Lipids

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Summer 2020

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

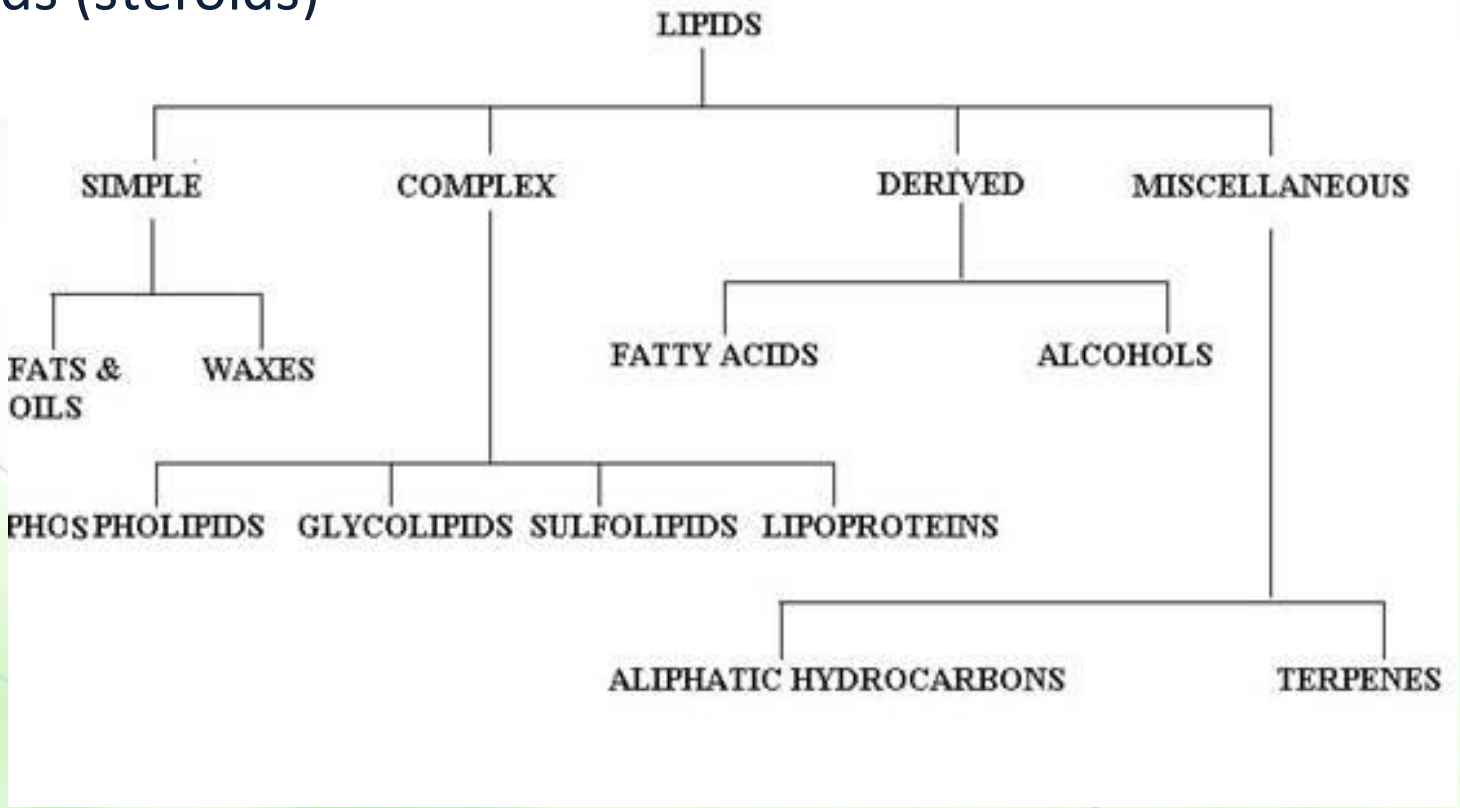
Lipids

- 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

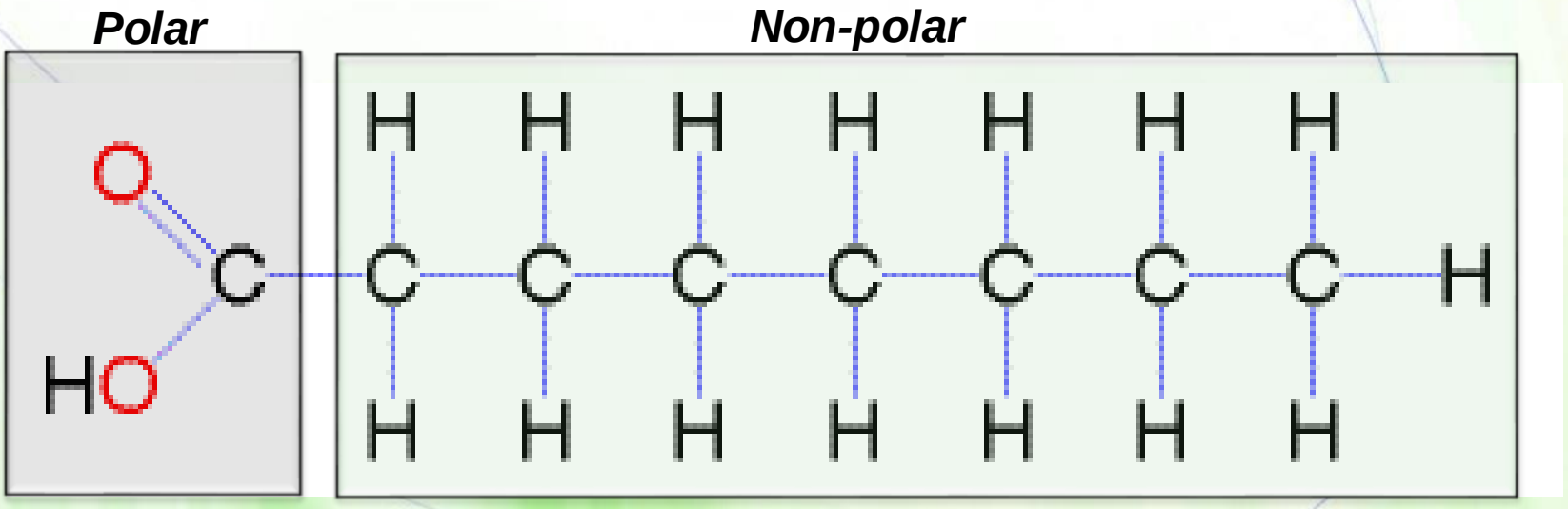
- Lipids include:
  - Storage lipids
  - Structural lipids in membranes
  - Lipids as signals, cofactors & pigments
- They are a major source of energy
  - They are storable to unlimited amount (vs. carbohydrates)
  - They provide considerable amount of energy to the body (25% of body needs) & provide 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

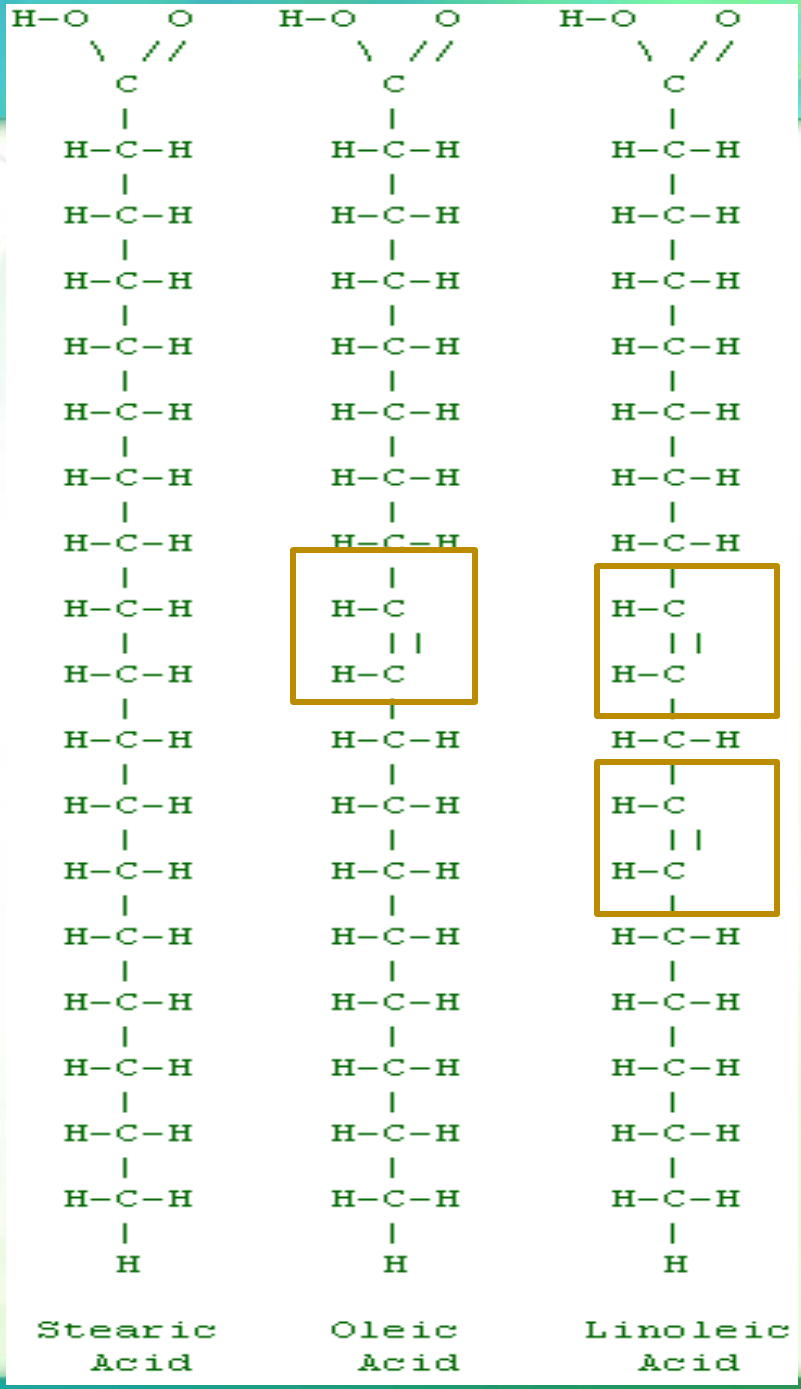
Functions:

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

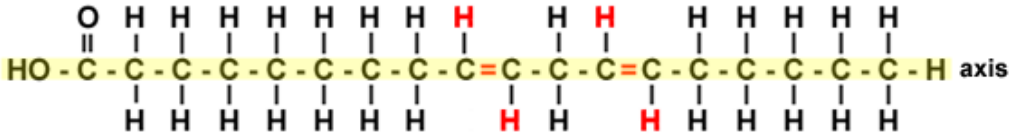


Types of fatty acids

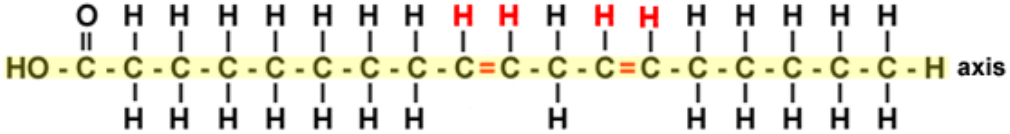
- Saturated fatty acids are those with all of C-C bonds being single.
- Unsaturated fatty acids are those with one or more double bonds between carbons
  - Monounsaturated fatty acid: a fatty acid containing one double bond.
  - Polyunsaturated fatty acids contain two or more double bonds.



Cis vs. trans bonds



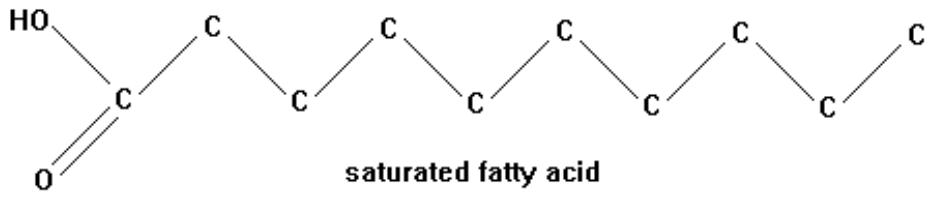
linoleic acid: *trans* configuration (*trans* isomer)



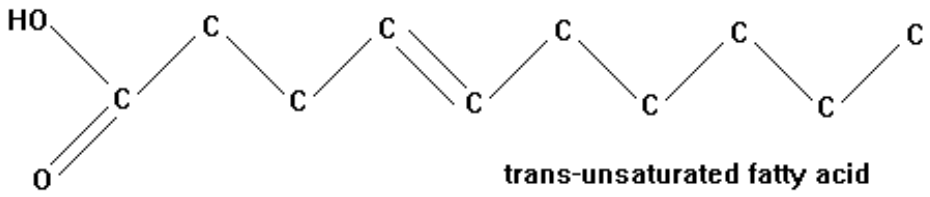
linoleic acid: *cis* configuration (*cis* isomer)

cis isomer predominates; trans is rare

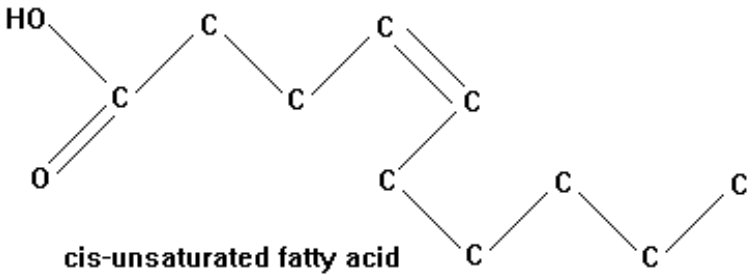
cis- vs. trans-fatty acids



saturated fatty acid



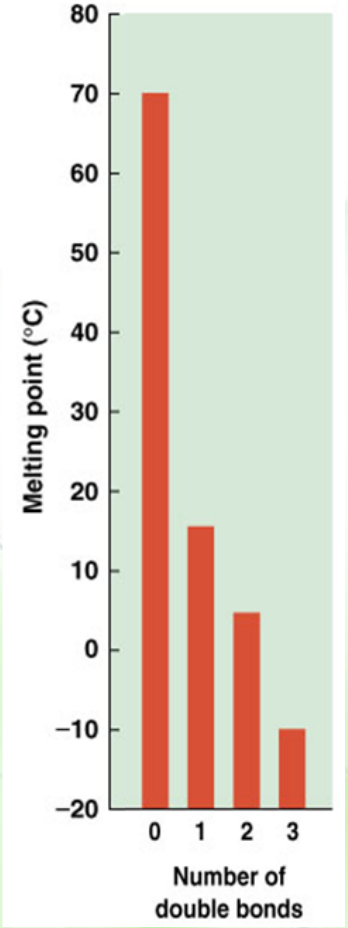
trans-unsaturated fatty acid

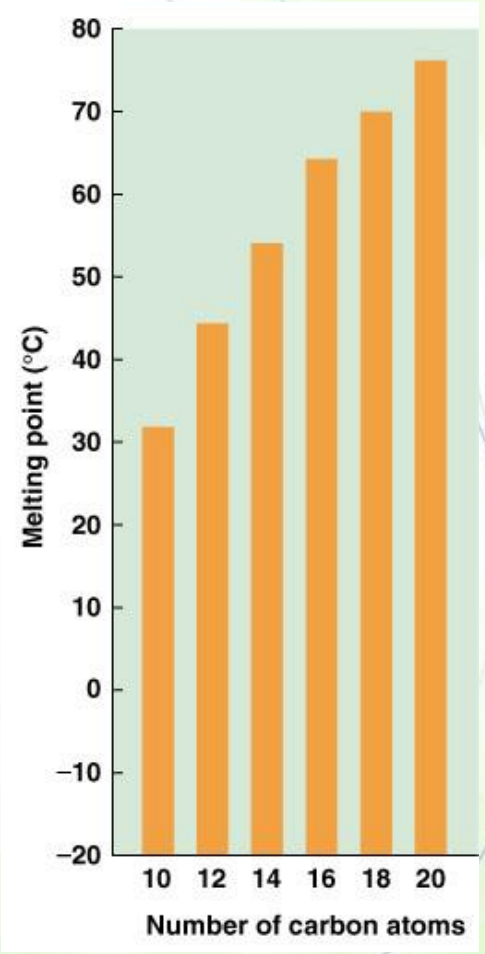


cis-unsaturated fatty acid

Properties of fatty acids

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





Properties of saturated 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 at RT	Non-volatile at RT	Non-volatile
Acetic, butyric, caproic FA	Caprylic & capric F.A.	Palmitic and stearic F.A

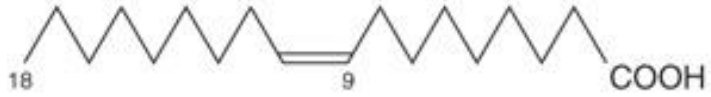
Greek number prefix

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

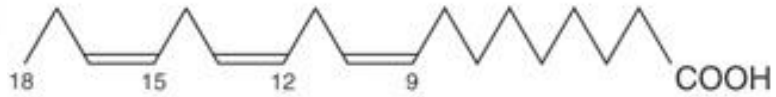
- Alkane to oic
  - Octadecane (octa and deca) is octadecanoic acid
    - One double bond = octadecenoic acid
    - Two double bonds = octadecadienoic acid
    - Three double bonds = octadecatrienoic acid
- Designation of carbons and bonds
  - 18:0 = a C18 fatty acid with no double bonds
    - stearic 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})

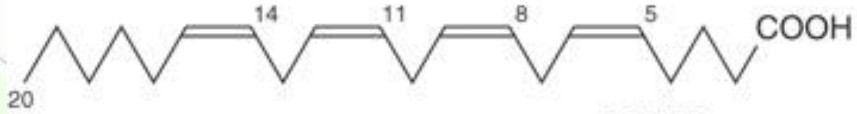


Oleic acid (ω9, 18:1, Δ^{9})

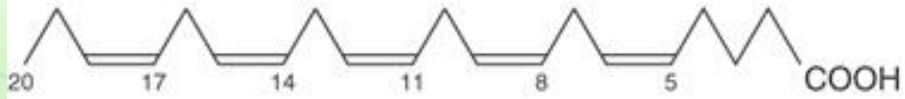
***Linoleic acid (ω6, 18:2, $\Delta^{9,12}$)**



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



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

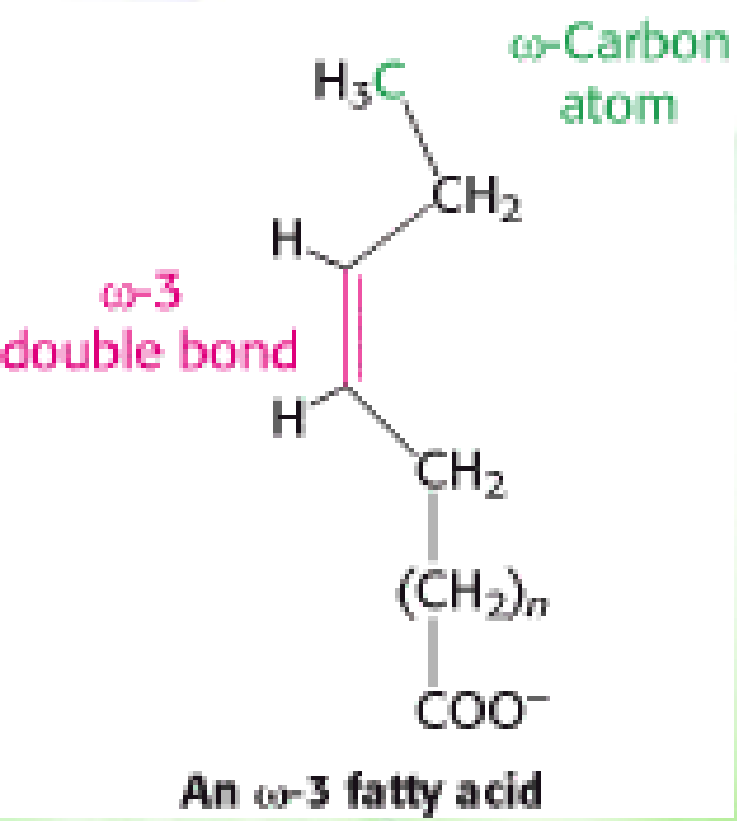


Eicosapentaenoic acid (ω3, 20:5, $\Delta^{5,8,11,14,17}$)

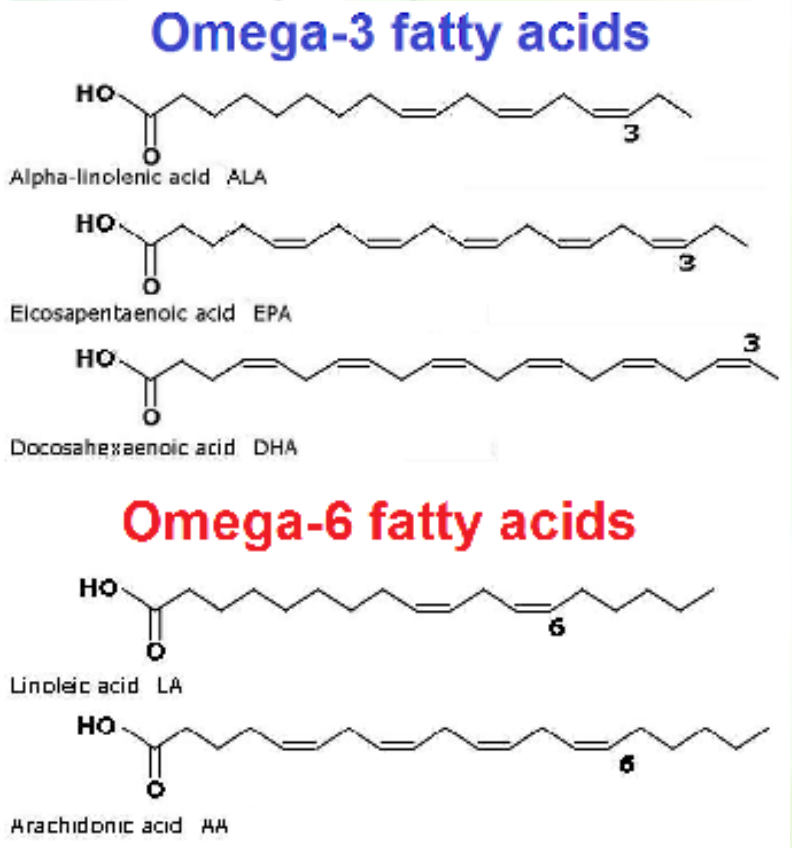
Number of carbons	Number of double bonds	Common name	Systematic name	Formula
14	0	Myristate	n-Tetradecanoate	$CH_3(CH_2)_{12}COO^-$
16	0	Palmitate	n-Hexadecanoate	$CH_3(CH_2)_{14}COO^-$
18	0	Stearate	n-Octadecanoate	$CH_3(CH2)_{16}COO^-$
18	1	Oleate	cis-Δ^9-Octadecenoate	$CH_3(CH_2)_7CH=CH(CH_2)_7COO^-$
18	2	Linoleate	cis,cis-Δ^9,Δ^{12}-Octadecadienoate	$CH_3(CH_2)_4CH=CHCH_2CH(CH_2)_7COOH$
18	3	Linolenate	all-cis-$\Delta^9,\Delta^{12},\Delta^{15}$-Octadecatrienoate	$CH_3CH_2(CH=CHCH_2)_3(CH_2)_6COOH$
20	4	Arachidonate	all-cis-$\Delta^5,\Delta^8,\Delta^{11},\Delta^{14}$-Eicosatetraenoate	$CH_3(CH_2)_4(CH=CHCH_2)_4(CH_2)_2COOH$

Another way of naming

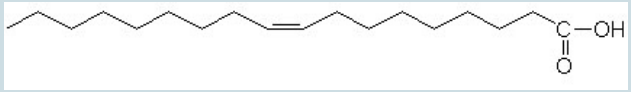
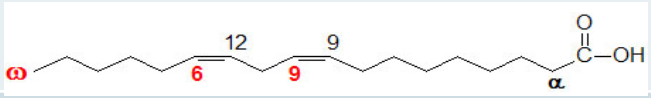
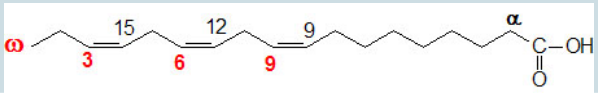
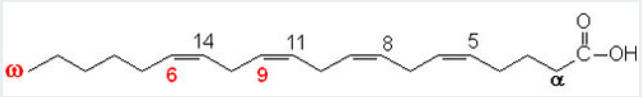
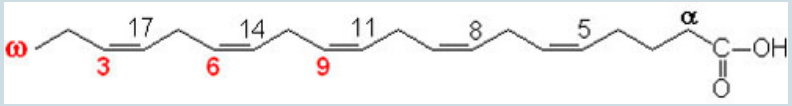
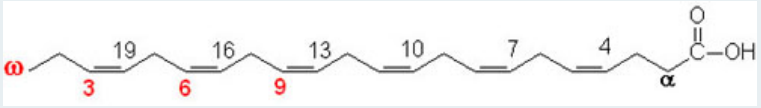
- (ω)-C: distal methyl C as #1



An ω-3 fatty acid



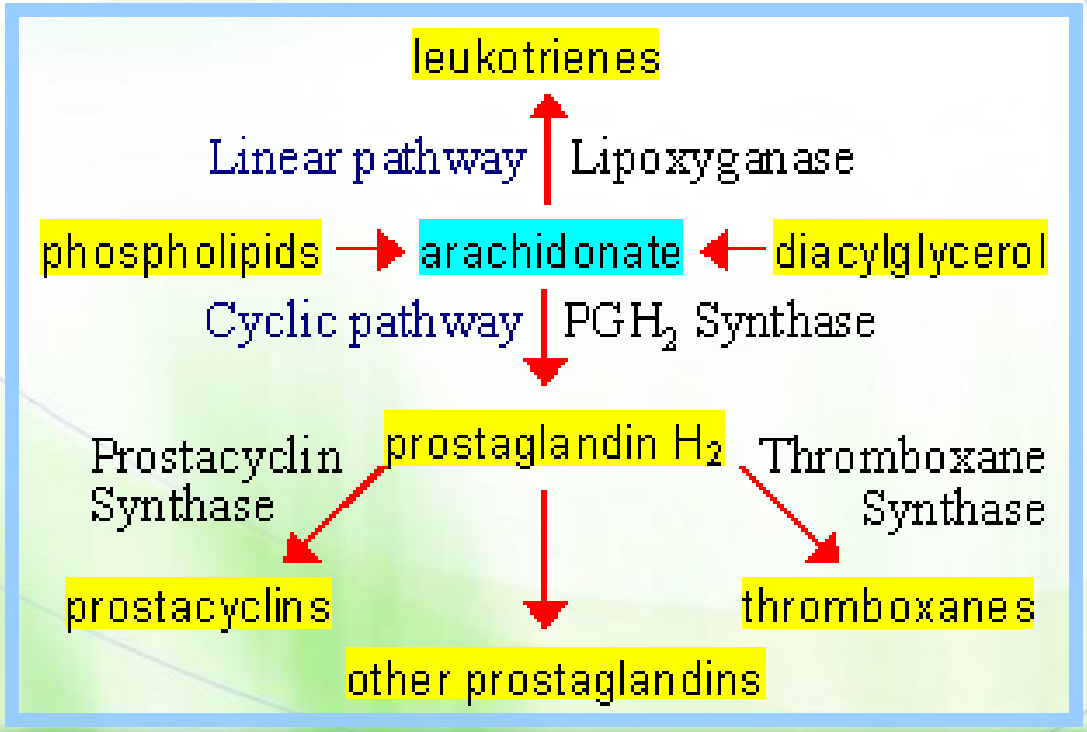
- **Linoleic acid: precursor of arachidonates**
- **Linolenic acid: precursor of EPA and DHA**

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

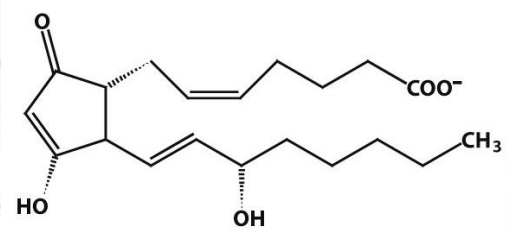
Arachidonate

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

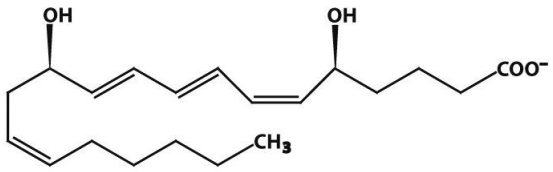


Eicosanoids and their functions

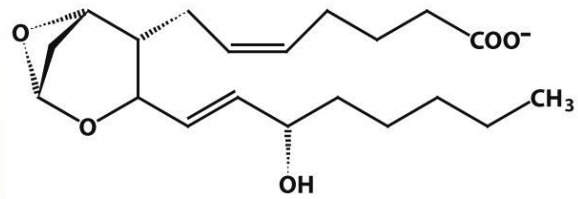
- Prostaglandins
  - Induction of inflammation
  - Inhibition of platelet aggregation
    - Inhibition of blood clotting
- Leukotrienes
  - Constriction of smooth muscles
    - Asthma
- Thromboxanes
  - Constriction of smooth muscles
  - Induction of platelet aggregation
- Prostacyclins
  - An inhibitor of platelet aggregation
  - A vasodilator



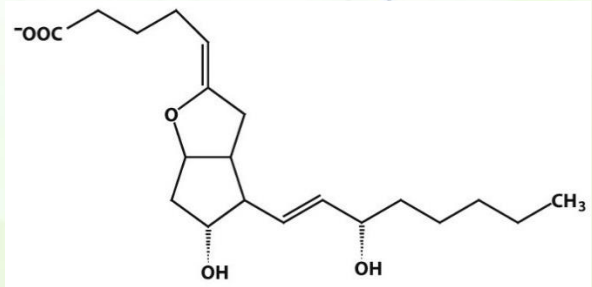
Prostaglandin E_2



Leukotriene B_4

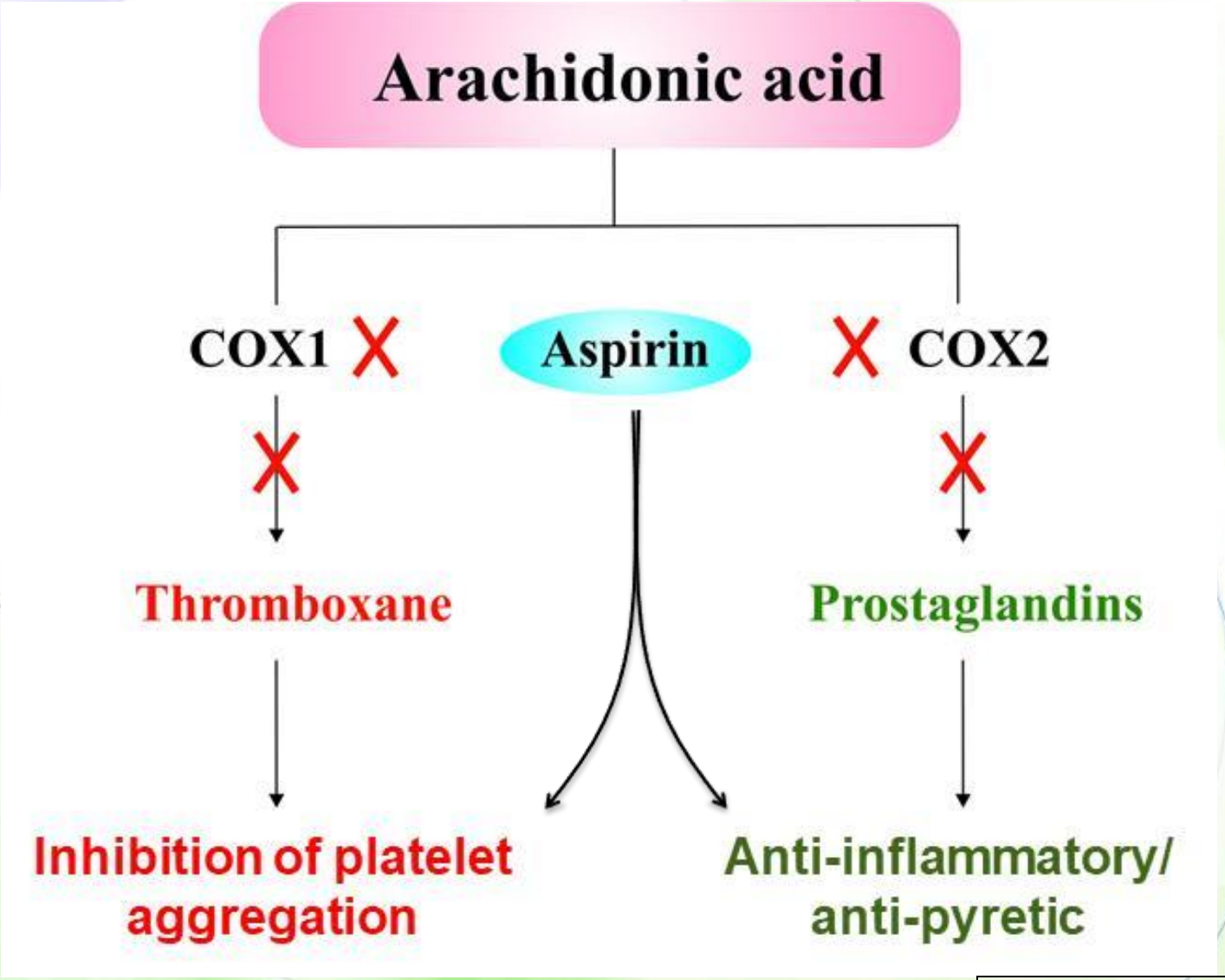


Thromboxane A_2 (TXA_2)



Prostacyclin (PGI_2)

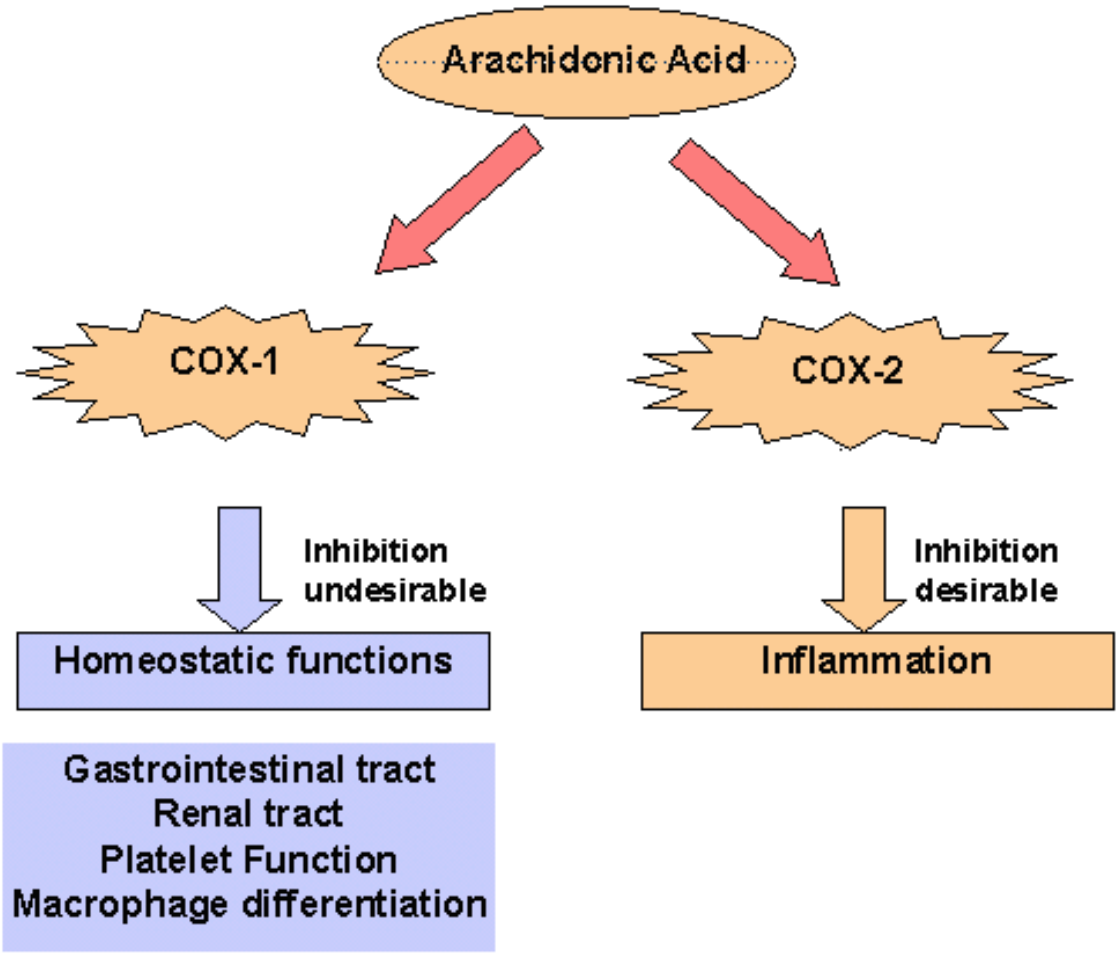
Aspirin is good



COX: Cyclooxygenase

Targets of Aspirin

- Cyclooxygenase is present in three forms in cells, COX-1, COX-2, and COX-3.
- Aspirin targets both, but COX-2 should only be the target.



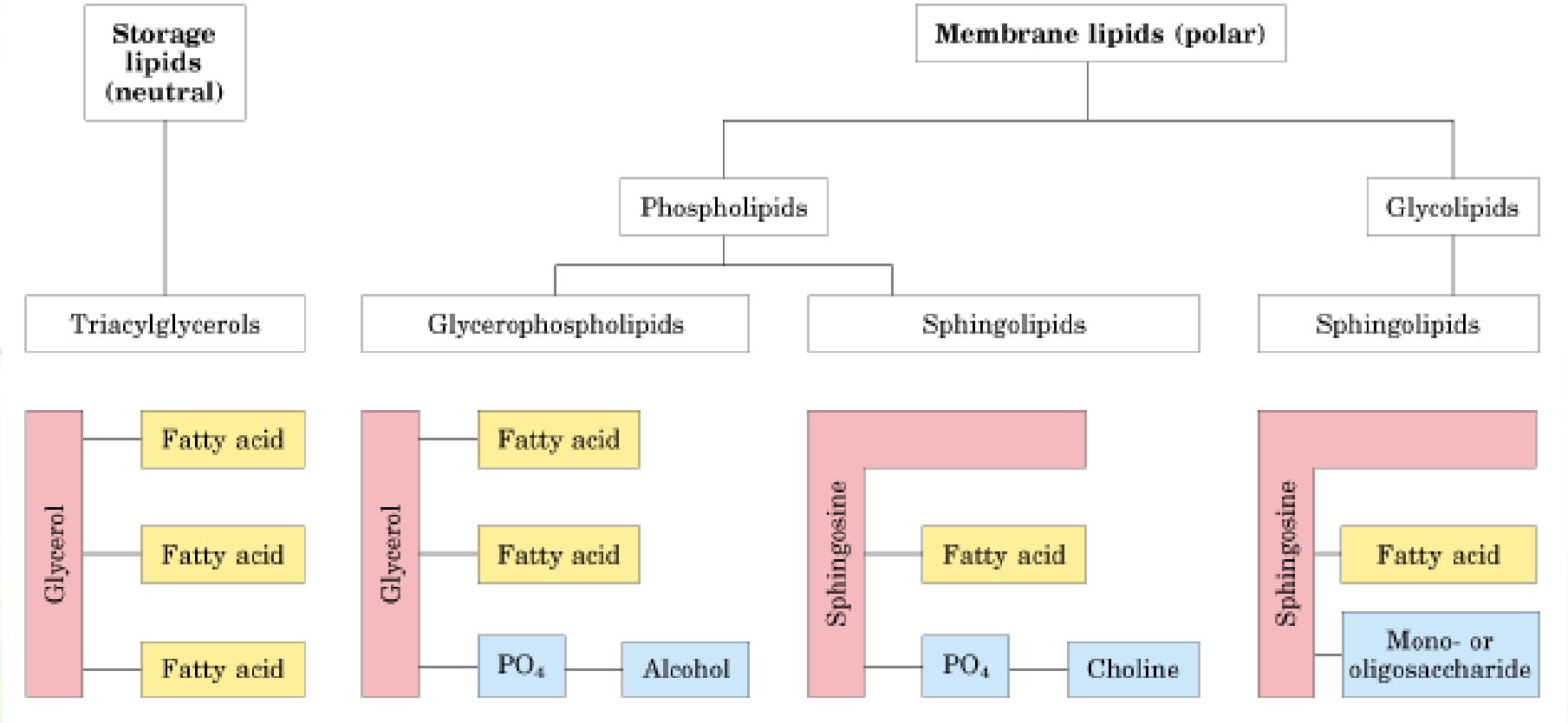
Celebrex

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

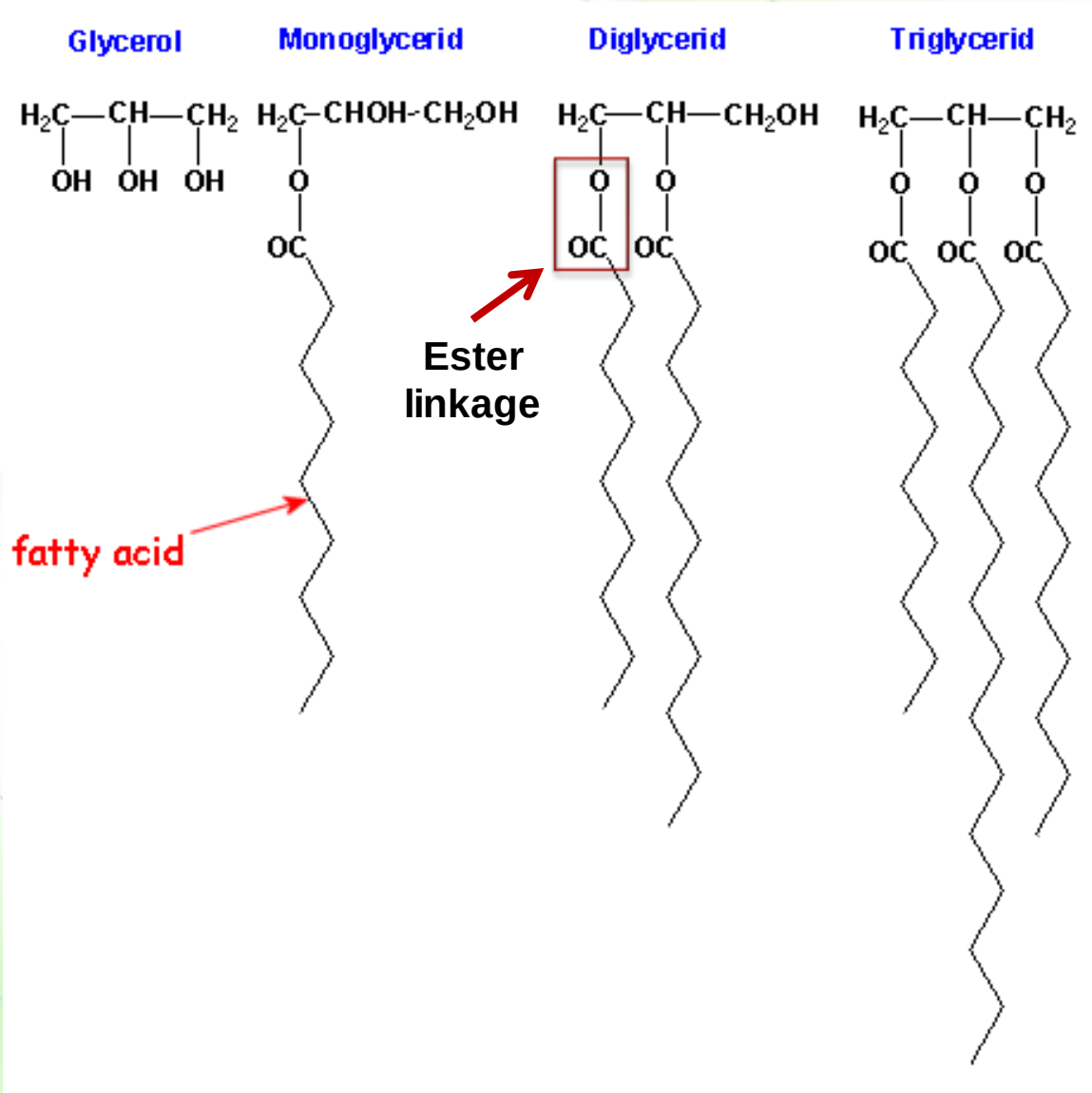
Omega fatty acids

- 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

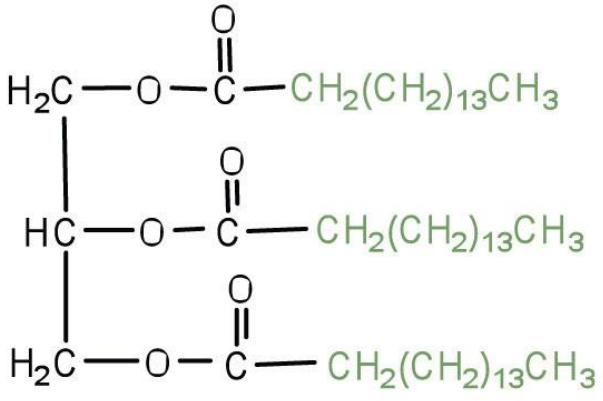
Complex lipids


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

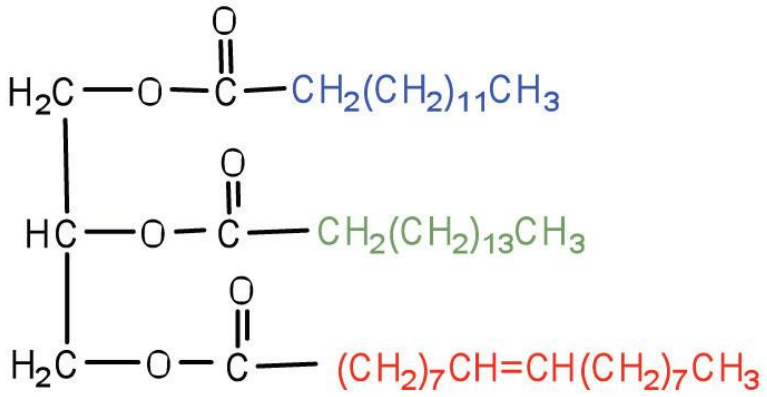
Triglycerides



Types of glycerides



Tristearin
a simple triglyceride

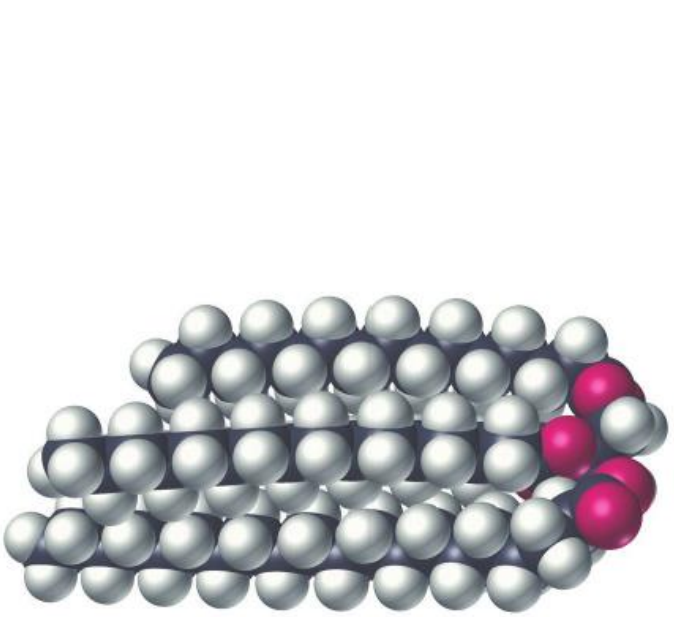


a mixed triglyceride

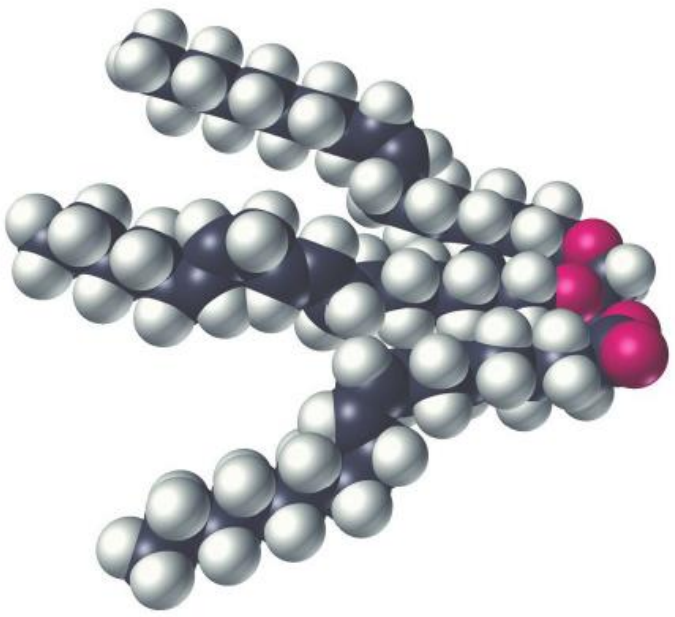
How soluble will a triglyceride be if fatty acids are unsaturated?

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



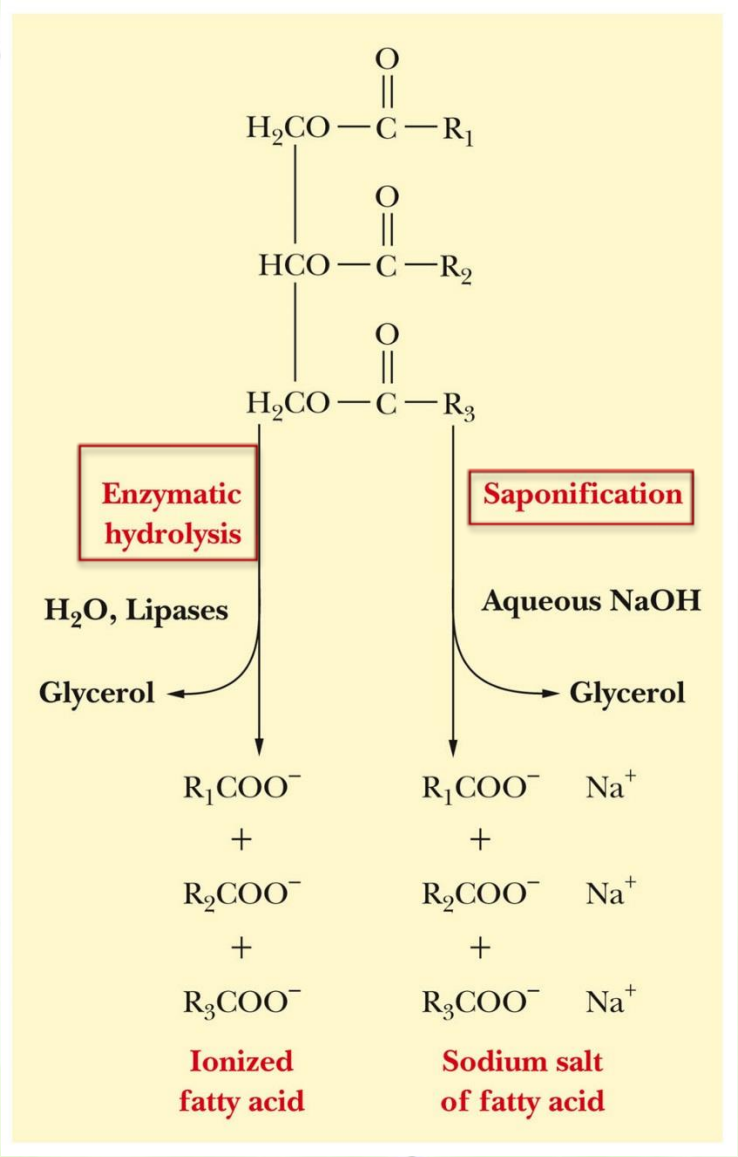
A fat



An oil

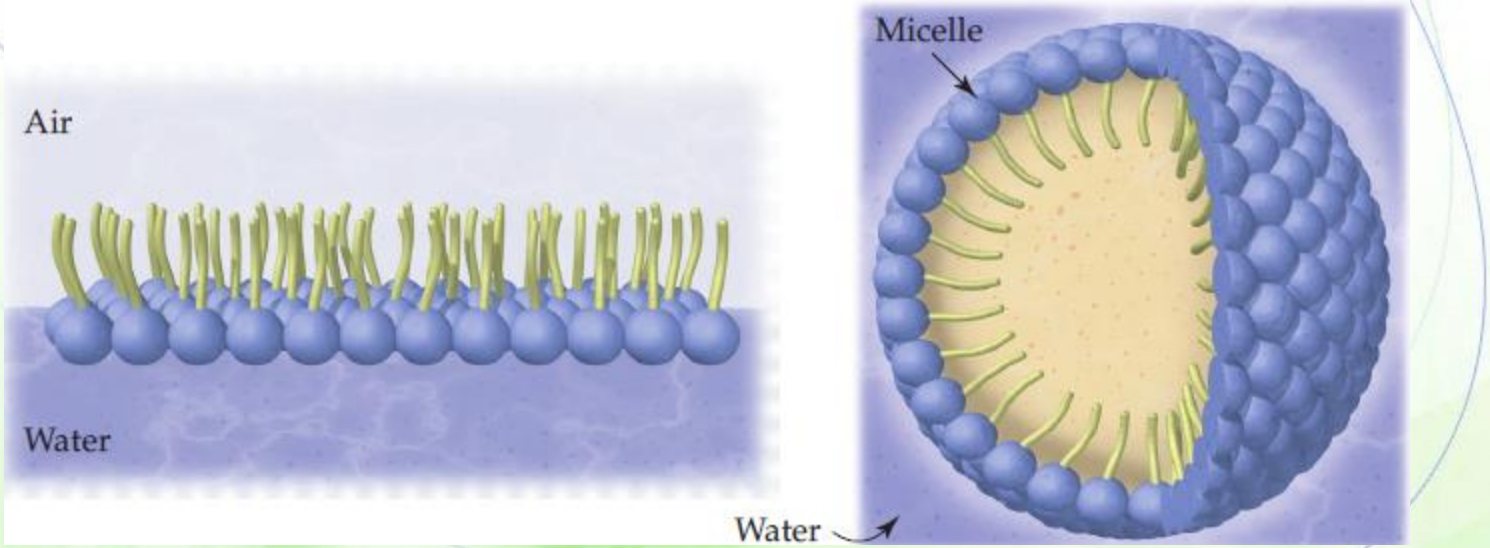
Saponification

- Hydrolysis: steam, acid, enzyme (e.g., lipase of pancreas)
- Saponification: Alkaline hydrolysis produces salts of fatty acids (soaps). Soaps cause emulsification of oily material.



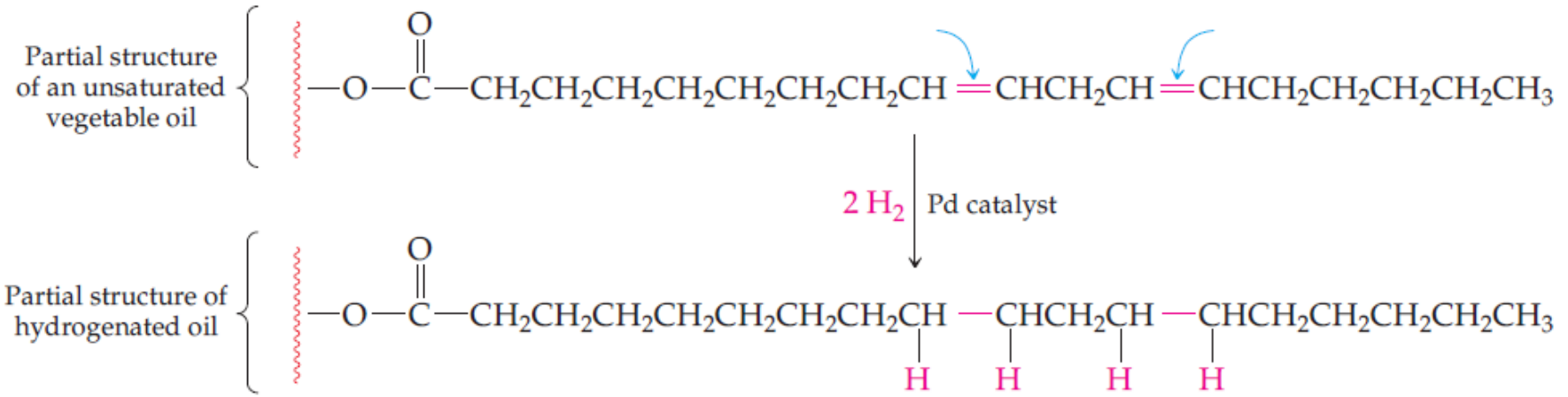
How does soap work?

- 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

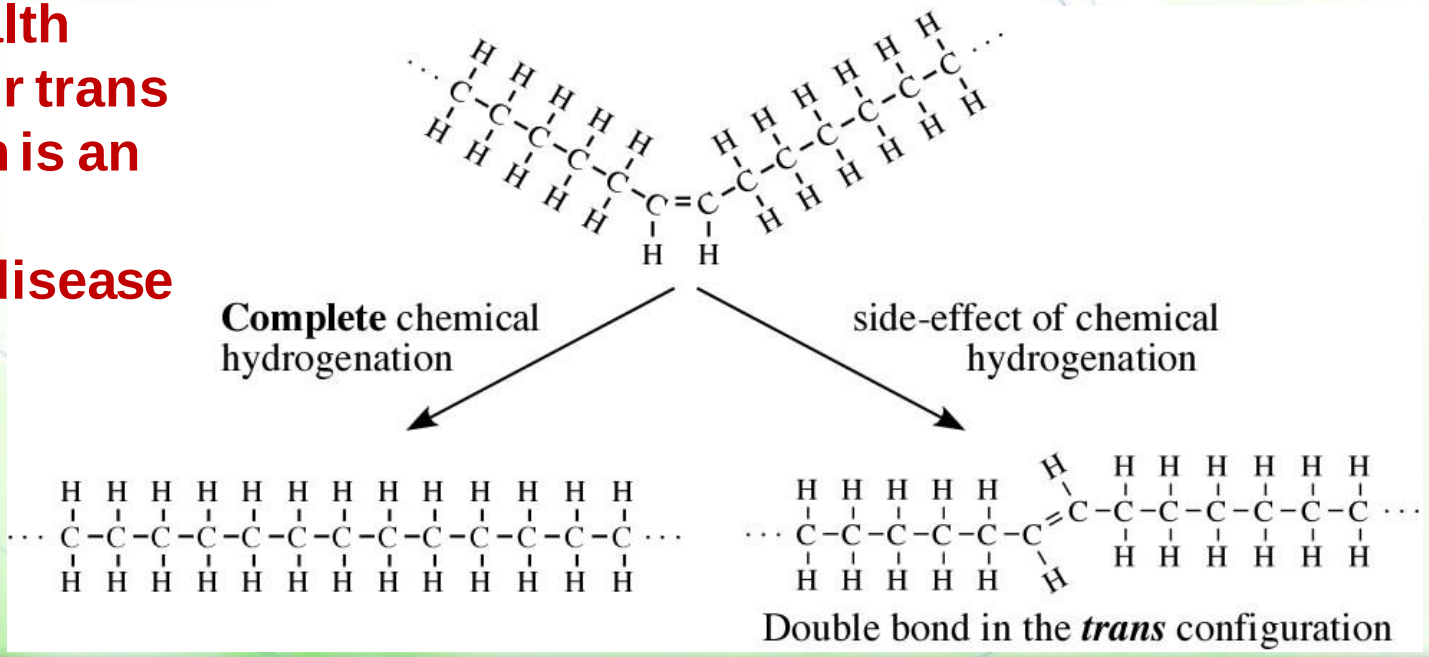
- The carbon-carbon double bonds in vegetable oils can be hydrogenated to yield saturated fats in the same way that any alkene can react with hydrogen to yield an alkane.



Trans fat

- Although the animal fat is unhealthy, it has better cooking properties and better taste.
- Therefore, chemists invented a method of converting unsaturated oil 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 melts on warm toast.

Nutrition Facts

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

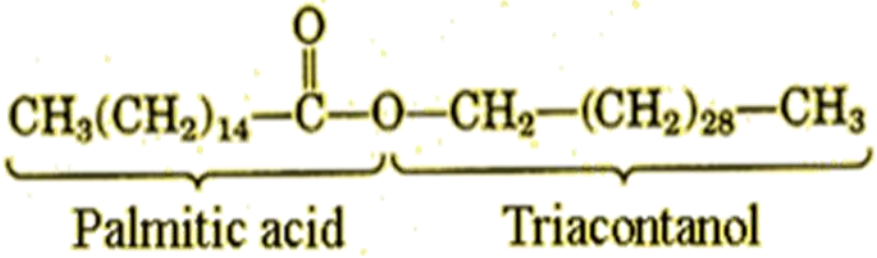
*Percent Daily Values (DV) are based on a 2,000 calorie diet.

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

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.

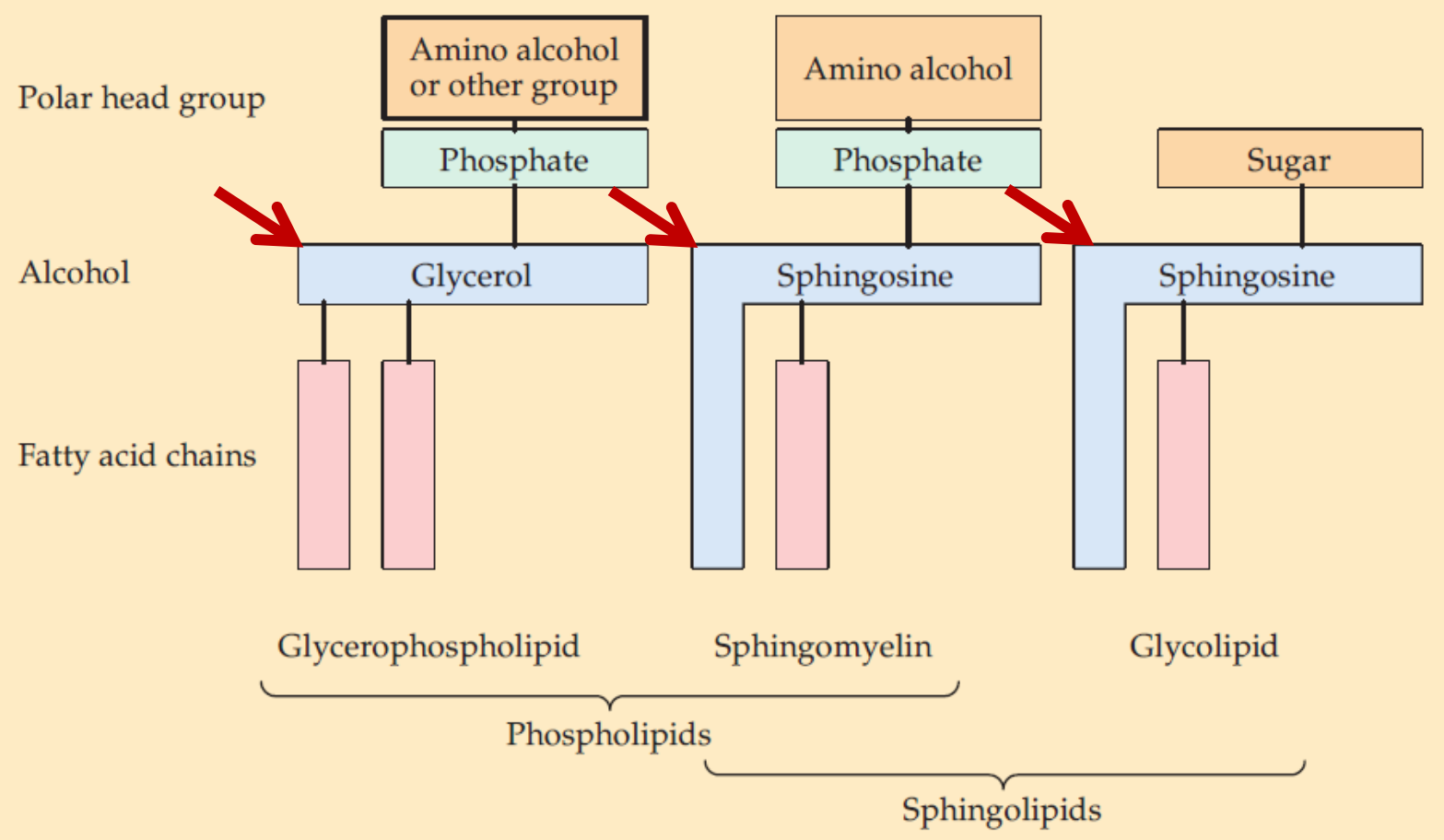
Waxes



- 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 acrolin 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

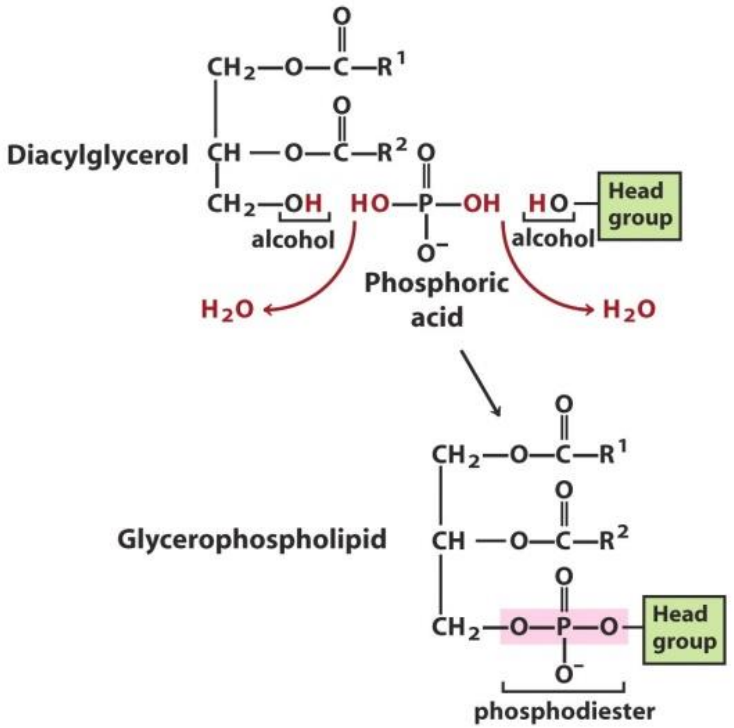
Type	Structural Formula	Source	Uses
Beeswax	$CH_3(CH_2)_{14}-C(=O)-O-(CH_2)_{29}CH_3$	Honeycomb	Candles, shoe polish, wax paper
Carnauba wax	$CH_3(CH_2)_{24}-C(=O)-O-(CH_2)_{29}CH_3$	Brazilian palm tree	Waxes for furniture, cars, floors, shoes
Jojoba wax	$CH_3(CH_2)_{18}-C(=O)-O-(CH_2)_{19}CH_3$	Jojoba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

Membrane lipids



The most prevalent class of lipids in membranes is the glycerophospholipids

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	$-CH_2-\underset{\displaystyle COO^-}{\underset{\displaystyle |}{CH}}-\overset{+}{N}H_3$

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

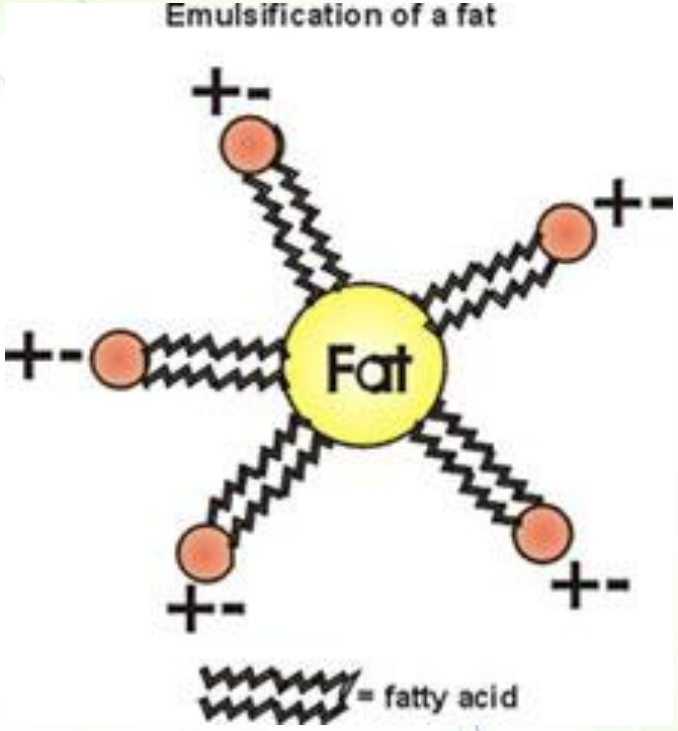
Glycerophospholipids - Lecithins

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

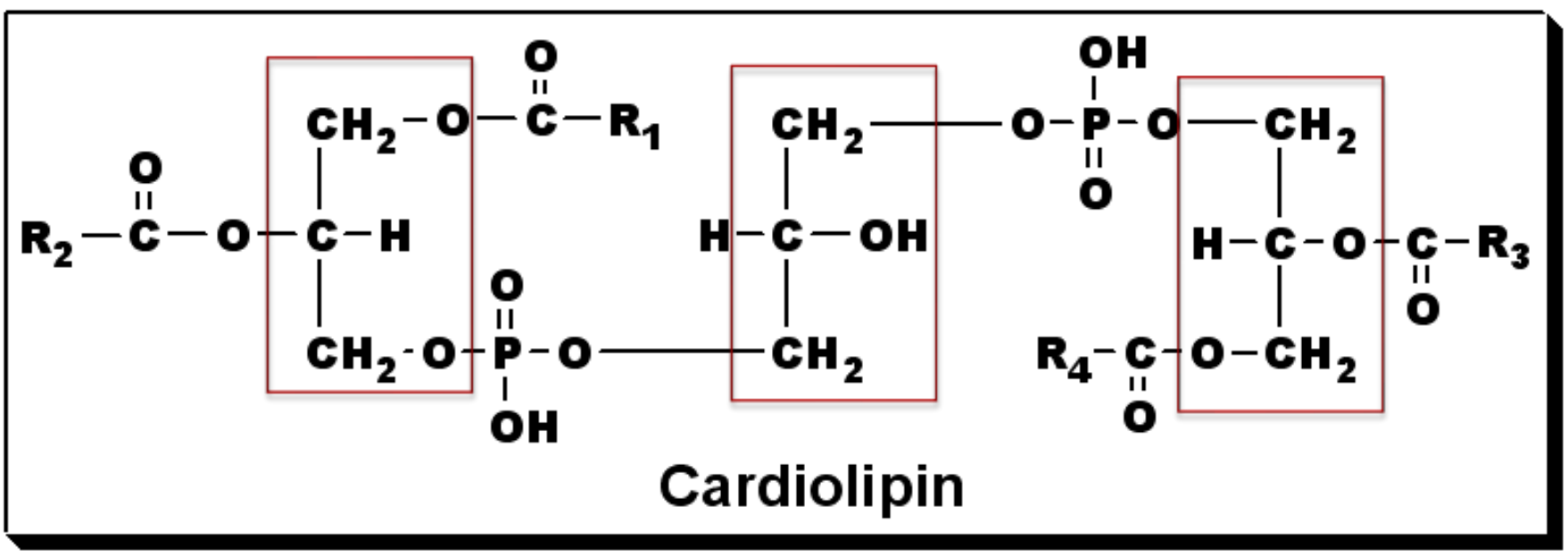
Emulsification

- 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.



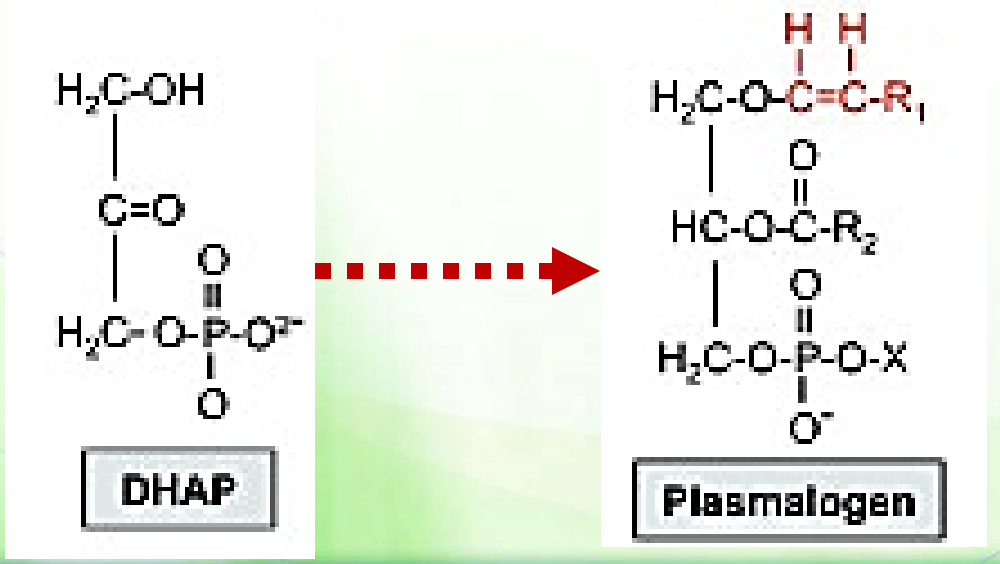
Glycerophospholipids - Cardiolipins

- 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



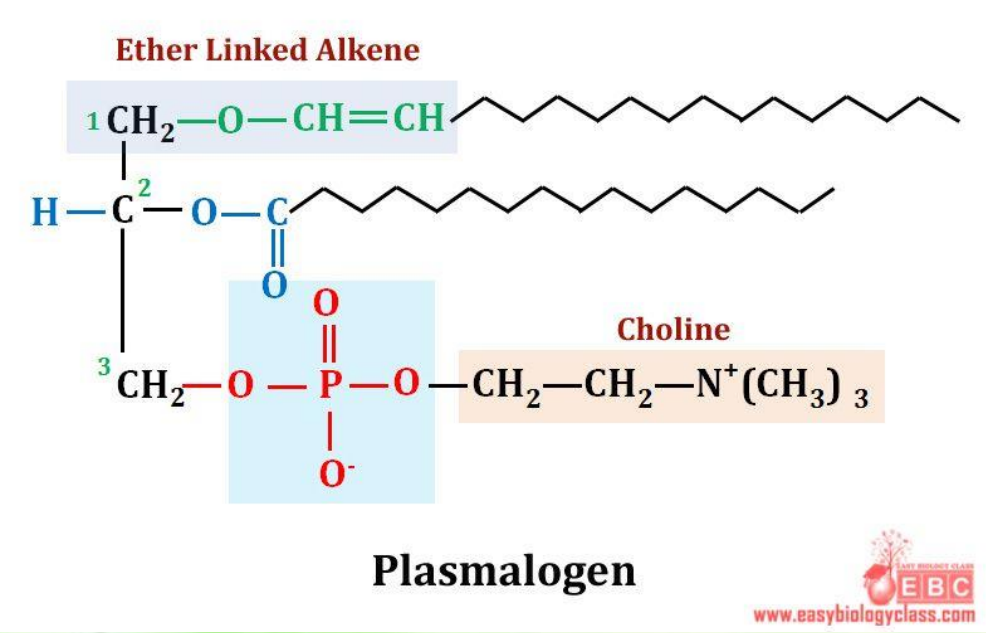
Plasmalogens

- 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



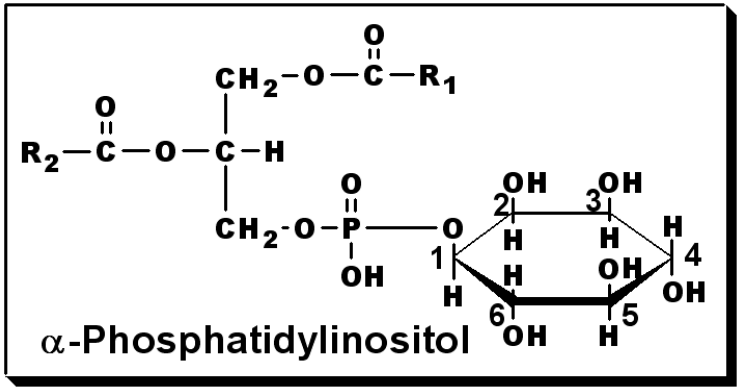
Major classes of plasmalogens

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



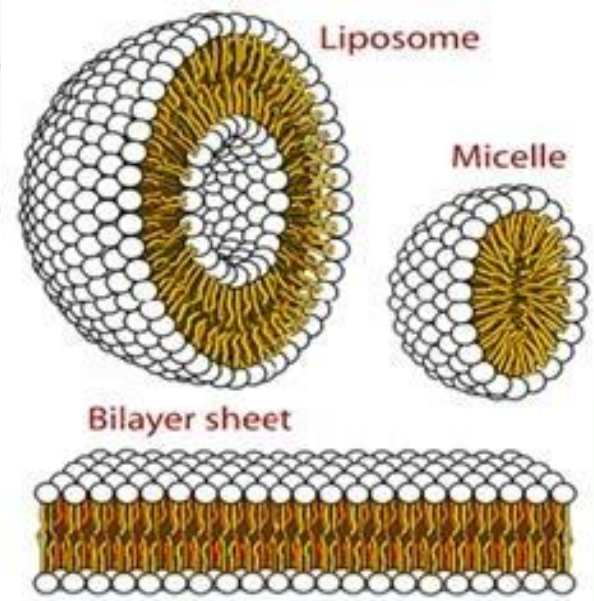
Glycerophospholipids - Inositides

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

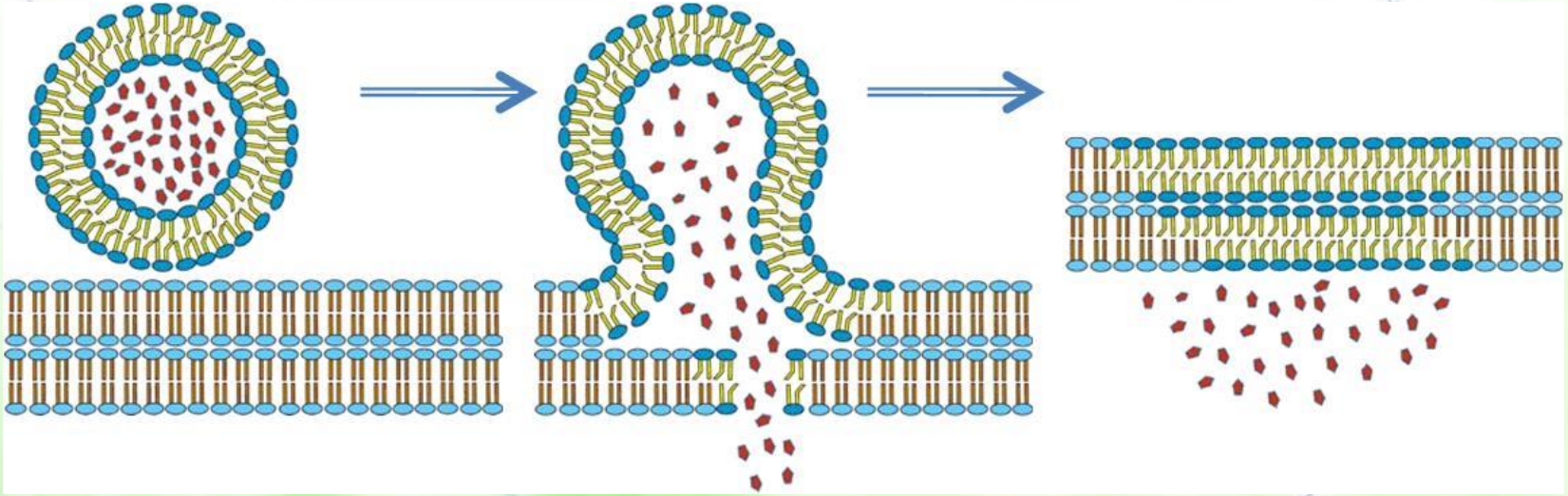


- Functions:
  - Major component of cell membrane
  - Second messenger during signal transduction
  - On hydrolysis by phospholipase C, phosphatidyl-inositol-4,5-diphosphate produces diacyl-glycerol (DAG) & inositol-triphosphate (IP3); which liberates calcium

The different structures of phospholipids

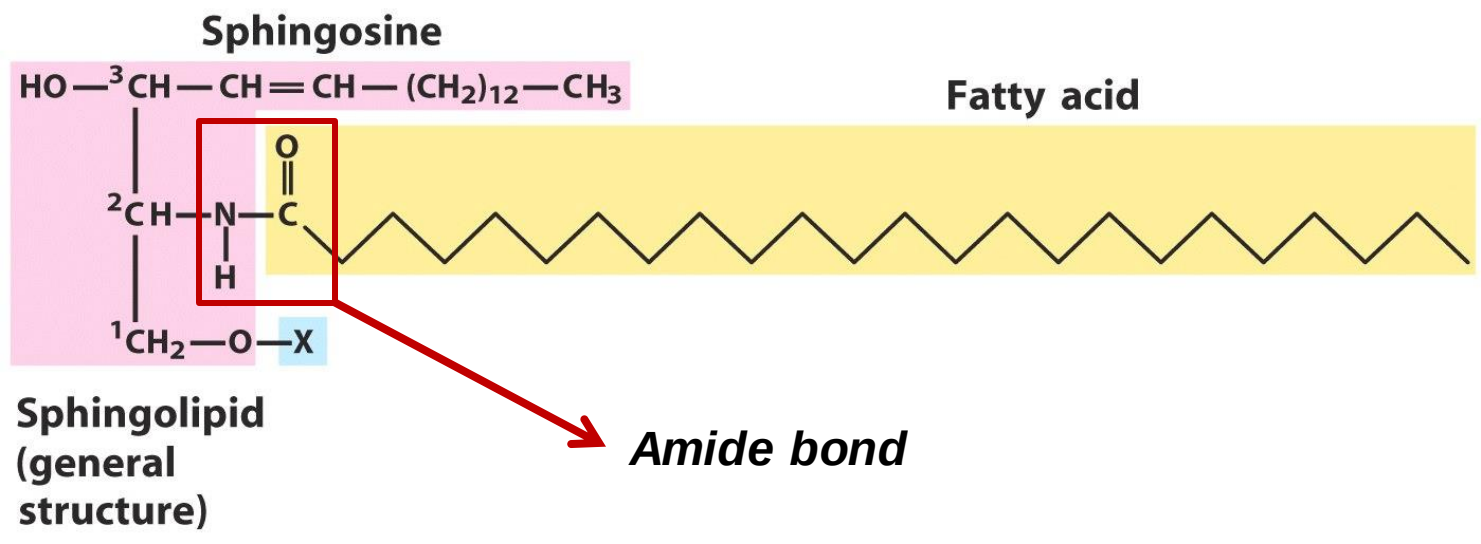


Uses of liposomes: delivery

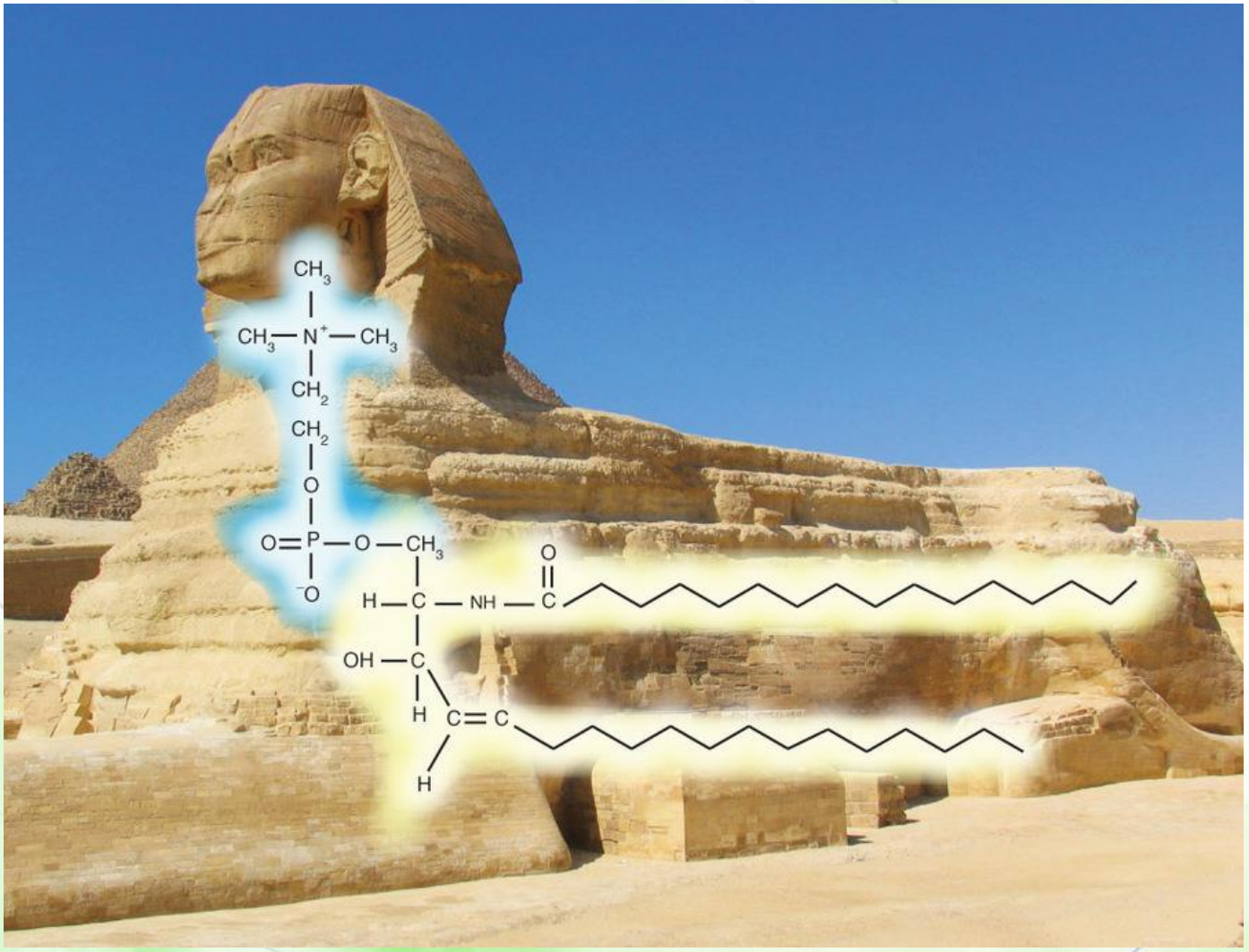


Sphingolipids

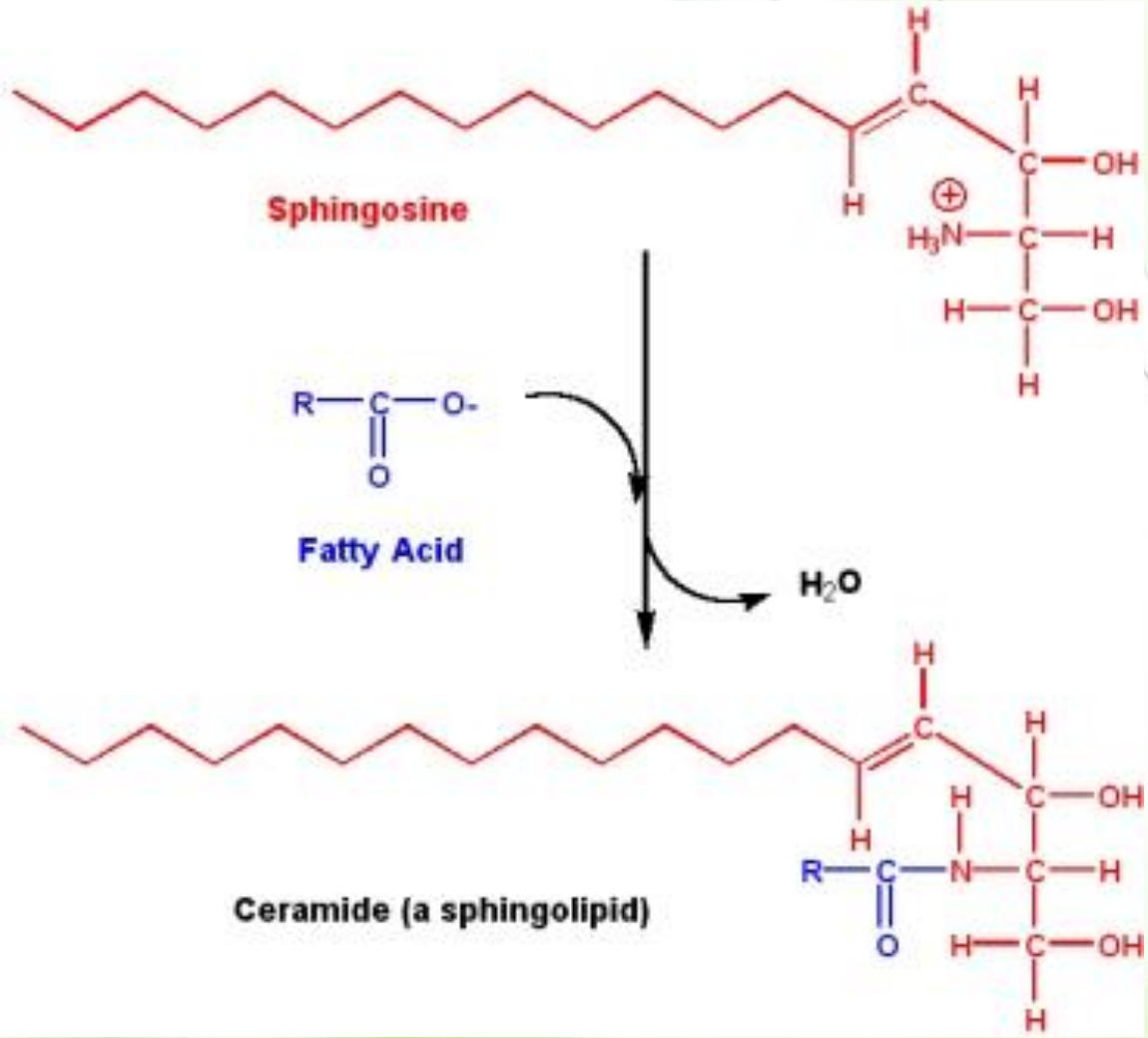
- Sphingolipids are found in the plasma membranes of all eukaryotic cells and is highest in the cells of the central nervous system
- The core of sphingolipids is the long-chain amino alcohol, sphingosine



Mysterious lipids



Ceramide

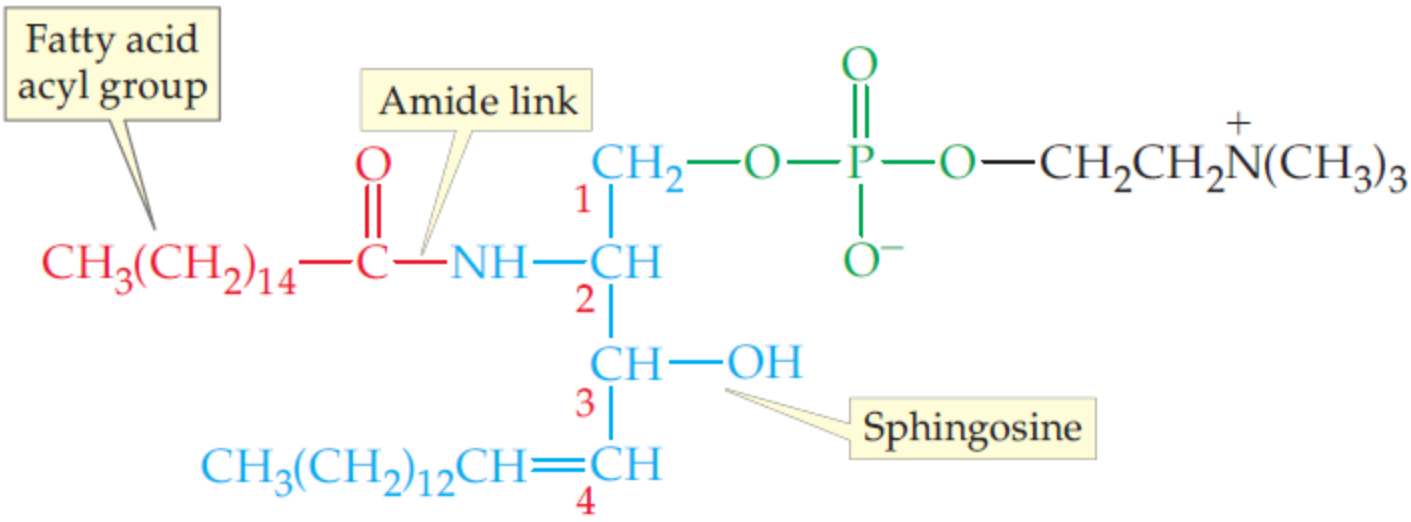


Types of sphingolipids

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

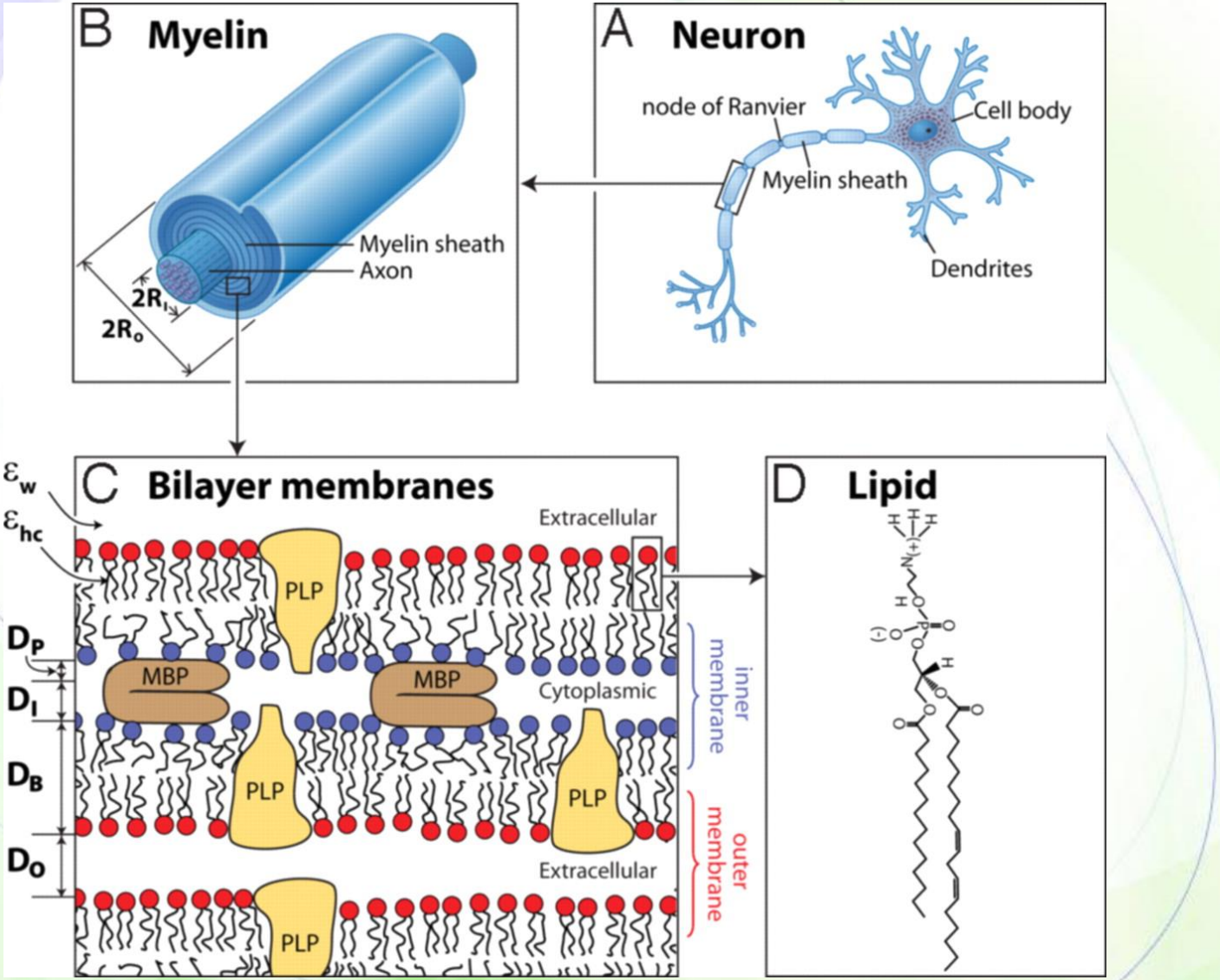
Sphoingomyelin

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



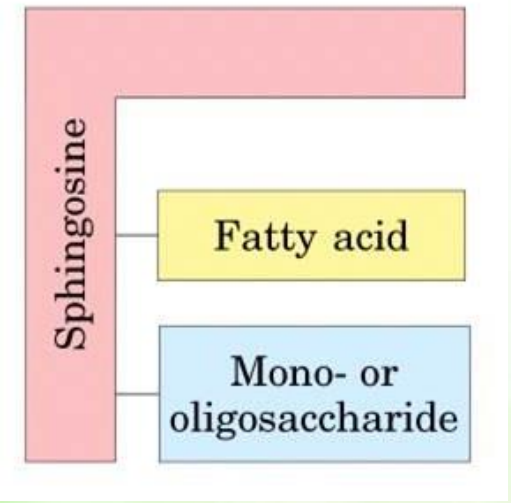
A sphingomyelin (a sphingolipid)

Zooming into the myelin



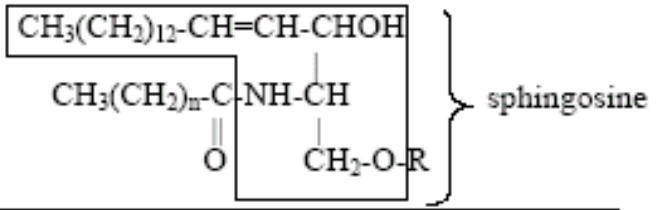
Glycolipids

- 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



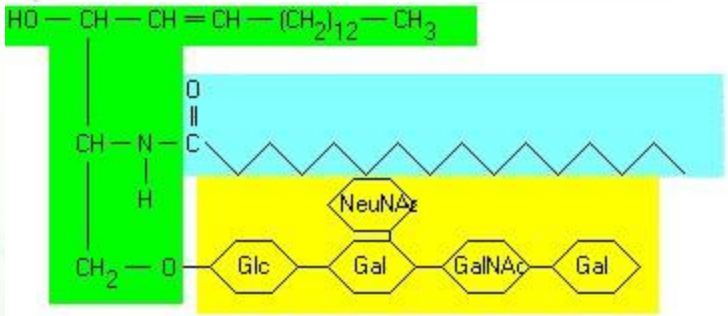
Glycolipids

- **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.**

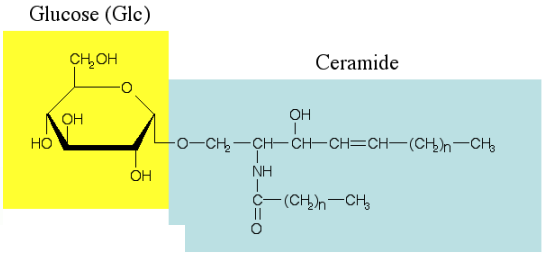


Sphingolipid type	R group
Ceramide	H
Sphingomyelin	phosphocholine
Cerebroside	monosaccharide (galactose or glucose)
Globoside	two or more sugars (galactose, glucose, N-acetylglucosamine
Ganglioside	three or more sugars including at least one sialic acid

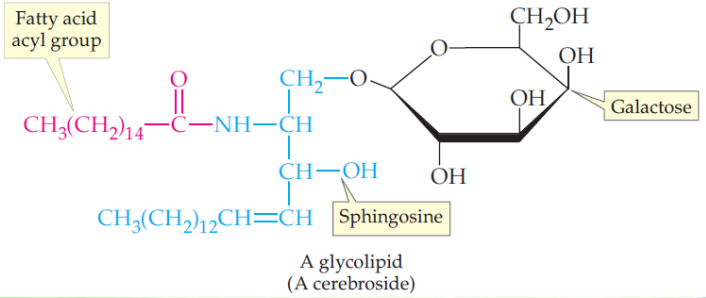
glycolipids



Glucocerebroside



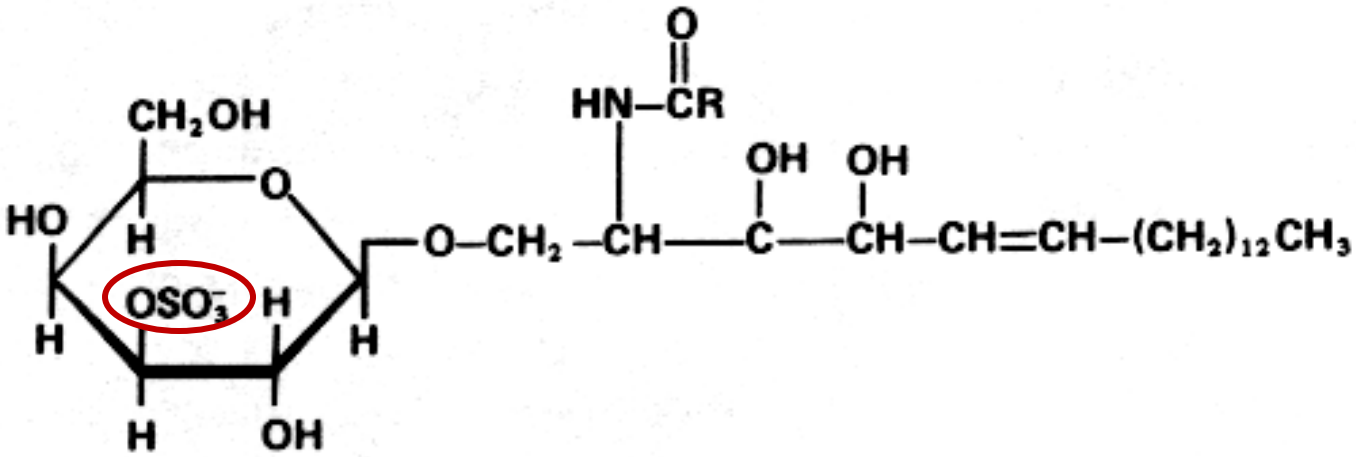
Gangliosides are targeted by cholera toxin in the human intestine.

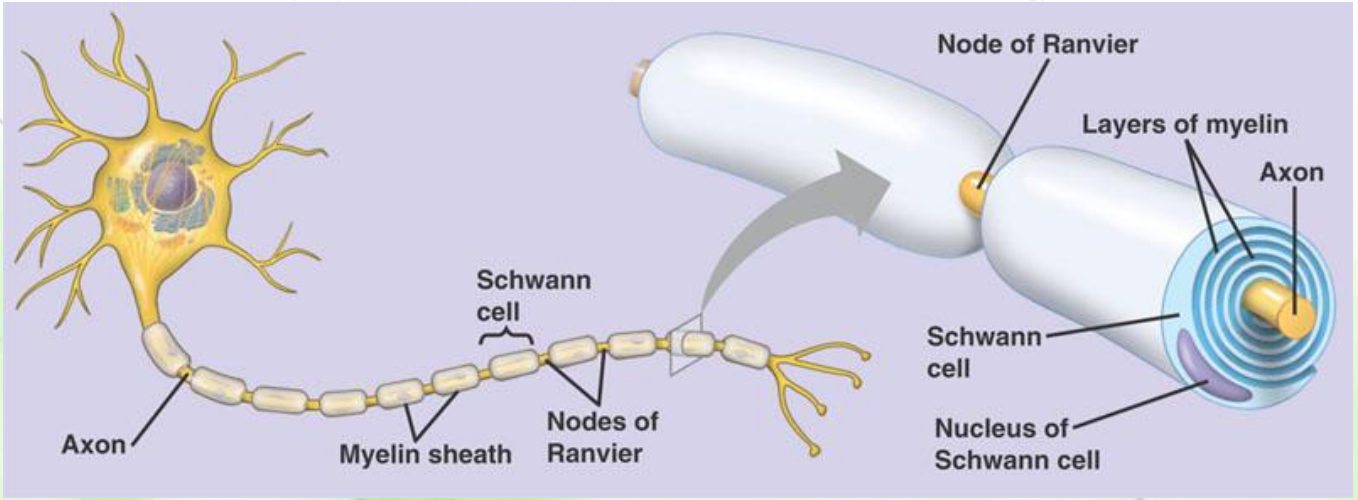


A glycolipid
(A cerebroside)

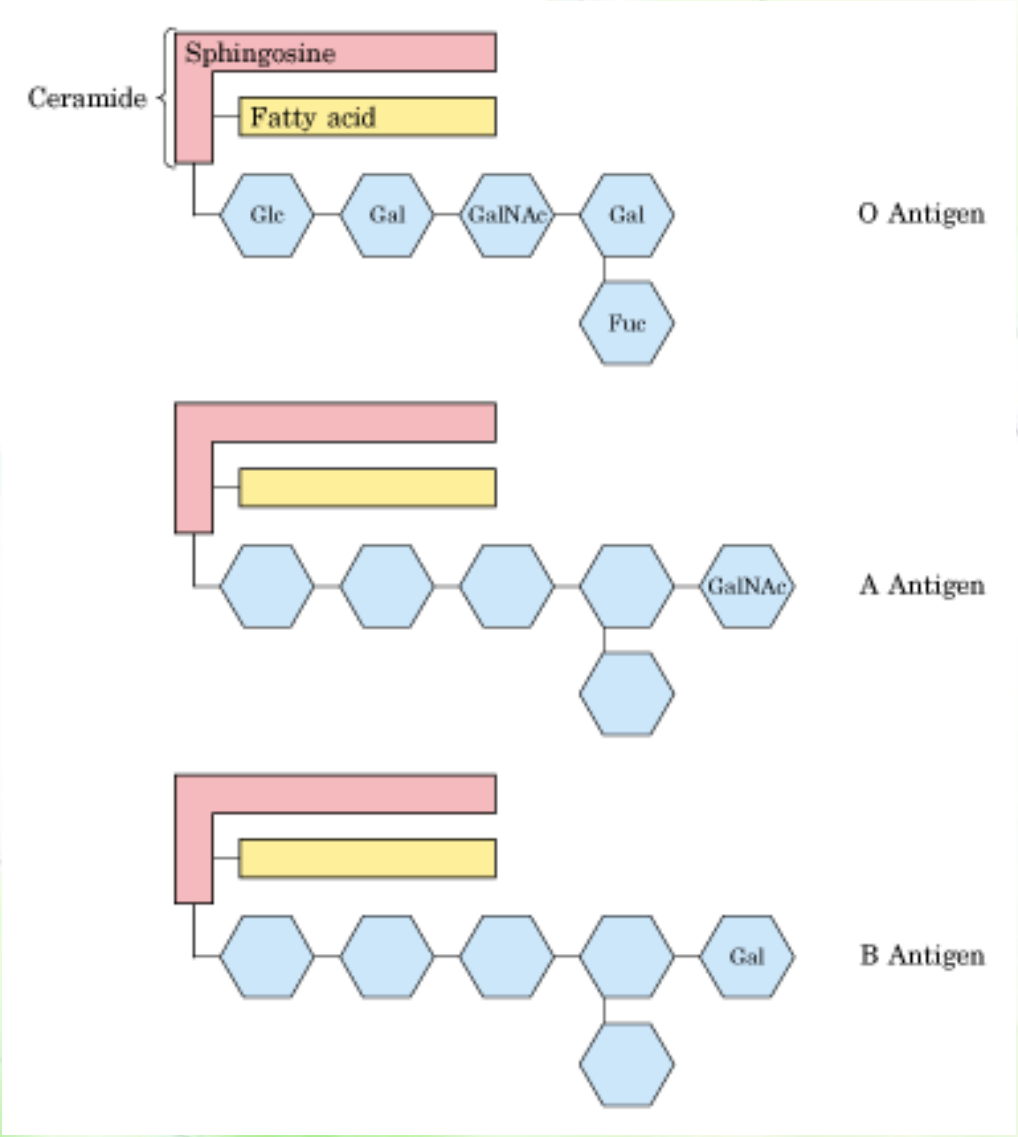
Sulfatides

- Synthesized from galactocerebroside
- Abundant in brain myelin

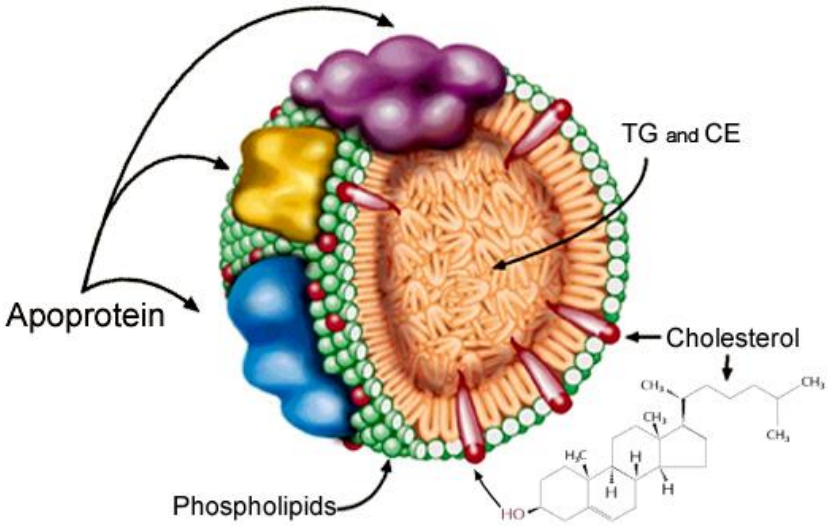




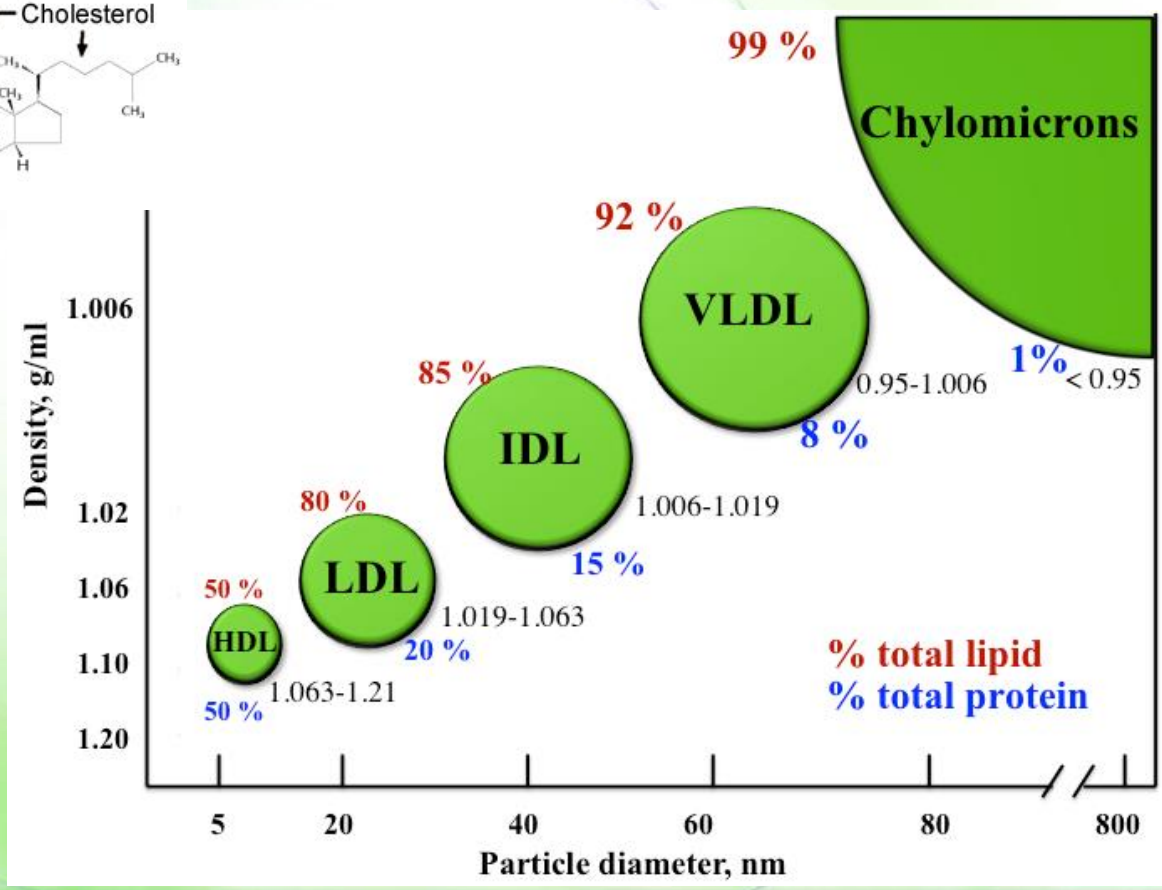
Sphingolipids and blood groups



Lipoproteins



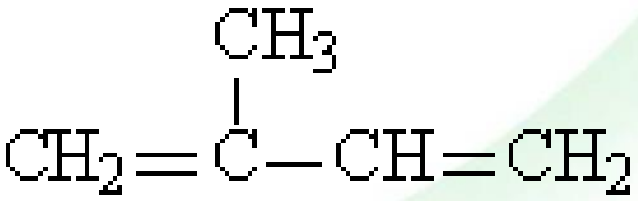
Function: transport of different types of lipids (cholesterol, cholesterol esters, phospholipids & triacylglycerols) in blood plasma.



As lipid content increases, the density decreases

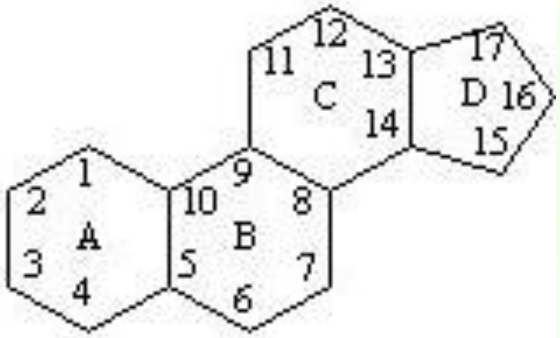
Steroids

The precursor



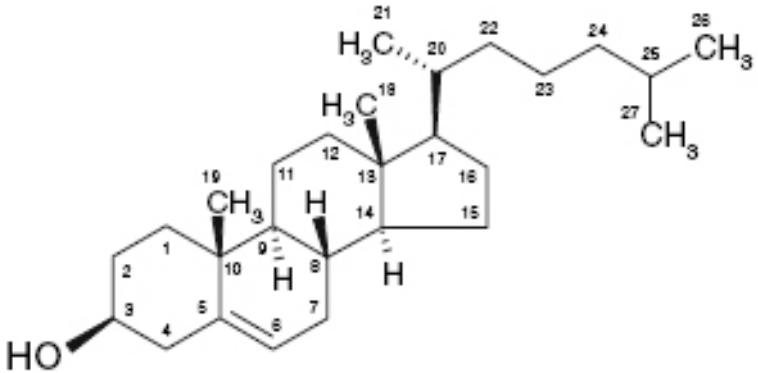
Isoprene

The nucleus

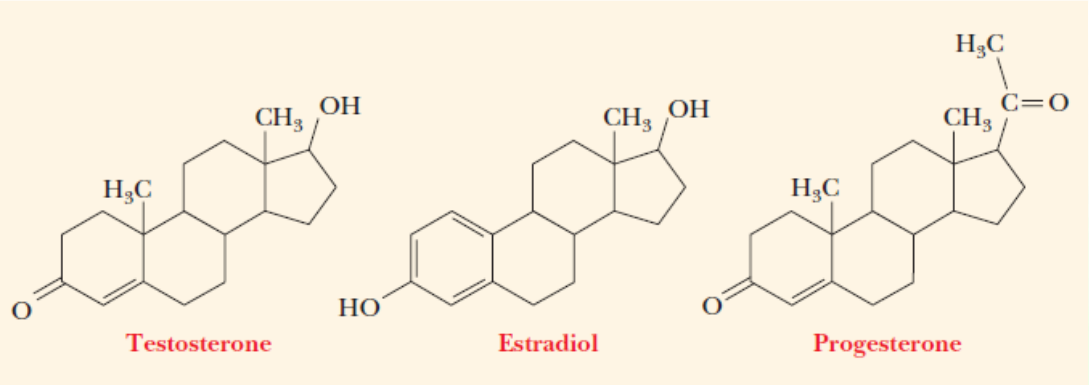


Steroid nucleus

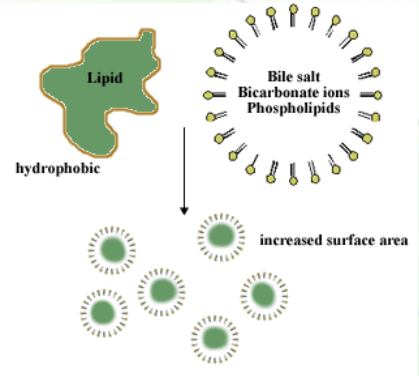
The most common steroid

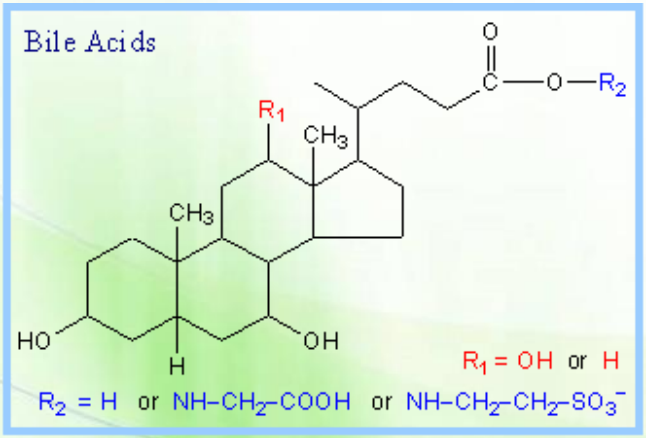


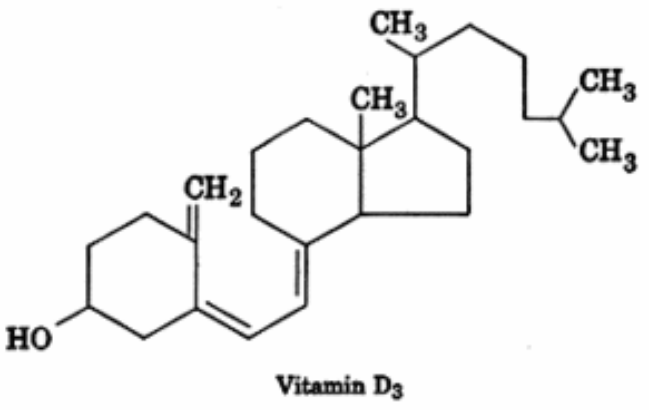
Products of cholesterol



- 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)

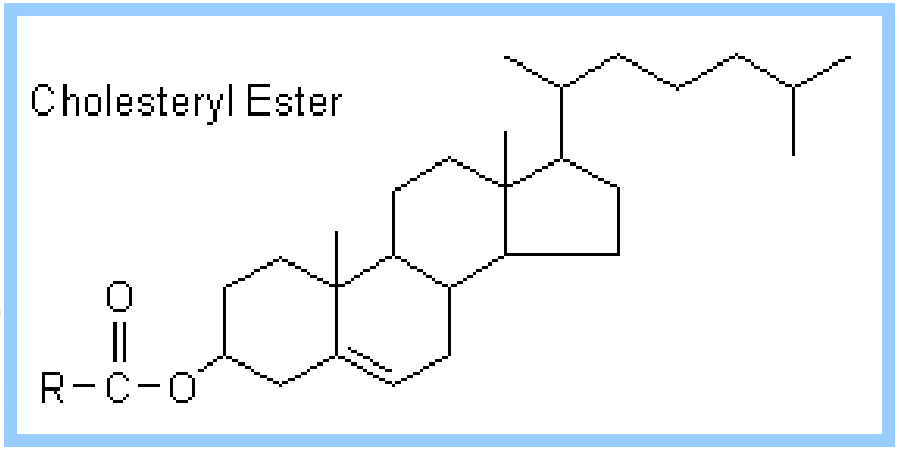


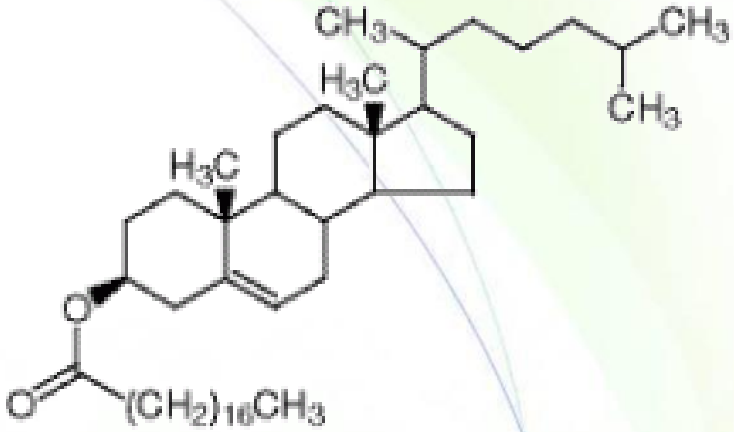




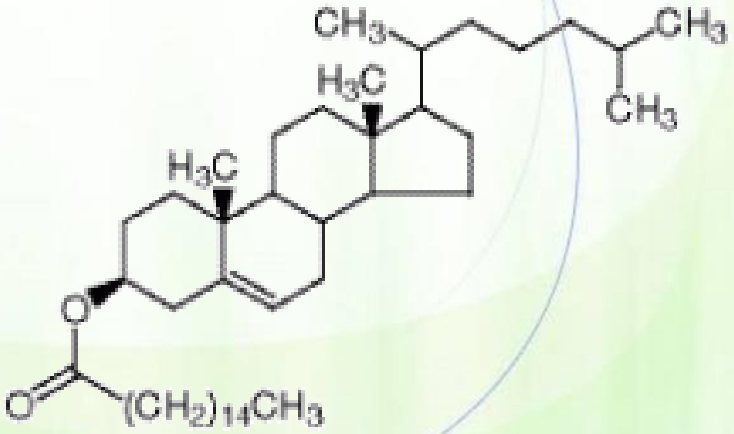
Cholesterol esters

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



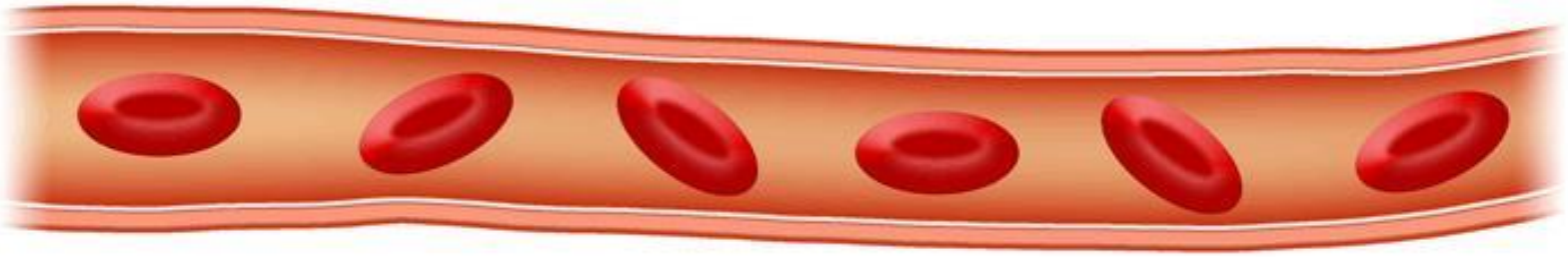


Name the molecules?

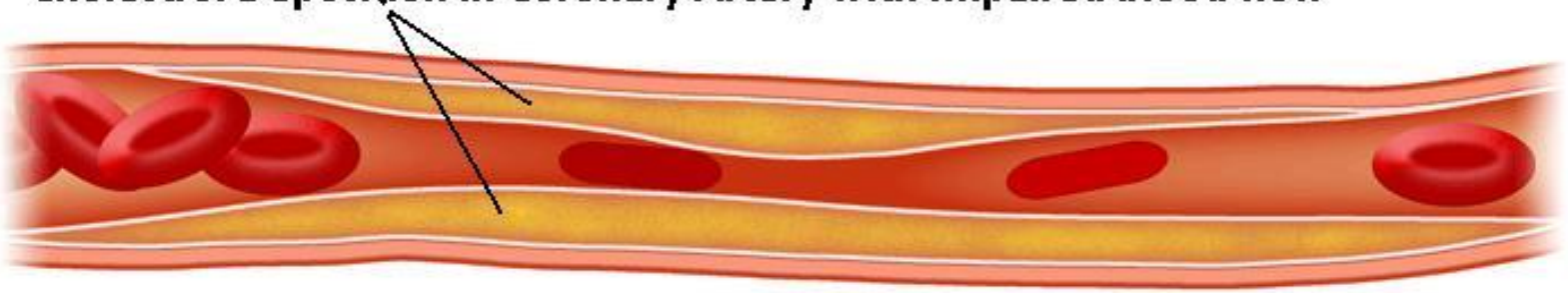


Atherosclerosis

Normal Coronary Artery with Normal blood flow

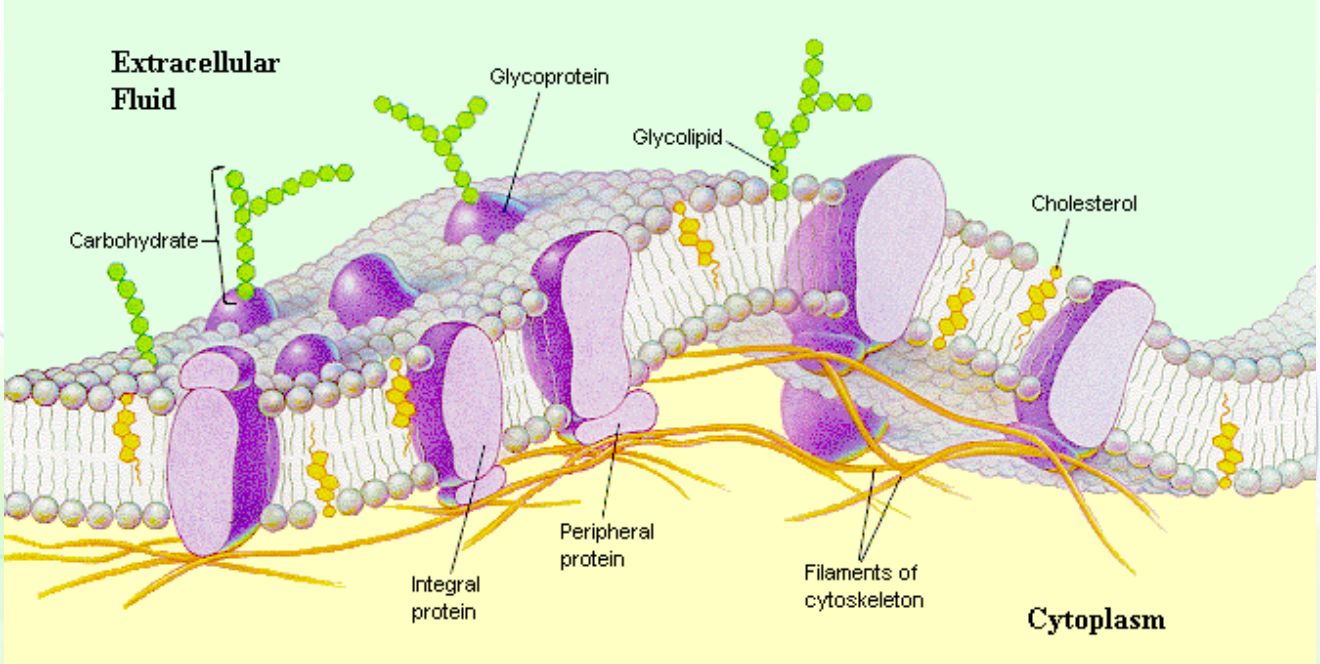


Cholestrol Deposition in Coronary Artery with Impaired blood flow



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.

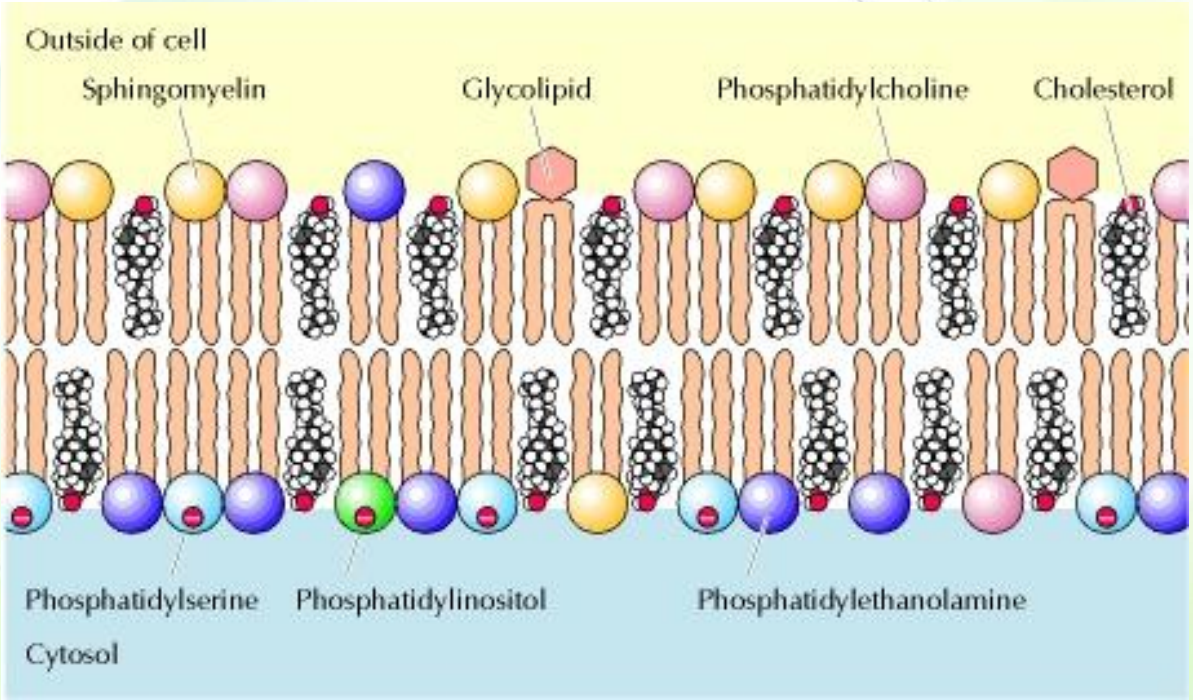


Phospholipids

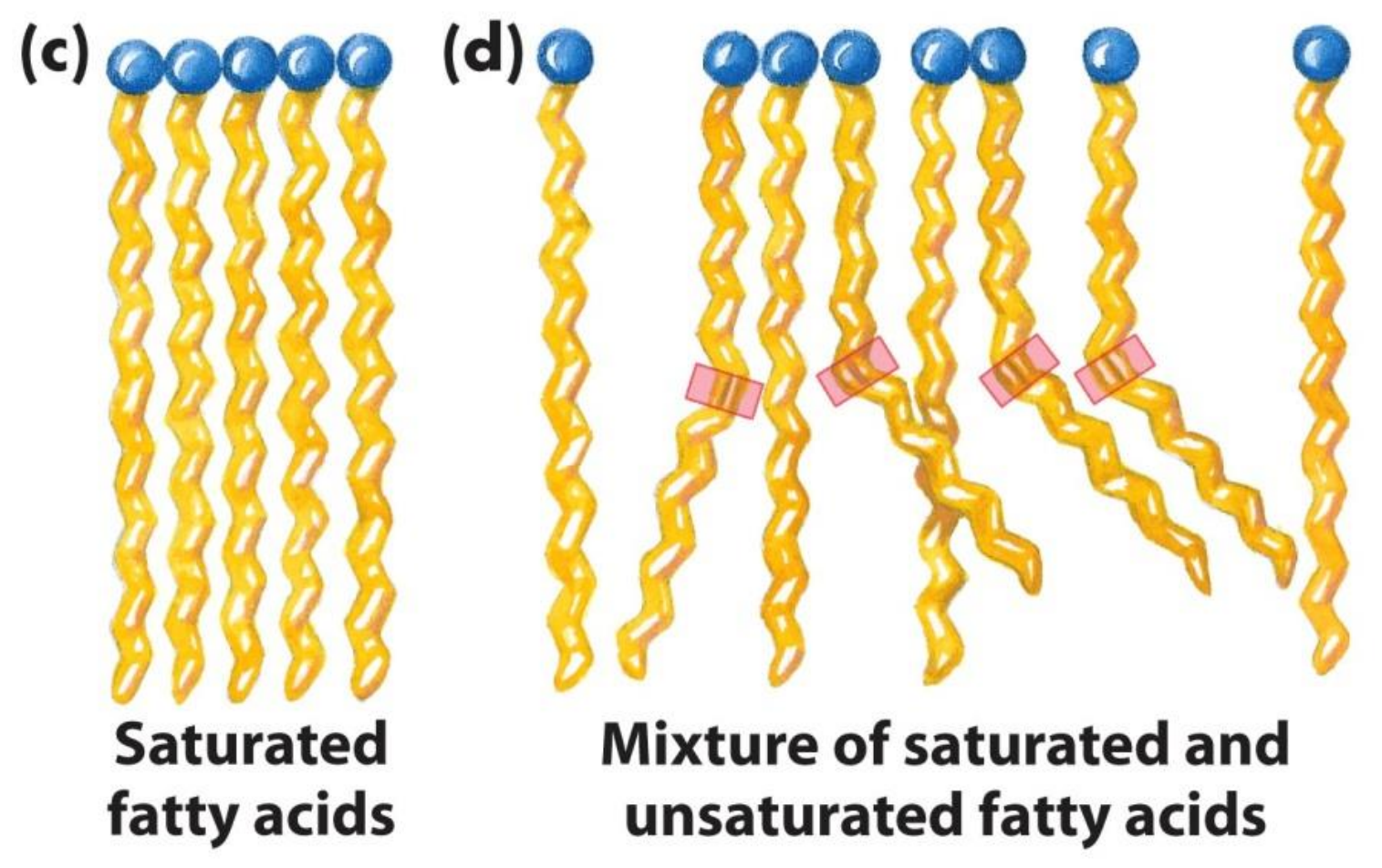
- The outer: phosphatidylcholine, sphingomyelin, and glycolipids(cell recognition)
- The inner: phosphatidylethanolamine, phosphatidylserine, and phosphatidylinositol (signaling)

Cholesterol is distributed in both leaflets

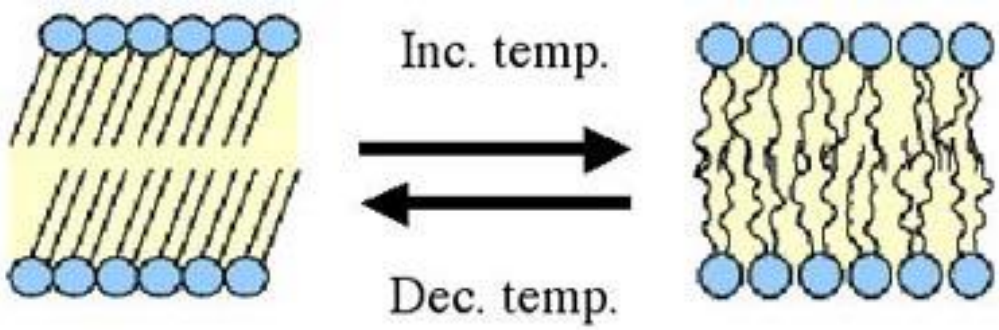
Animal cells vs. plant cells vs. prokaryotic cells



Fatty acids and membrane fluidity

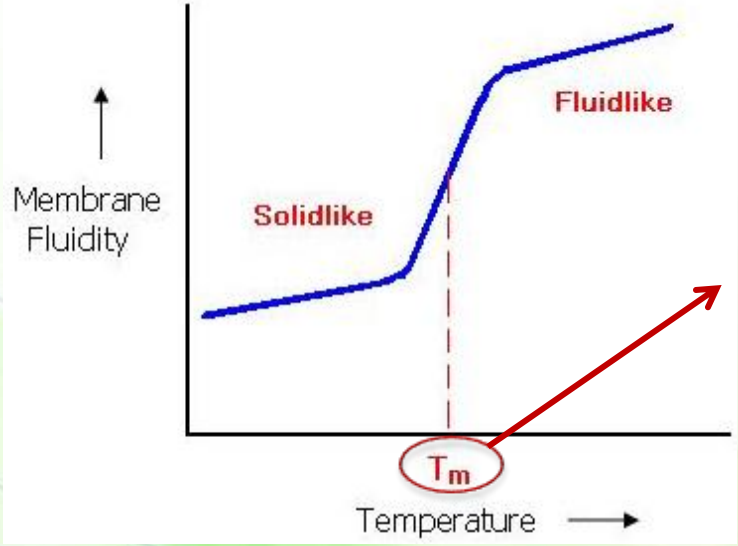


Membrane fluidity and temperature



Very regular,
Ordered structure

Less tightly packed,
Hydrocarbon tails
Disordered.

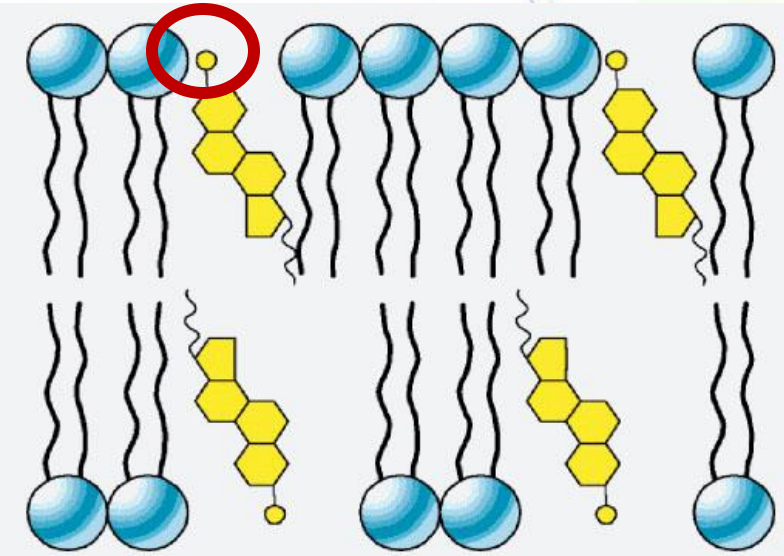


Melting temperature (transition temperature

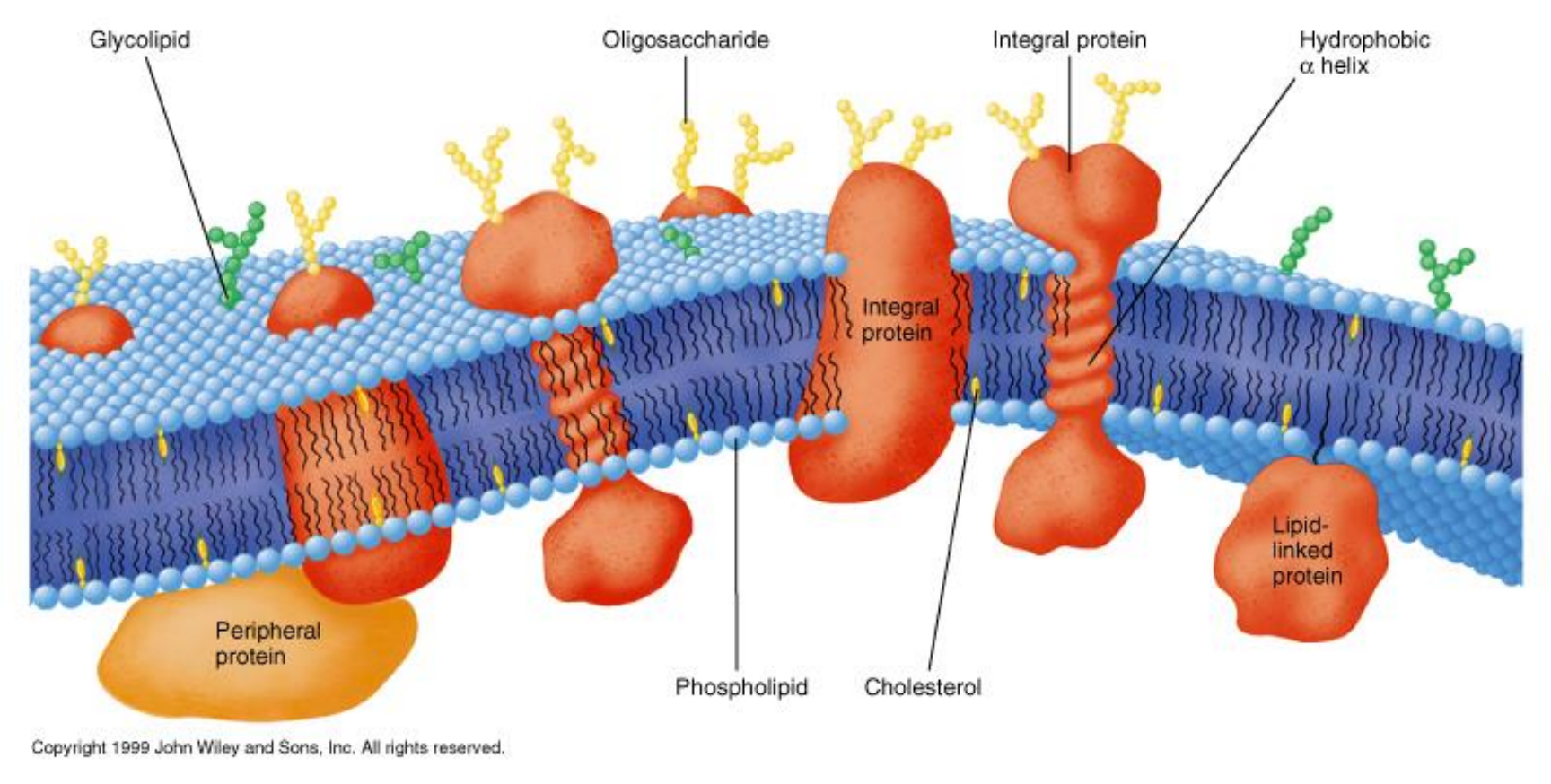
Cholesterol and membrane fluidity

- 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



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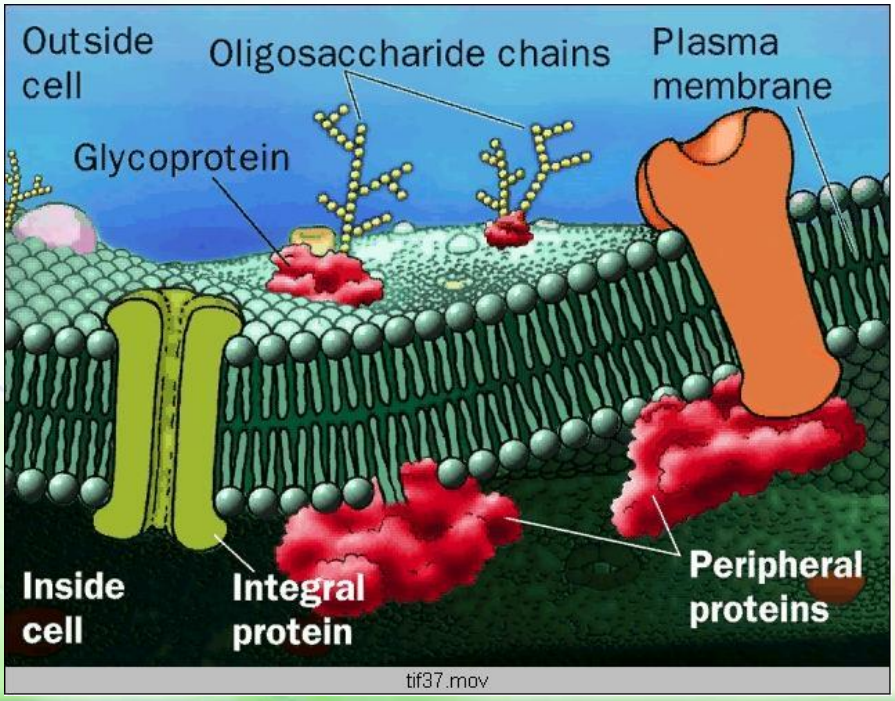
Types of membrane proteins

- 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

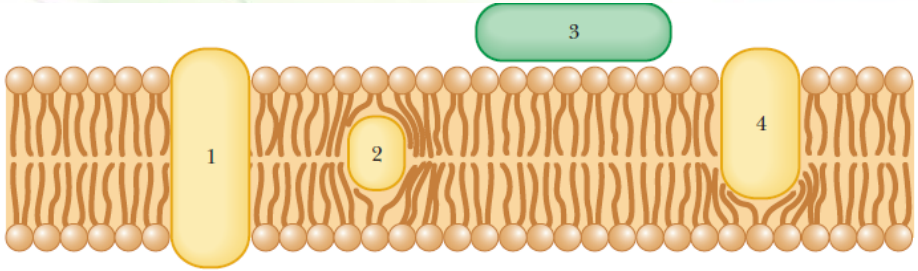
Peripheral membrane proteins

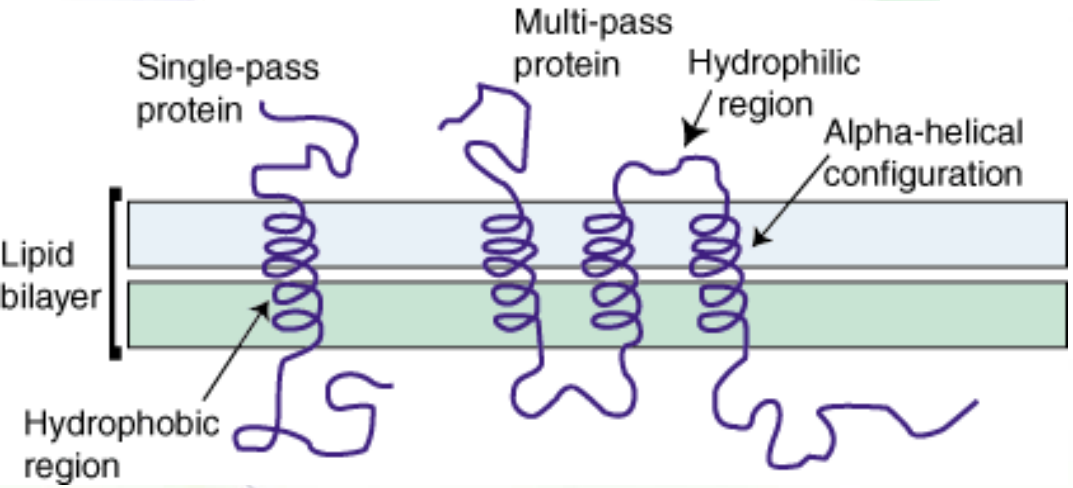
- They are associated with membranes but do not penetrate the hydrophobic core of the membrane
  - often associated with integral membrane proteins
- They are not strongly bound to the membrane and can be removed without disrupting the membrane structure
  - treatment with mild detergent



Integral membrane proteins

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



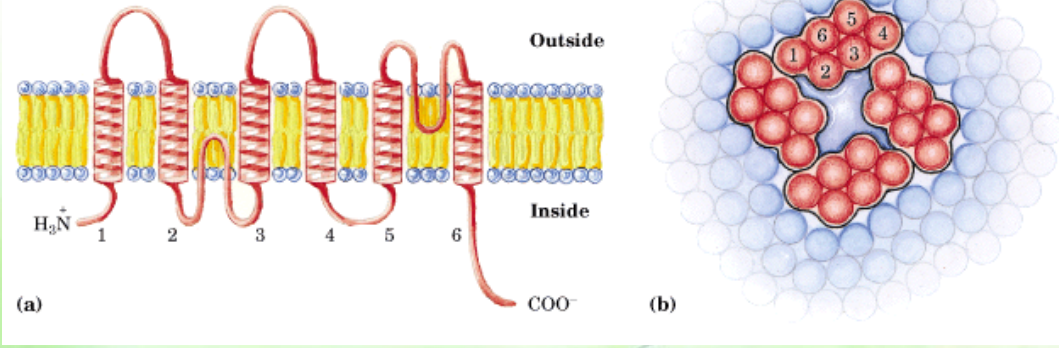


The membrane integral domains are:

1. Single or multiple

2. α-helix or β-sheet

Some can form channels.



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