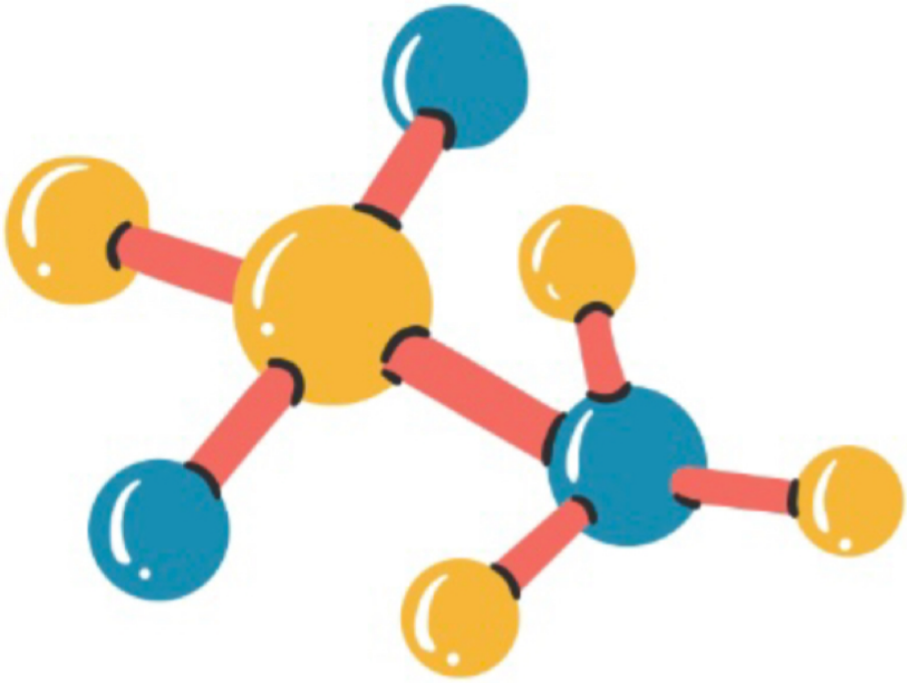
Sheet no.13

Biochemistry



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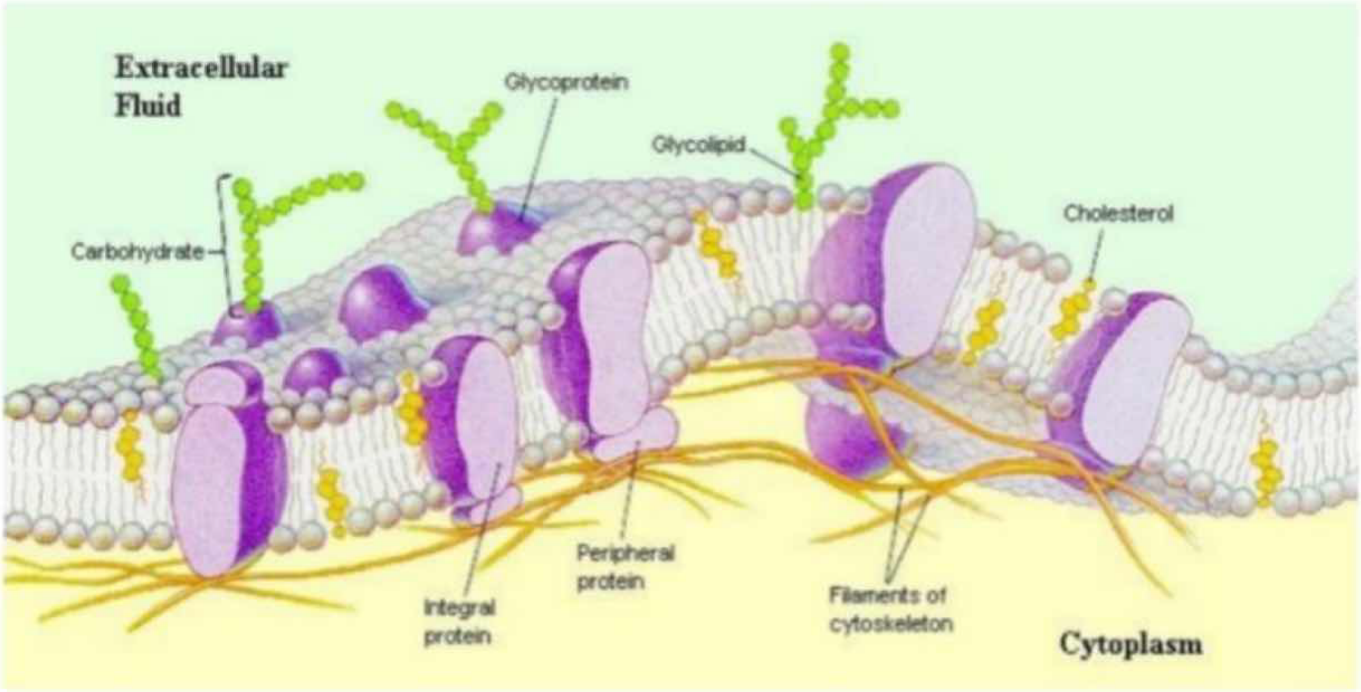
• Cell membranes

Recall that the plasma membrane is a **phospholipid bilayer** composed of two different leaflets : an outer leaflet and an inner leaflet , each with its unique chemical composition of **lipids, proteins and carbohydrates that are associated with several types of glycoproteins as well as glycolipids**.

- The Plasma membrane is hypothesized in a model known as the **fluid mosaic model**
  Fluid: all the components of the membrane in a constant state of flux and movement
  Mosaic: a variety different types of molecules making the composition of the membrane.
- **Components**: 45% lipid, 45% protein and 10% carbohydrate. They exist side by side without forming some other substance of intermediate nature.



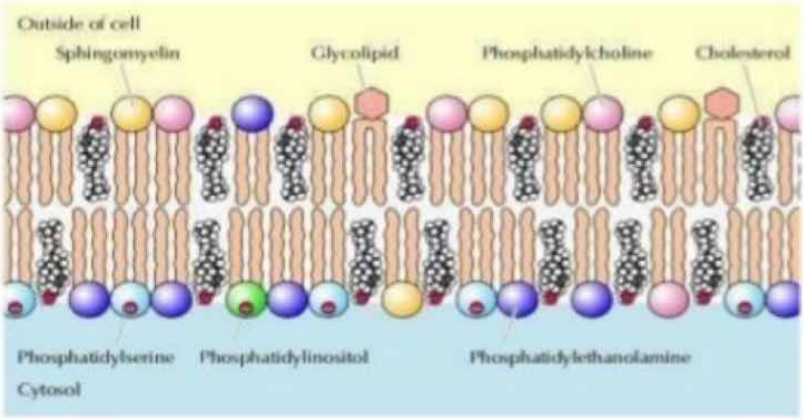
Notice from the figure above the following:-

1- Some membrane proteins can penetrate the lipid bilayer either completely or partially and these are known as Integral membrane proteins.
2- Other proteins are attached to the lipid bilayer without penetrating it and these are known as peripheral membrane proteins.
3- Glycolipids and glycoproteins are found exclusively in **the outer leaflet of the plasma membrane**, with their carbohydrate portions exposed on the cell surface.
4- Cholesterol molecules are embedded between the membrane phospholipids and sphingolipids.

Lipid molecules (glycerophospholipids & sphingolipids) are distributed in different proportions across the leaflets.

- **The contents of the Plasma membrane are distributed as the following**:-
  - **The outer leaflet contains:**
    1. Phosphatidylcholine
    2. Sphingomyelin
    3. Glycolipids (The sugar component is essential for **recognizing cell-types**)
    4. Cholesterol
  - **The inner leaflet contains**:
    1. Phosphatidylethanolamine
    2. phosphatidylserine
    3. phosphatidylinositol **(signaling)**
    4. Cholesterol

-Notice that Cholesterol Is evenly distributed between the leaflets (1:1 Ratio).
-Distribution of lipids differs among organisms, (animals, plants, prokaryotes, etc.) depending on cellular membrane functions



-Several factors affect the membrane fluidity, including cholesterol, fatty acids & temperature,

• membrane fluidity and Fatty acids

Recall from previous lectures that glycerophospholipids mainly composed of the 2 fatty acid chains that can be either saturated or unsaturated (thus introducing cis kinks in the structure of the molecule). Regarding membrane fluidity , there are two different scenarios :-

1. Saturated fatty acyl chains:- These have straight chains without kinks. According to this, fatty acids are densely aligned next to each other, thus their whole surface area is available for non-covalent interactions such as Van der Waals and hydrophobic interactions causing the membrane to be more rigid in structure.

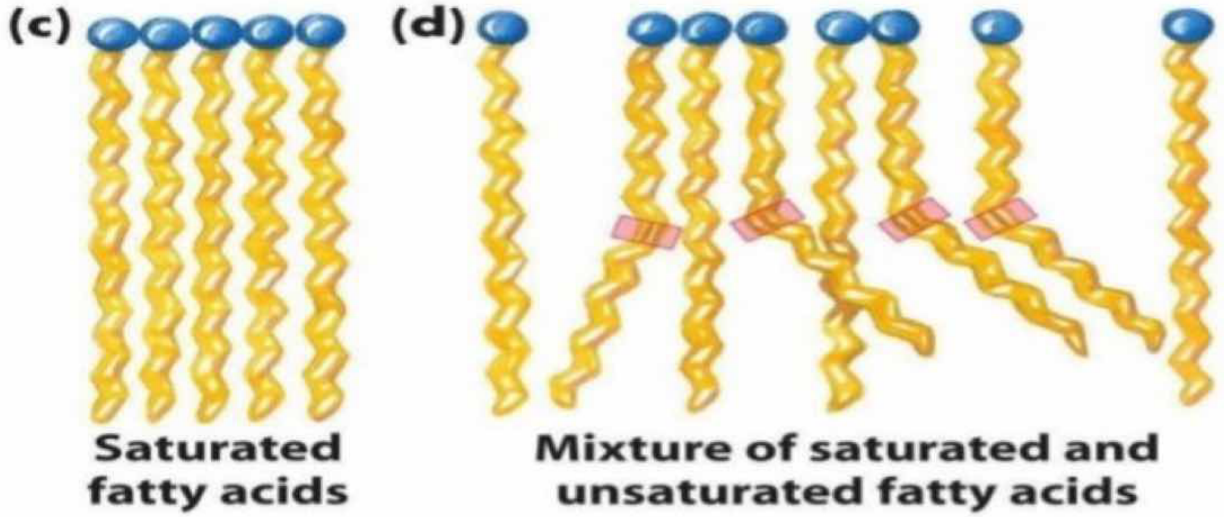
2. Unsaturated fatty acyl chains: These chains contain unsaturated double bonds mostly in cis configuration that introduces kinks in the structure of the molecule pushing and increasing the space between lipid molecules leading to less non-covalent interactions and subsequently, a less rigid structure.

Note:- different regions within the plasma membrane can have different fluidities due to their different composition of fatty acids whether saturated or unsaturated.

To summarize :-

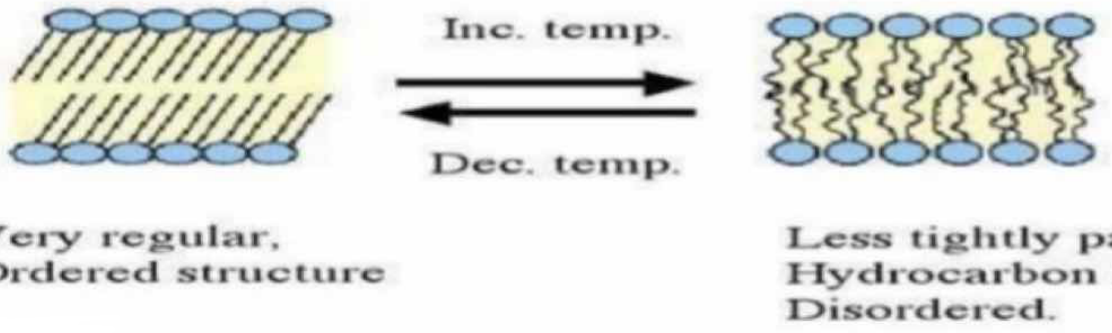
Saturated → linear and exposed surface → more non-covalent interactions → more rigidity

Unsaturated → kinked structure-less space → less non-covalent interactions → more fluidity

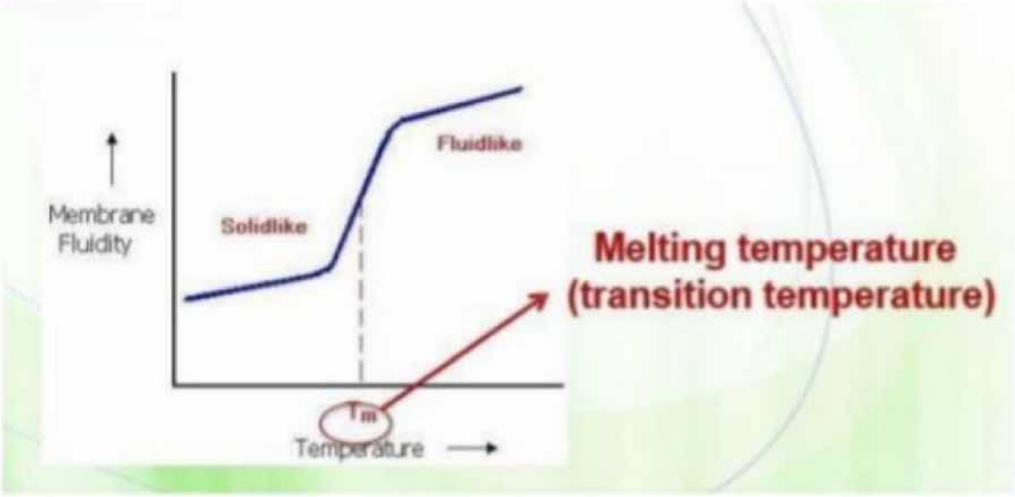


• Membrane fluidity and temperature

Changes in temperature above or below the normal physiological temperature could lead to different effects on membrane fluidity. When there is an increase in temperature, Phospholipid molecules gain more kinetic energy causing a disruption in their interactions as they move faster and away from each other, leading to a decrease in membrane rigidity and vice versa. (**When we revert the temperature back to normal, the membrane goes back to the normal rigid state**)



- The term **Transition temperature or Melting temperature** refers to the **temperature required to induce a change in the lipid physical state from the ordered gel phase**, (where the hydrocarbon chains are fully extended and closely packed) **to the disordered liquid crystalline phase** (where the hydrocarbon chains are randomly oriented and fluid) and vice versa.

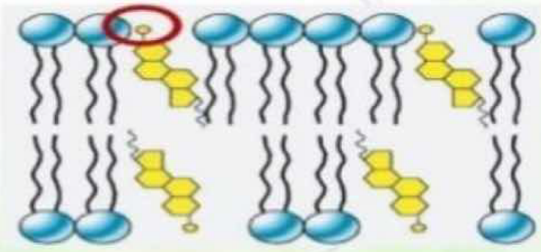


• Membrane fluidity and Cholesterol

Notice that the rigid steroid-ring structure of cholesterol is embedded between membrane phospholipids (leaving the polar OH group near the polar heads). A large number of van der Waals interactions form between the rigid steroid-ring structure and fatty acids, due the presence of large number of atoms in the rigid structure of cholesterol, these interactions stabilizes the extended straight-chain arrangement of saturated fatty acids. Furthermore, Cholesterol acts as a fluidity buffer resisting changes in membrane fluidity by intercalating in between and preventing the close packing of fatty acid tails in the crystal state at low temperatures and conversely, it decreases the mobility of the hydrocarbon tails at high temperatures effectively increasing the melting temperature for that membrane.

- 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.

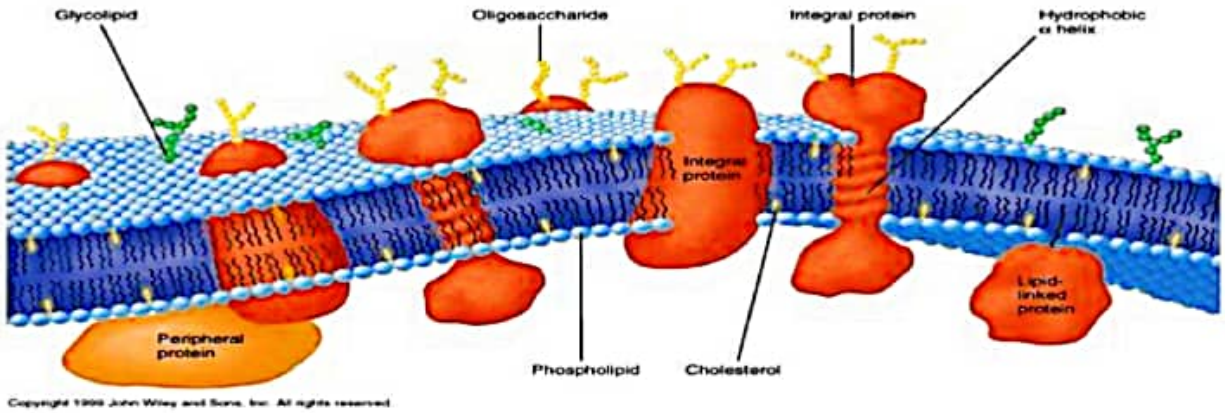


In summary, Cholesterol functions as a buffer, preventing lower temperatures from inhibiting fluidity and preventing higher temperatures from increasing fluidity.

• Membrane Proteins

We mentioned previously that one of the major contents of the plasma membrane is proteins , which can be classified into 3 types:

1. Integral membrane proteins: **(Anchored into membrane via Hydrophobic regions).**
2. Peripheral membrane proteins: **(Associated with the exterior of membranes via weak non-covalent interactions).**
3. Lipid-anchored proteins: **(Associated with the membrane via a lipid group through covalent bonds).**



• Peripheral membrane proteins

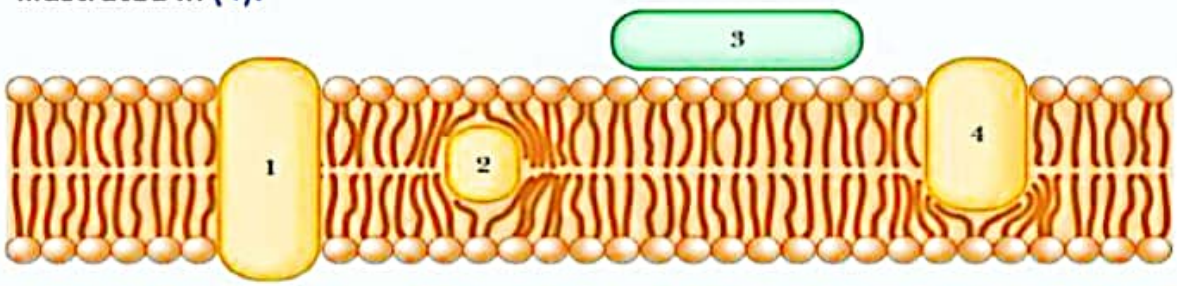
- These proteins are attached to membranes but do not penetrate the hydrophobic core of the bilayer, which means that they lack the presence of hydrophobic amino acids on their surface. Instead, they associate with the plasma membrane either **directly** by interacting with the lipid polar heads or **indirectly** by interacting with other integral membrane proteins (Often associated with integral membrane proteins).

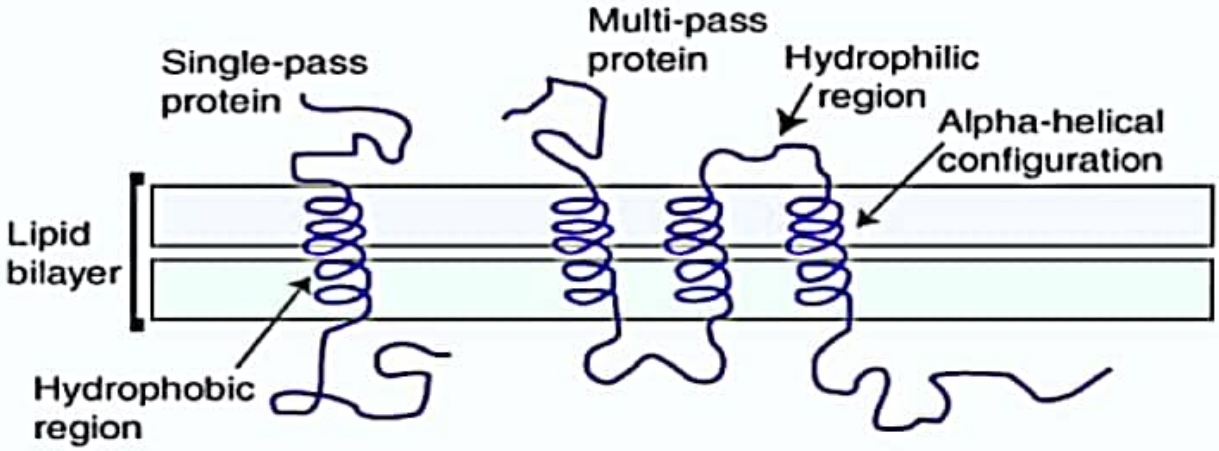
- They are weakly bound to the membrane via **non-covalent interactions** that can be easily broken effectively removing them without disrupting the structure of the membrane (Example : Treatment with mild detergents).

• Integral membrane proteins

Proteins inserted into the two leaflets of membrane. Integral membrane proteins are **amphipathic molecules** that can be associated with the lipid bilayer in several ways ,in which the **Hydrophilic regions** protrude outside facing the aqueous surrounding environment while the **Hydrophobic regions** (non- polar amino acids) anchor the protein within the bilayer by forming non-covalent interactions (this is why detaching these proteins is harder compared to peripheral proteins)

1. They could fully penetrate the lipid bilayer thus being exposed to both sides, we refer to such proteins as Transmembrane integral proteins (1).
2. They could be embedded within the lipid bilayer without being exposed to any of the sides as illustrated in (2).
3. They could partially penetrate the lipid bilayer thus being exposed to one side as illustrated in (4).





- Notice from the figure above that the membrane integral domains can be :
  1. **Single or multiple:** Some membrane proteins are composed of multiple helices inserted in the bilayer or a single helix in other cases.
  2. **a-helix or b-sheet:** Most integral proteins are made from **alpha helices;** however, there are some examples where **beta sheets** are inserted into the membrane.

     - Alpha helices can be organized to form channels that transport several ions (K+ ,Na+ ,Ca++)

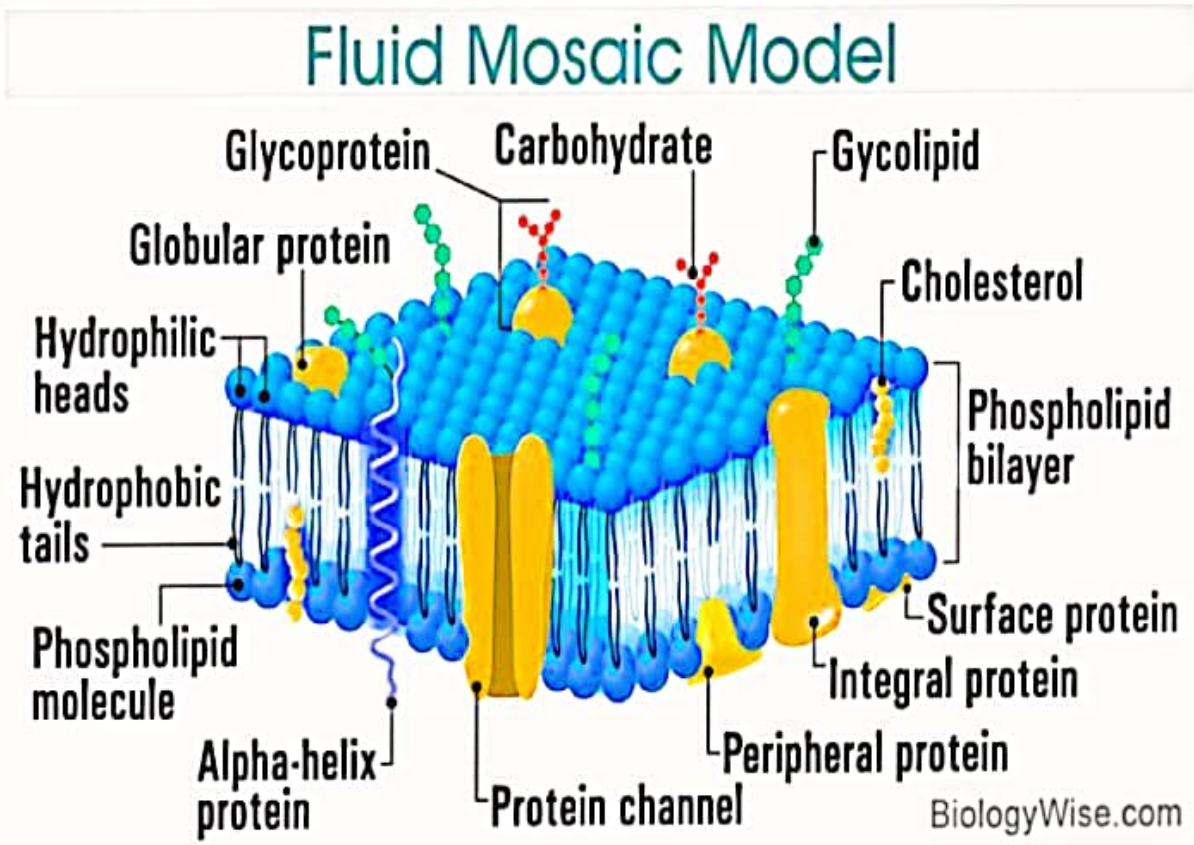
     -beta sheets organize themselves into beta barrels forming pores such as **Aquaporins.**(Proteins responsible for the transport of water across the bilayer)

• Structure-Function of Membranes

- **Transport: Cellular membranes are impermeable barriers** , that is they permit the passing of certain (Hydrophobic-water insoluble) molecules while permitting the passing of large hydrophilic substances. Therefore**, integral membrane proteins come to the rescue by acting as carriers (transporters) or channels** that facilitate the crossing of many materials that cannot cross the lipid bilayer (Ions for instance).

- **Signaling: Protein receptors and small molecules (some can be lipids themselves).**

- **Catalysis (speeding chemical reactions): Enzyme linked receptors** which can be integral or peripheral membrane proteins.



The End

Self-assessment Questions

1. Fatty acids are a component of A) carotenes.
   A. cerebrosides.
   B. sterols.
   C. vitamin D.
   D. vitamin K.

2. Which of the following is true of sphingolipids?
   A. Cerebrosides and gangliosides are sphingolipids.
   B. Phosphatidylcholine is a typical sphingolipid.
   C. They always contain glycerol and fatty acids.
   D. They contain two esterified fatty acids.
   E. They may be charged but are never amphipathic.

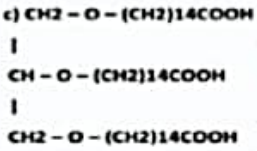
3. A compound containing N-acetylneuraminic acid (sialic acid) is:
   A. cardiolipin.
   B. ganglioside GM2.
   C. phosphatidylcholine.
   D. platelet-activating factor.
   E. sphingomyelin.

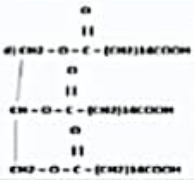
4.

5)Which of the following structures is a triglyceride?

A) 

B) 

C) 

D) 

Answer : A

5. Which of the following is a characteristic of both triacylglycerols and glycerophospholipids?
   a) Both contain carboxyl groups and are amphipathic
   b) Both contain fatty acids and are saponifiable.
   c) Both contain glycerol and ether bonds.
   d) Both can be negatively charged at cellular

6. Which is a characteristic of sphingolipids?
A. They all contain a fatty acid joined to glycerol.
B. They all contain a long-chain alcohol joined to isoprene.
C. They all contain ceramide joined to a polar group.

12. Which of the following best describes the cholesterol molecule?

A) Amphipathic

B) Nonpolar, charged

C) Nonpolar, uncharged

D) Polar, charged

E) Polar, uncharged 2)

13. Which of the following contains an ether-linked alkyl group?

A) Cerebrosides

B) Gangliosides

C) Phosphatidyl serine

D) Platelet-activating factor

E) Sphingomyelin

14. Which of the following is not a fat-soluble vitamin?

A) A

B) C

C) D

D) E

E) K

15. Which vitamin is derived from cholesterol?

A) A

B) B12

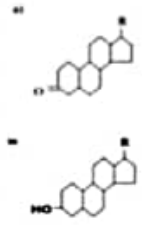
C) D

D) E

E) K

16.

5) Which of the following structures is a sterol?



A or B

Answer : B

17. Which is a characteristic of the lipids in a biological membrane?
a) Specific glycerophospholipids are distributed equally on the two membrane surfaces.
b) Lipid molecules are held in fixed positions by non-covalent bonds with proteins.
c) The fluidity of the membrane decreases with lower levels of saturated fatty acids.
d) The fatty acids of lipid molecules are found in the interior of the membrane

18. Which is a property of integral membrane proteins?
a) All integral membrane proteins contain hydrophilic regions.
b) All integral membrane proteins span the entire membrane.
c) All integral membrane proteins contain carbohydrate groups within the membrane.
d) All integral membrane proteins transport non-polar molecules through the membrane.

19. Which will be a characteristic of a steroid that is part of a cell membrane?
A. It will contain a hydroxyl group.
B. It will contain four aromatic rings.
C. It will contain choline.
D. It will contain an amide bond.

20. Which characteristic is shared by a cell membrane and a chylomicron?
a) Both contain specific proteins.
b) Both have a bilayer structure.
c) Both contain a high proportion of triglycerides.
d) Both contain a high proportion of sterols.