10

BIOCHEMISTRY

Faculty of medicine – JU2018

◉ Sheet ○ Slides

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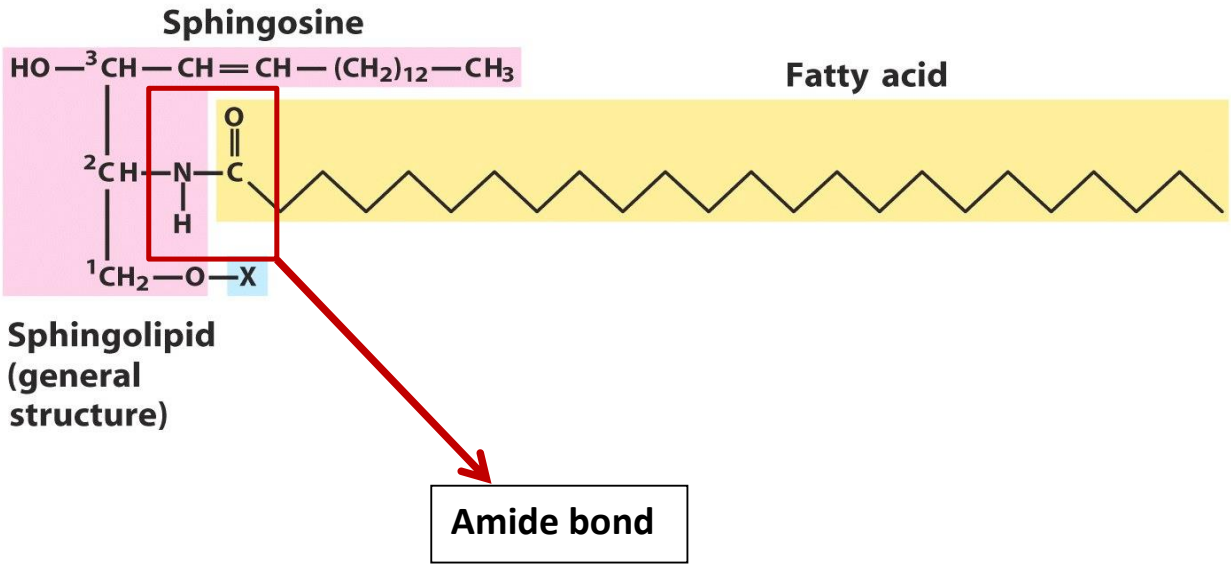
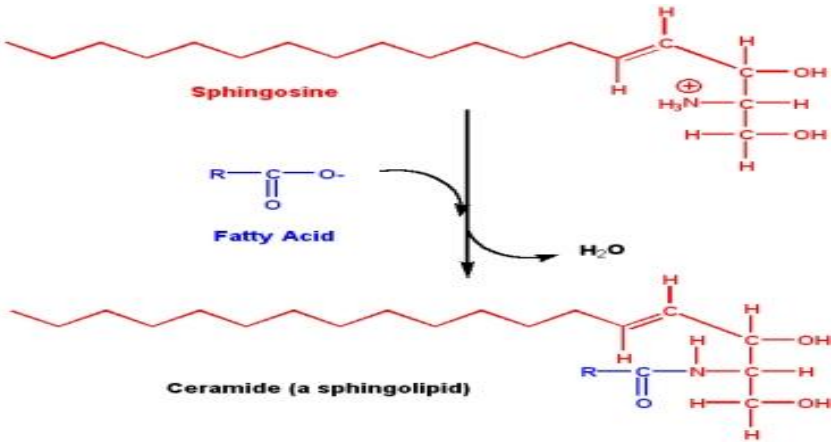
❖ Sphingolipids:

- Are a class of complex lipids containing backbone of sphingosine rather than glycerol , that are amide-linked to an acyl group, such as a fatty acid (usually saturated),and o-linked to a (usually) charged head group such as ethanolamine, serine, or choline.

- Sphingolipids are found in the plasma membranes of all eukaryotic cells, but exist in the central nervous system more than any other type of tissues .



- Ceramide is the simplest sphingolipid.

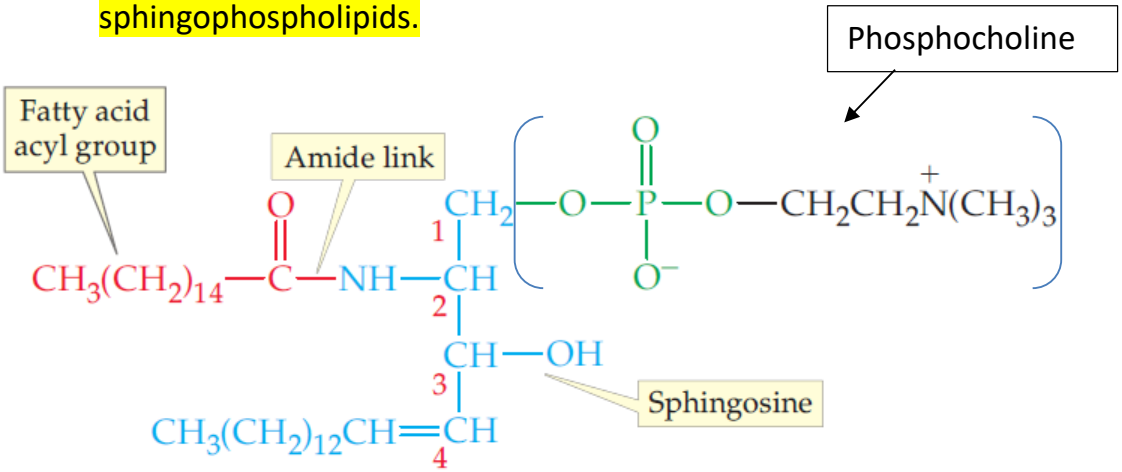


❖Types of sphingolipids:

- The sphingolipids are divided into the two subcategories:

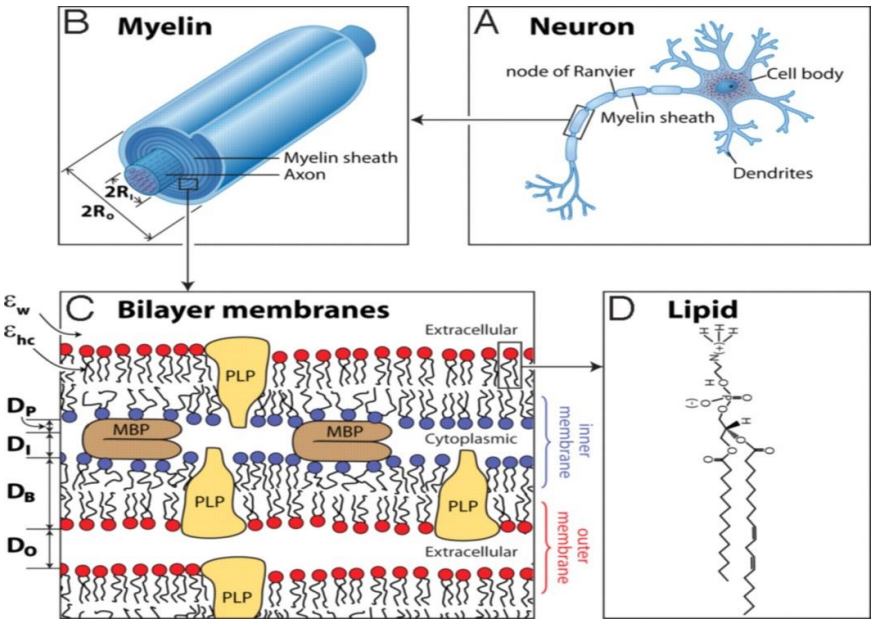
  a)Sphingomyelins ➡

  - is a type of sphingolipid found in animal cell membranes, especially in the membranous myelin sheath that surrounds some nerve cell axons. It usually consists of phosphocholine, or a phosphoethanolamine head group; therefore, sphingomyelins can also be classified as sphingophospholipids.



A sphingomyelin (a sphingolipid)

  - Sphingomyelin is a major component of central nervous system ,it covers neurons axon ;forming myelin sheeth.



- As a result of the autoimmune disease **multiple sclerosis (MS)**, the myelin sheath of neuronal cells in the brain and spinal cord is degraded, resulting in loss of signal transduction capability. **[Extra Info.]**

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b) Glycosphingolipid (or 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 depending on ;the complexity of the structure ,and the presence of certain molecule:

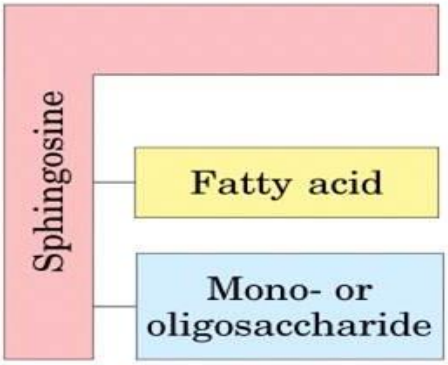
1.<u>Cerebroside (glactocerebroside , glucocerebroside)</u>

the simplest glycolipids, contain a single hexose (galactose or glucose).

2.<u>Globoside</u>

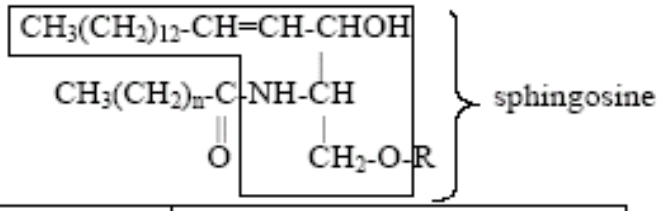
3.<u>ganglioside</u>

- Globosides and gangliosides are more complex glycolipids.
- Both contain glucose, galactose, and N-acetylgalactosamine, but gangliosides must also contain sialic acid.



<u>Notes:</u>

- These glycolipids mainly exist in the CNS , but can be present in other tissue as well.
- Glycolipids have no phosphate in there components.
- Gangliosides are targeted by cholera toxin in the human intestine

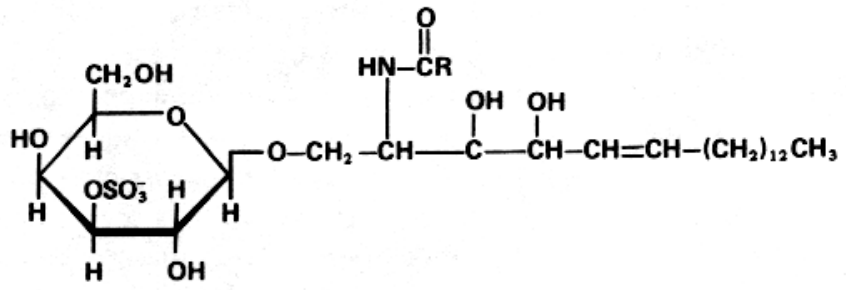


Sphingolipid type	R group
Ceramide	H
Sphingomyelin	phosphocholine
Cerebroside	monosaccharide (galactose or glucose)
Globoside	two or more sugars (galactose, glucose, N-acetylglucosamine
Ganglioside	three or more sugars including at least one sialic acid

glycolipids

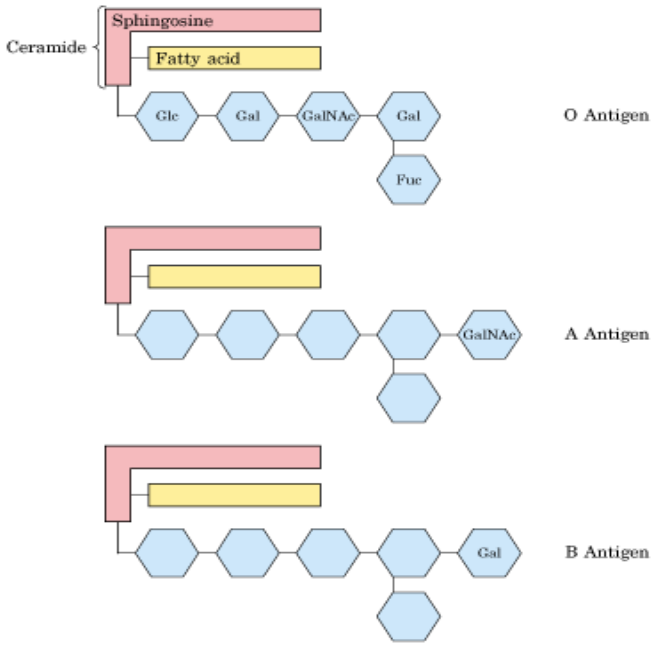
Sulfatides:

- Synthesized from galactocerebroside by adding a sulfate group .
- Abundant in brain myelin.



❖Sphingolipids and blood typing:

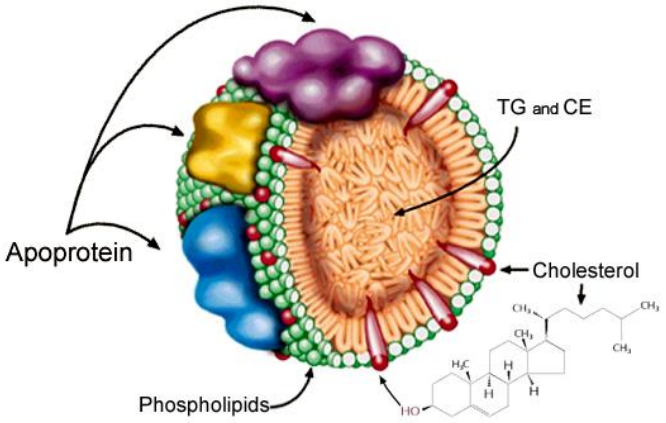
- Blood typing depends on the sugar molecule that presents on the cell surface of RBCs.
- They all have the same backbone exept that in **B antigen** there are an additional galactose molecule , and in **A antigen** there are an additional N-Acetylgalactoseamine (GalNAc) ;there for **group o** can be given to any one because it has a common backbone ,but can't take blood from A and B groups because they have additional sugar.



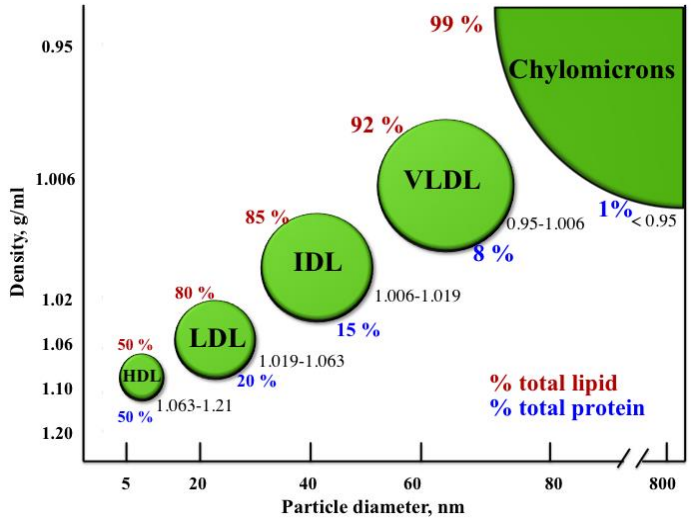
❖Lipoproteins:

- They consists of two major components(lipids + proteins).
- They look like micelle (They have a single-layer phospholipid and cholesterol outer shell, with the hydrophilic portions oriented outward toward the surrounding water and lipophilic portions of each molecule oriented inwards toward the lipids molecules within the particles).

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



- There are different types of lipoproteins , each one of them has structural features , and functional features as well.
- The basic different between these lipoproteins ; is the ratio between **lipids** and **proteins** content ➡ as lipid content increases , the size increases as well , and the density decreases.

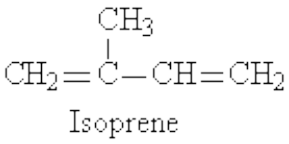


Explain :

- ✓ The highest lipid to protein ratio , the largest size and the least density they have ,which are called: **(Chylomicrons)**
- ✓ The least lipid to protein ratio , the smallest size, and the highest density it has; (**HDL**)

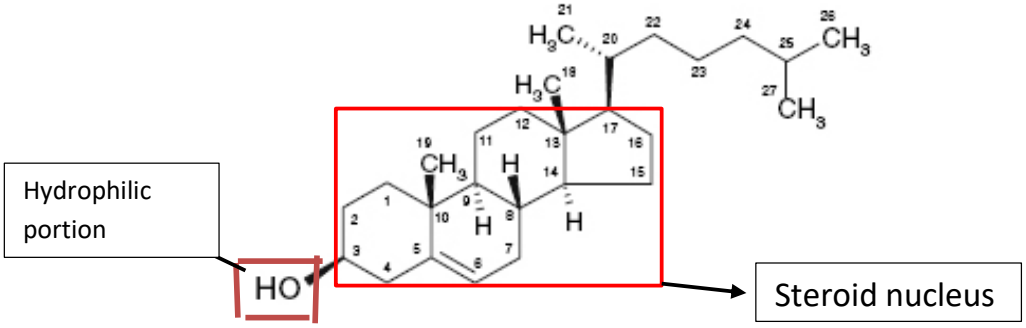
❖Steroids :

- They are derivatives of cholesterol, composed of seventeen carbon atoms, bonded in four "fused" rings: three six-member cyclohexane rings and one five-member cyclopentane ring.
- Cholesterol is made of five carbon molecule as a precursor , known as **isoprene :**



- Cholesterol is made of 27 carbon atoms by the assembly of **isoprene** molecules .

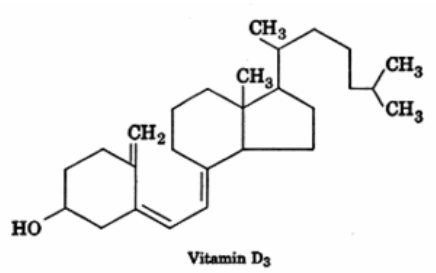
Cholesterol structure



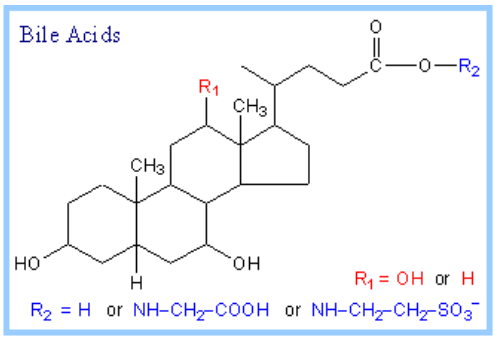
❖ products of cholesterol:

1) **Hormones** , such as: **[**Sex hormones (androgens,. estrogens, progestins)**]**
2) some **vitamins** such as **vitamin D**

   Note that Vitamins A, D, E, and K are made from isoprenoids.

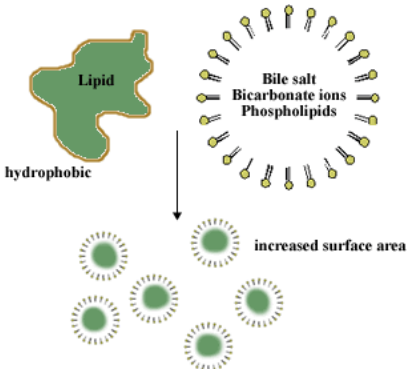


3) **Bile acids**



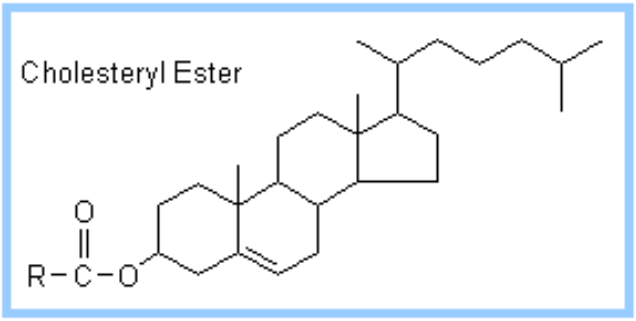
How bile acids work ?

They take lipid droplets in our intestines and break them down into smaller droplets , allowing for intestinal cells to absorb lipids and emulsify lipids in the intestines.



❖ Cholesteryl ester :

- It is formed by forming an ester bond between the carboxylate group of a fatty acid and the hydroxyl group of cholesterol.
- Cholesteryl esters have a lower solubility in water due to their increased hydrophobicity.



- Examples : **Name the molecules?**
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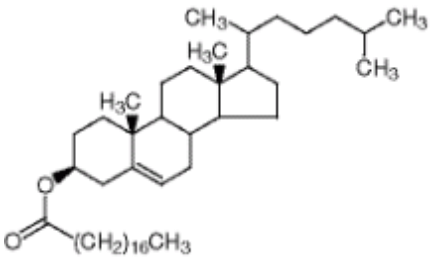
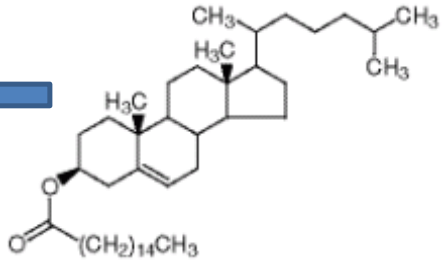
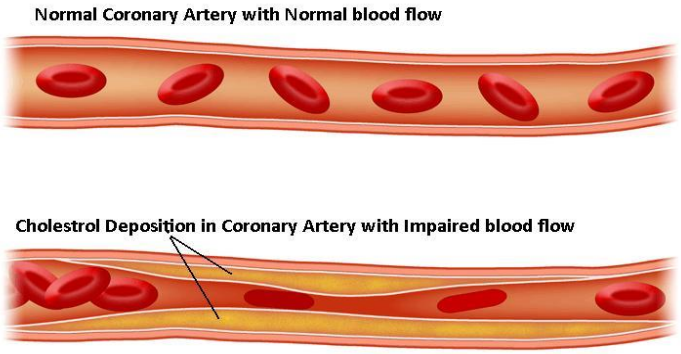


Sterol cholestrol

Polmetoyl cholestrol



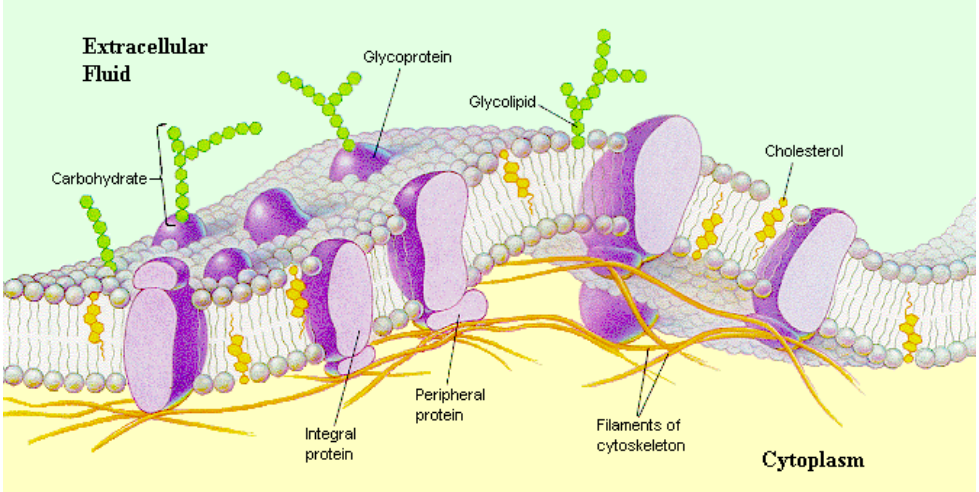
- Cholesterol and lipids in general related to certain condition known as Atherosclerosis (which is abnormal accumulation of lipids in blood vessels impeding blood flow).



❖ Cell membrane:

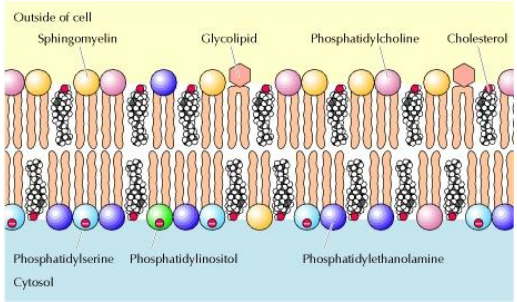
- The membrane is hypothesized in a model known as the fluid mosaic model (it is a dynamic structure not rigid)
- Components: in general ,45% lipid, 45% protein and 10% carbohydrate
- The ratio of membrane components are different between different tissues , organs and organelles as well.
- The predominant fatty acid in plasma membrane is phosphotidycholine.
- Sugar molecules exist outside in the cell, exept one ,is called inositol ;for signaling.

These components exist side by side without forming some other substance of intermediate nature.

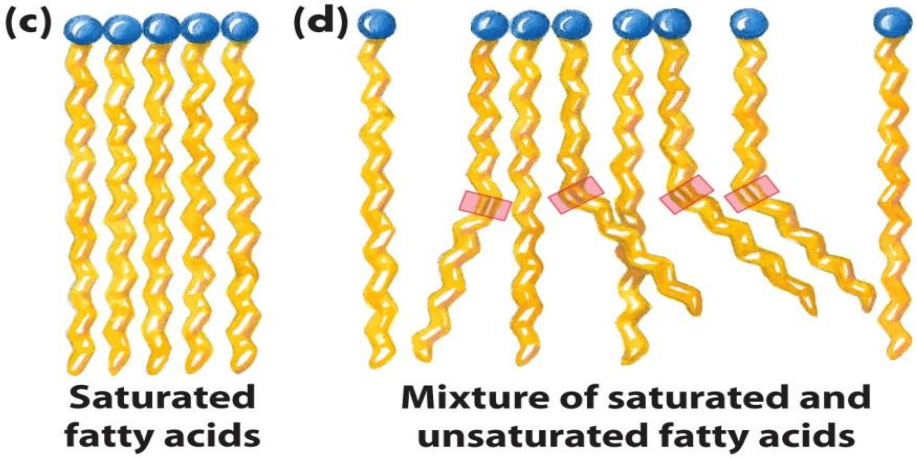


- **Phospholipid content of plasma membrane:**
  - The outer leaflet: phosphatidylcholine, sphingomyelin, and glycolipids(cell recognition)

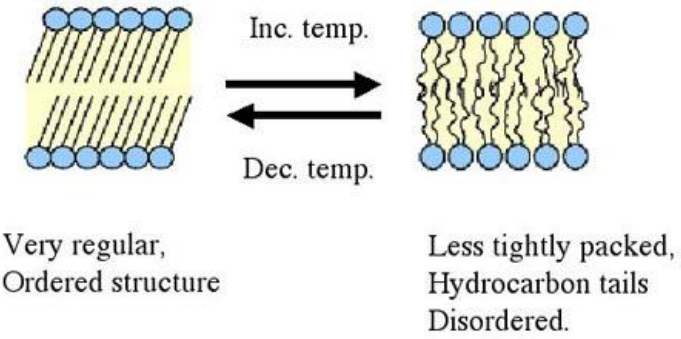
- The inner: phosphatidylethanolamine, phosphatidylserine, and phosphatidylinositol (signaling)
- Cholesterol is not present in bacteria, and it is equaly distributed in both leaflets of animal cell.



- **Fatty acid and membrane fluidity:**
  - Membrane fluidity is inversely proportional with amount of saturated fatty acid ; as there are high amount of saturated fatty acid , the membrane will be more rigid.
  - Because of the present of unsaturated fatty acid in larger ratio than saturated fatty acid ; the membrane looks fluidic .



- **Membrane fluidity and temperature:**
  - Membrane fluidity is directly proportional with temperature , if the **temperature** increases, for example during a high fever, the **cell membrane** can become more fluid because the fatty acid tails of the phospholipids become less rigid and allow more movement of proteins and other molecules



- **Cholesterol and membrane fluidity:**
  - Cholesterol is realy important for the fluidity of plasma membrane ; at high temperature and low temp. as well.
  - 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.

❖ Membrane proteins

- **Types of membrane proteins:**

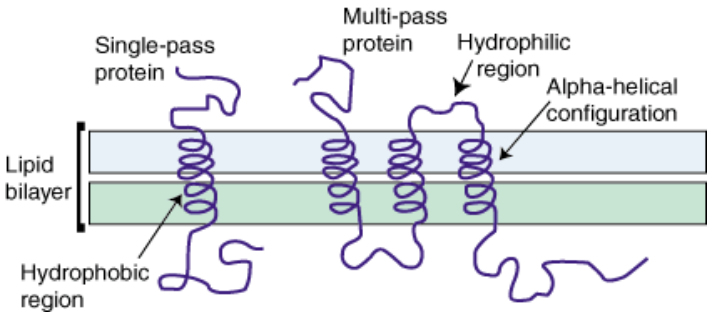
- **1) <u>Peripheral proteins</u>:**
  are associated with the exterior of membranes via noncovalent interactions.
  often associated with integral membrane proteins
  They are not strongly bound to the membrane and can be removed without disrupting the membrane structure (treatment with mild detergent)

  2) <u>Integral membrane proteins</u>:

- anchored into membrane via hydrophobic regions
- **The membrane integral domains are:**

  1.Single or multiple

  2.α-helix or β-sheet



- Some can form channels

3) **<u>Lipid-anchored:</u>**

- associated via a lipid group

❖ Structure-Function of Membranes:

<u>1)Transport:</u>

Membranes are impermeable barrier

Proteins can be carriers or channels

<u>2)Signaling</u>

Protein receptors and small molecules (some can be lipids themselves)

<u>3)Catalysis</u>

Enzyme-linked receptors.

Good luck