بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

BioChemistry

وَلَقَدْ خَلَقْنَا الْإِنسَانَ وَنَعْلَمُ مَا تُوَسْوِسُ بِهِ نَفْسُهُ ۖ وَنَحْنُ أَقْرَبُ إِلَيْهِ مِنْ حَبْلِ الْوَرِيدِ

MID | Lecture #11

Lipid pt.4

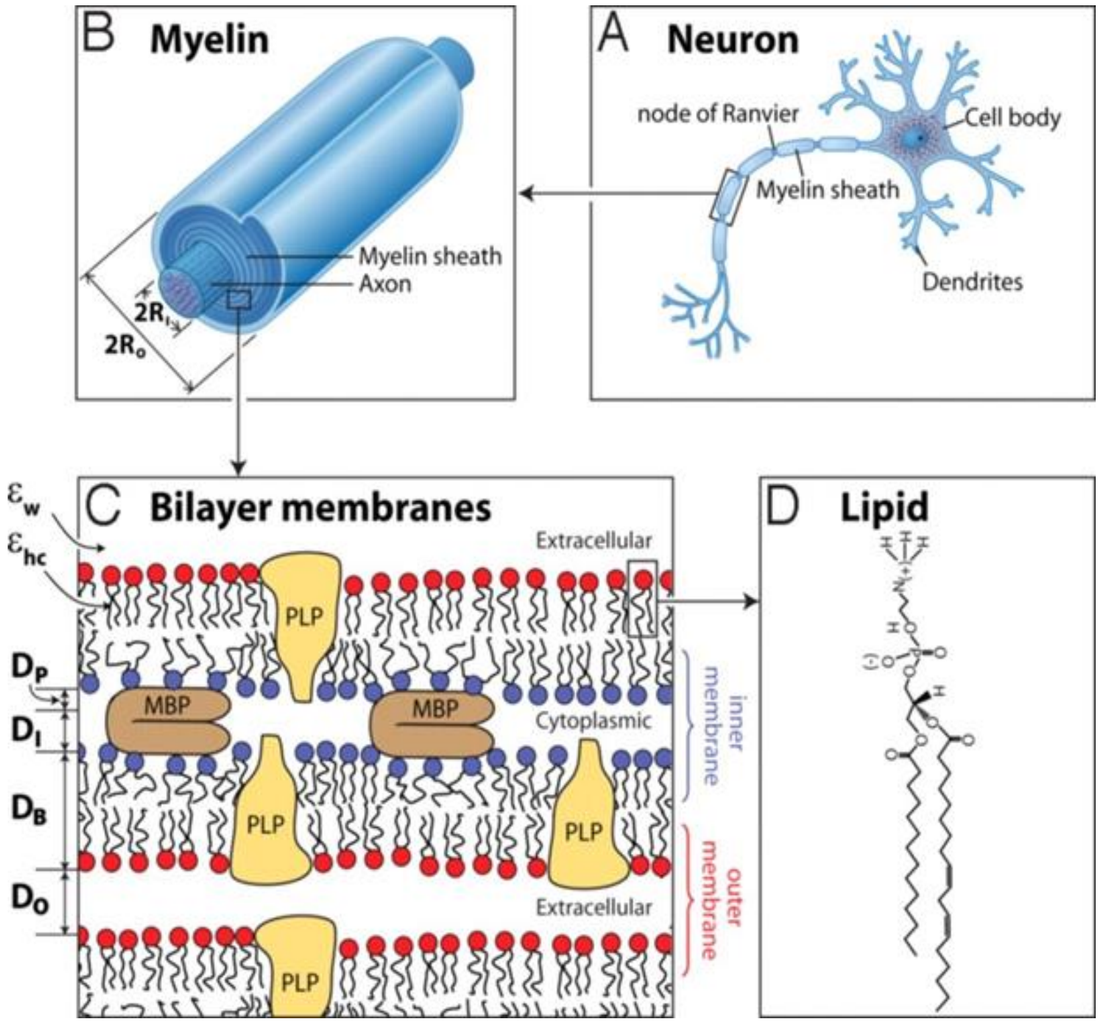
Written by : Yaman Khalil
Ahmad Mohy
Ali Al-sharaeah

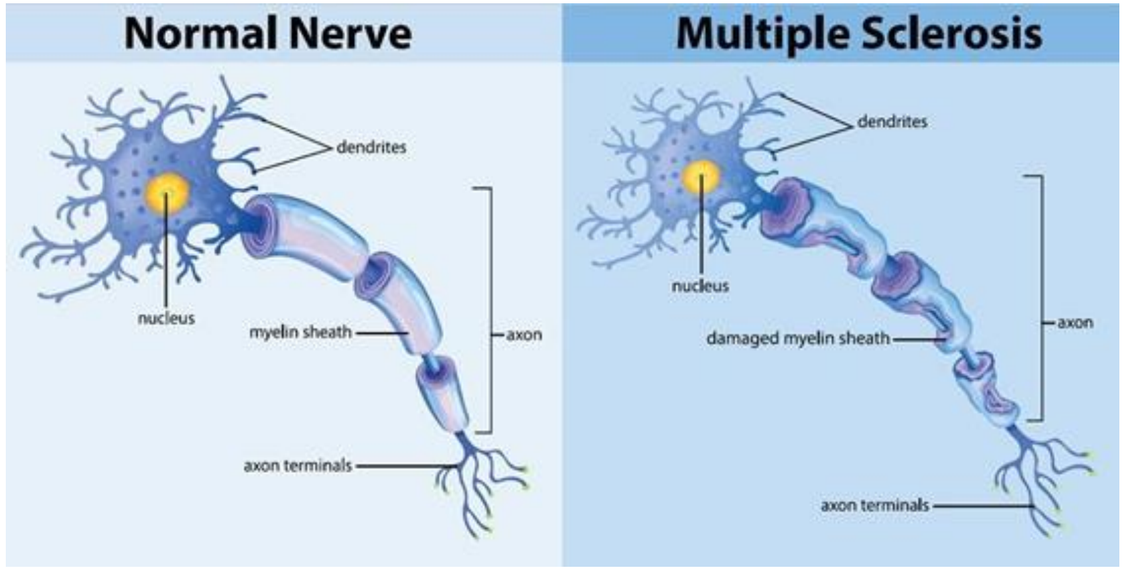
Reviewed by : Yamen Aljarrah

Color coding used in the modified:

- *Black: the original slides*
- *Navy Blue: the doctor’s explanation/words*
- *Gray: additional information and explanation*
- *Red: important information*

Zooming into the myelin





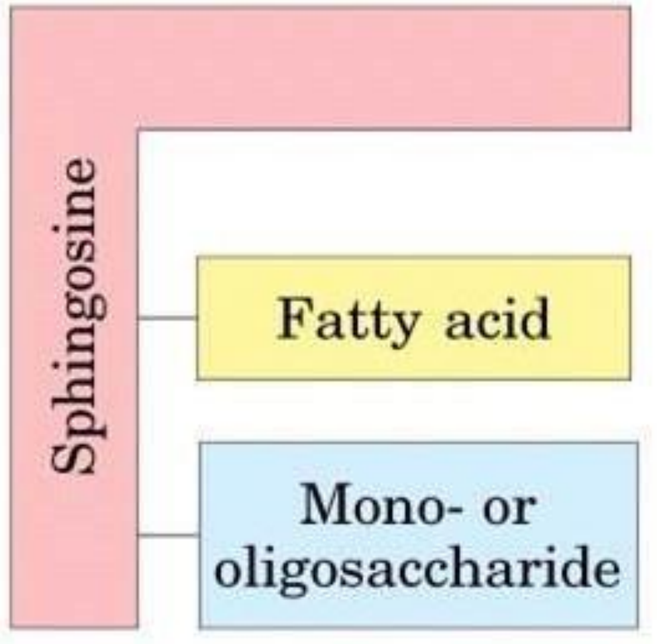
- Sphingomyelin is the main component of the coat of axons (myelin sheath)
- It contain (preserve) the electrical signal like the insulator layer of a copper wire
- In certain diseases such as multiple sclerosis (a degenerative nervous systam disorder) the immune cells attack the myelin sheath leading to its -myelin sheath- degeneration. As a result, the conduction of electrical signal become slower (no saltatory conduction)

Glycolipids

Instead of phosphocholine in sphingomyelin (the only sphingophospholipid)

- 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**

They are located mainly in the CNS, but also can be located in other cell types.

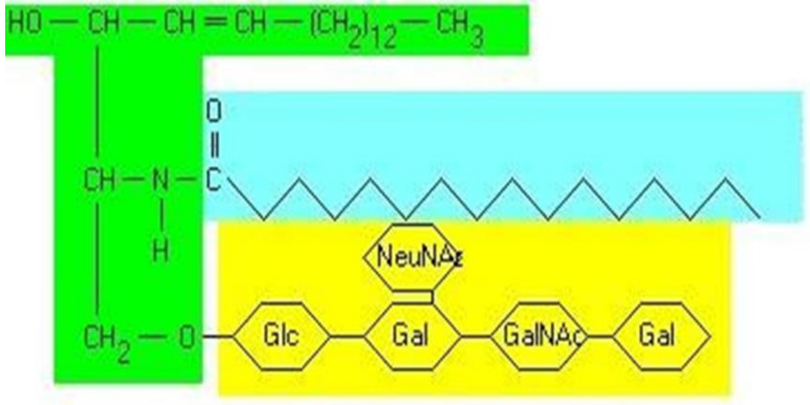


Glycolipids (or glycosphingolipids specifically) **contains:**

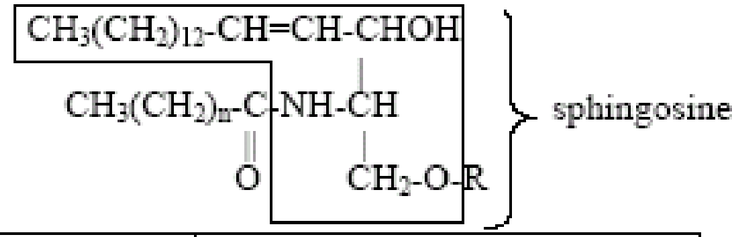
- **Sphingosine backbone**
- **Amide linkage with a fatty acid (usually palmitic acid)**
- **A sugar molecule at C1**

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.**



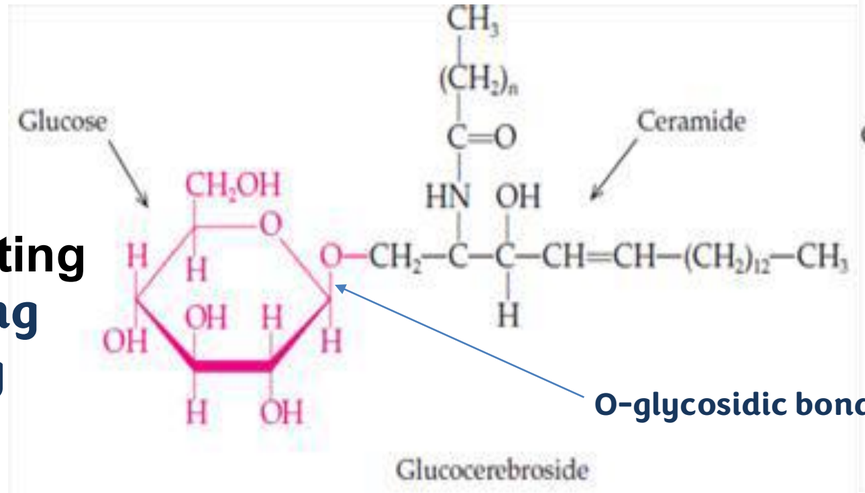
Gangliosides are bound by cholera toxin in the human intestine facilitating its endocytosis into the cells causing cholera (excessive diarrhea causing death because of dehydration).



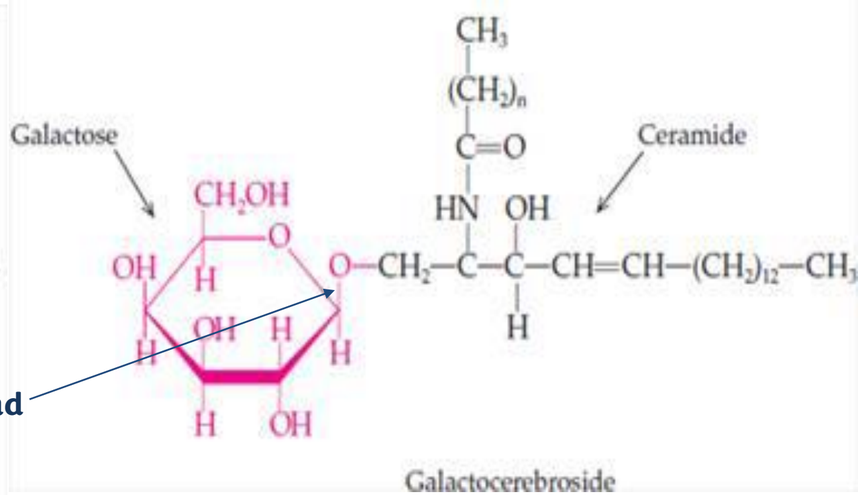
Sphingolipid type	R group
Ceramide	H
Sphingomyelin	phosphocholine
Cerebroside	monosaccharide (galactose or glucose)
Globoside	two or more sugars (galactose, glucose, N-acetylglucosamine
Ganglioside	three or more sugars including at least one sialic acid

glycolipids

Glucocerebroside



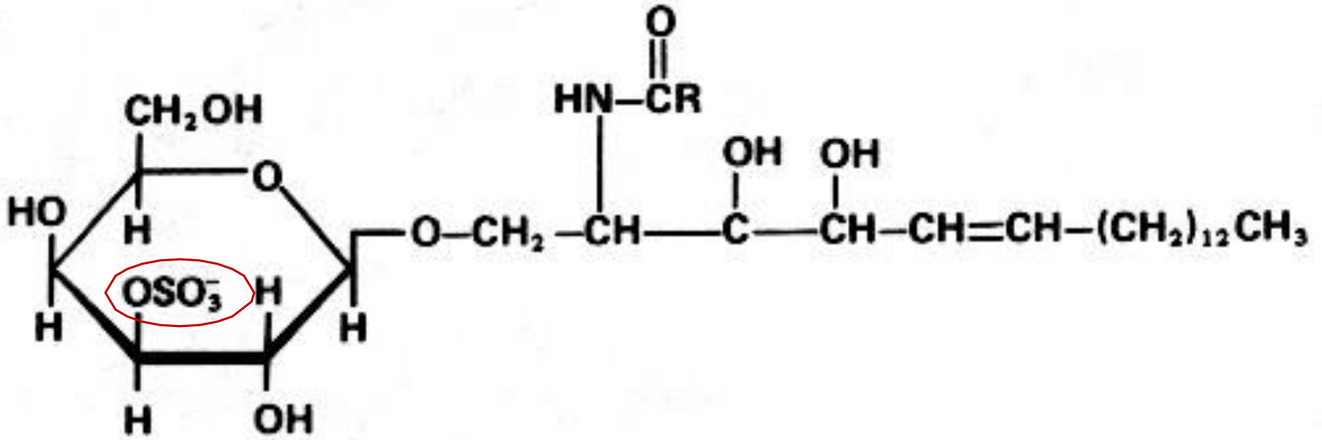
Galactocerebroside

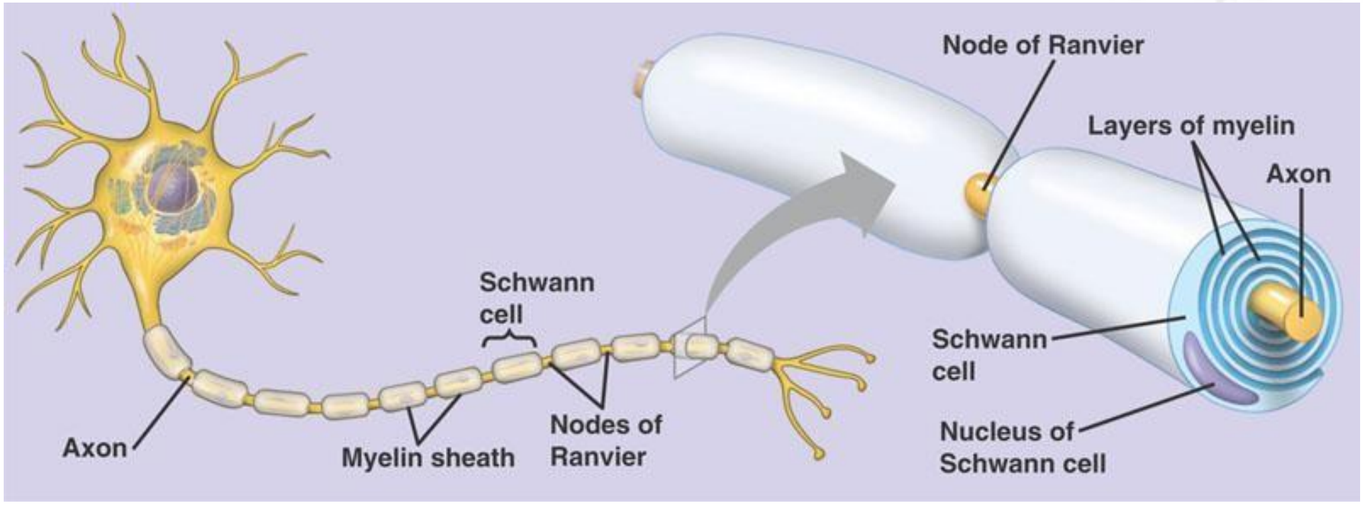


Sulfatides

Modified galactocerebrosides by adding a sulfate group (negative charge) absolutely they are sphingolipids (glycolipids)

- Synthesized from **galactocerebroside**
- Abundant in **brain myelin**

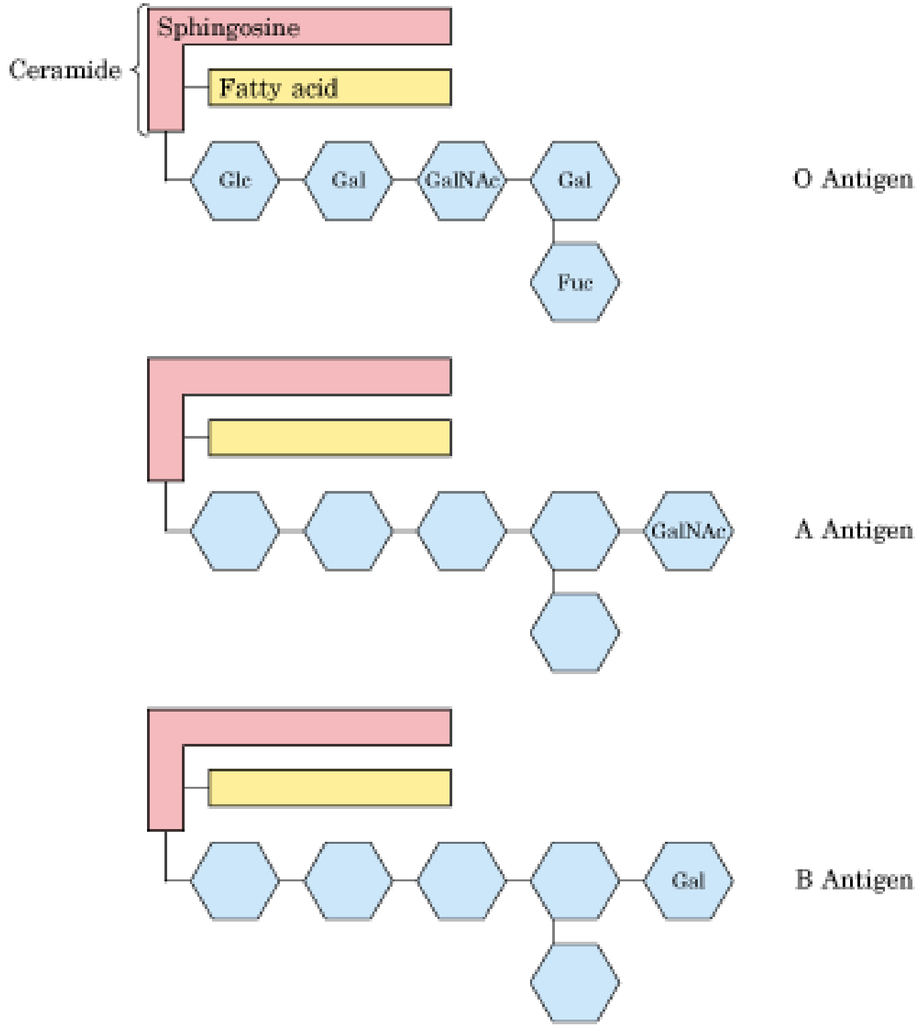




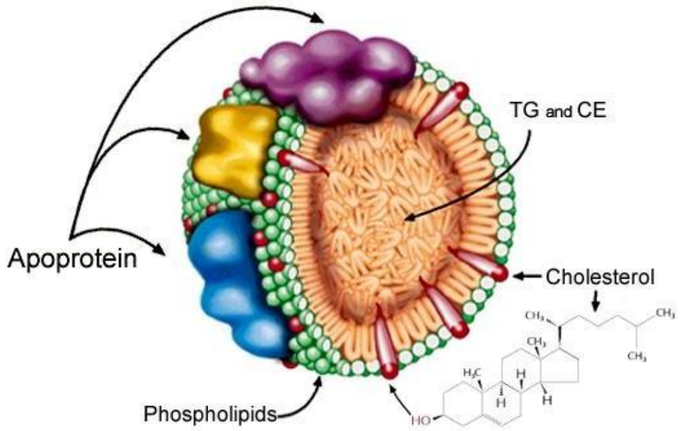
Sphingolipids and blood groups

- Sphingolipids serve in **inter**cellular communication and as the antigenic determinants of the ABO blood groups.
- Some are used as receptors by viruses and bacterial toxins. Like gangliosides and cholera

Sphingolipids (glycolipids) –**specifically globosides** are also located on the surface of RBCs and they have a role in blood typing (A,B,AB,O). Glycoproteins may have a role also (we will talk about them later).



Lipoproteins



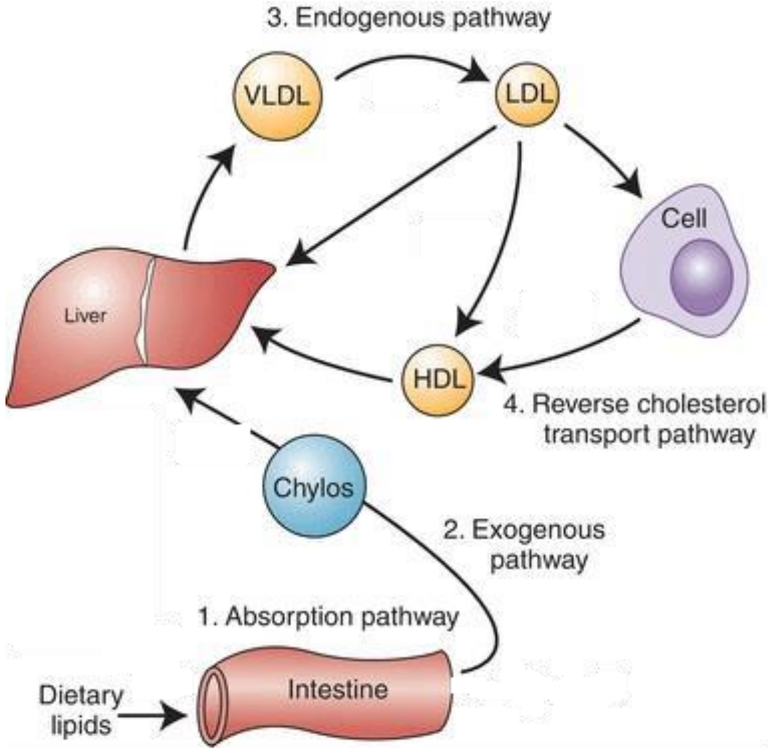
Function: transport of different types of lipids (cholesterol, cholesterol esters, phospholipids & triacylglycerols) in blood plasma.

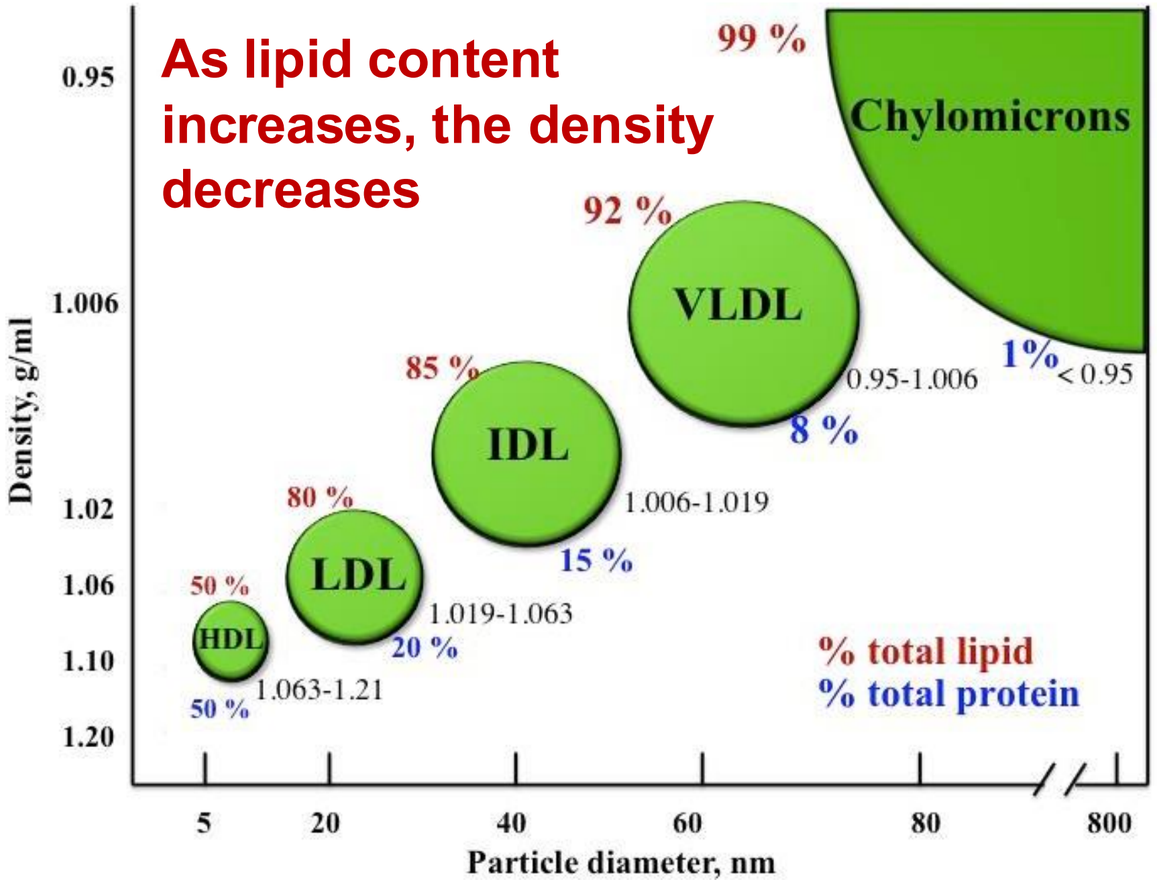
VLDL: very low-density lipoprotein

LDL: low-density lipoprotein

IDL: intermediate-density lipoprotein

HDL: high-density lipoprotein

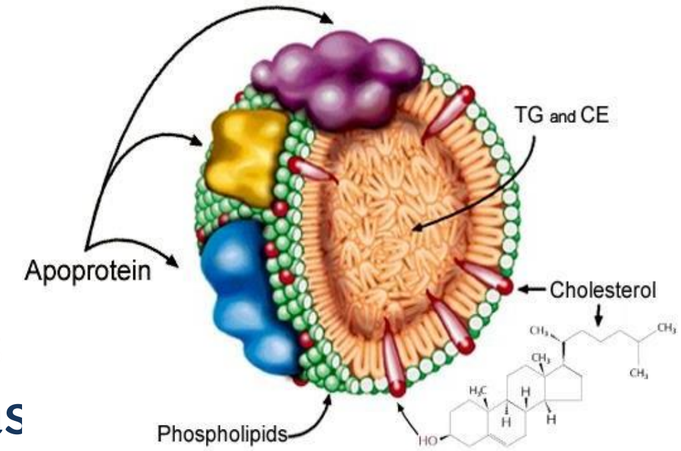




- Lipoproteins are large structures that transport different types of lipids throughout the body (via blood plasma) because lipids are hydrophobic and can't be transported in a hydrophilic medium(blood) on its own. If we put lipids without a carrier (lipoprotein in this case) it would aggregate and cause heart attacks.

- The phospholipids that participates in forming lipoproteins forms micelles
- We have the phosphate groups of the phospholipids (mainly glycerophospholipids in lipoproteins) directed outward
- We have the hydrophobic tails (of the phospholipids) directed inward

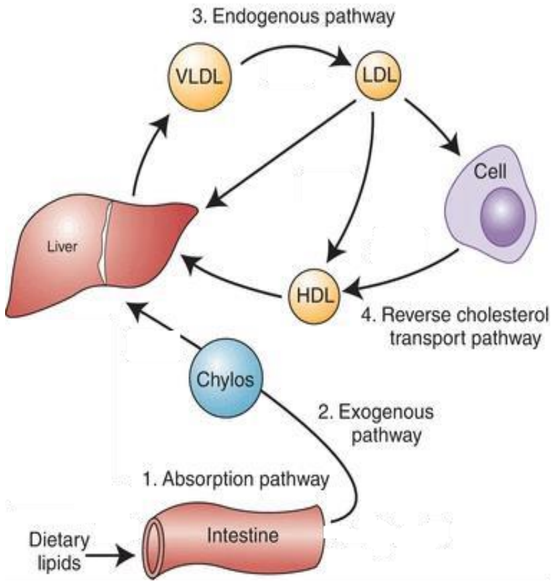
- This structure is bounded to proteins (thus it is called lipoprotein)



- It has many types (Chylomicrons, VLDL, LDL, IDL, HDL) . A key difference is the density which depends on the ratio of protein to lipids. As the ratio of protein to lipid increases the density increases and the volume decreases. Another difference is the type of proteins on each type, this protein control from where to where the lipoprotein will move.

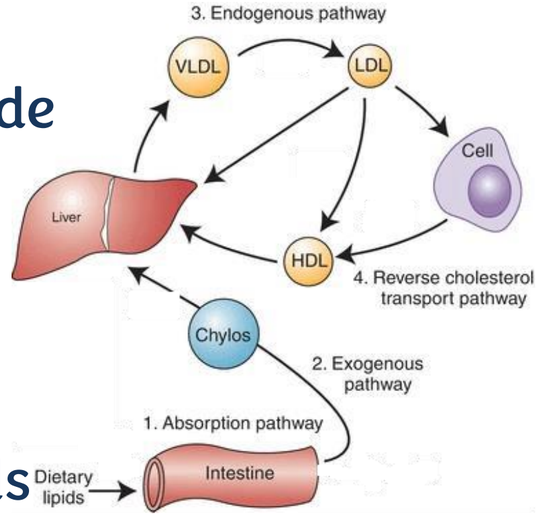
Chylomicrons have the highest density, largest volume and lowest percentage of proteins, while HDL has the highest density, smallest volume and biggest percentage of proteins .

- When we eat something that contains fat, intestinal cells absorb the fats inside them ,This is called absorption pathway.
- Then these intestinal cells package those lipids inside a Chylomicrons => that means Chylomicrons contain “dietary lipids”. The process of transporting exogenous lipids (lipids that came from outside of the body “food”) through the lymphatic system first then reaching the bloodstream to the liver is called exogenous pathway. (Chylomicrons are too large to enter blood capillaries so they go first through the lymph).
- The endothelial cells of the blood vessels remove ‘through enzymes’ the fatty acids from triacylglycerol and use it as energy source. Then, When Chylomicrons reach the liver they will be mainly composed of cholesterol and very small amount of fatty acids.
- The functions of the Liver : 1) To store dietary molecules like cholesterol, fatty acids, and glucose in the form of glycogen.
  2) Detoxification : to remove the toxicity from substances.



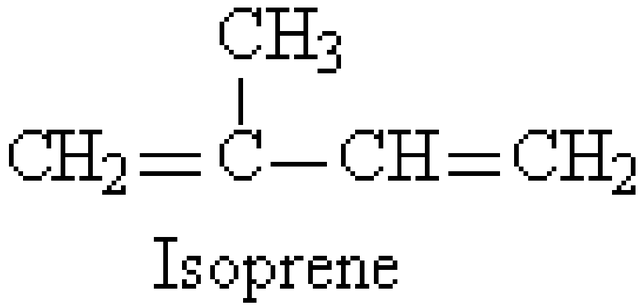
- When a specific signal reaches the liver because of the demand of fatty acids => liver cells release fatty acids, triacylglycerol, and cholesterol inside VLDL.
- Endogenous pathway (internal pathway) is the process of transporting lipids to the peripheral tissues in the form of VLDL. (Release is directly through bloodstream 'no lymph')
- In the blood, enzymes 'hydrolysis the triacylglycerol' releasing fatty acids to tissues like muscle tissue. As VLDL loses fatty acids it becomes LDL. LDL mainly contains cholesterol, and a small amount of fatty acids and triacylglycerol. (VLDL=> LDL) .
- LDL then is delivered to peripheral tissues to do its function, such as being a precursor for different derivatives (we will cover them later in this file).
- Liver also produce HDL(small in size), which retains the excess cholesterol from the peripheral tissues to the liver. (Reverse cholesterol transport pathway)
- When we do a lipid profile, we mainly focus on : 1) The amount of cholesterol in the blood . 2) The amount of {bad cholesterol}=> LDL.

  3) The amount of {good cholesterol}=> HDL.



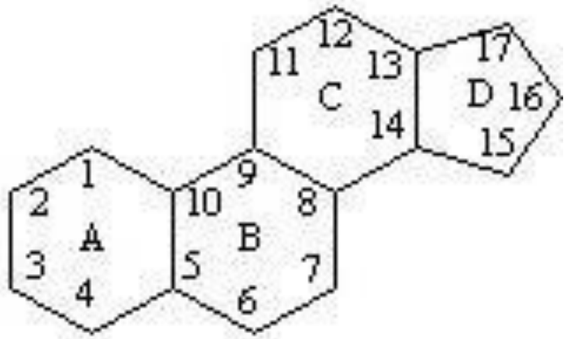
Steroids **A type of lipids.**

The precursor



Isoprene

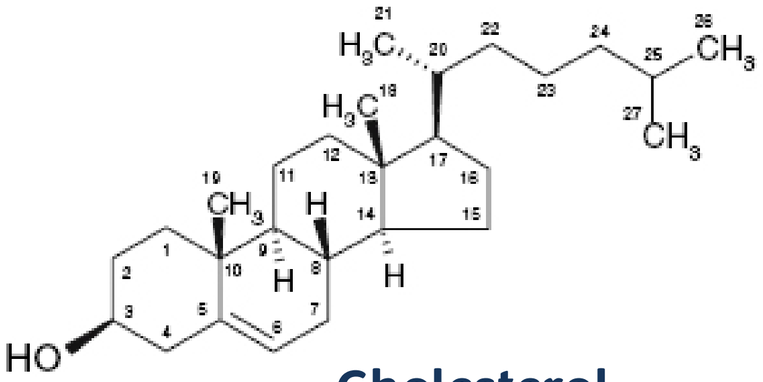
The nucleus



Steroid nucleus

- Cholesterol (lipid)is a 27 C molecule.
- It's synthesised through the precursor (Isoprene). We add them together up to 30 C then we remove 3C of them.
- It's a 4 ringed structure designated as (A B C D) containing 17 carbons, with a 10C hydrophobic chain. It also has a hydroxyl group (OH) making the molecule amphipathic (can be separated into two parts, one is hydrophilic and the other is hydrophobic (and this is why it's considered a lipid).

The most common steroid



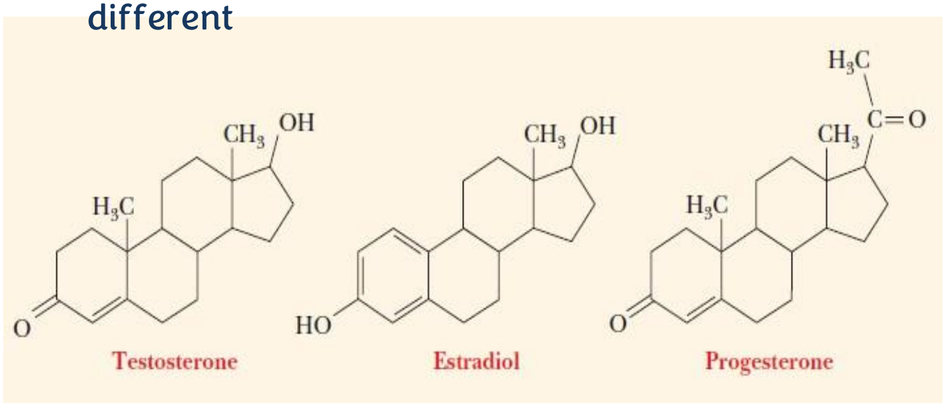
Cholesterol

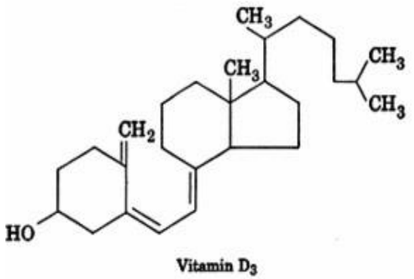
Products of cholesterol

A type of lipids.

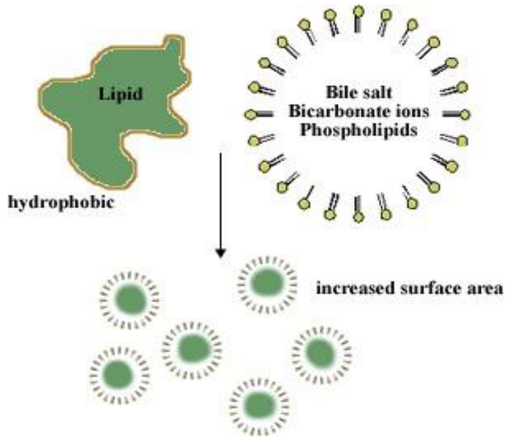
- Precursor of Hormones (important for the body):
  - **Sex hormones (androgens,. estrogens, progestins)**
  - Glucocorticoid and cortisol
- Vitamin D (the sun)
- Bile acids (intestinal absorption of fat):
  - Yellow in color found in gallbladder
  - Does emulsification: dissolving a hydrophobic substance in a hydrophilic environment (when we eat food that contains fats, it reaches the intestines which is a hydrophilic environment, so emulsification is important here.
  - Amphipathic molecule

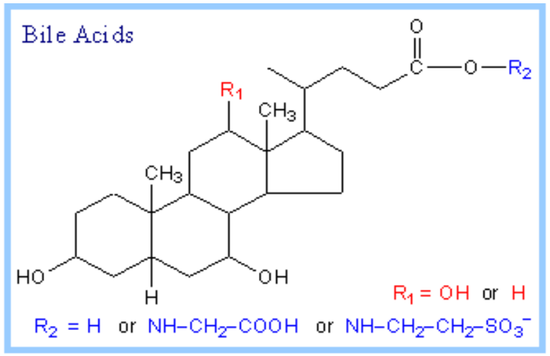
Don't memorize the structure, but know that the different sub groups is what makes them different





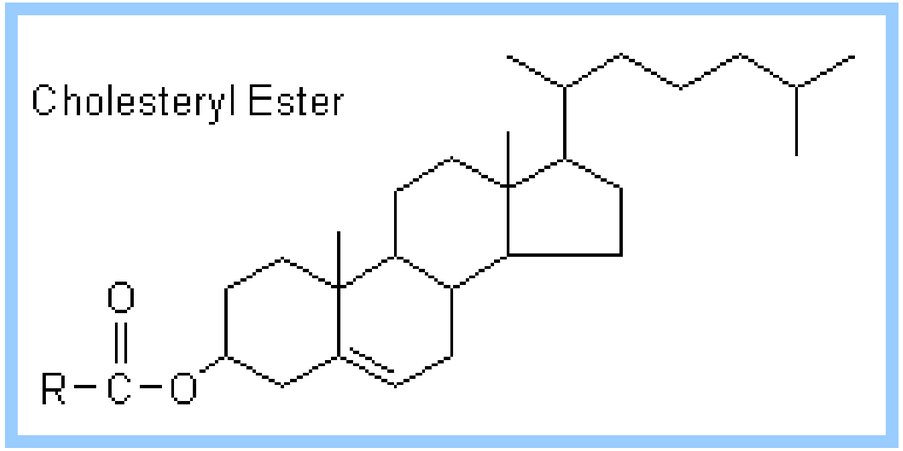
- Bile acids also break down lipids into droplets to make it easier to get absorbed, then in the intestines it gets transferred using Chylomicrons.
- People who have to remove their gall bladder do not produce enough bile acids, which will result in failure to absorb the lipids in the intestines which causes diarrhea.



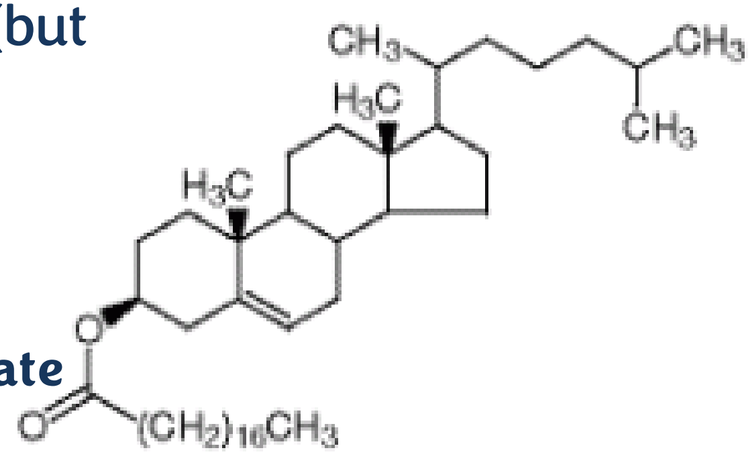


Cholesterol esters

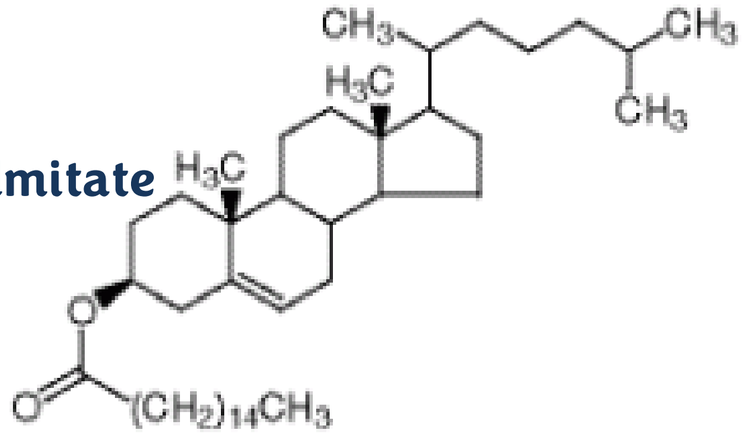
- A cholesterol with a fatty acid attached at (-OH) of C3, not amphipathic (hydrophobic).
  - This molecule can be considered a way to store fatty acids (but mainly fatty acids are stored as triacylglycerols).



Cholesterol sterate



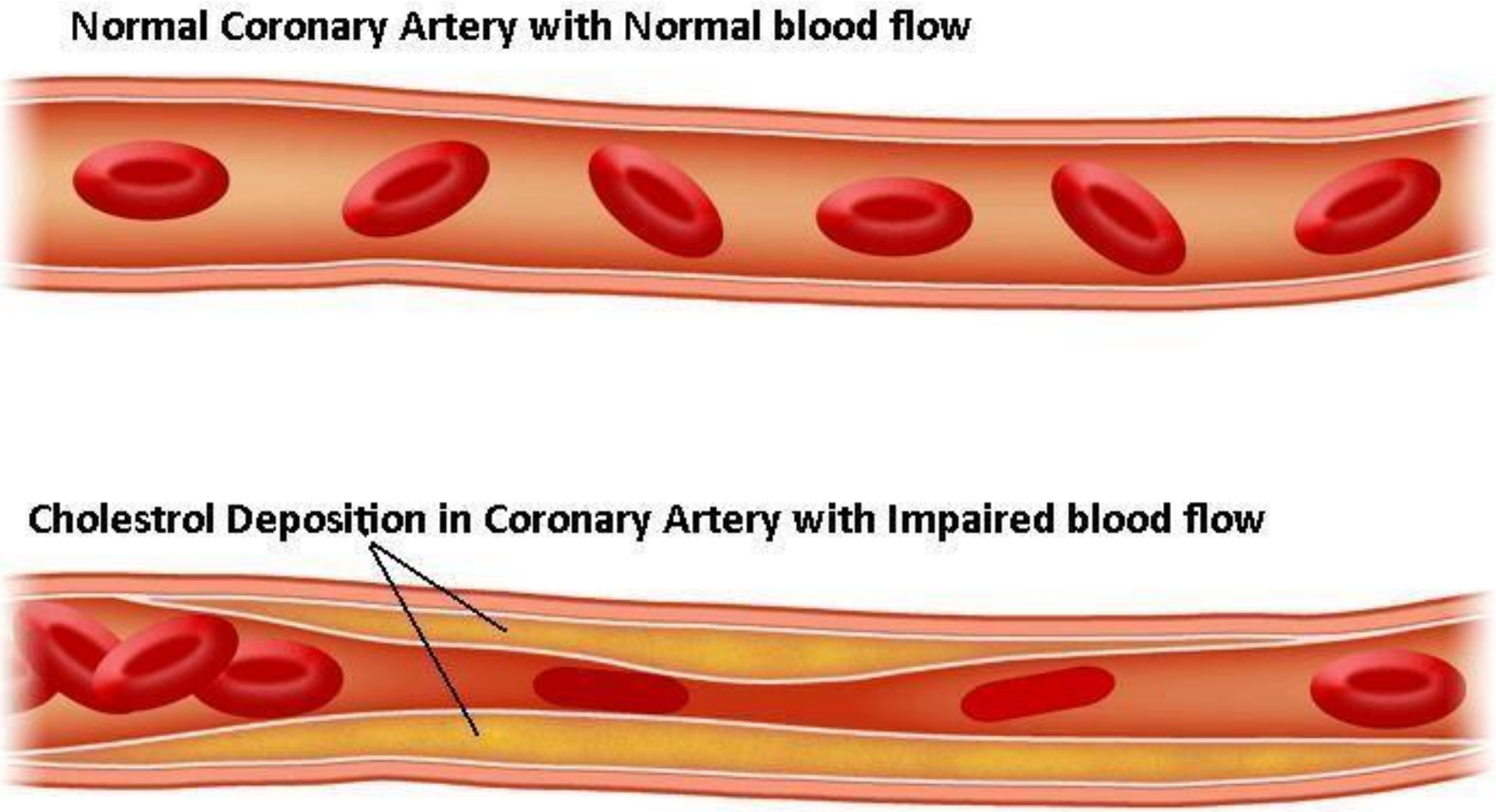
Cholesterol palmitate



Name the molecules?

1. Cholesteryl stearate (or cholesteryl octadecanoate)
2. Cholesteryl palmitate (or cholesteryl hexadecanoate)

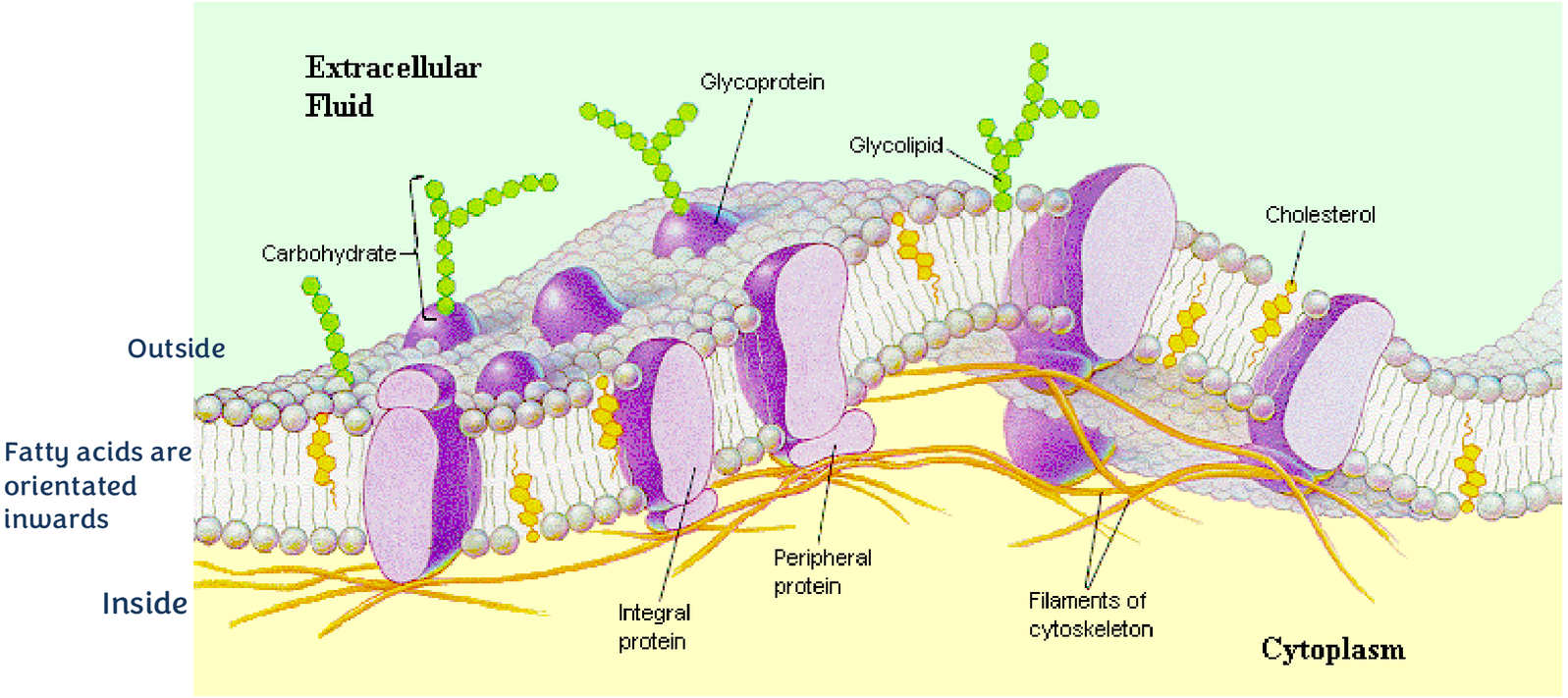
Atherosclerosis



LDL (bad cholesterol) accumulates and aggregates in blood vessels causing atherosclerosis

Cell membranes : bilayer structure of Glycerophospholipids

- The membrane is hypothesized in a model known as the fluid mosaic model.
- Components: 45% lipid, 45% protein and 10% carbohydrate(extracellular, helpful for recognition and cell-cell interactions, these carbohydrates can be found on sphingolipids “glycolipids” and proteins “glycoproteins”)
  - They exist side by side without forming some other substance of intermediate nature.



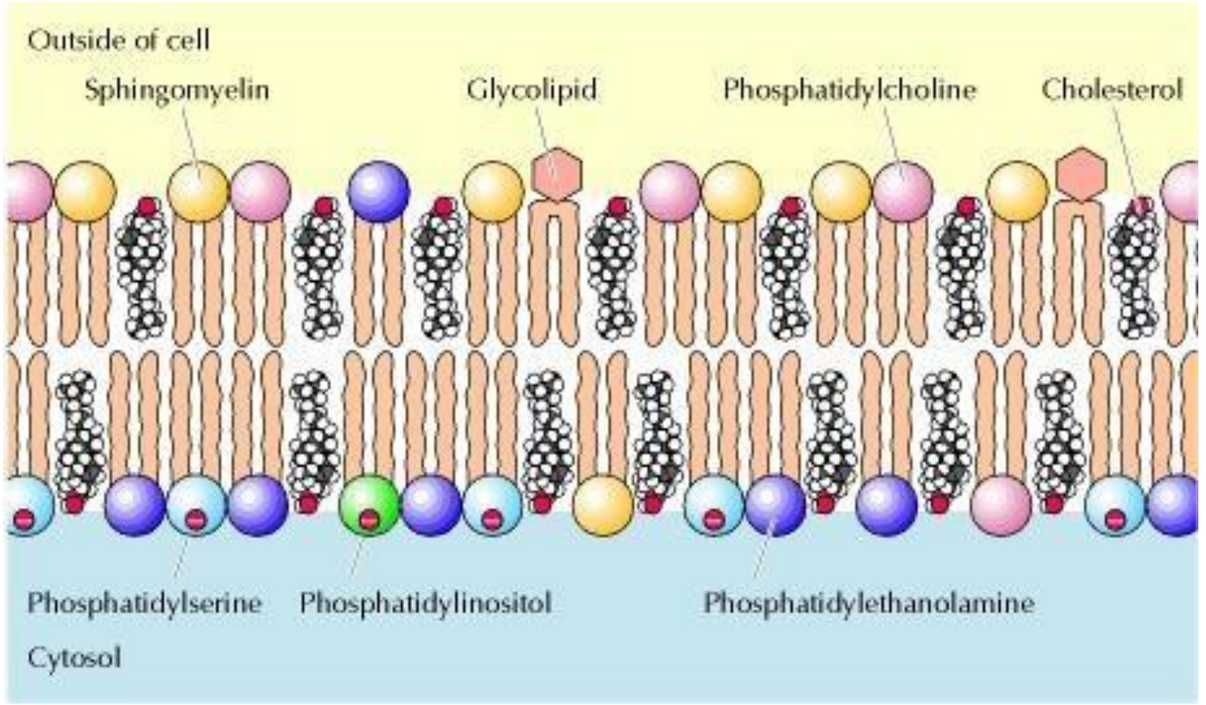
Phospholipids

- The outer: phosphatidylcholine, sphingomyelin, and glycolipids(cell recognition)
- The inner: phosphatidylethanolamine, phosphatidylserine, and phosphatidylinositol (signaling)
  - The distribution between the two layers is **not** in equal quantities

Cholesterol is distributed equally in both leaflets

Animal cells vs. plant cells vs. prokaryotic cells

Cholesterol is not found in bacteria or plants (but plants have something similar to it)

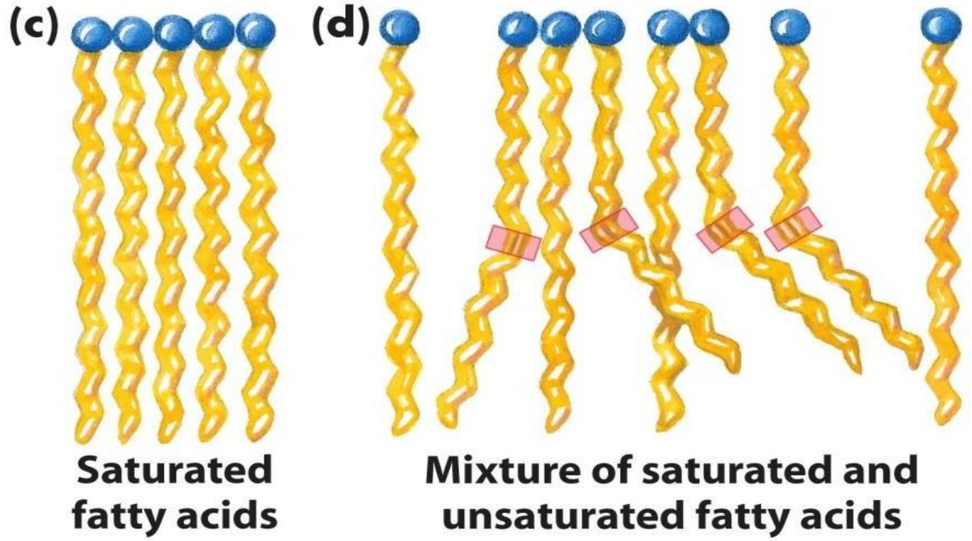


Fatty acids and membrane fluidity

the membrane is dynamic, not static (this feature is important for cell signaling and transferring nutrients into the cell), the lipids could move either laterally (on the same side) or vertically (flip from outside to inside or vice versa)

- Saturated fatty acids have straight hydrocarbon tails, allowing them to pack closely together, creating a rigid membrane.

- Unsaturated fatty acids have kinks in their tails due to double bonds, preventing tight packing and increasing membrane fluidity (helping molecules move around in it)



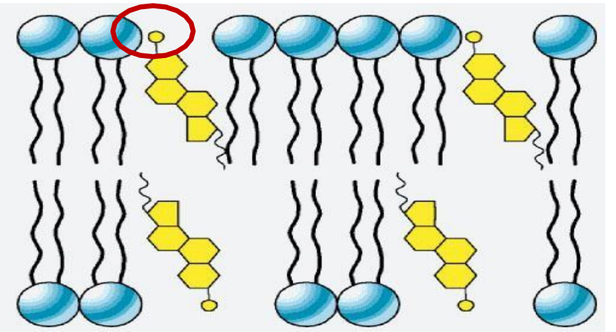
- **Unsaturated fatty acids provide more fluidity to the membrane.**

- **The structure of the cell membrane is actually different between different populations around the world. For example:**

- **In Africa, people's fatty acids in the cell membrane will be saturated fatty acids because the excessive heat there makes the molecules separate (makes the membrane more fluid) so saturated fatty acids help keeping the stability and rigidity of the membrane.**

- **People who live in very cold places around the world have cell membranes which is mainly made of unsaturated fatty acids,because the cold weather forces molecules to come closer to each other, so having unsaturated fatty acids helps keeping the stability and fluidity of the membrane in these harsh weather conditions. (That's why people who live in these places mostly have a diet that consists of a lot of fish, because it has A LOT of omega-3 fatty acids "unsaturated fatty acids" which is very healthy for them and doesn't cause heart attacks.)**

Cholesterol and membrane fluidity

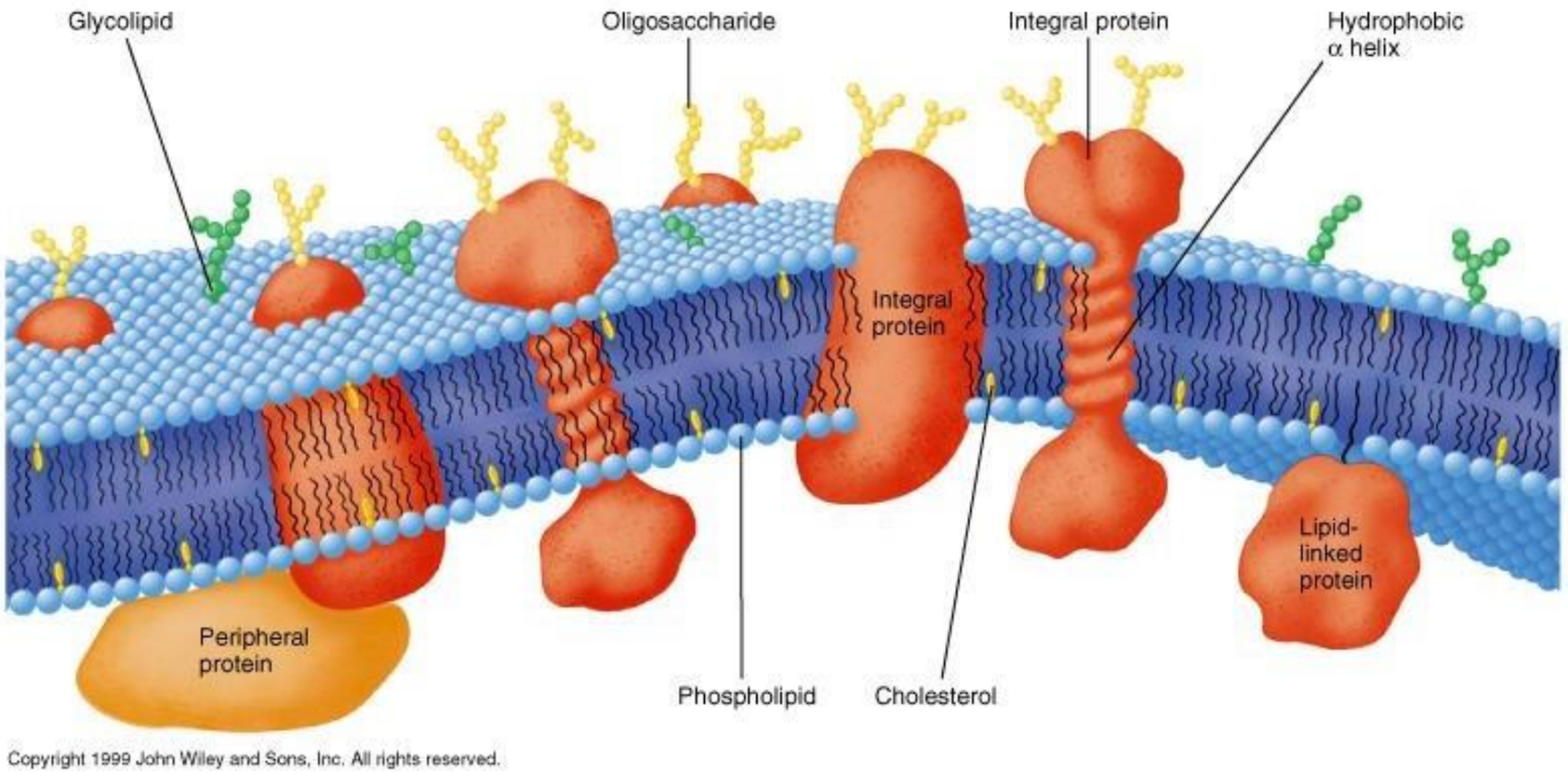


Cholestorl's hydroxyl group interacts with the phosphate group on the phospholipid, and the ring part of the cholesterol is oriented inward in the cell membrane (in the hydrophobic region).

- The presence of cholesterol and the cis unsaturated fatty acids in the membrane prevents the hydrophobic chains from packing too closely together, allowing free membrane proteins and lipid molecules to move laterally in the plane of the leaflet, making the membrane a dynamic environment.
- Cholesterol **(has duel roles)** can also stabilize the fluidic membranes**(despite the temperature)** by increasing interactions between the fatty acids of phospholipids through hydrophobic interactions with the cholesterol ring structure.
- Note the significance of cholesterol at low and high temperatures:
  - **When cold: cholesterol seperates the fatty chains away from each other so no interactions occur making it fluid and dynamic.**
  - **When hot: cholesterol prevents collision of molecules which makes the membrane more rigid and less fluid.**

The prof stopped explaining here because we will take these topics in the proteins section 💙

Membrane proteins

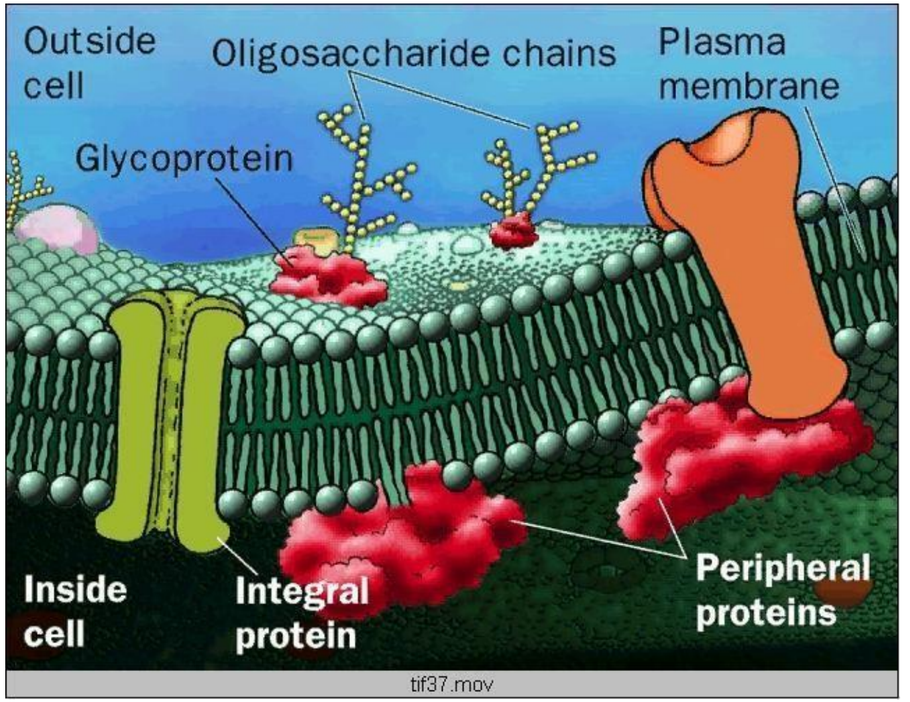


Types of membrane proteins

- 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

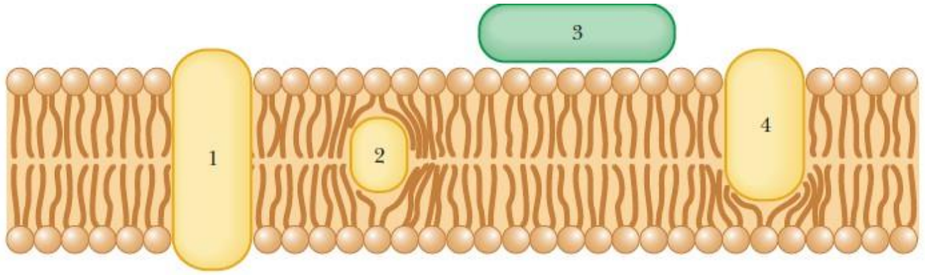
Peripheral membrane proteins

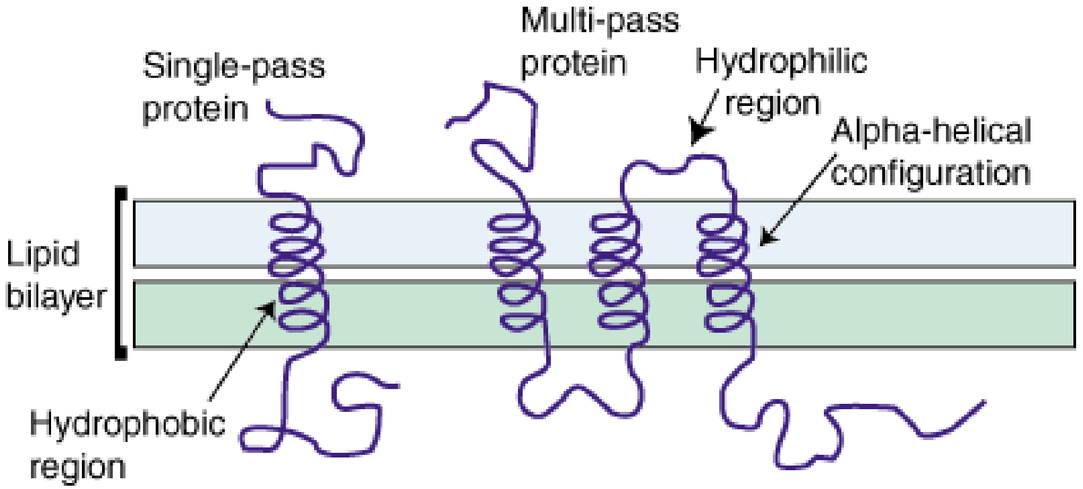
- They are associated with membranes but do not penetrate the hydrophobic core of the membrane.
  - They can be associated with integral membrane proteins.
- They are not strongly bound to the membrane and can be removed without disrupting the membrane structure.
  - Treatment with mild detergent



Integral membrane proteins

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



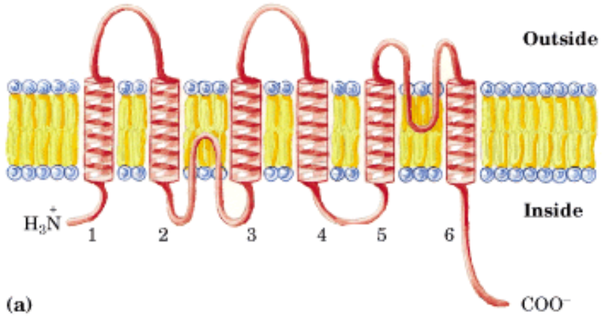


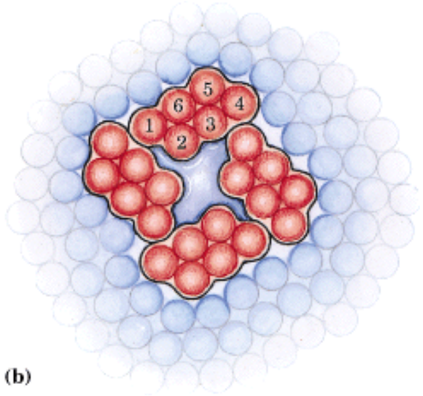
The membrane integral domains are:

1. Single or multiple

2. α-helix (human) or β-sheet (bacteria)

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
  - Enzymes

Quiz!

Good luck!

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			

Additional Resources:

رسالة من الفريق العلمي:

Reference Used:

Prof. Mamoun Ahram recorded lecture
“Lipids pt.4”

Extra References for the Reader to Use:

Marks’ Basic Medical Biochemistry (6th edition)

لا تنسوا أنفسكم ولا تنسونا من صالح دعائكم💙💙