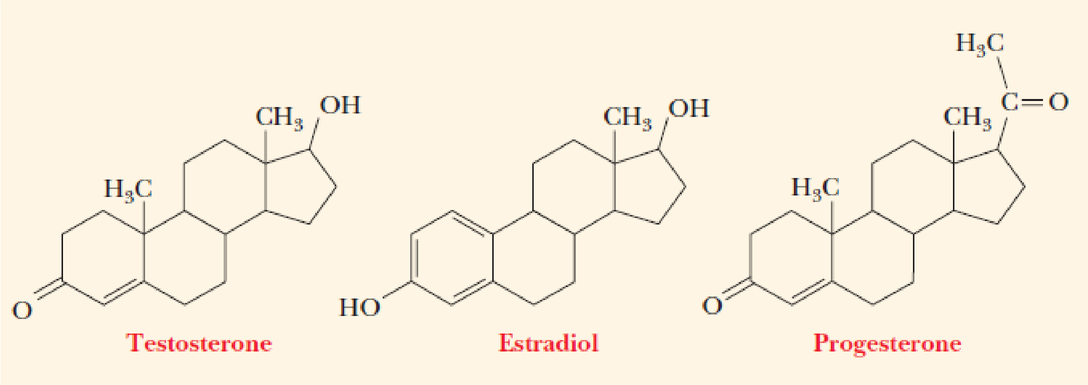


Steroid nucleus

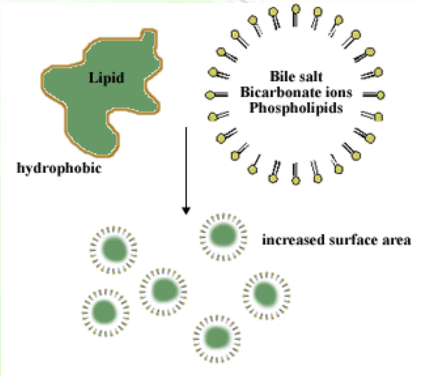
The most common steroid

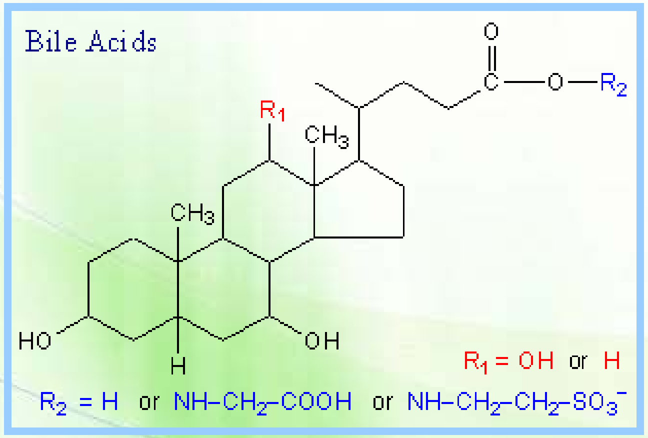


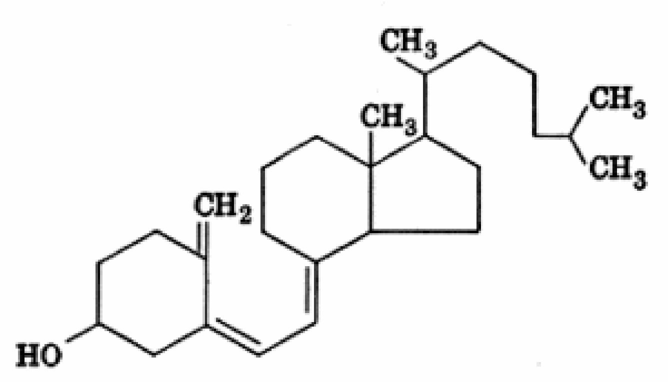
Products of cholesterol



- Hormones
  - sex hormones (androgens,. estrogens, progestins)
- Some vitamins such as vitamin D
  - Vitamins A, D, E, and K are made from isoprenoids
- Bile acids (intestinal absorption of fat)



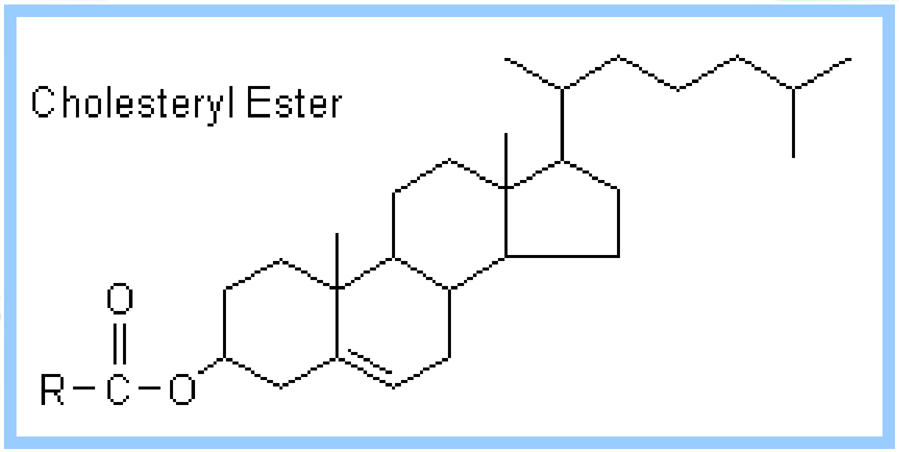


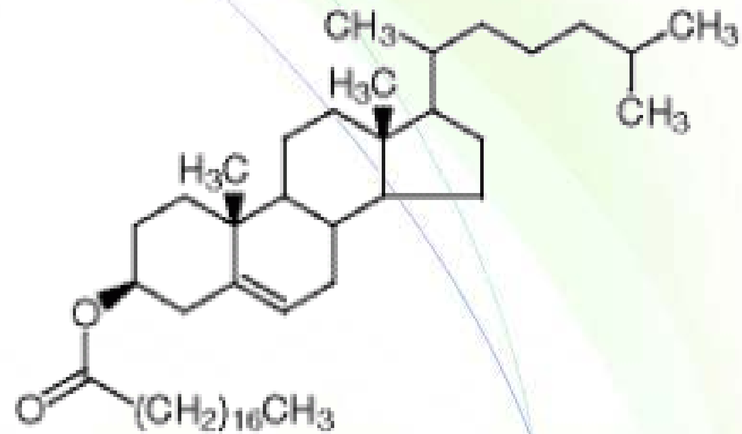


Vitamin D_3

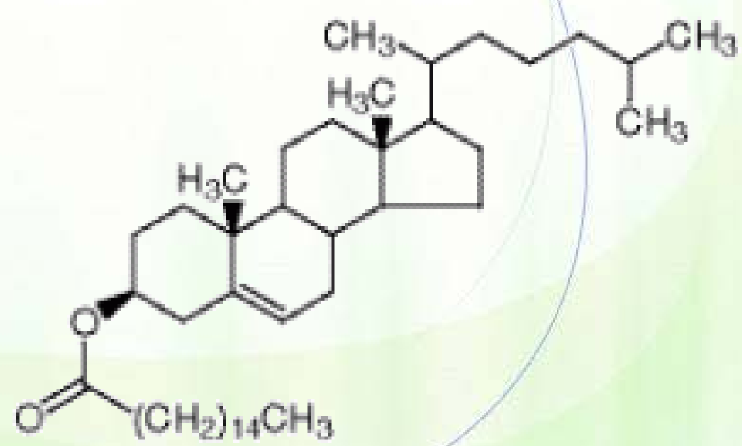
Cholesterol esters

- A cholesterol with a fatty acid attached at (-OH) of C3

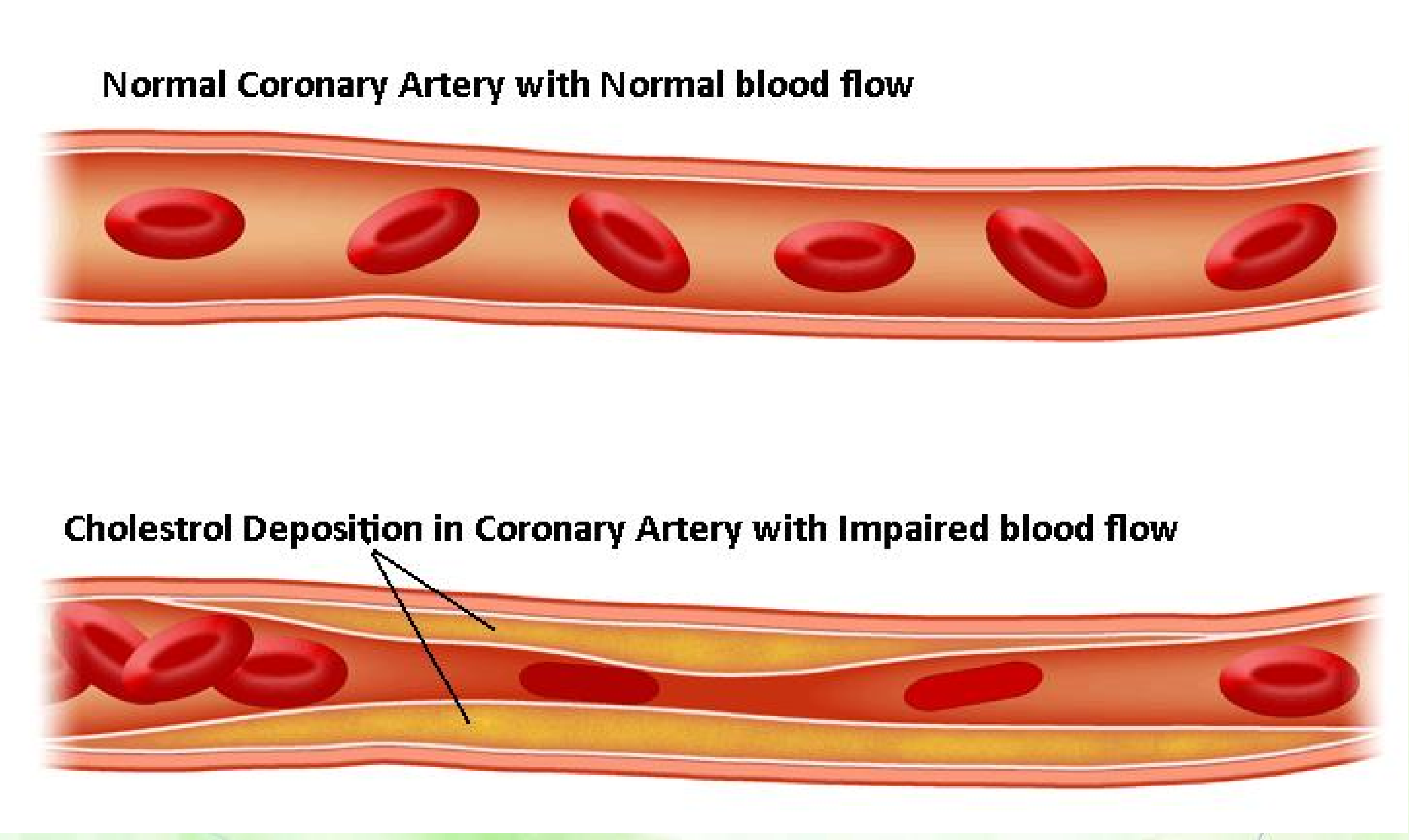




Name the molecules?

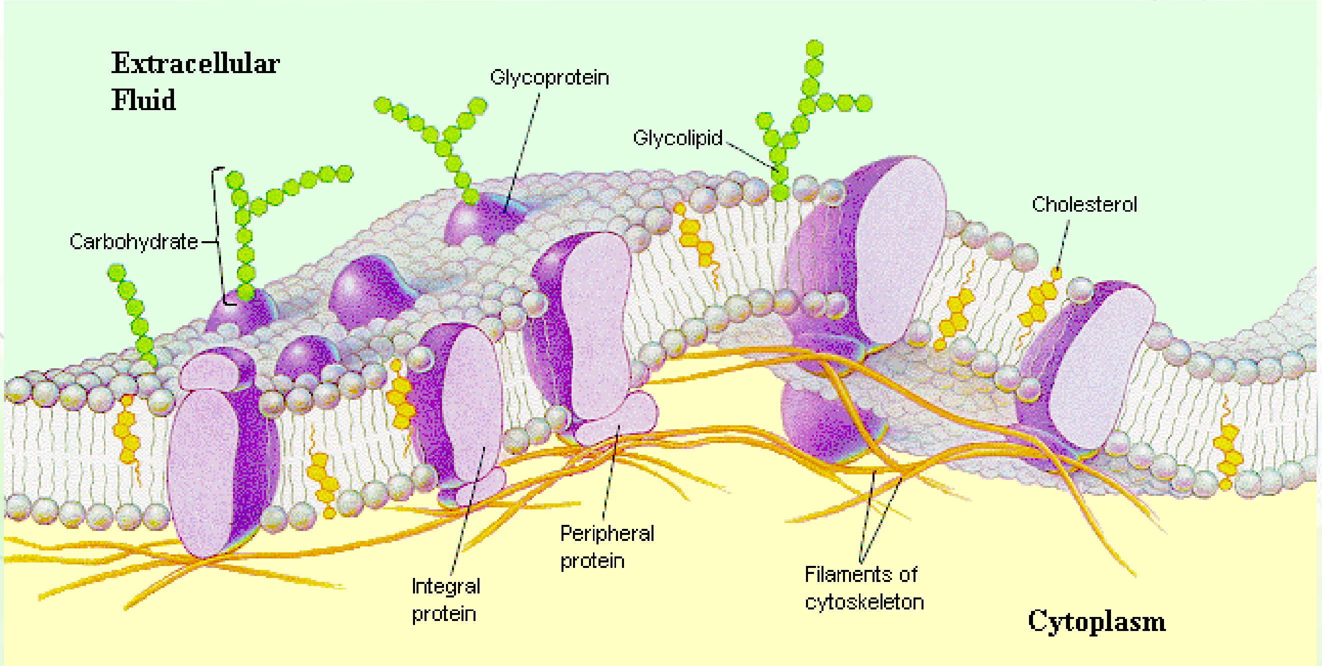


Atherosclerosis



Cell membranes

- The membrane is hypothesized in a model known as the fluid mosaic model.
- Components: 45% lipid, 45% protein and 10% carbohydrate
- They exist side by side without forming some other substance of intermediate nature.

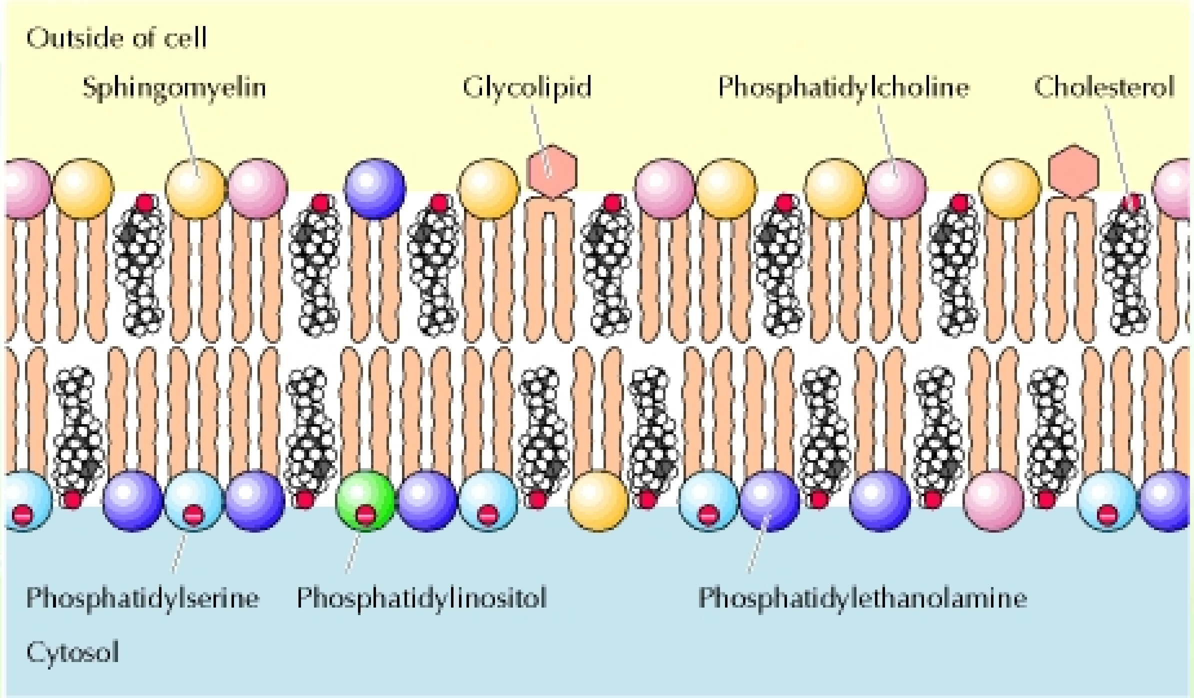


Phospholipids

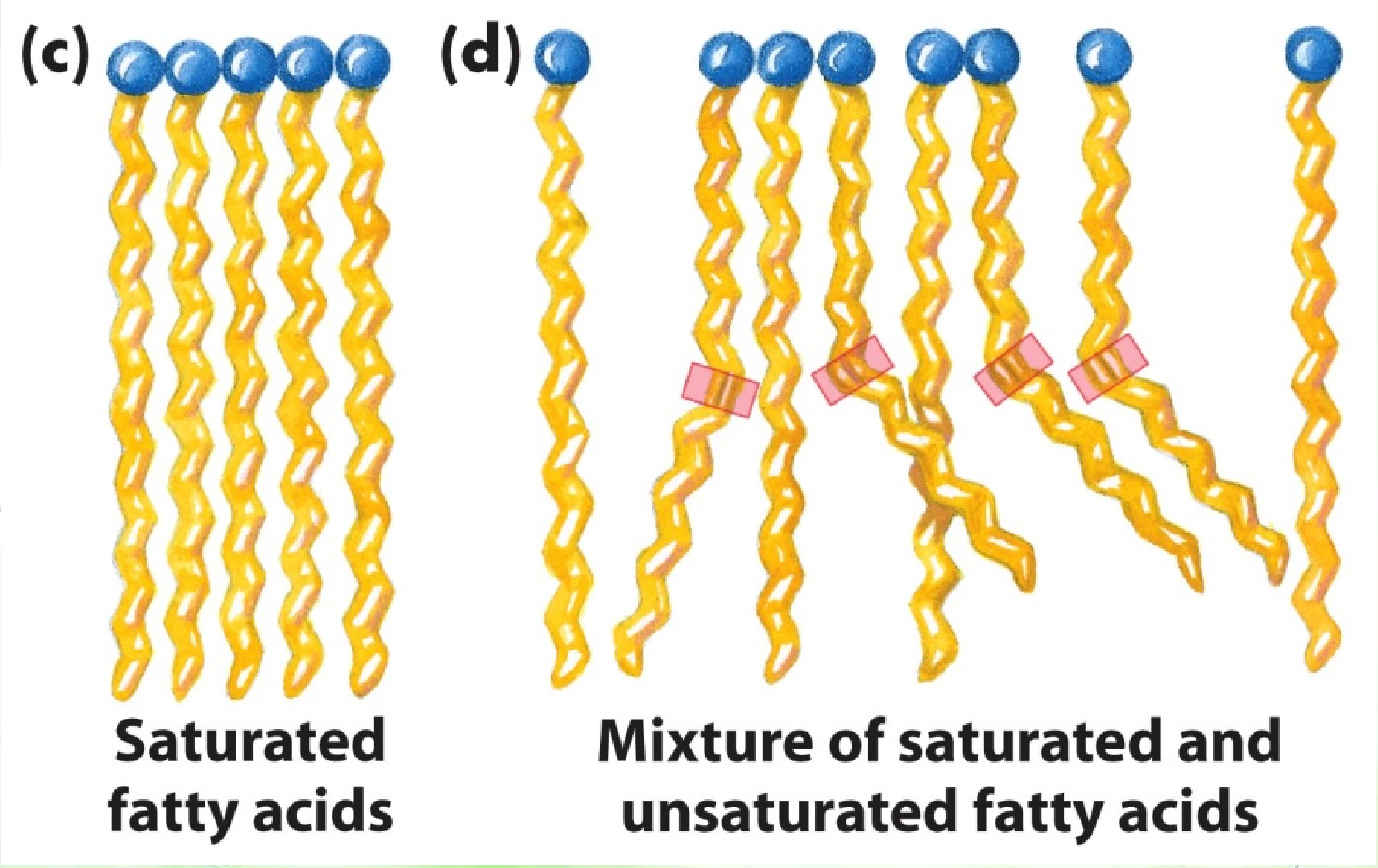
- The outer: phosphatidylcholine, sphingomyelin, and glycolipids(cell recognition)
- The inner: phosphatidylethanolamine, phosphatidylserine, and phosphatidylinositol (signaling)

Cholesterol is distributed in both leaflets

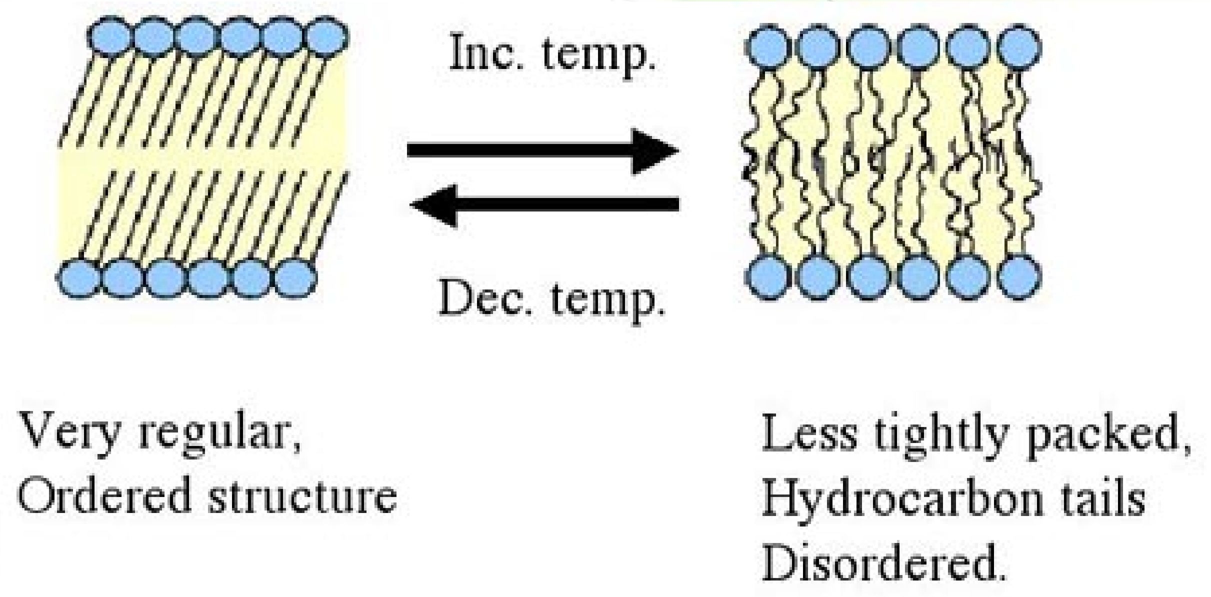
Animal cells vs. plant cells vs. prokaryotic cells

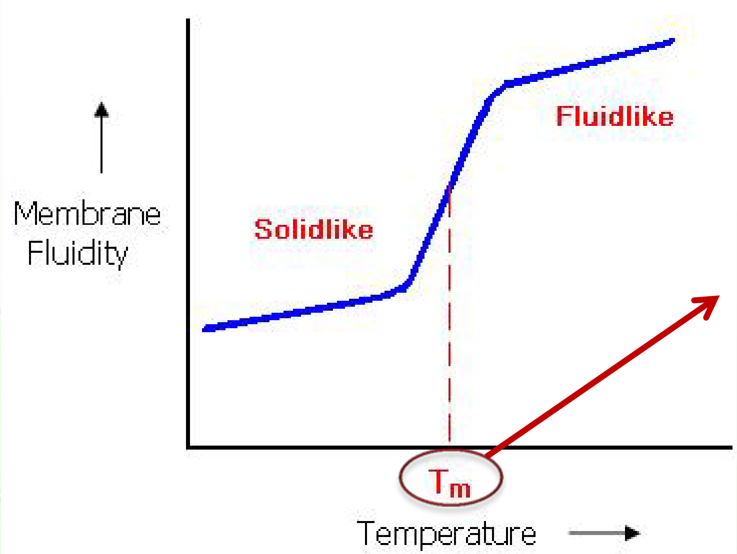


Fatty acids and membrane fluidity



Membrane fluidity and temperature



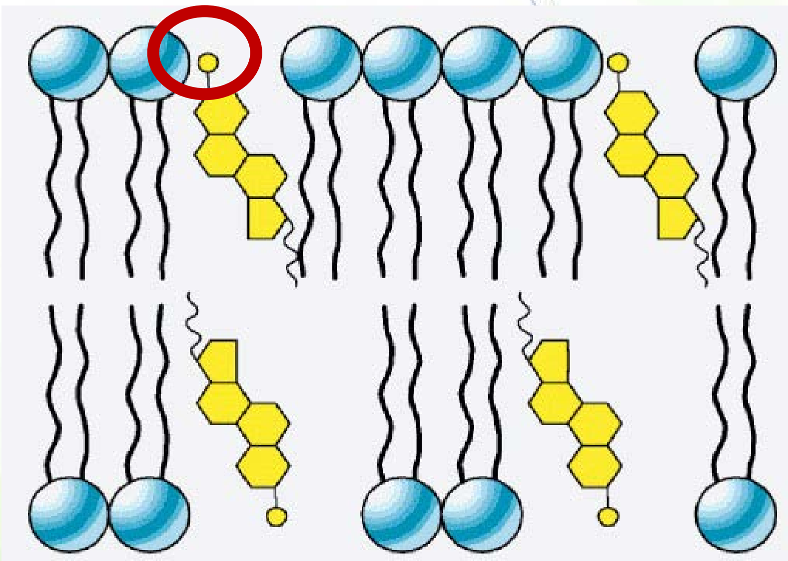


Melting temperature (transition temperature

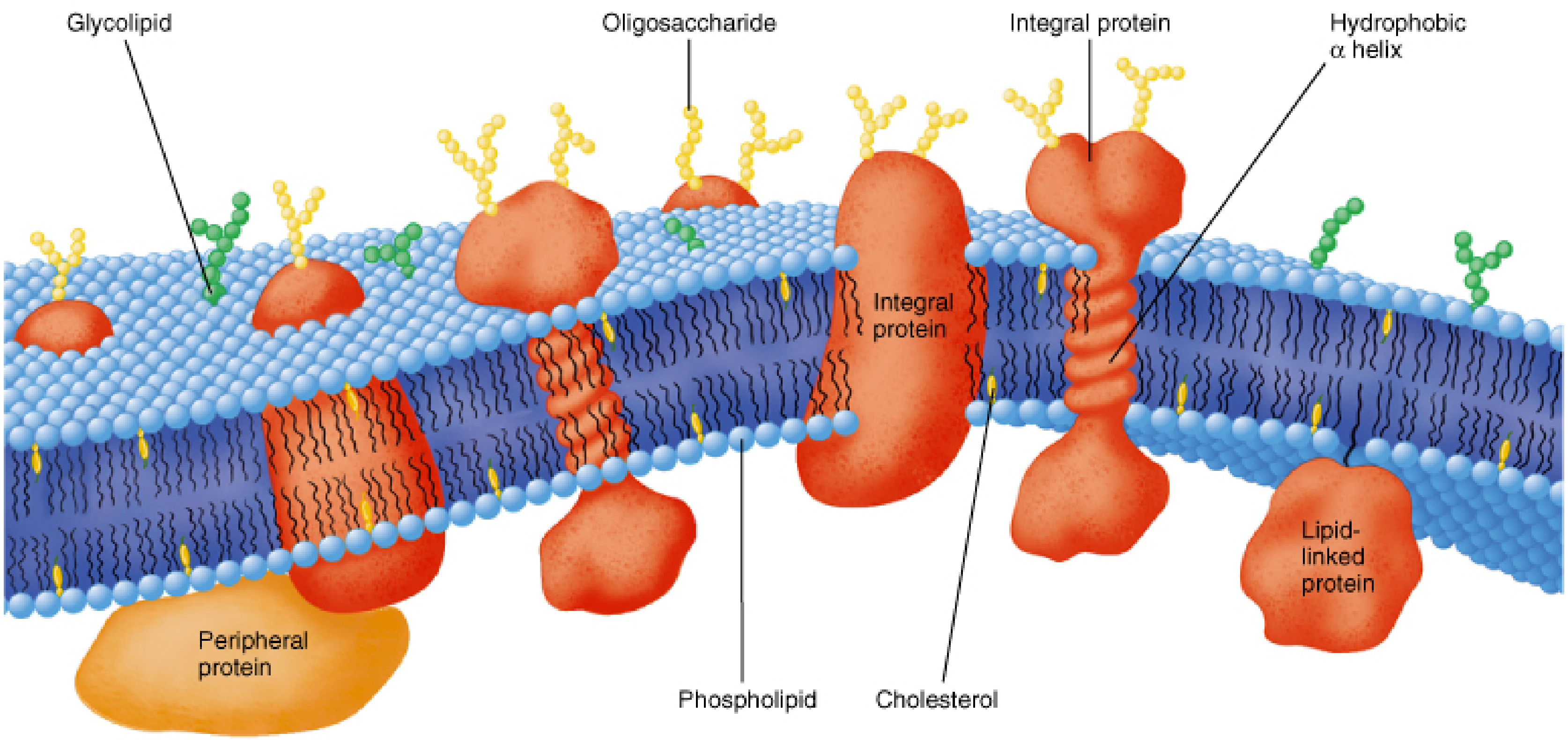
Cholesterol and membrane fluidity

- The presence of cholesterol stabilizes the extended straight-chain arrangement of saturated fatty acids by van der Waals interactions.
- Cholesterol makes a membrane less solid at low temperatures and more solid at high temperatures.

- **It decreases the mobility of hydrocarbon tails of phospholipids.**
- **It interferes with close packing of fatty acid tails in the crystal state.**



Membrane proteins

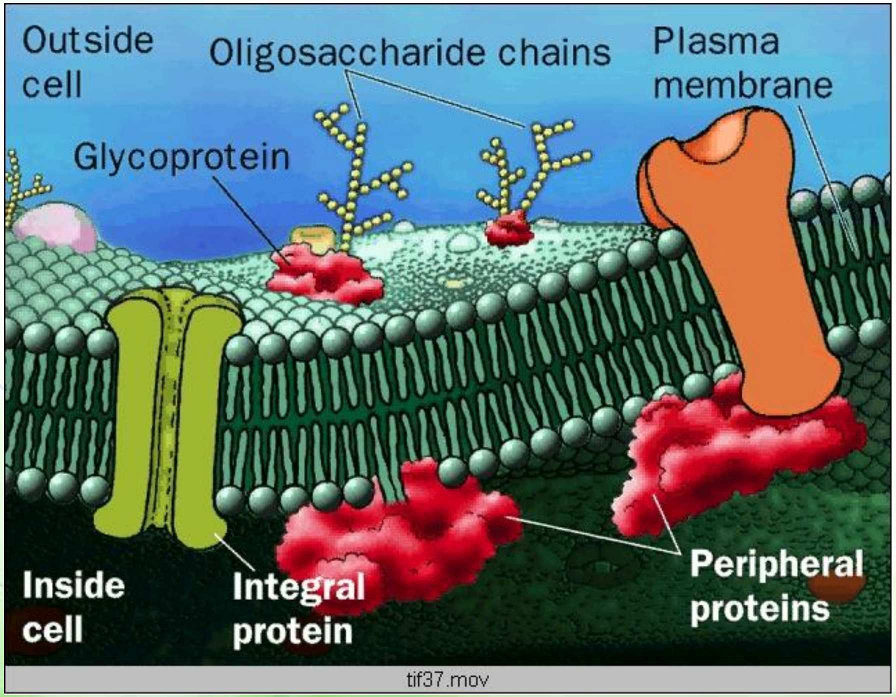


Types of membrane proteins

- Peripheral proteins:
  - are associated with the exterior of membranes via noncovalent interactions
- Integral membrane proteins:
  - anchored into membrane via hydrophobic regions
- Lipid-anchored:
  - associated via a lipid group

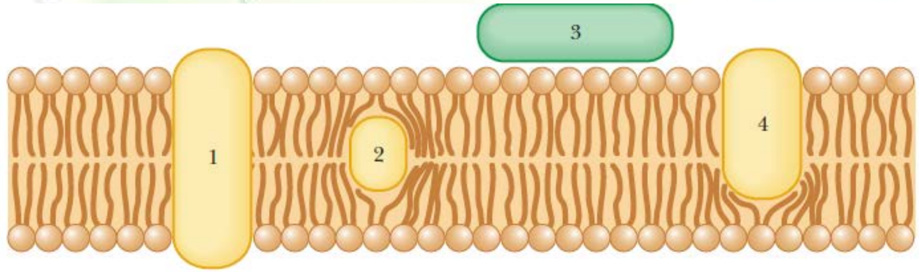
Peripheral membrane proteins

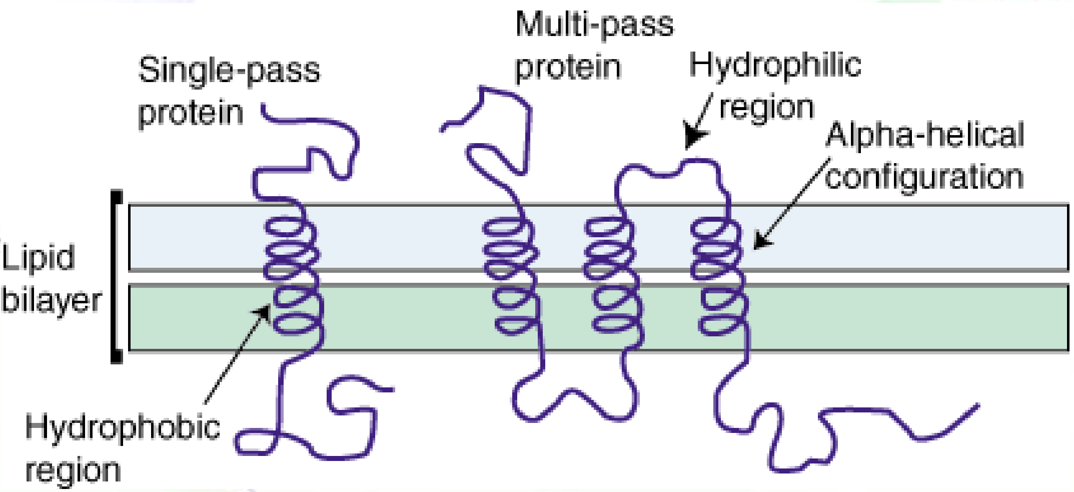
- They are associated with membranes but do not penetrate the hydrophobic core of the membrane
  - often associated with integral membrane proteins
- They are not strongly bound to the membrane and can be removed without disrupting the membrane structure
  - treatment with mild detergent



Integral membrane proteins

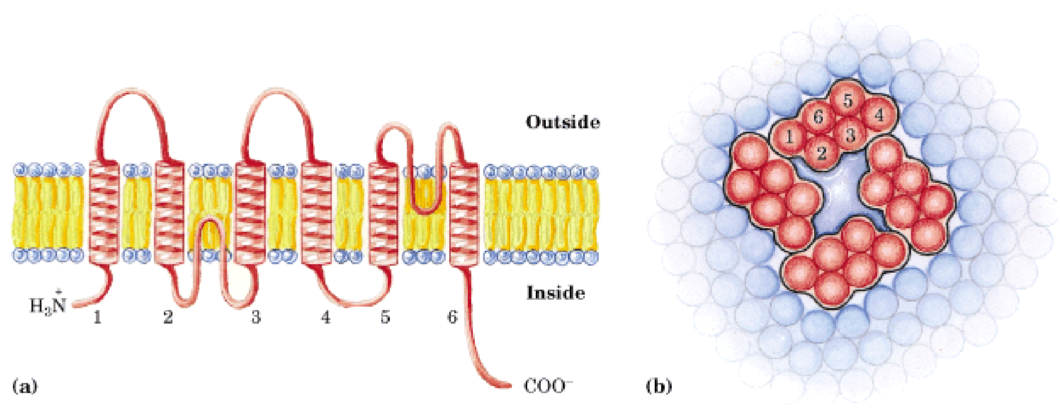
The integral proteins can be associated with the lipid bilayer in several ways.





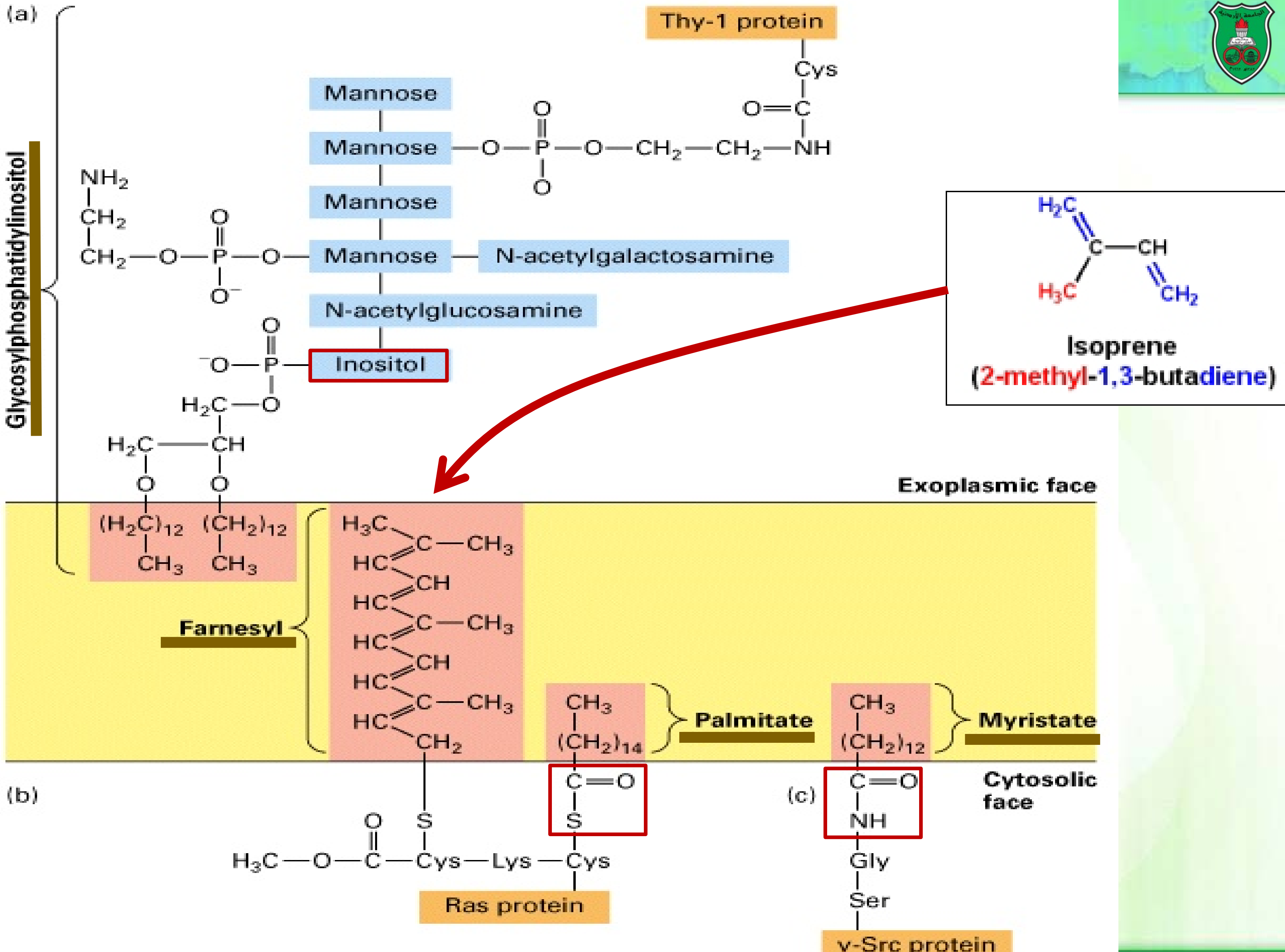
The membrane integral domains are:
1. Single or multiple
2. α-helix or β-sheet

Some can form channels



Lipid-anchored membrane proteins

- Four types have been found:
  - Amide-linked myristoyl anchors
    - Always myristic acid
  - Thioester-linked fatty acyl anchors
    - myristate, palmitate, stearate, oleate
  - Thioether-linked prenyl anchors
    - Prenylation refers to linking of "isoprene"-based groups
  - Glycosyl phosphatidylinositol anchors
    - Ethanolamine links to an oligosaccharide linked in turn to inositol of PI


(a)
Glycosylphosphatidylinositol
Thy-1 protein
Cys
Mannose
Mannose
Mannose
Mannose
N-acetylgalactosamine
N-acetylglucosamine
Inositol
Isoprene
(2-methyl-1,3-butadiene)
Exoplasmic face
Farnesyl
Palmitate
Myristate
Cytosolic face
(b)
(c)
Ras protein
v-Src protein

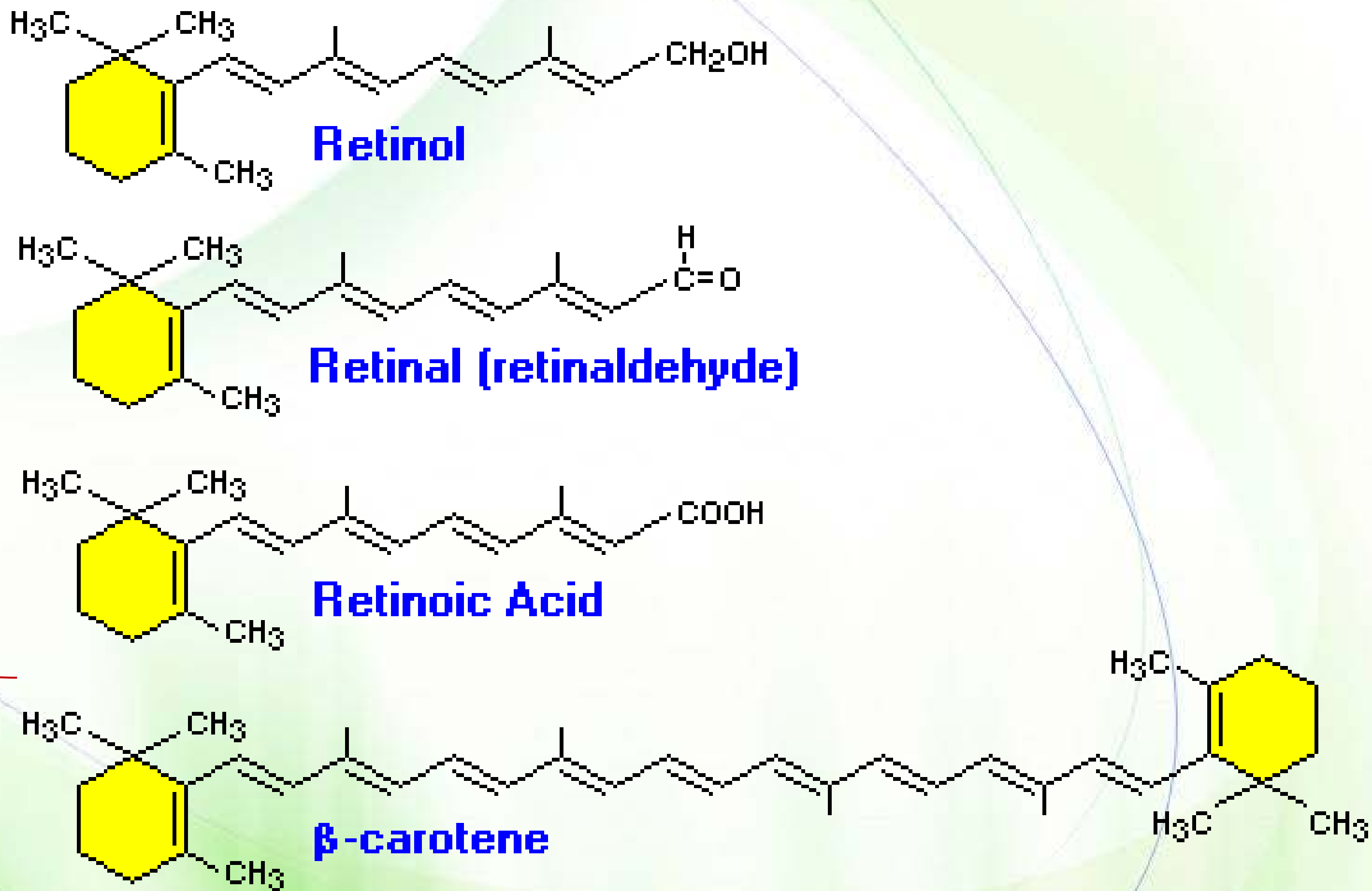
Structure-Function of Membranes

- Transport:
  - Membranes are impermeable barrier
  - Proteins can be carriers or channels
- Signaling
  - Protein receptors and small molecules (some can be lipids themselves)
- Catalysis
  - Enzyme-linked receptors

Vitamins

Vitamin A

Forms of vitamin A

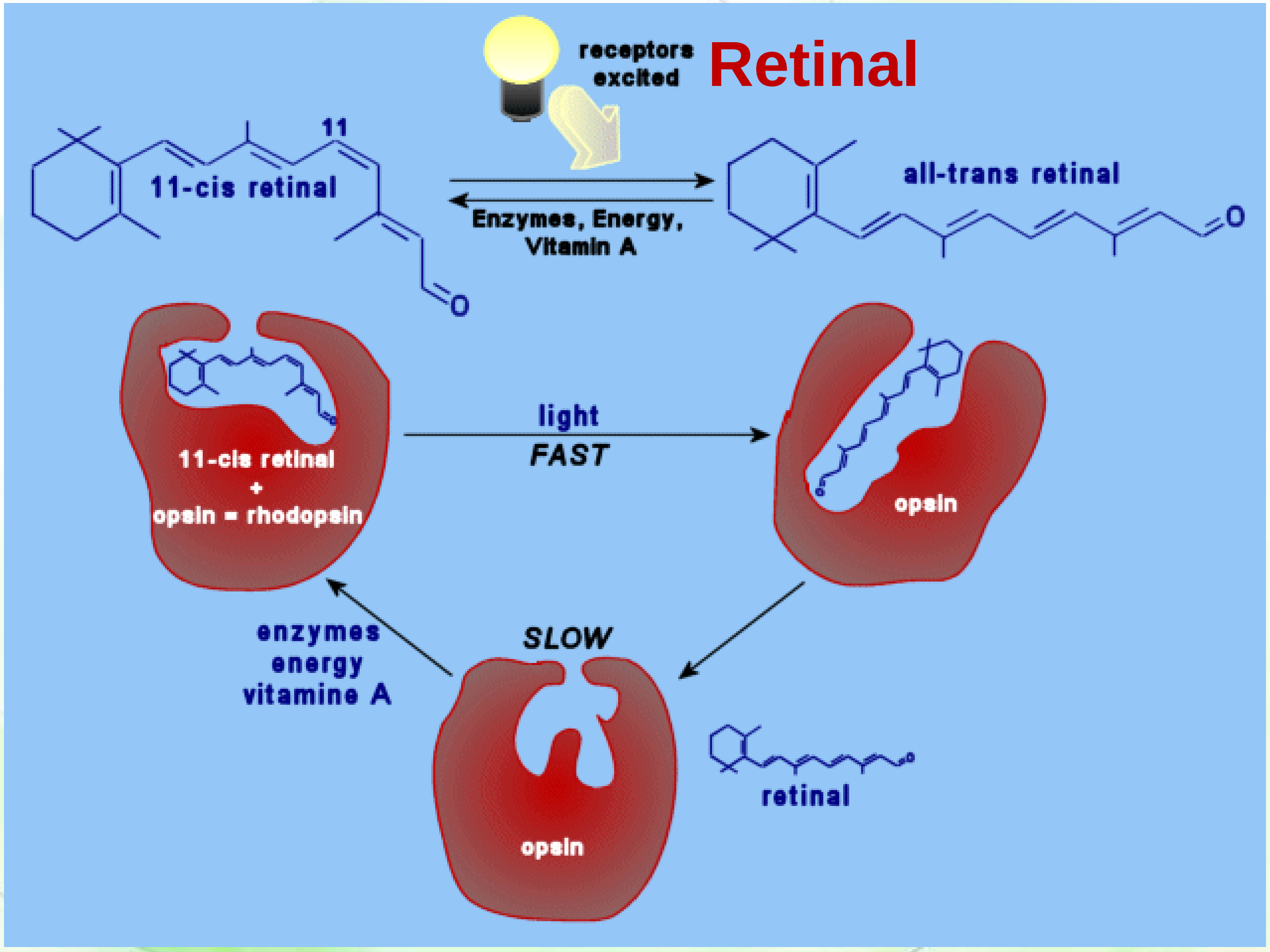


precursor

Vision

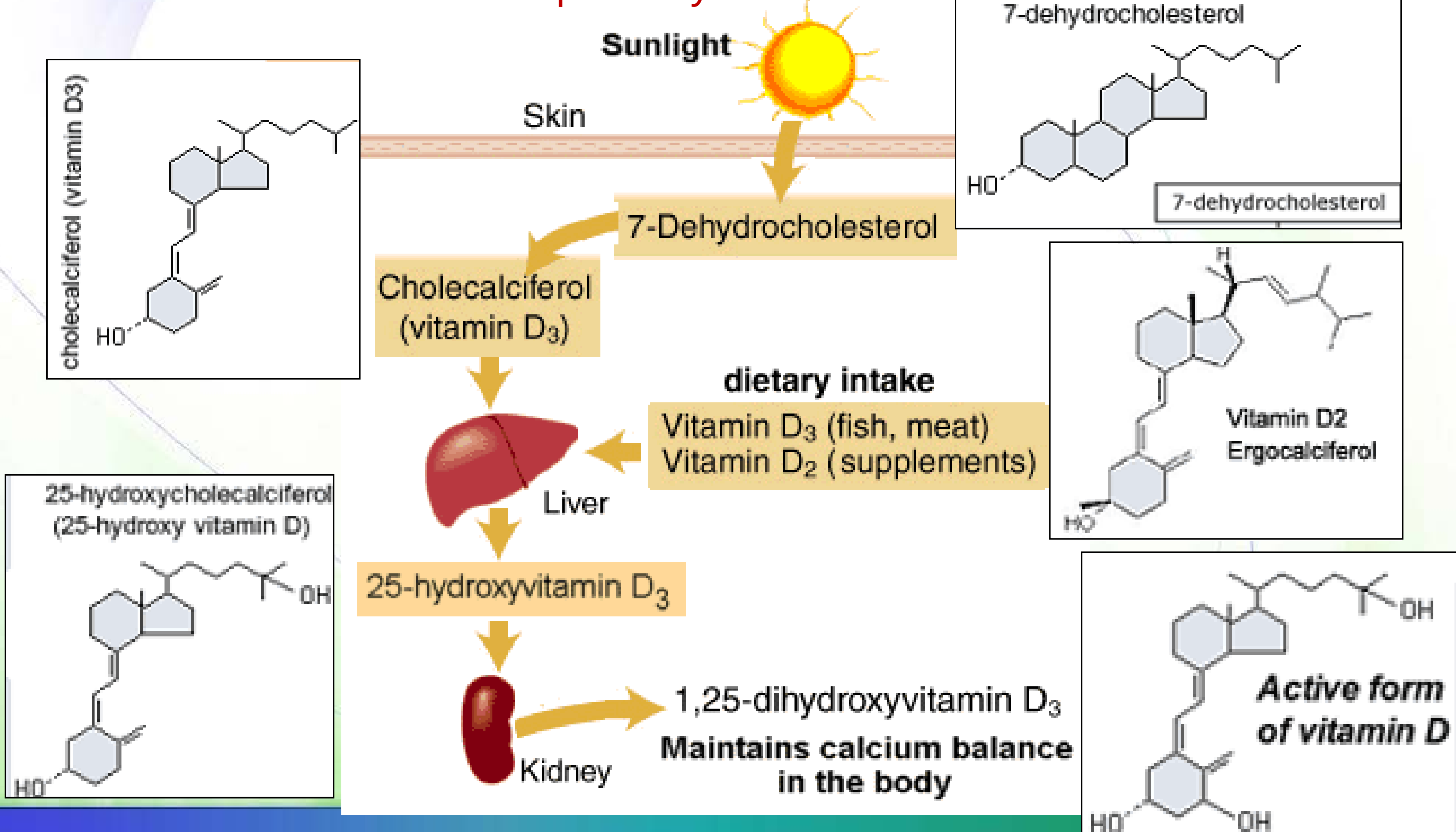
- The outer segment of rod cells contains flat membrane enclosed discs, the membrane consisting of about 60% rhodopsin and 40% lipid.

How viscous is membrane of rod cells?



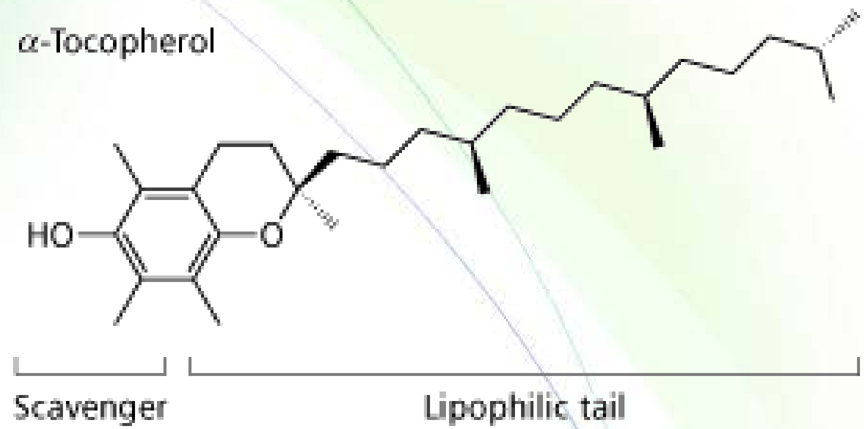
Vitamin D

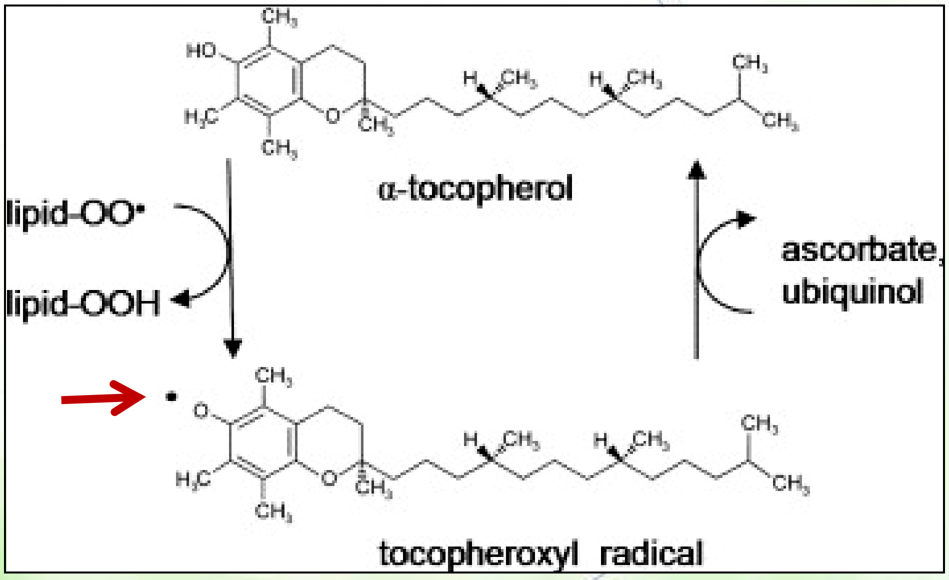
- Vitamin D3 increases synthesis of a Ca^{2+}-binding protein, which increases the absorption of dietary calcium in the intestines and calcium uptake by the bones.



Vitamin E

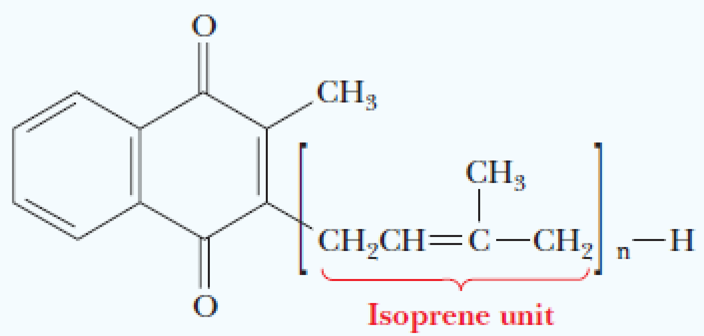
- **Vitamin E is a good reducing agent and an antioxidant (it reacts with oxidizing agents before they can attack other biomolecules).**

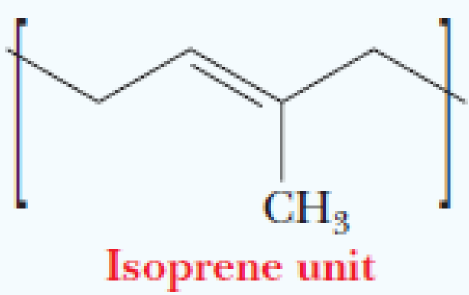




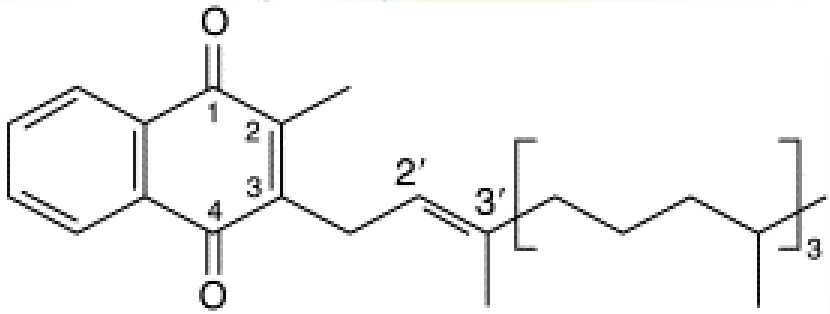
Vitamin K

The bicyclic ring system contains two carbonyl groups and a long unsaturated hydrocarbon side chain that consists of repeating *isoprene* Units.

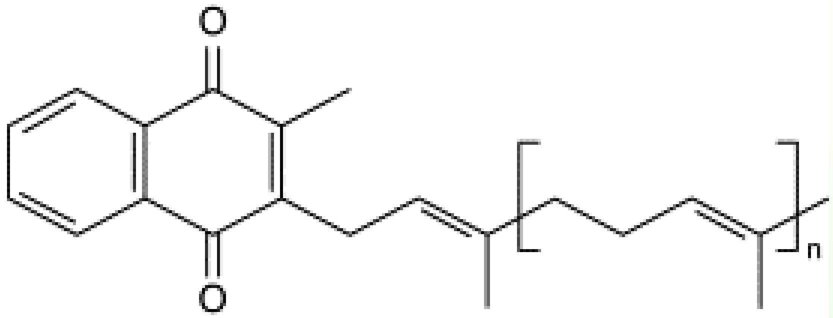




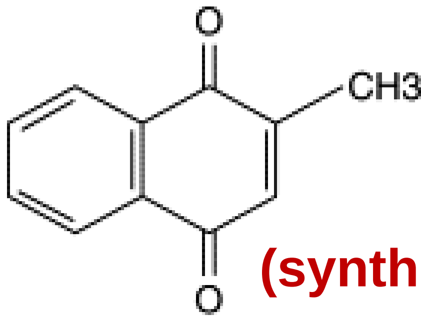
Vitamin K1



Vitamin K2



Vitamin K3



(synthetic vitamin K)

Biological function of vitamin K

- Vitamin K is important in the carboxylation of glutamate producing γ-carboxyglutamate residues in the prothrombin protein.
- The two carboxyl groups bind Ca2+ ion form a *bidentate ("two teeth") ligand,* which is required for blood clotting.
- Two well-known anticoagulants, dicumarol and warfarin (a rat poison), are vitamin K antagonists.