

بيو كيمياء

BioChem

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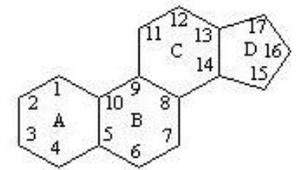
Doctor: Mamoun Ahram

❖ Lipids

- ✓ In this Lecture we will talk about cyclic lipids (steroid) and then we will talk about the membrane structure in cells and different types of membrane protein.

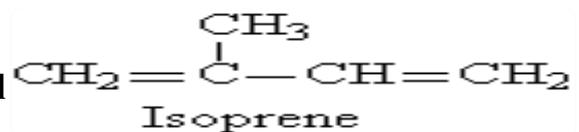
❖ Steroids

- composed of seventeen carbon atoms
- They contain a **steroid nucleus** (a four rings structure), this structure is derived from **isoprene** (5 carbon molecule), so we have condensation of multiple isoprene units :



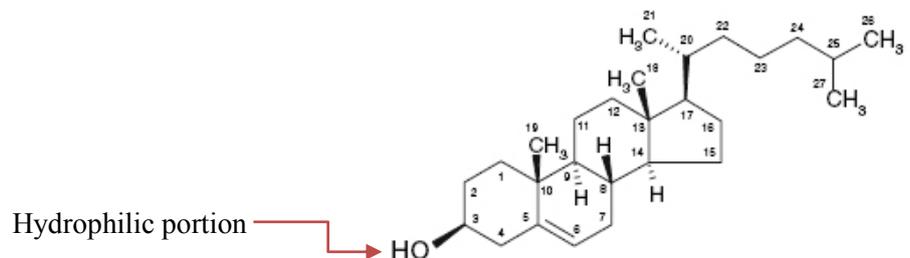
Steroid nucleus

- The most common steroid is **cholesterol** (is made of 27 carbon atoms by the assembly of isoprene molecules)



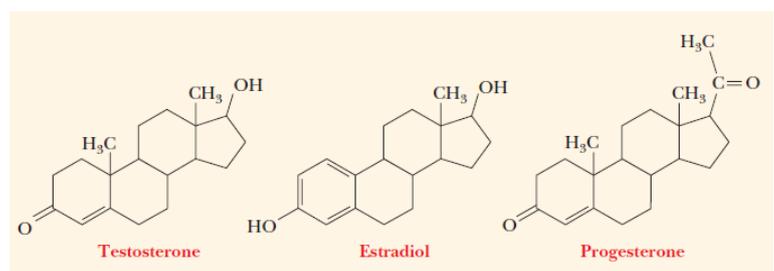
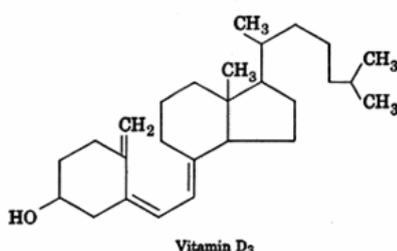
Cholesterol structure

Cholesterol is an **amphipathic** molecule (that have both **polar** and **nonpolar** regions, giving it both **hydrophilic** (**water-loving**) and **lipophilic** (**fat-loving**) properties)

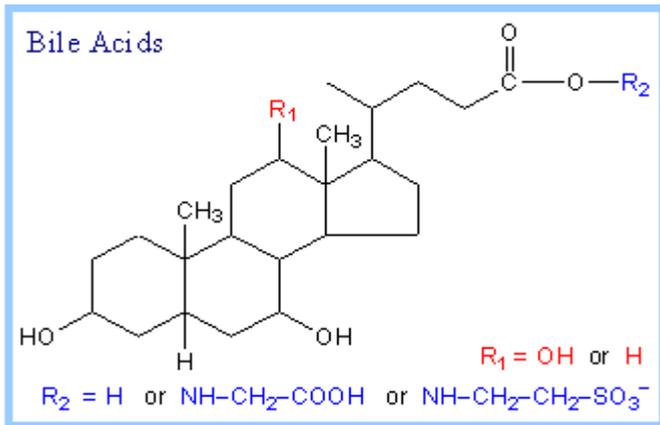


❖ products of cholesterol:

- **Hormones**, such as: [Sex hormones (androgens, estrogens, progestins)]
- some **vitamins** such as vitamin **D**
- **Note** that Vitamins A, D, E, and K are made from isoprenoids.

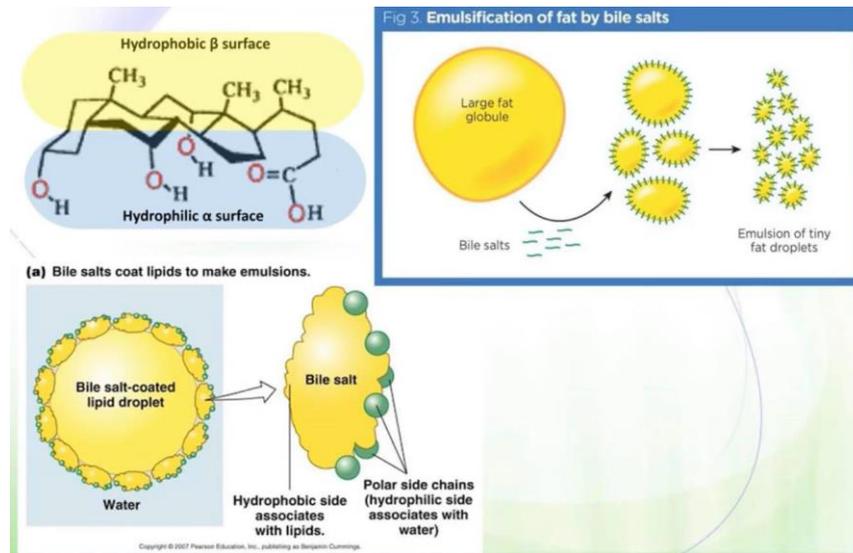


➤ **Bile acids** (most important Derivatives of cholesterol):

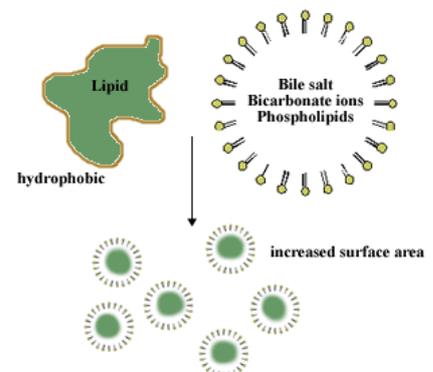


- amphipathic molecules
- Are synthesized and secreted from the gallbladder المرارة .
- **Main function** (facilitate absorption of fat), they emulsify molecules (dissolved fat).

- ✓ How can we call it an amphipathic molecule despite the fact that hydrophilic groups are distributed unevenly (where we can draw the line)?
- We have to look at the molecule in a 3D form, so we see all hydrophilic groups localized below the ring structure, and all hydrophobic groups localized above the ring .

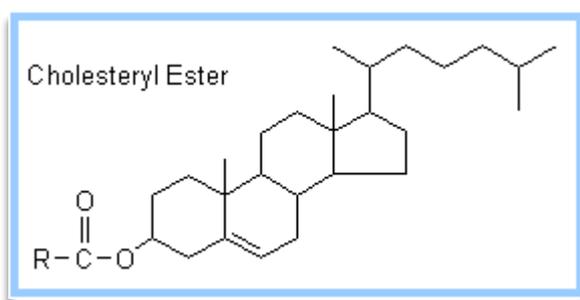


- ✓ **How bile acids work?** They take fatty lipid droplets (لما تاكل لية بالمنسف) in our intestines and break them down into smaller droplets, allowing for intestinal cells to absorb lipids and emulsify them in the intestines

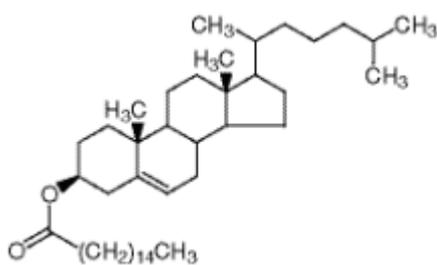


❖ Cholesteryl ester:

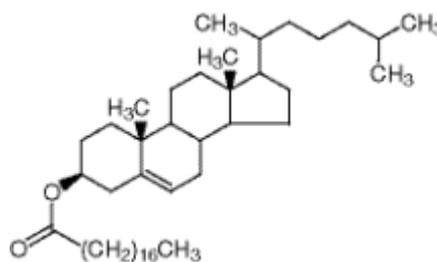
- It is formed by forming an ester bond between the carboxylate group of a fatty acid and the hydroxyl group of a cholesterol molecule . (producing a very hydrophobic molecule)
- Cholesteryl esters have a lower solubility in water due to their increased hydrophobicity.



Name the molecules?



Polmetoylester cholesterol



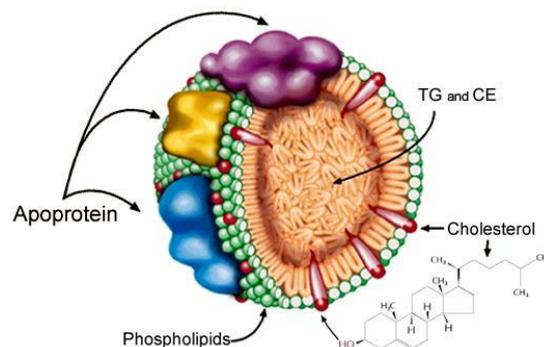
Sterol cholesterol

❖ Lipoproteins:

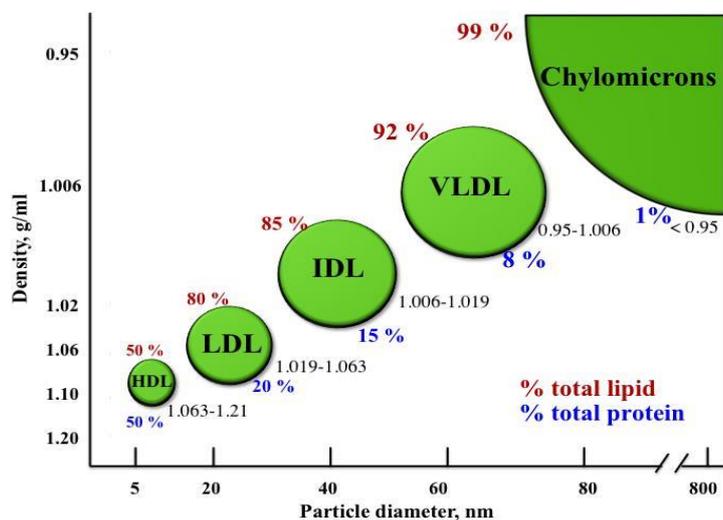
- ✓ When we eat cholesterol, lipid triacylglycerols will be absorbed by intestinal cells and then they'll run in our blood stream to be then stored in our liver as well as adipose tissues leaving them later on and running again in our blood stream to reach our peripheral tissues (they can't dissolve in blood as these lipids are hydrophobic),**SO HOW ARE THEY CARRIED? By molecule called Lipoprotein**

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

- They consist of two major components (lipids + proteins).
- They look like **micelles** (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 particle)



- There are different types of lipoproteins, each one of them has structural features, and functional features as well.
- The main difference between these lipoproteins is their composition of both lipids and proteins. **[in another words ; is the ratio between lipids and proteins content, as protein content increases, the size decreases , and the density increases]**



VLDL : very-low-density lipoprotein
IDL: Intermediate-density lipoprotein
LDL: Low-density lipoproteins
HDL: High-density lipoproteins

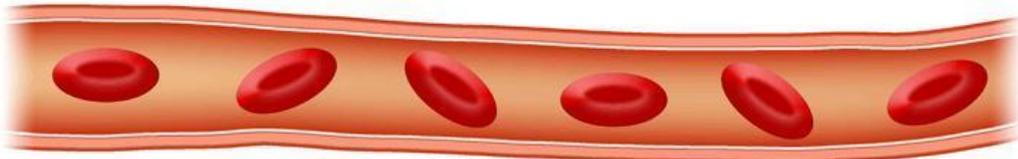
Explain:

- ✓ The highest lipid to protein ratio , the largest size and the least density goes to molecules called: **(Chylomicrons)**
- ✓ The least lipid to protein ratio , the smallest size, and the highest density goes to molecules called **(HDLs)**

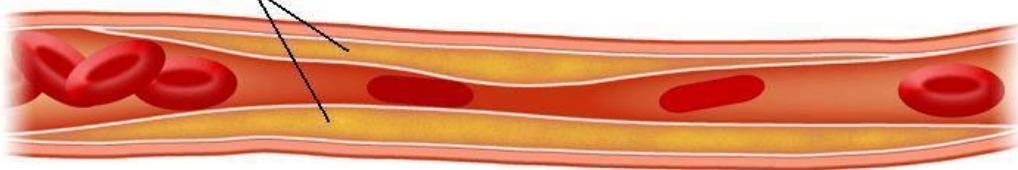
- ✓ Each one has a certain function, chylomicrons -for example- carry lipids from intestines to liver so they carry dietary lipids
- **HDL: the Good cholesterol** because it removes excess cholesterol from the body (peripheral tissue) back to liver and liver eliminates it.
- **LDL: the bad cholesterol**, for two reasons:
 - carries cholesterol from liver to peripheral tissue [doesn't remove excess cholesterol]
 - Has tendency to accumulate in blood (at the walls of blood vessels)

- ❖ **Atherosclerosis** (which is an abnormal accumulation of lipids in blood vessels impeding blood flow... heart attack and strokes)
LDL, is directly associated with risk for **atherosclerosis**

Normal Coronary Artery with Normal blood flow

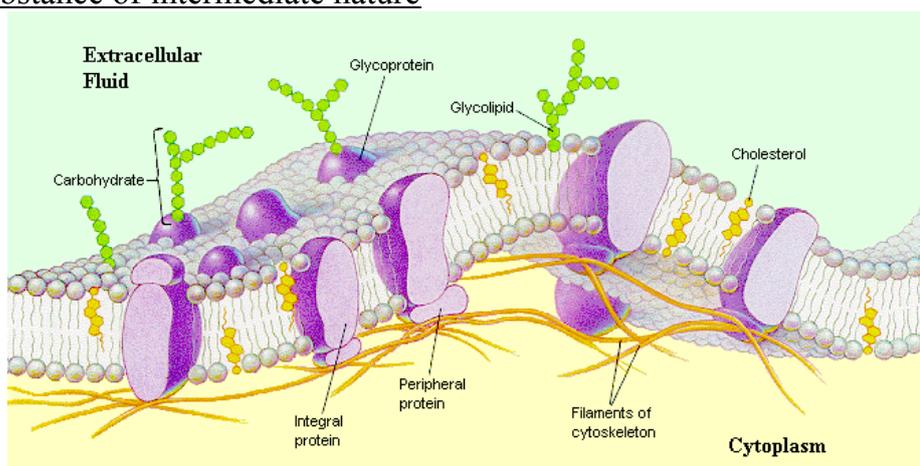


Cholesterol Deposition in Coronary Artery with Impaired blood flow



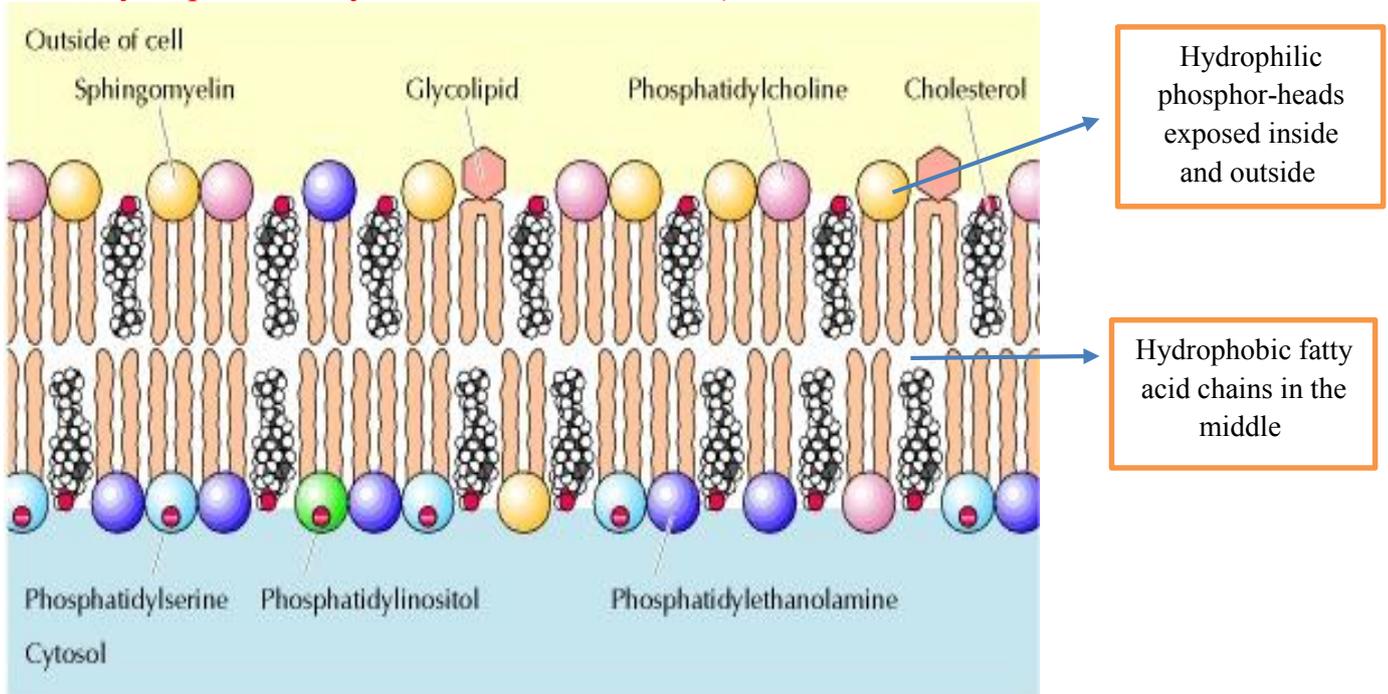
❖ Cell membrane:

- The membrane is hypothesized in a model known as **the fluid mosaic model** (it is a dynamic structure not a rigid one).
- **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.
- ✓ These components exist side by side without forming some other substance of intermediate nature



❖ Phospholipids

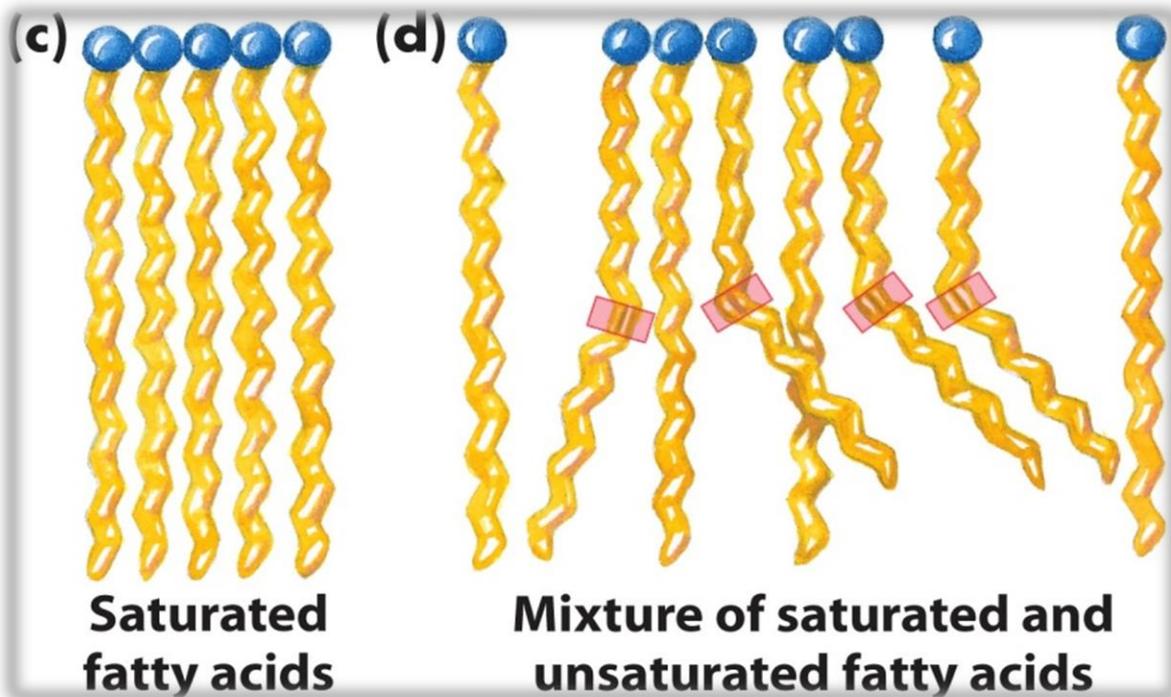
- If you look at the lipid composition of plasma membrane, you will notice that actually it's not symmetrical (as phosphor hydrophilic heads are exposed and hydrophobic fatty acid chains are hidden).



- ❖ The type of lipids exist in the outer leaflet of the bilayer is different from that which exists in the inner leaflet:
 - The outer:
 - phosphatidylcholine, sphingomyelin, and glycolipids(cell recognition)
 - you find a lot of sugars exposed to the outside of the cell because one function of membrane lipids is cell-cell recognition...this is how immune cells can be recognized by looking at the sugars that are present at the surface of cells.
 - The inner:
 - phosphatidylethanolamine, phosphatidylserine, and phosphatidylinositol (we said that phosphatidyl inositol is involved in cell signaling so it's exposed to the cytoplasm).
 - wherever something binds to a receptor on the cell surface , the phosphatidyl inositol molecule senses the presence of this ligand and sends a signal to another molecule within the cell.
 - We also have cholesterol in the plasma membrane, equally distributed on both parts of leaflets. And it's present mainly in animal cells, so there is no cholesterol in plants or prokaryotic cells...plant cells have a different type of steroids that replaces this buffering molecule ...

❖ Fatty acids and membrane fluidity

- Plasma membrane is supposed to be fluidic in order to allow the molecules to pass through and to allow the molecules within the membrane itself to move freely specially in certain cell types like retinal cells (our visual cells), also in the inner membrane of the mitochondria as well (the Electron Transport Chain(ETC))
- The fluidity of the plasma membrane is controlled by the type of fatty acids that are

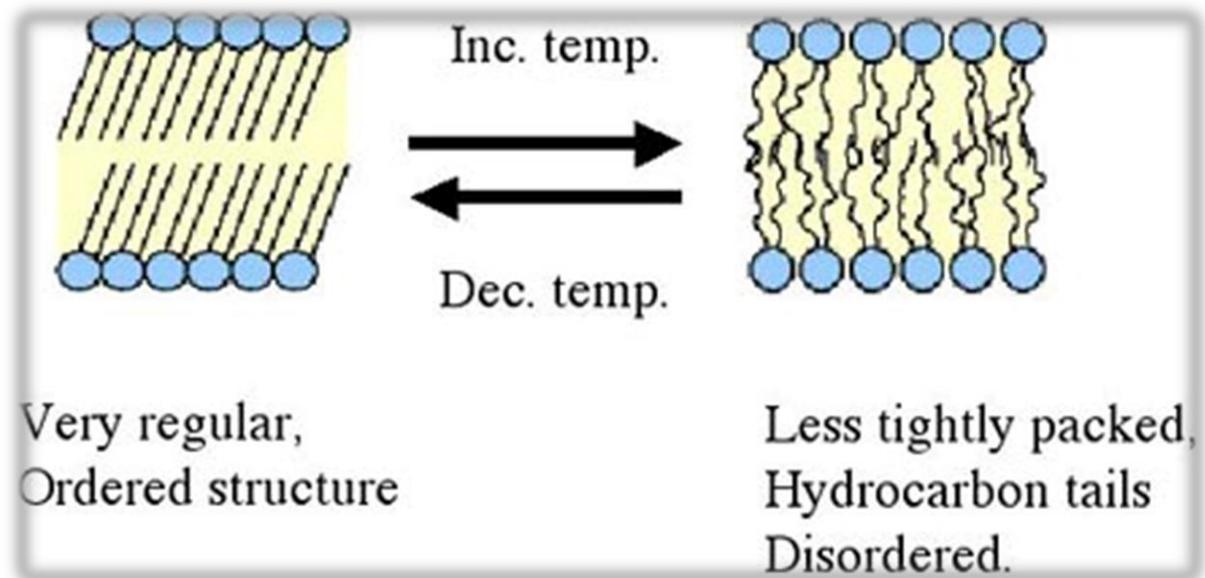


attached to the phosphate heads:

- If you have fully saturated fatty acids the membrane would be quite rigid (the greater the number of saturated fatty acids ,the higher the rigidity of the membrane and vice versa)
- The cis double bond that is present in the hydrocarbon chain of the fatty acid create a kink in the molecule which creates spaces between the molecules, the greater the number of unsaturated fatty acids , the higher the fluidity of the membrane.

❖ Membrane fluidity and temperature

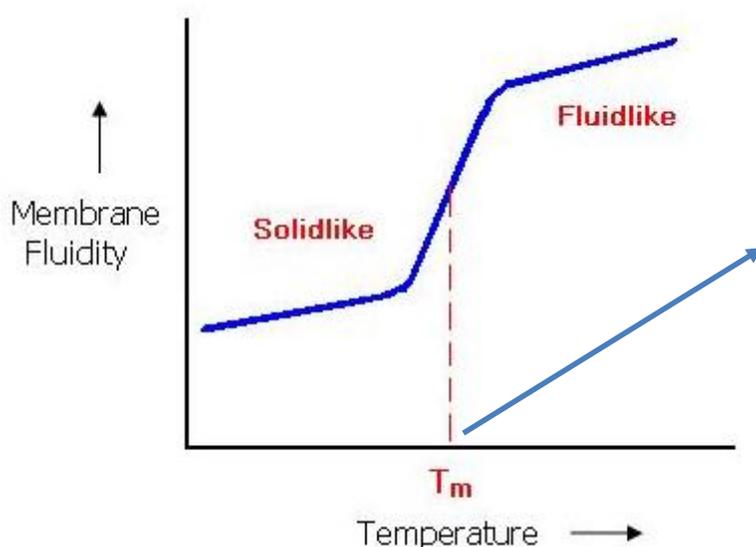
- The fluidity of the membrane is also controlled by the temperature (higher temperatures lead to less ordered / packed membranes and vice versa)



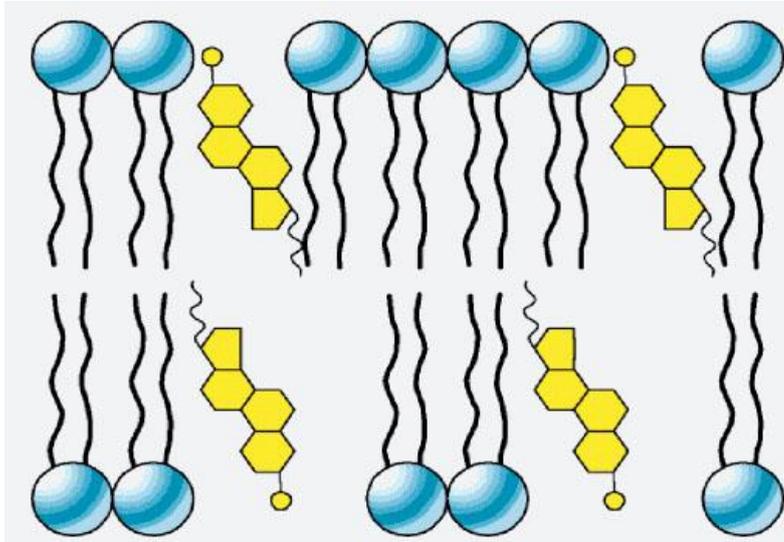
- For creatures living in high temperature areas , cells' membranes need to have more saturated fatty acids in order to have a more packed structure .On the other hand , in areas where the temperature is low , cells' membranes need to have more unsaturated fatty acids (in comparison with saturated ones) in order to prevent membrane packing
- That's why in the eskimo- for example- where it's really cold , animals feed mainly on fishes which contain a lot of omiga-3 fatty acids (unsaturated fatty acids) which plays a role in reducing there membranes' rigidity .

❖ Cholesterol and membrane fluidity

- In the plasma membrane we have the hydrophobic ring of cholesterol interacting with the fatty acid chains , and the hydroxyl group interacting with the phospholipid hydrophilic heads .



Here we have what is known as **melting temperature** which is a **transition temperature** where the membrane runs really fast between being solid-like versus fluid-like



The importance of cholesterol in membranes :

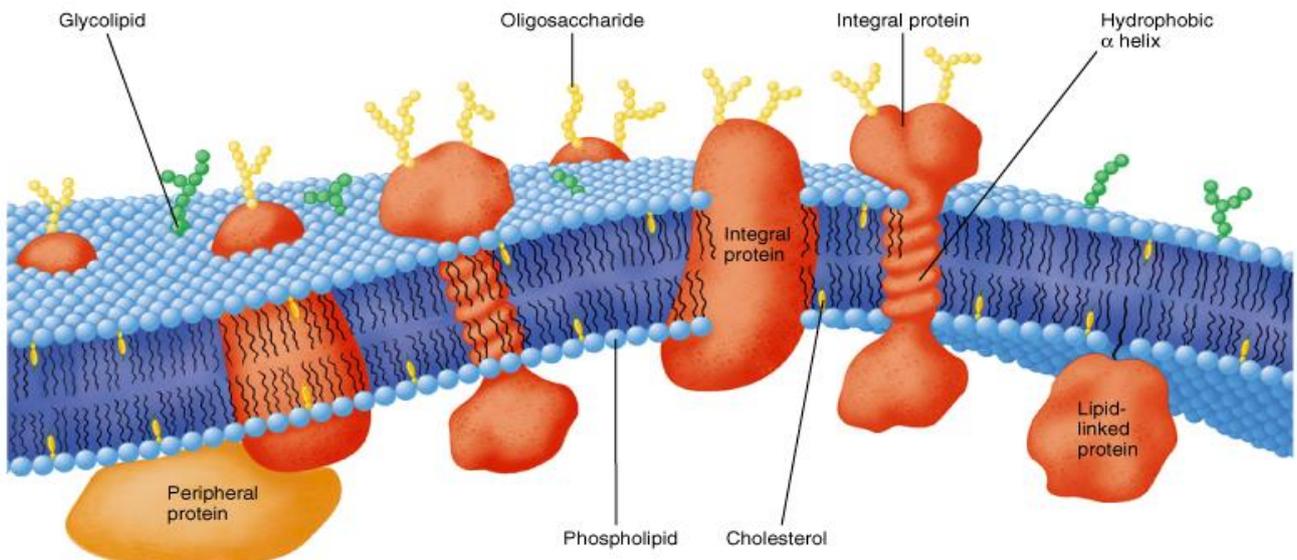
- The presence of cholesterol stabilizes the extended straight-chain arrangement of saturated fatty acids by van der Waals interactions, so it strengthens the membrane at high temperatures protecting the membrane from collapsing.
- Also , Cholesterol molecules make the membrane less solid at low temperatures by creating spaces between the fatty acid chain.
- It decreases the mobility of hydrocarbon tails of phospholipids.
- It interferes with close packing of fatty acid tails in the crystal state

❖ Membrane proteins

✓ Membrane proteins exist in different types, forms, and structures:

- **Integral membrane proteins:**
 - They insert themselves inside the plasma membrane
 - Can have parts present outside the membrane and others inside it
 - The parts present inside the lipid bilayer are linked to the membrane by hydrophobic interactions with fatty acid chains.
 - They have different structures within the membrane.
- **Peripheral membrane protein:**
 - anchored to the membrane via non-covalent interactions .
 - They interact with other integral membrane proteins.
 - Present attached either to the inner or outer leaflet of the membrane.
- **Lipid-anchored membrane proteins:**
 - associated via a lipid group

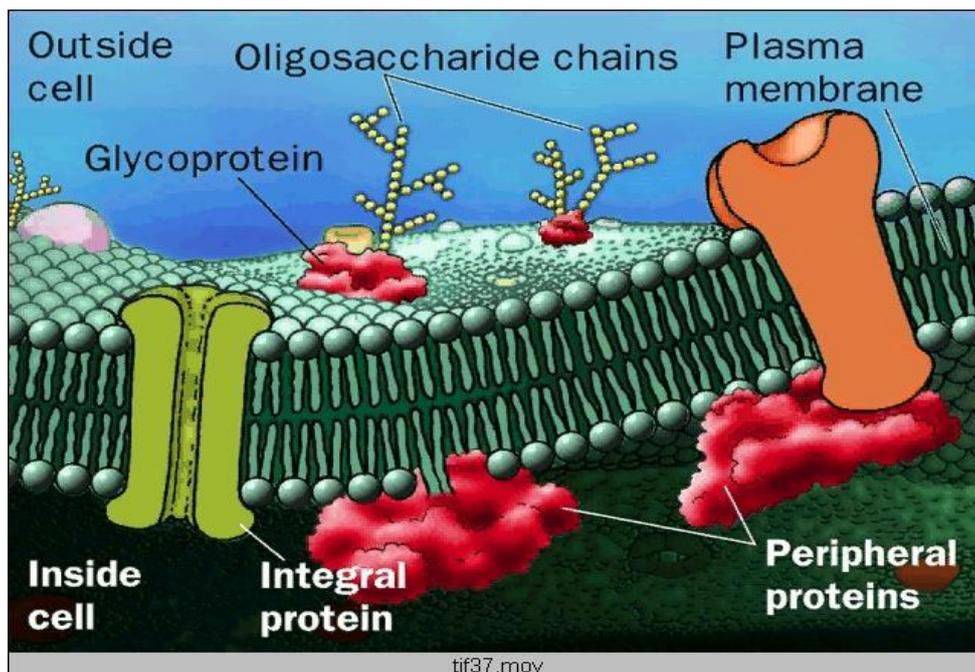
✓ Note that sometimes the extracellular part of the integral proteins is glycosylated (an oligosaccharide is attached to it)



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❖ Peripheral membrane proteins

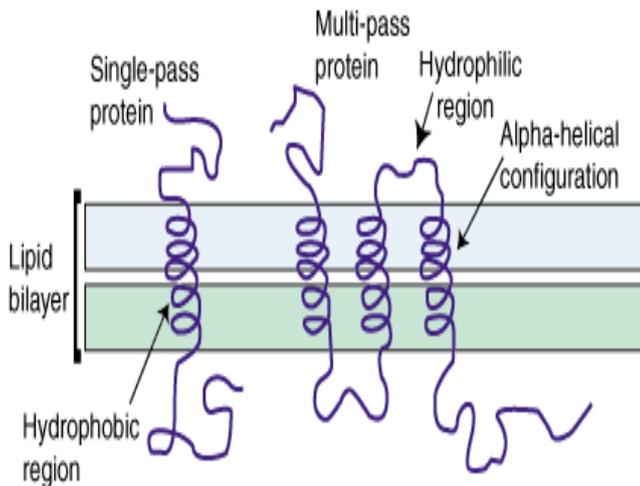
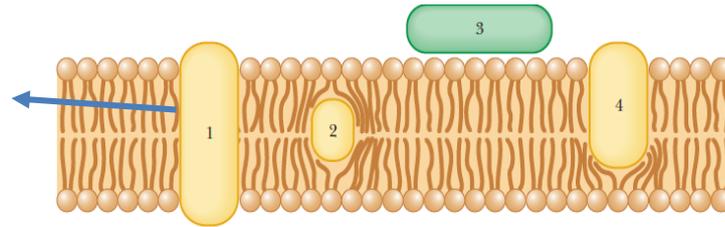
- They are attached to the membranes but do not penetrate the hydrophobic core of the membrane
 - often attached to integral membrane proteins
- They are not strongly bound to the membrane and can be removed without disrupting the membrane structure
 - treatment with mild detergent



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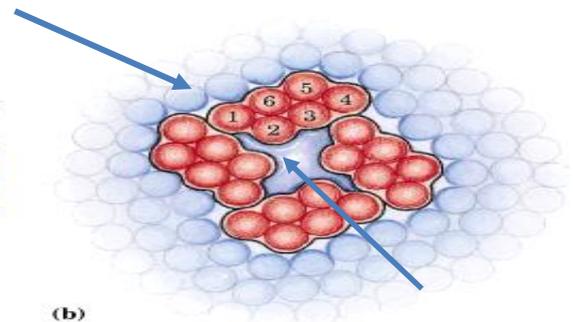
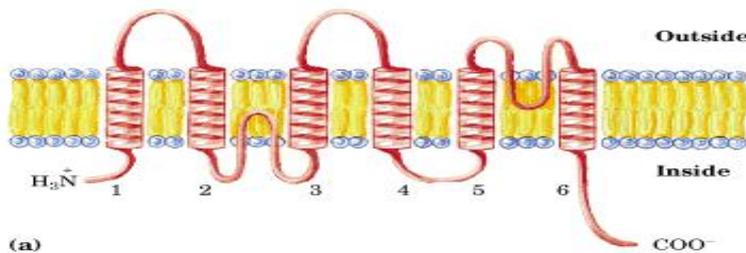
❖ Integral proteins

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



- **Integral proteins can have one single transmembrane domain** integrating just once and inserting itself into the plasma membrane OR can have **multiple transmembrane domains** integrating the membrane multiple times.
- **α-helix** (in mammalian cells) or **β-sheet** (in bacterial cells)

Some integral proteins can form channels by the in and out movement of their transmembrane domains .



❖ Membranes' functions :

- **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

Opening whereby ions or other molecules can pass through

Best Wishes



SHORT QUIZ

1) Which of the following best describes the cholesterol molecule?

- A) Amphipathic
- B) Nonpolar, charged
- C) Nonpolar, uncharged
- D) Polar, charged
- E) Polar, uncharged

2) Which of the following contains an ether-linked alkyl group?

- A) Cerebrosides
- B) Gangliosides
- C) Phosphatidyl serine
- D) Platelet-activating factor
- E) Sphingomyelin

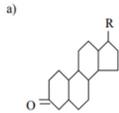
3) Which of the following is not a fat-soluble vitamin?

- A) A
- B) C
- C) D
- D) E
- E) K

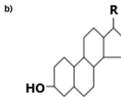
4) Which vitamin is derived from cholesterol?

- A) A
- B) B12
- C) D
- D) E
- E) K

5) Which of the following structures is a sterol?



A or B



6) 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.

7) 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.

8) 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.

9) 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.

ANSWERS

Q1	Q2	Q3	Q4	Q5
A	D	B	C	B
Q6	Q7	Q8	Q9	Hotel
D	A	A	A	Trivago



