بسم الله الرحمن الرحيم

BioChemistry | Lecture 11

Lipids pt.3 & Nucleic acids pt.1

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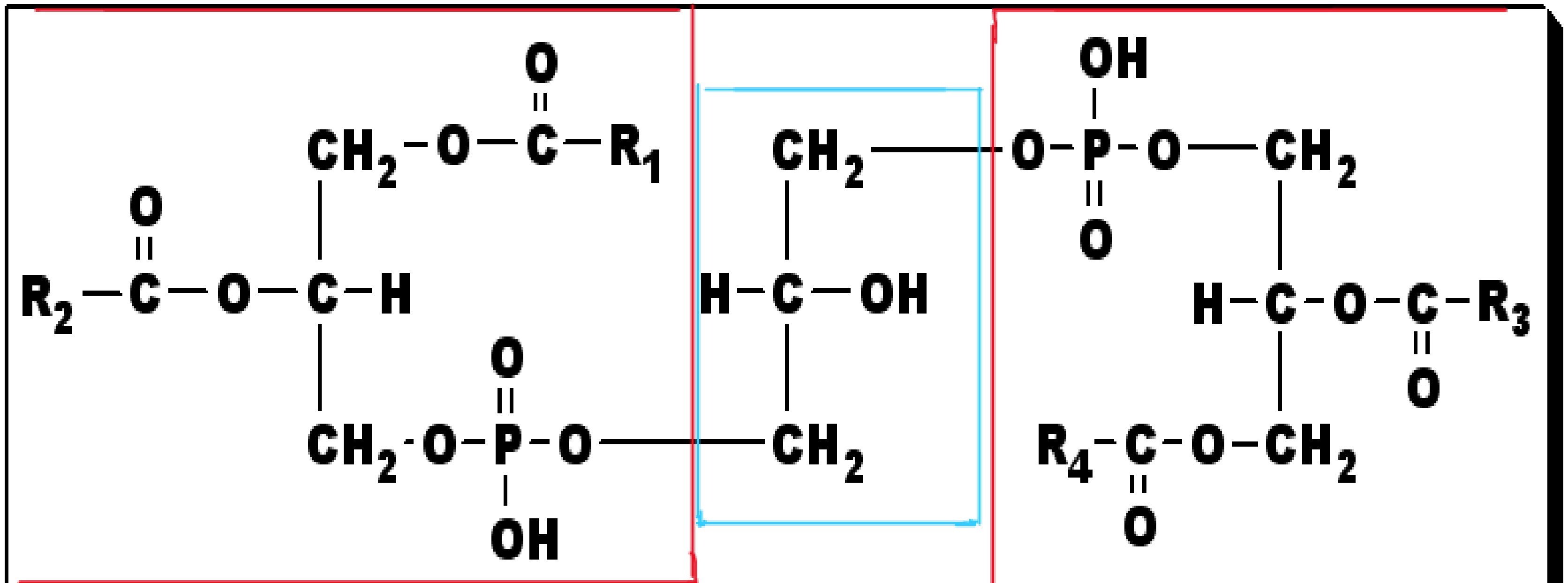
Cardiolipins

- Diphosphatidyl-glycerol
- Inner membrane of mitochondria



Cardiolipin

Cardiolipins

Cardiolipins have a unique and complex structure.
They are composed of three glycerol molecules connected by phosphate groups. The name "cardiolipin" is a common name, derived from the fact that it was first discovered in the heart muscle (cardiac cells), and later identified in other types of cells.

Cardiolipin is also known by its **systematic name diphosphatidylglycerol**, which accurately reflects its chemical structure: it consists of two phosphatidic acid molecules linked to a central glycerol backbone.

Cardiolipins are highly hydrophobic in nature. In most biological membranes, their concentration ranges from 2% to 3%, which helps regulate membrane density and prevents excessive tightness. This regulation is essential because dense membranes hinder the passage of ions and charged molecules.

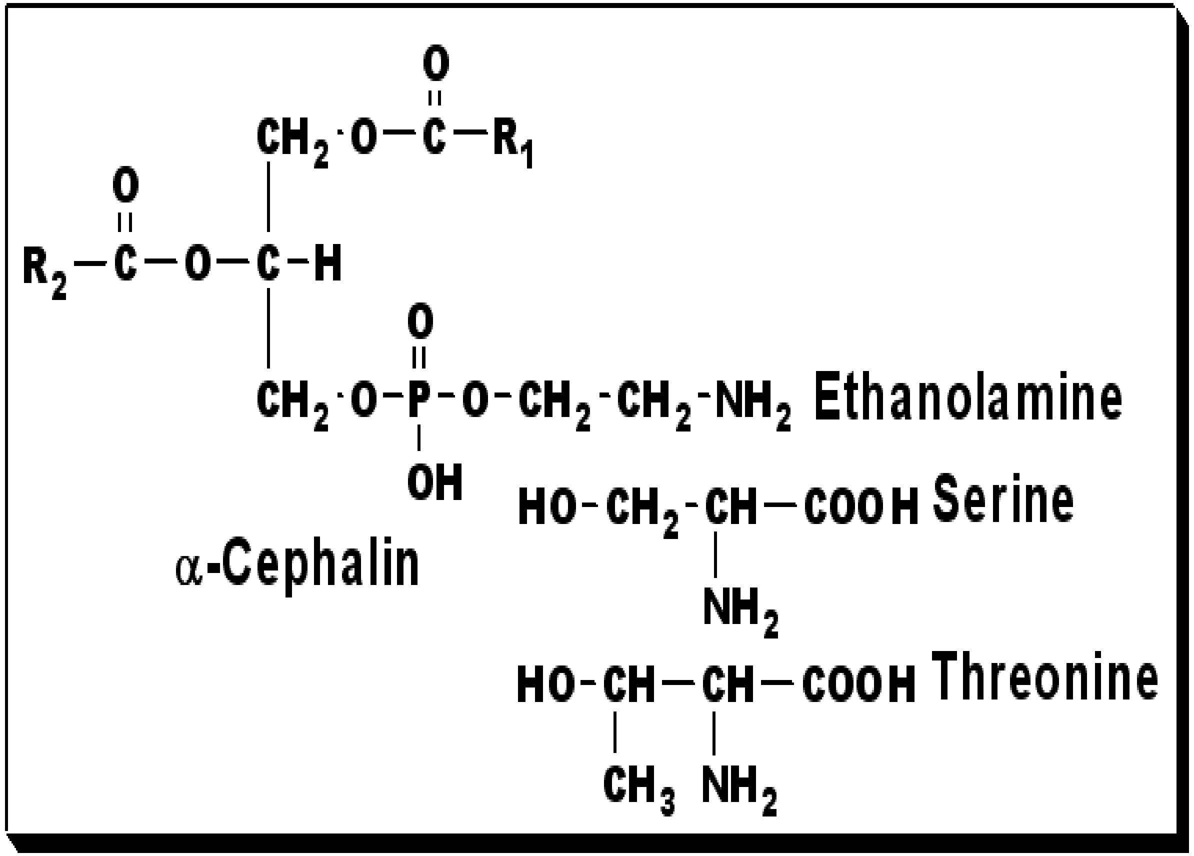
As you may know, cell membranes have limited permeability for charged molecules, generally up to a molecular size of about 5 kilodaltons. Molecules larger than this size cannot easily pass through.

However, **there is one exception: the inner mitochondrial membrane**, which is structurally and functionally distinct from other membranes in the body. As it is completely impermeable, even to protons—the smallest and simplest charged particles in nature.

One of the reasons the inner mitochondrial membrane has this special property is its high protein content and exceptionally high cardiolipin concentration, reaching approximately 22%, which is about ten times higher than in other membranes

This impermeability is vital for energy production. Protons are pumped across the inner mitochondrial membrane during cellular respiration. Then, they return through ATP synthase, driving the synthesis of ATP, the energy currency of the cell. If protons are pumped and do not return through the ATP synthase, the process becomes inefficient, and energy production fails.

Cephalins or Kephalins



Cephalins were first discovered in brain cells, which is why they were given this name—since "cephalic" refers to the head. Later, they were found to exist in all cells. They are glycerol-based molecules in which the phosphate group is attached to a nitrogenous base.

This nitrogenous base can be:

Ethanolamine

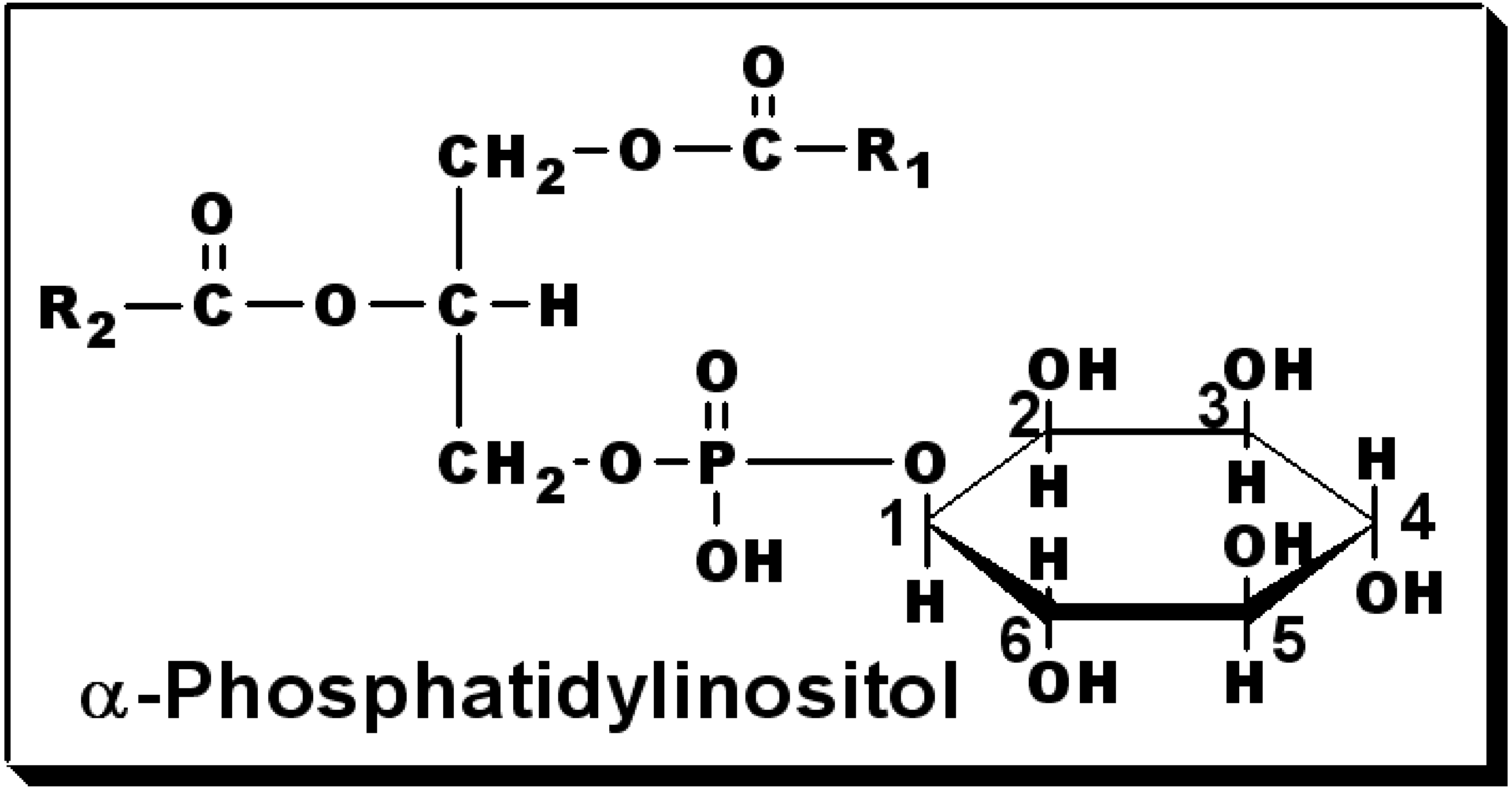
Serine

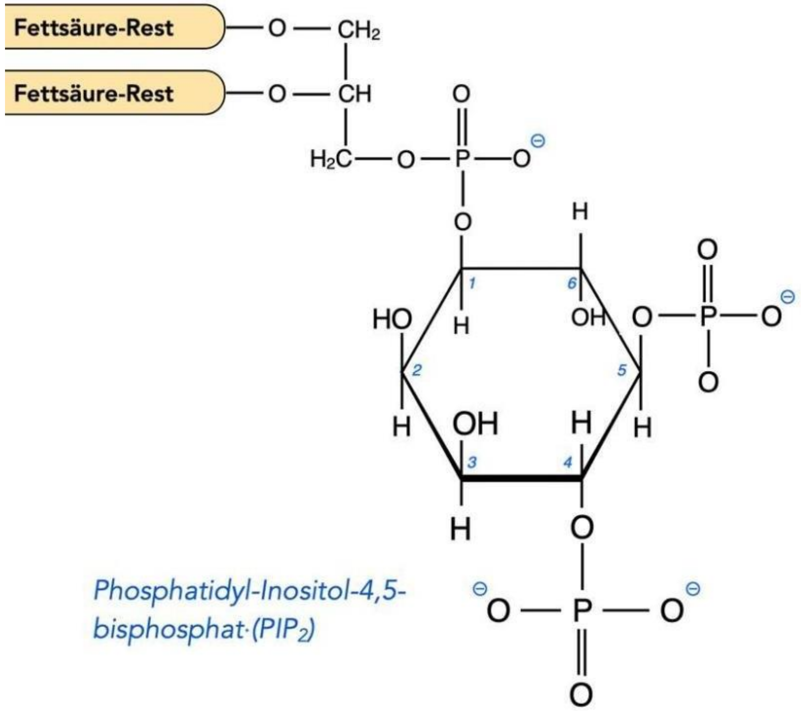
Threonine

These three are considered the main types of cephalin structures.

Serine and threonine are also classified as amino acids.

Inositides





Phosphatidyl-Inositol-4,5-bisphosphat (PIP$_2$)

Inositides

Phosphatidylinositol is composed of a phosphatidyl structure attached to inositol, which is an alcohol molecule. It is not considered a sugar, since oxygen is not part of the ring. The inositol ring contains six carbon atoms, and each carbon carries a hydroxyl group, making it a hydroxyl-rich structure.

This molecule is found in cell membranes, and it can undergo modifications by the addition of two phosphate groups to the inositol ring—one at carbon 4 (C4) and another at carbon 5 (C5). The resulting molecule is called **phosphatidylinositol 4,5-bisphosphate (PIP_2).**

When a hormone binds to its receptor on the cell surface, this activates an enzyme inside the membrane, triggering a signaling cascade. As a result, PIP_2 is broken down into two important second messengers:

1) IP_3 (inositol trisphosphate):

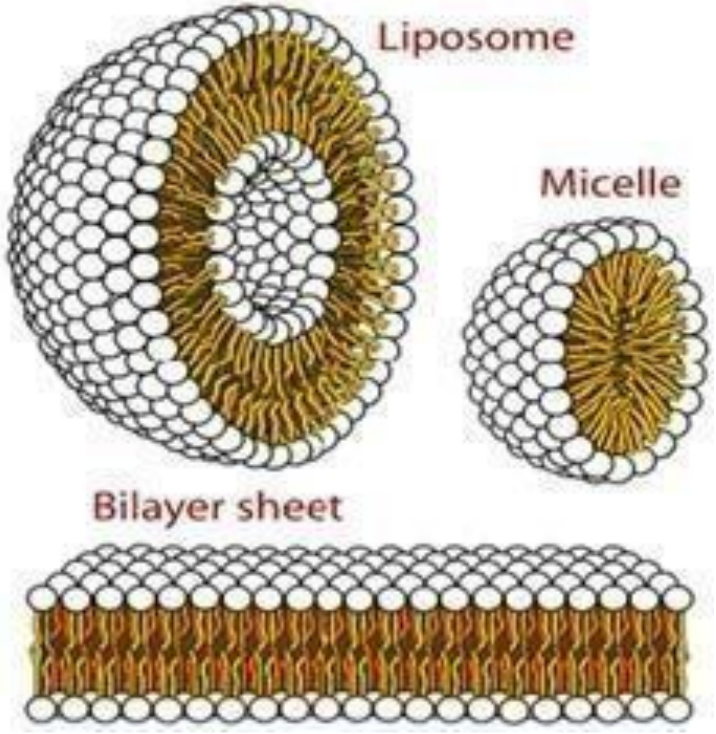
A highly soluble alcohol-based molecule with three phosphate groups. Because of its solubility, it leaves the membrane and moves into the cytosol, where it reaches the smooth endoplasmic reticulum. There, it binds to specific receptors and causes the release of calcium ions by opening calcium channels. The released calcium then functions as a second messenger, activating various proteins and enzymes in the cell.

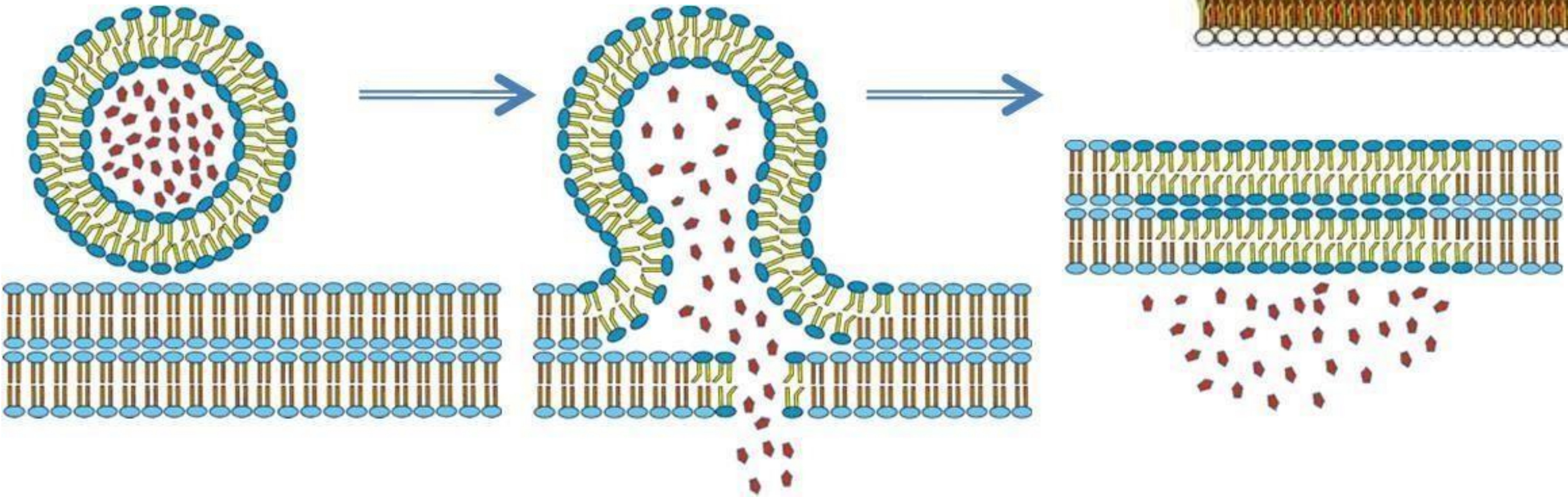
2) DAG (diacylglycerol):

A lipid-soluble molecule that remains in the membrane. It functions as another second messenger, and it activates protein kinase C (PKC). This enzyme initiates downstream phosphorylation reactions that regulate cellular responses.

Uses of liposomes: delivery

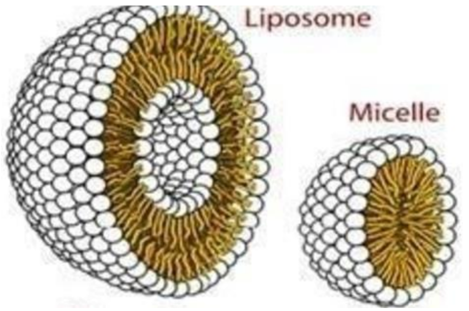
Structures of phospholipids





Structures of Phospholipids

Phospholipids are components of cell membranes. When emulsification occurs, some lipids form small droplets of fat, leading to the formation of micelles. These structures have hydrophilic phosphate groups that face outward toward water, while the lipid portions are arranged inward.



Through further modifications, liposomes can be formed. A liposome is a spherical structure composed of a phospholipid bilayer, similar to the structure of a biological membrane. Since the interior of cells is aqueous, the inside of a liposome can hold water or water-soluble drugs.

Liposomes are used as delivery systems for drugs. Normally, when a drug enters the body (e.g., via IV), it spreads through the bloodstream and reaches all cells, not just the target cells. This can result in side effects, because the drug affects healthy cells as well.

To solve this issue, researchers developed targeted liposomes. These liposomes are engineered to carry specific markers on their outer surface. These markers are designed to recognize and bind only to certain target cells.

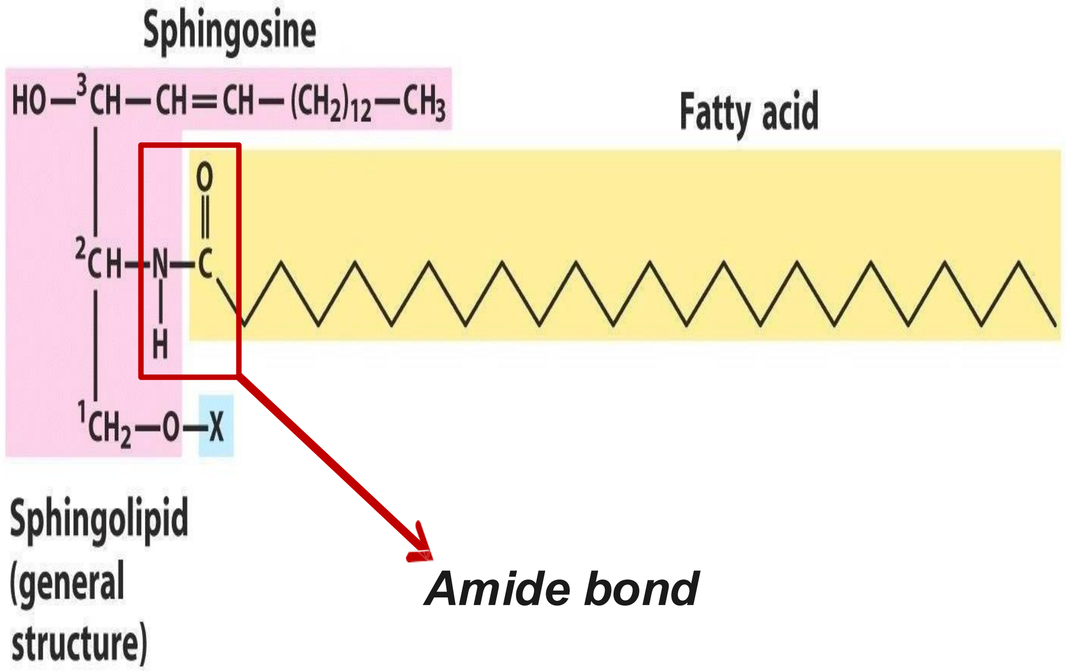
The main challenge lies in finding a marker that is specific to the target cell and attaching it effectively to the surface of the liposome. Once in circulation, the liposome carrying the drug will not bind to any cell except the target cell.

Upon reaching the target, the liposome membrane fuses with the cell membrane, releasing the drug directly inside the target cell. This enhances the beneficial effects of the drug and reduces side effects.

Sphingolipids

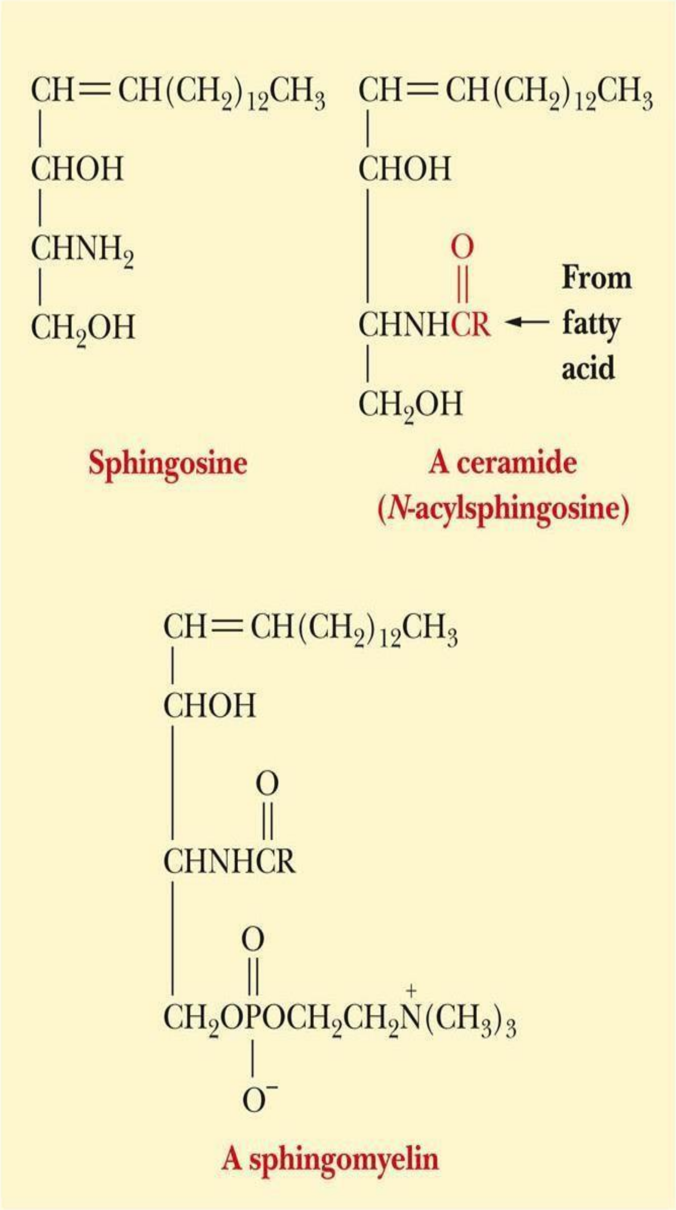
The core: long-chain amino alcohol, sphingosine

Highest in cells of CNS

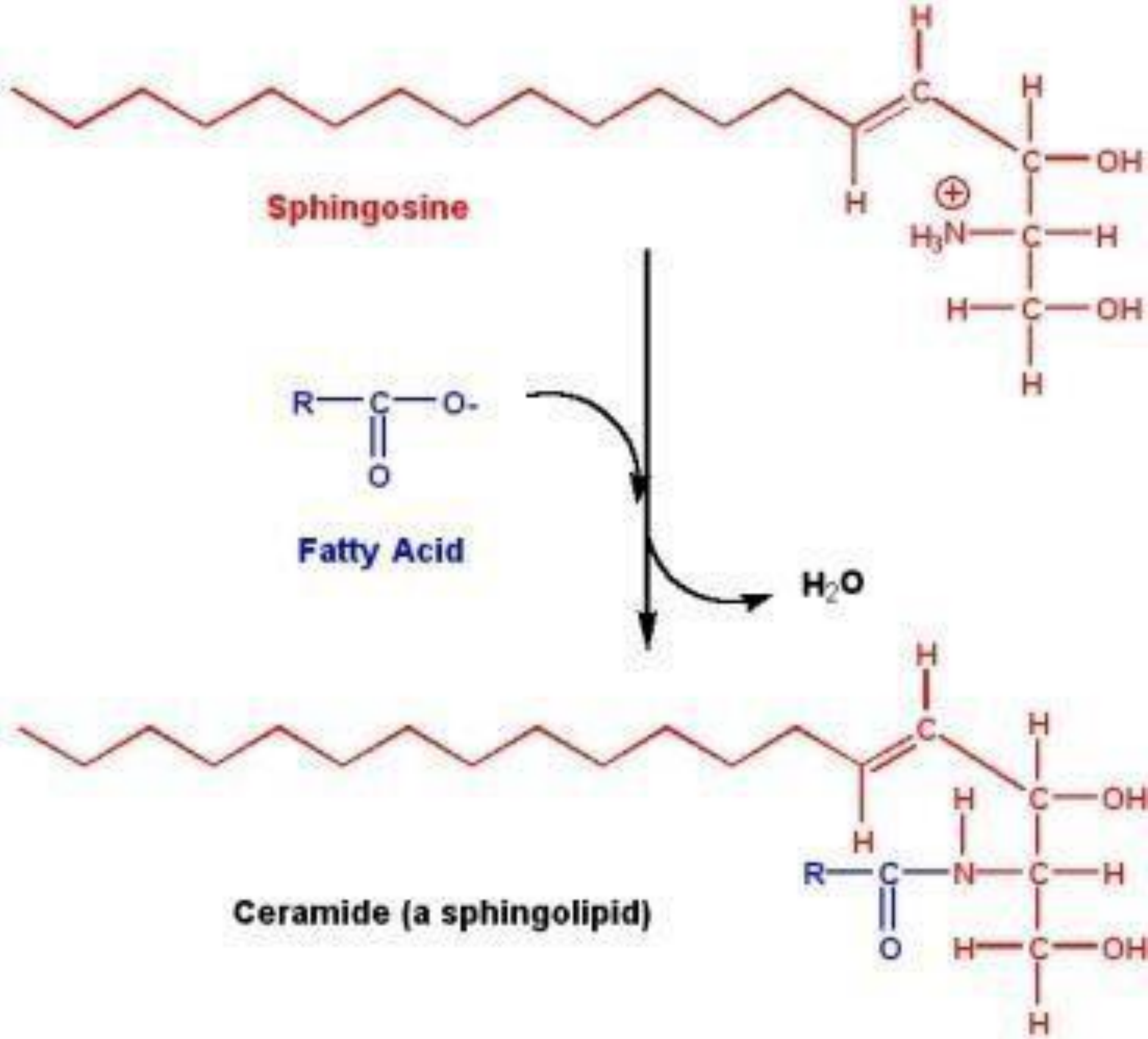


Sphingolipids are lipids that use sphingosine as their structural backbone. Sphingosine is a long-chain amino alcohol, and it binds to a fatty acid through its nitrogen group, forming an amide bond.

When no modifications are made to the terminal hydroxyl group (–OH), the resulting molecule is called a ceramide.



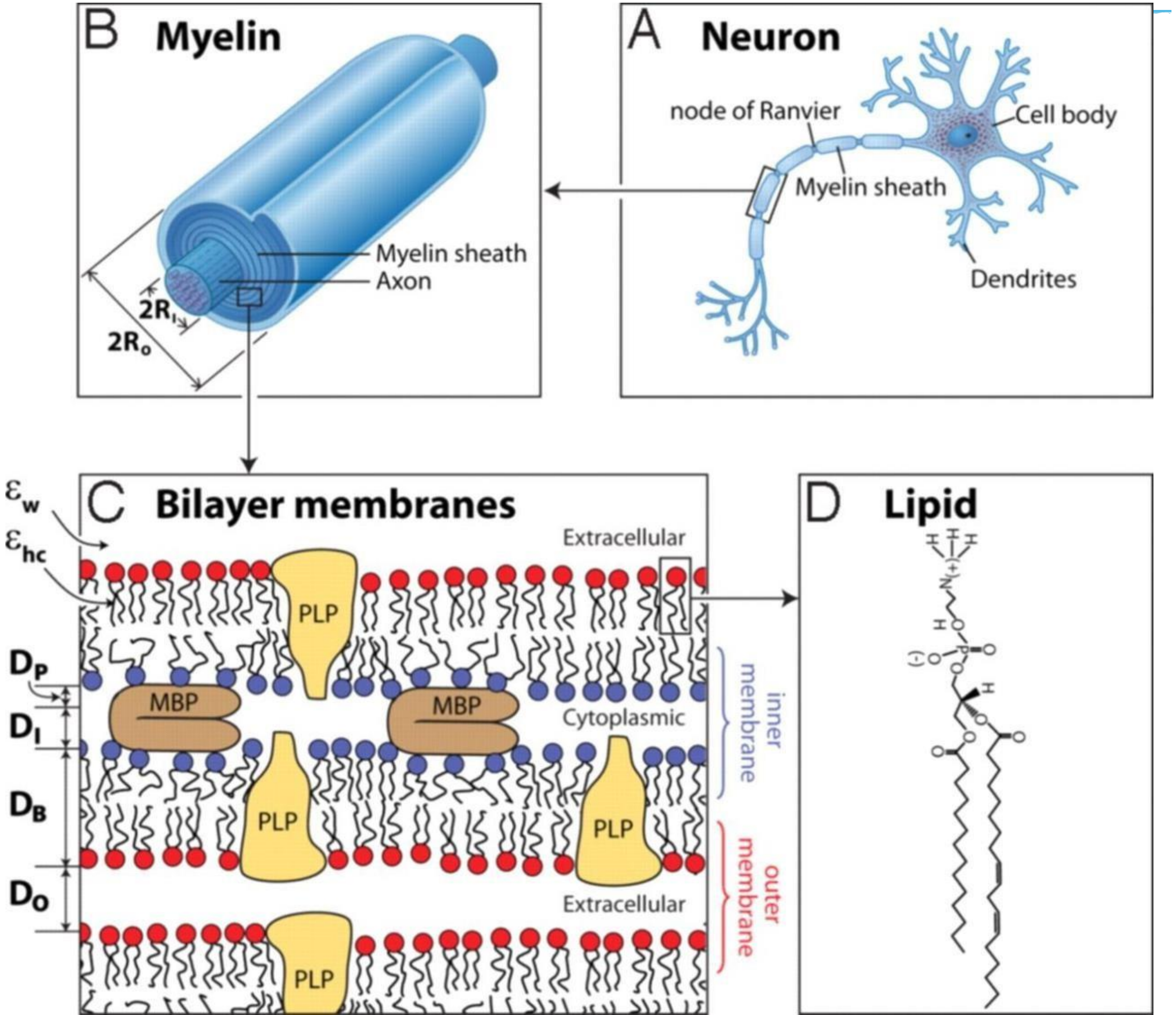
Ceramide

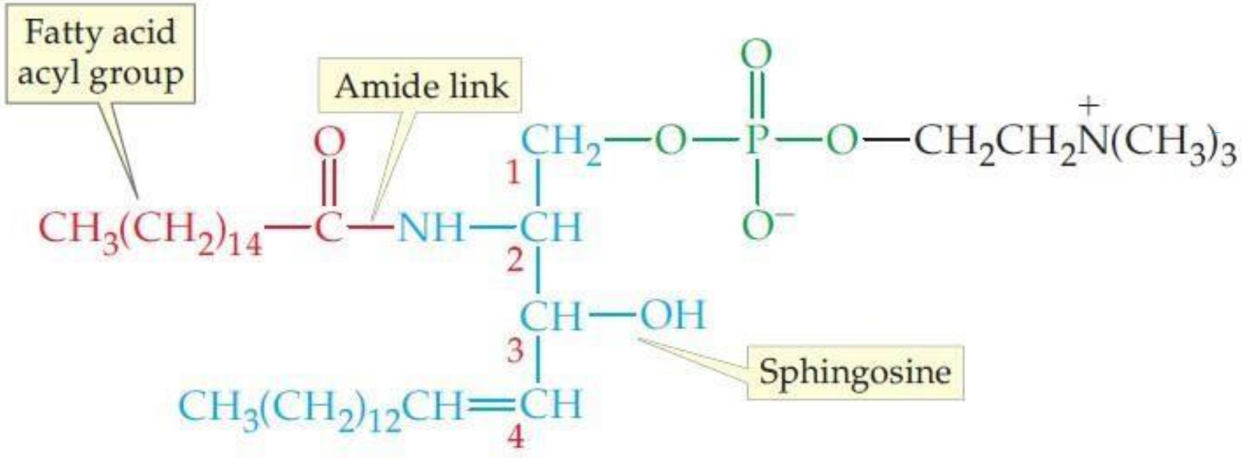


The simplest lipid formed from sphingosine is called ceramide.

Remember: just like the simplest phosphoglycerolipid is phosphatidic acid, the simplest sphingolipid is ceramide.

Classes - Sphingomyelins





A sphingomyelin (a sphingolipid)

Sphingomyelins are formed by modifying the structure of ceramide through the addition of a phosphate group and a choline group.

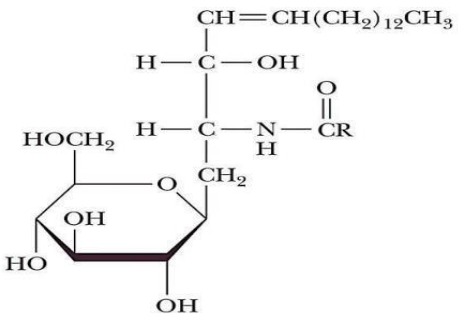
-The choline unit is a quaternary amine, meaning it contains a nitrogen atom bonded to three methyl groups, and is considered a nitrogenous base.

-Sphingomyelins are found in many cells, but they are present in high concentrations in the myelin sheath.
It is important that sphingosine-based lipids are more abundant in the central nervous system (CNS) and peripheral nervous system(PNS) because sphingomyelins are more hydrophobic, which is why they are needed in those locations.

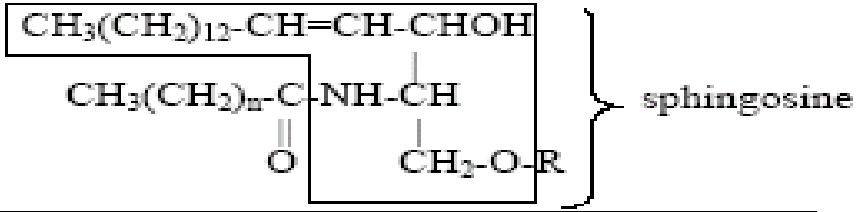
Classes – Glycolipids

There are three types of glycolipids

- Cerebrosides
- Globosides
- Gangliosides
- Sulfatides



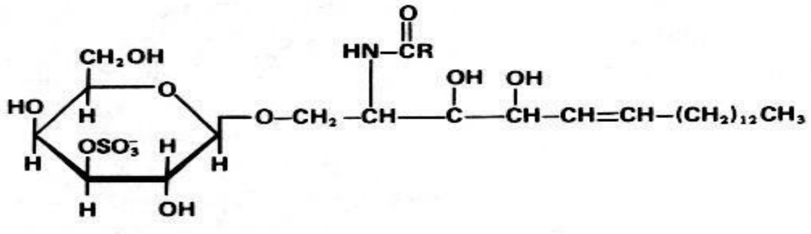
A Glucocerebroside



glycolipids:

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

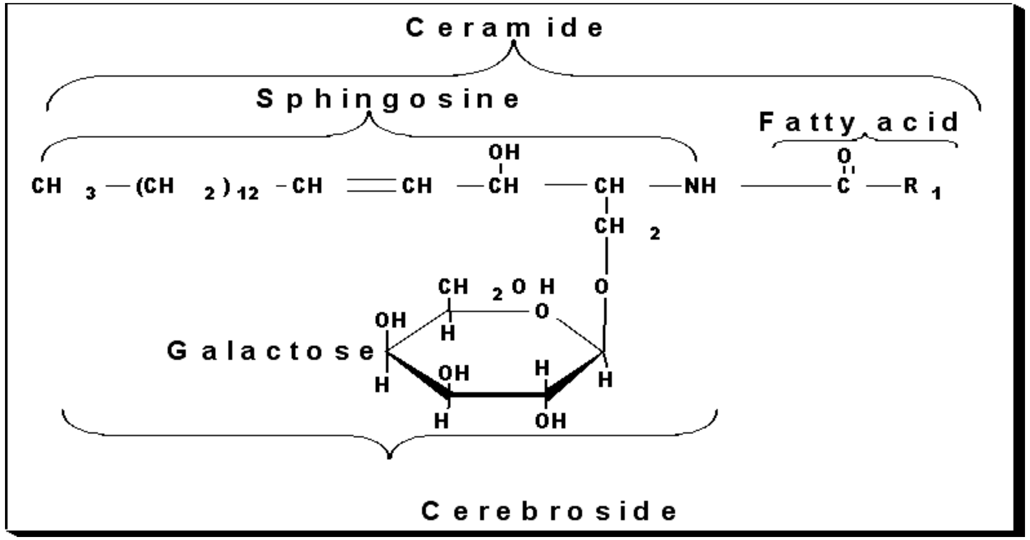
This table is required to be memorized



Ceramide-Glucose-Galactose-N-acetylgalactosamine-Galactose

Sialic acid

Monosialoganglioside



Glycolipids

Glycolipids are always built on a sphingosine backbone —> they are not based on glycerol.
The prefix “glyco–” refers to the presence of sugar units in their structure.
To attach carbohydrates to lipids, sphingosine must act as an alcohol.

There are three main types of glycolipids:

- **Cerebrosides:**

A sphingosine molecule is attached to one sugar unit —> either glucose or galactose.
If it contains galactose, it’s called galactocerebroside.
If it contains glucose, it’s called glucocerebroside.
Cerebrosides are found in large amounts in the cerebrum (brain), and in smaller amounts in other cells.

- **Globosides:**

These consist of sphingosine attached to two or more sugars.

- **Gangliosides:**

These contain oligosaccharides that must include at least one sialic acid.
They are highly abundant in ganglia, which are collections of nerve cell bodies located outside the CNS.

All these glycolipids are found in all body cells, but their concentration varies, being high in some cells and low in others.

Sphingolipids & blood groups

On the surface of red blood cells, blood group antigens can be attached either to proteins or to lipids.
If the antigen is attached to a lipid, then the lipid backbone is ceramide, which is linked to a chain of oligosaccharides.

There are three main types of antigens based on sugar attachments:

- **O Antigen:**

The sugar chain ends with galactose connected to fucose.

- **A Antigen**:

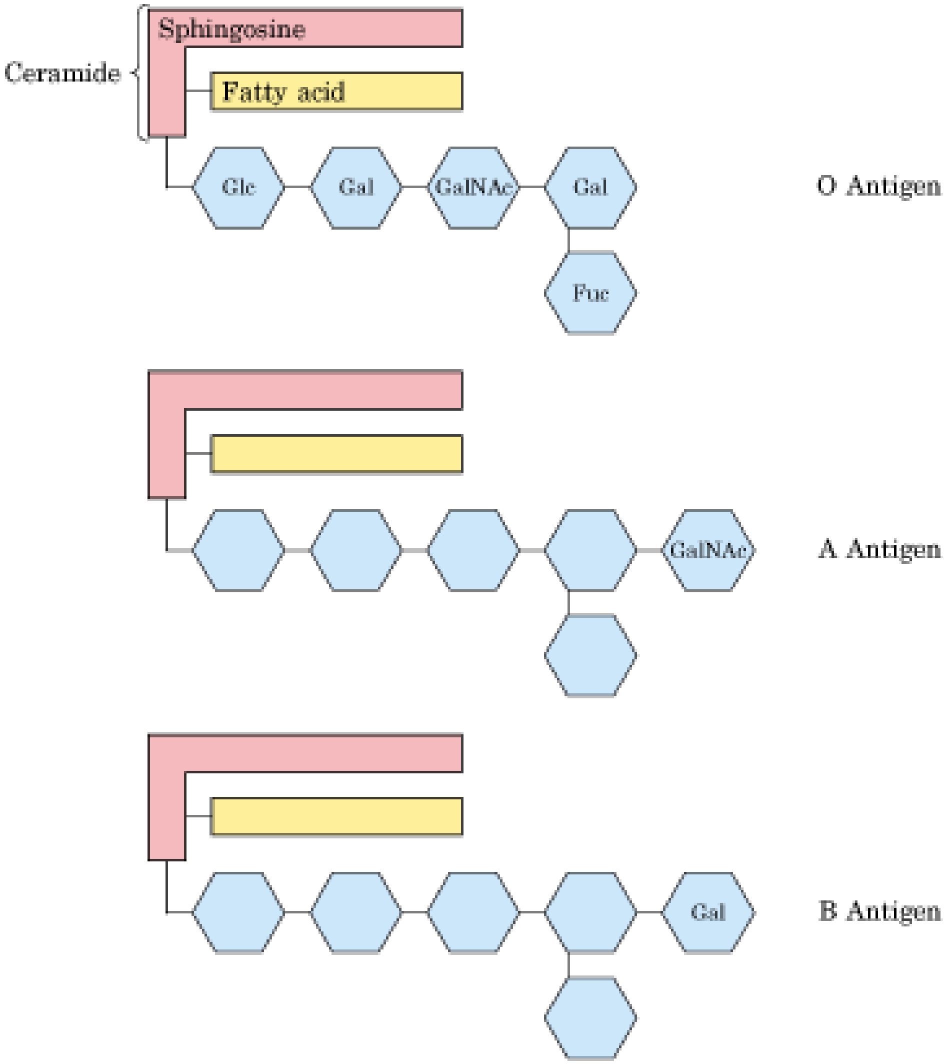
Galactose is connected to fucose and N-acetylgalactosamine.

- **B Antigen:**

Galactose is connected to another galactose.

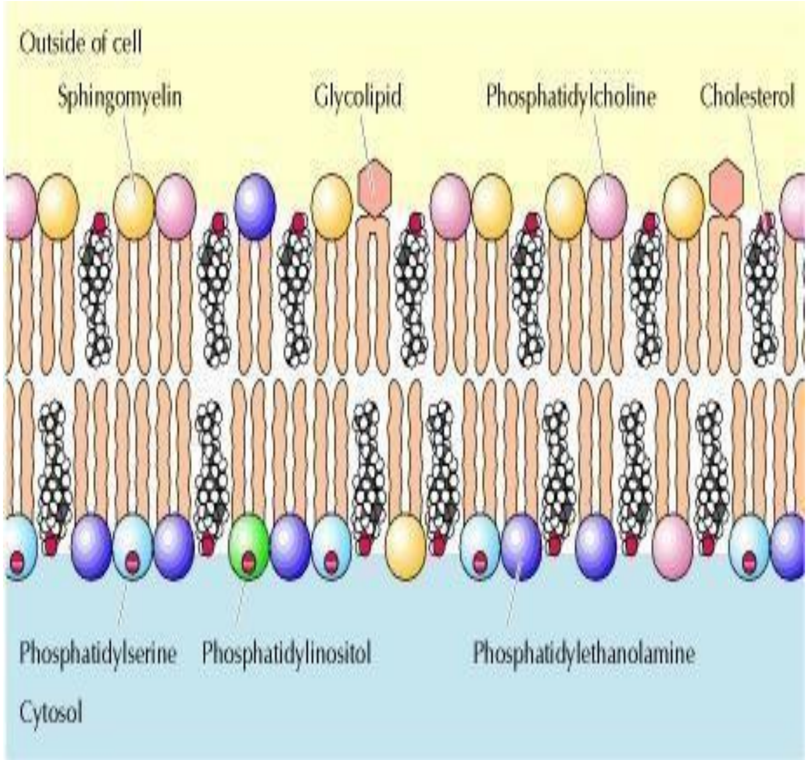
- **AB Blood Group:**

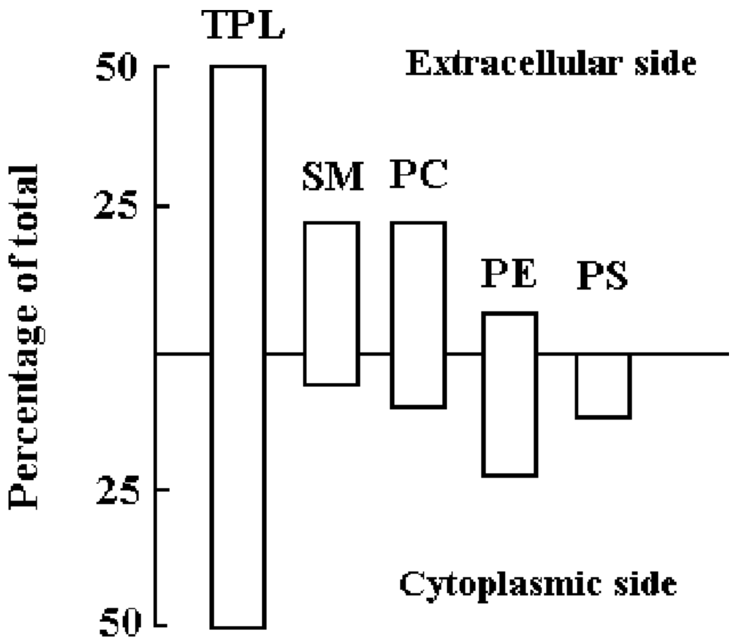
Red blood cells display both A and B antigens on their surface.



Phospholipids and membranes distribution

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





The distribution of phospholipids in cell membranes is not uniform and varies between different cells.
Although we describe membranes as phospholipid bilayers, their composition is not the same in every cell.

For example, cardiolipins are found in high concentrations in the inner mitochondrial membrane.

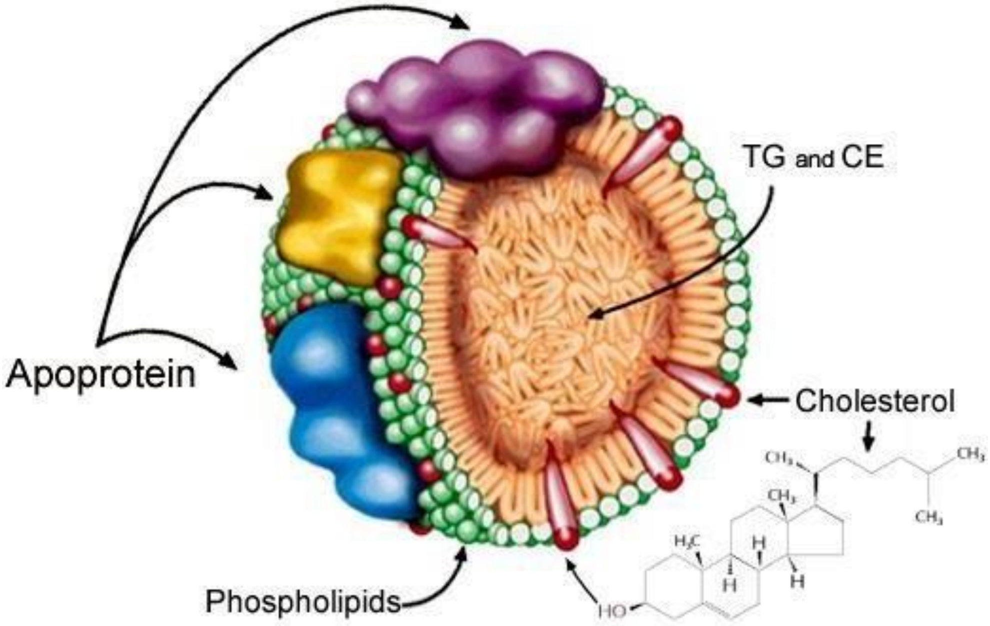
Some cells specialize in signal transduction, converting signals from outside the cell to inside. These cells often contain a high concentration of phosphatidylinositol in the **inner leaflet** of the membrane to support this function.

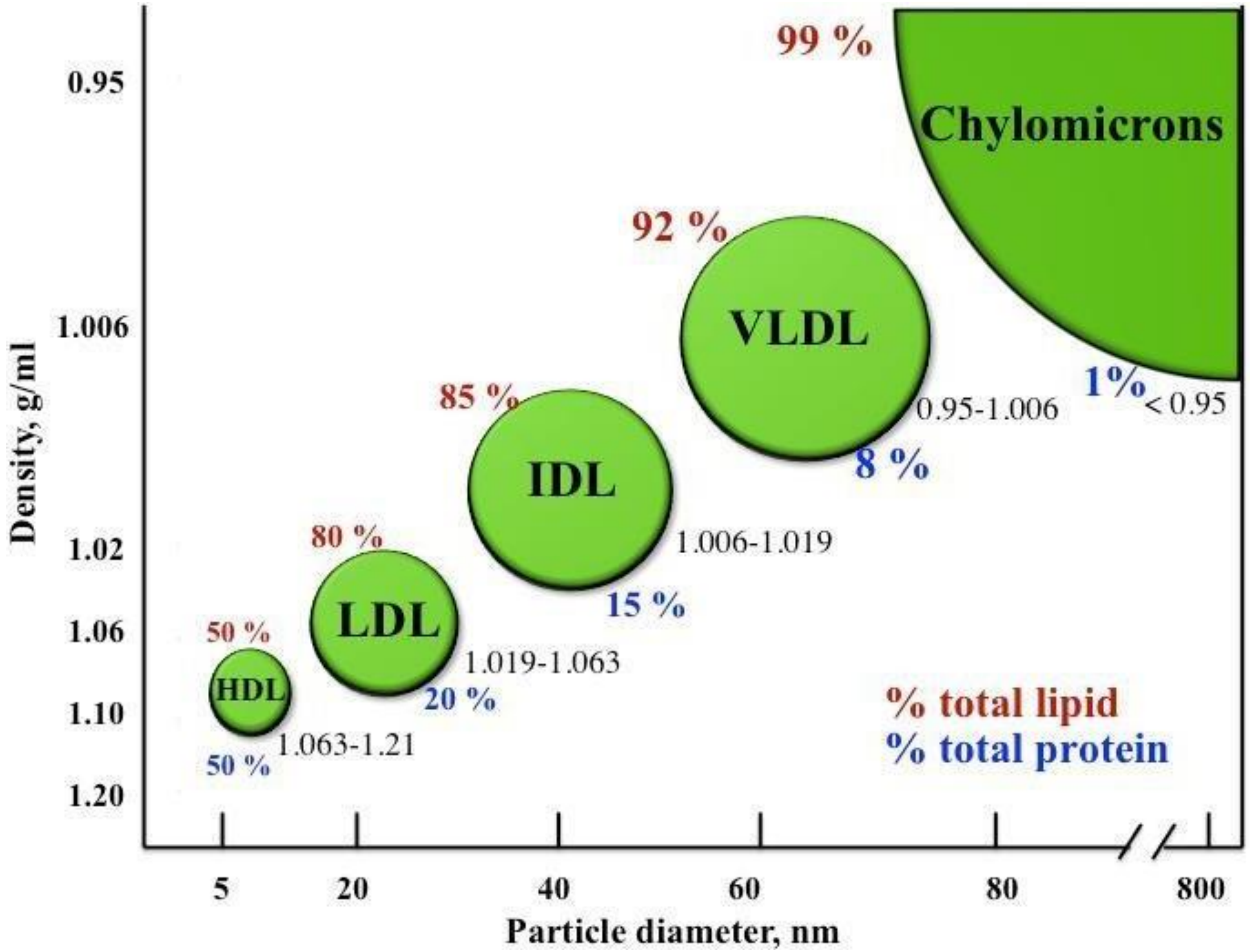
In general, the distribution of phospholipids between the inner and outer leaflets of the membrane is not equal.

Lipoproteins

Either structural

- or transport f different types of lipids (cholesterol, cholesterol esters, phospholipids & triacylglycerols) in blood plasma





Lipoproteins

Lipoproteins are a combination of proteins and lipids.

<u>Lipids and proteins attach together for two main reasons:</u>

Structural reason:

Lipids in membranes have a jelly-like or fluid structure. When they are attached to proteins in the membrane, this strengthens the membrane and helps maintain the shape of the cell.

Transport reason:

Lipids do not dissolve in water (like blood), so we attach them to something that does—such as proteins. This allows them to dissolve and be transported in the aqueous environment.

<u>Proteins are smaller and denser than lipids.</u>

If you take two pieces of equal size(one lipid, one protein)the protein will weigh more.
If the weight is equal, the lipid will take up more space(larger).

Lipoproteins

The combination of lipids and proteins is used to classify lipoproteins, based on how much lipid or protein they contain.

There are five main types:

- **Chylomicrons** ~> mostly lipid(98-99%); they transport dietary lipids from the GI tract to the liver. We get fatty acids, cholesterol, cholesterol esters, and triacylglycerols from the diet. These components come together and are coated with proteins to form lipoproteins. Due to their large size, they can't directly enter the blood, so they pass through the lymphatic system first, drain into the inferior vena cava, and then reach the liver.
- **VLDL** ~> Very Low Density Lipoprotein
- **IDL** ~> Intermediate Density Lipoprotein
- **LDL** ~> Low Density Lipoprotein
- **HDL** ~> High Density Lipoprotein
- As shown in the figure:, as you go down the diagram, lipid percentage decreases, and protein percentage increases.
- LDL (الكوليسترول الضار) and HDL (الكوليسترول النافع) are commonly tested in lipid profiles:
- LDL carries synthesized cholesterol from the liver to body cells. It's considered bad cholesterol, because high levels of LDL mean more cholesterol is being delivered to the circulation and cells.
- HDL carries cholesterol from dead cells in the body back to the liver. It's good cholesterol, and high levels are considered beneficial for health.
- HDL is higher in females, and it increases with exercise.
- LDL increases with smoking and lack of physical activity.

Steroids

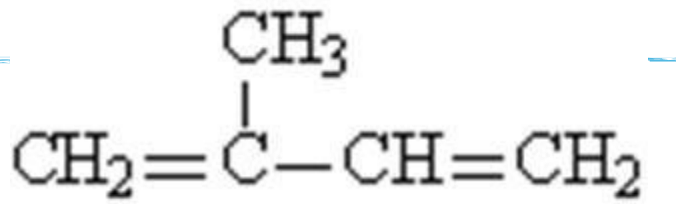
Steroids are based on a structure called the steroid nucleus, which consists of four fused rings named A, B, C, and D, (3 six-membered rings and 1 five-membered ring) and it contains 17 carbon atoms.

These rings can be synthesized in the liver from a unit called isoprene, which comes from acetyl-CoA (a two-carbon molecule attached to coenzyme A).

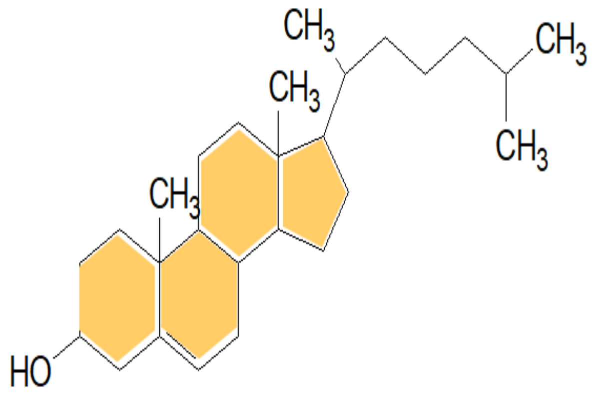
Once the steroid nucleus is formed, there is no metabolic pathway in the body to break it down.
However, it can be modified by adding more carbon atoms until it becomes a molecule with 27 carbon atoms, called cholesterol.

Cholesterol is a steroid-based molecule and the starting point of many metabolic processes in the body.
We don't start with the steroid nucleus and make small modifications, instead we first make cholesterol, and then use it to make other smaller molecules.

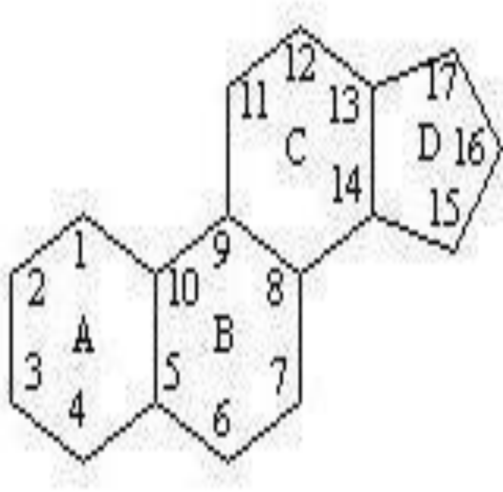
The precursor



Isoprene

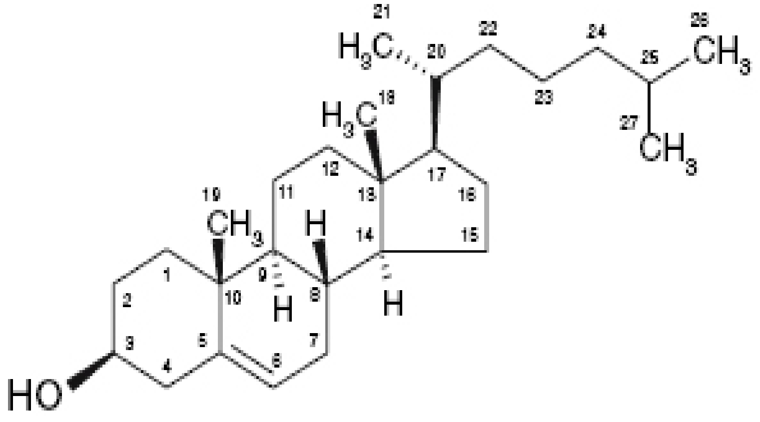


The nucleus



Steroid nucleus

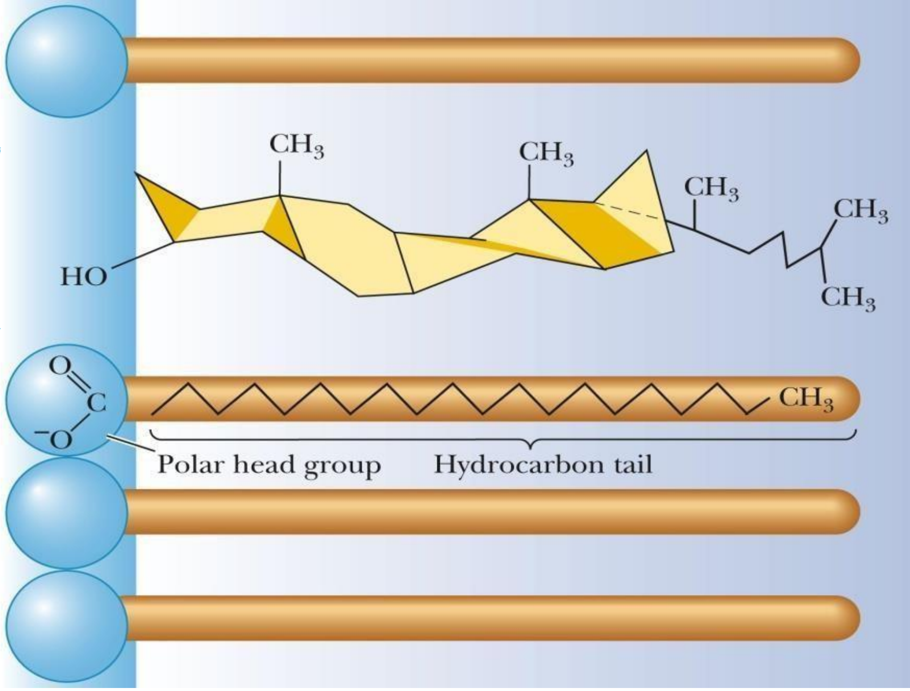
The most common steroid



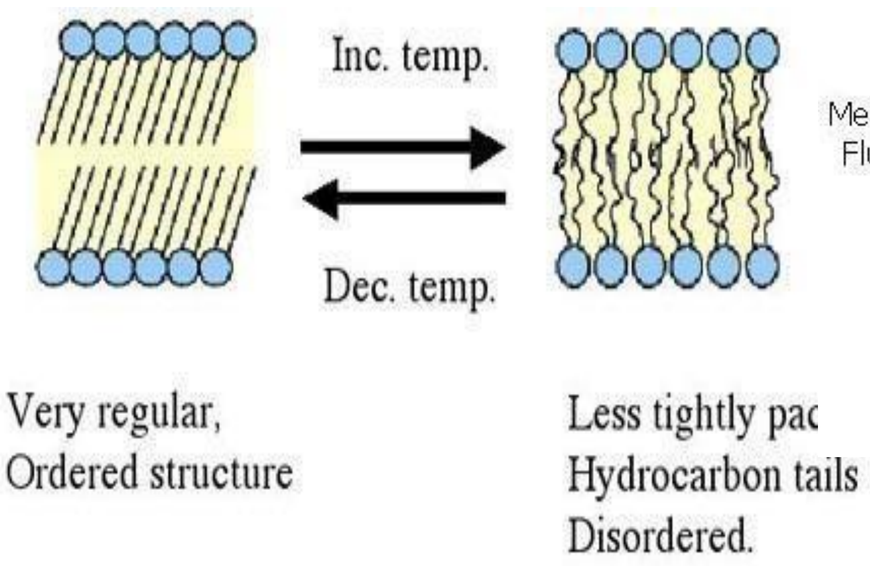
Cholesterol

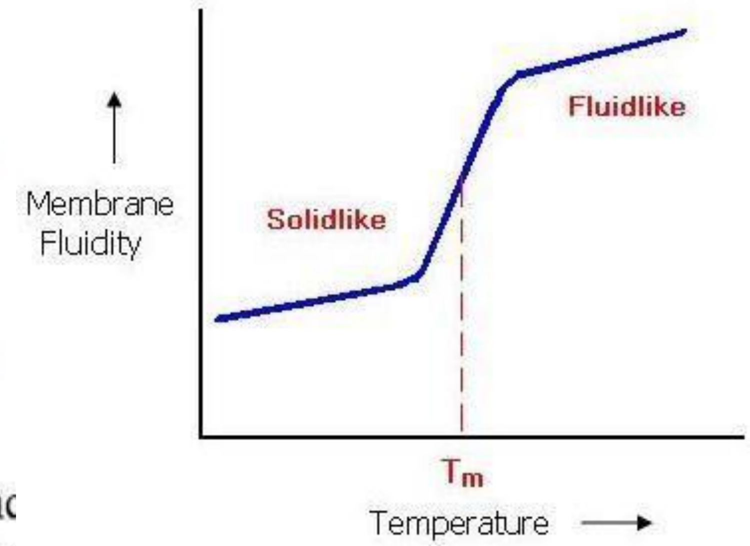
Vary among tissues

Acts as a fluidity buffer in membranes: makes a membrane less solid at low temperatures and more solid at high temperatures



Cholesterol is very important for membranes because it acts as a fluidity buffer. With respect to temperature, It doesn't make the membrane extremely fluid or very solid. The structure of cholesterol contributes to this because fatty acids are jelly-like. When cholesterol is present in high concentrations (especially from animal sources) it exists between phospholipids. Since it is rigid and not-twistable, it binds to the fatty acid tails via hydrophobic interactions and reduces their movement, preventing the membrane from becoming too fluid.





Products of cholesterol

Sterols

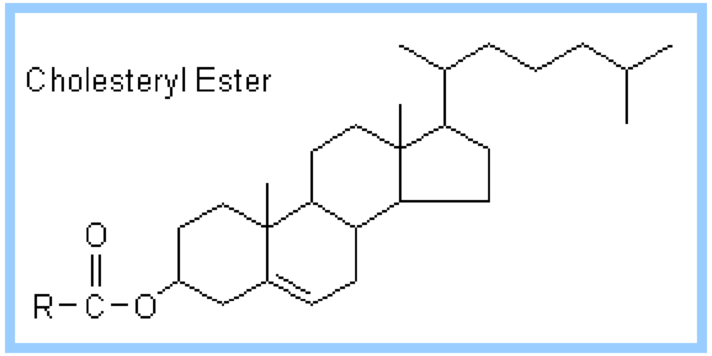
Adrenal cortical hormones

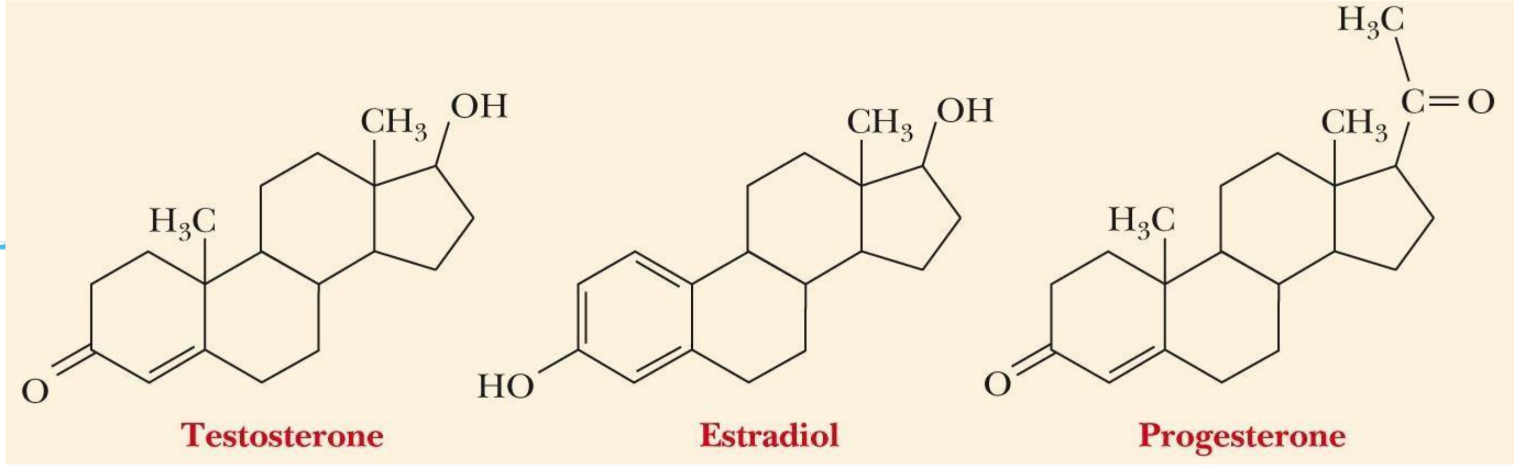
Male and female sex hormones

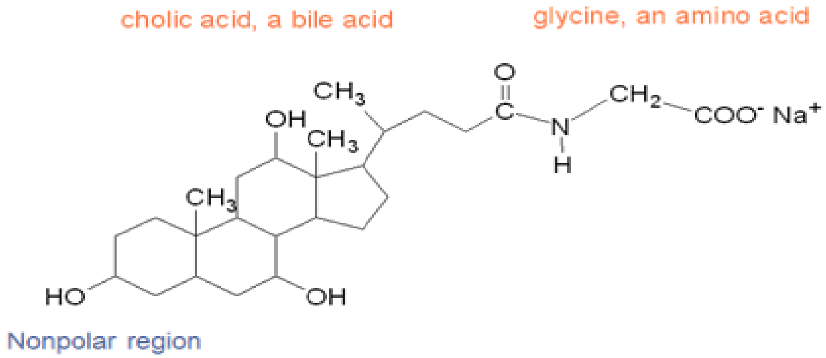
Vitamin D group

Bile acids

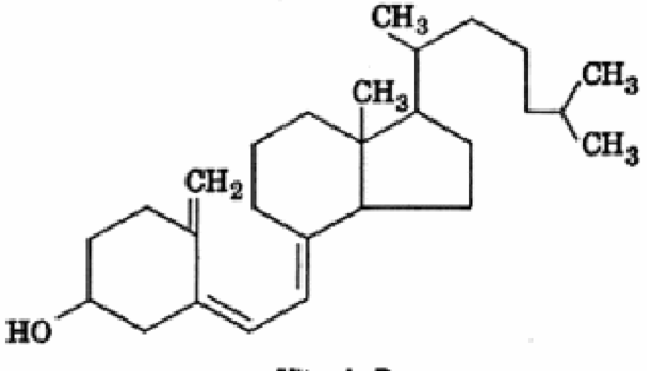
Cholesterol esters



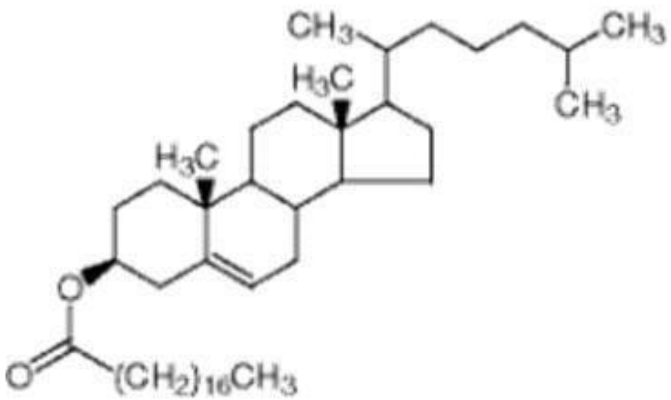


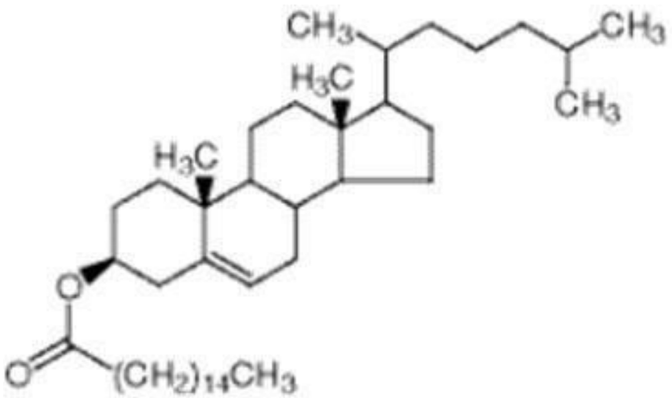


sodium glycocholate, a bile salt



Vitamin D_3





Products of cholesterol

The second reason behind the importance of cholesterol is its essential role in producing various biologically active molecules. These include adrenal cortical hormones, aldosterone, bile acids, vitamin D, and the male and female sex hormones.

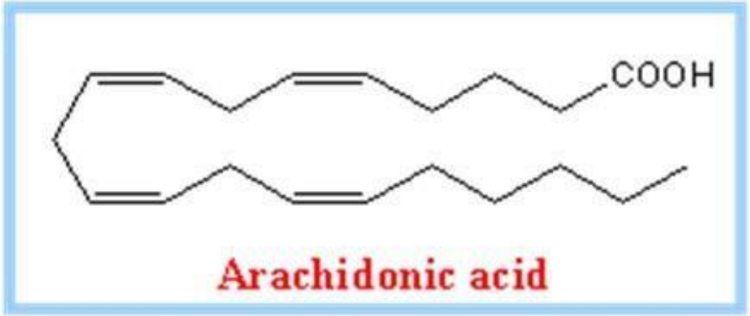
Among the sex hormones derived from cholesterol are **testosterone, estradiol, and progesterone.**
Testosterone is primarily responsible for male characteristics, while estradiol (the main form of estrogen) defines female characteristics. The key chemical difference between them lies mainly in a single carbon atom and the presence of either a carbonyl (found in testosterone) or a hydroxyl group (found in estradiol). It's often said that a difference of just one carbon atom can create different human beings.This highlights how incredibly specific our receptors must be,they can detect even a single atom difference or a functional group variation like a carbonyl versus a hydroxyl.

Bile acids are another important product of cholesterol. Cholesterol is modified by adding a carboxylic group, and then this molecule is converted into a salt. These bile salts act as emulsifiers in the intestine. The sodium component dissolves in water, making the carboxyl group hydrophilic and dissolve in water, while the rest of the molecule is hydrophobic and dissolves in lipids. This amphipathic nature initiates the emulsification process, allowing lipases to effectively digest dietary lipids.

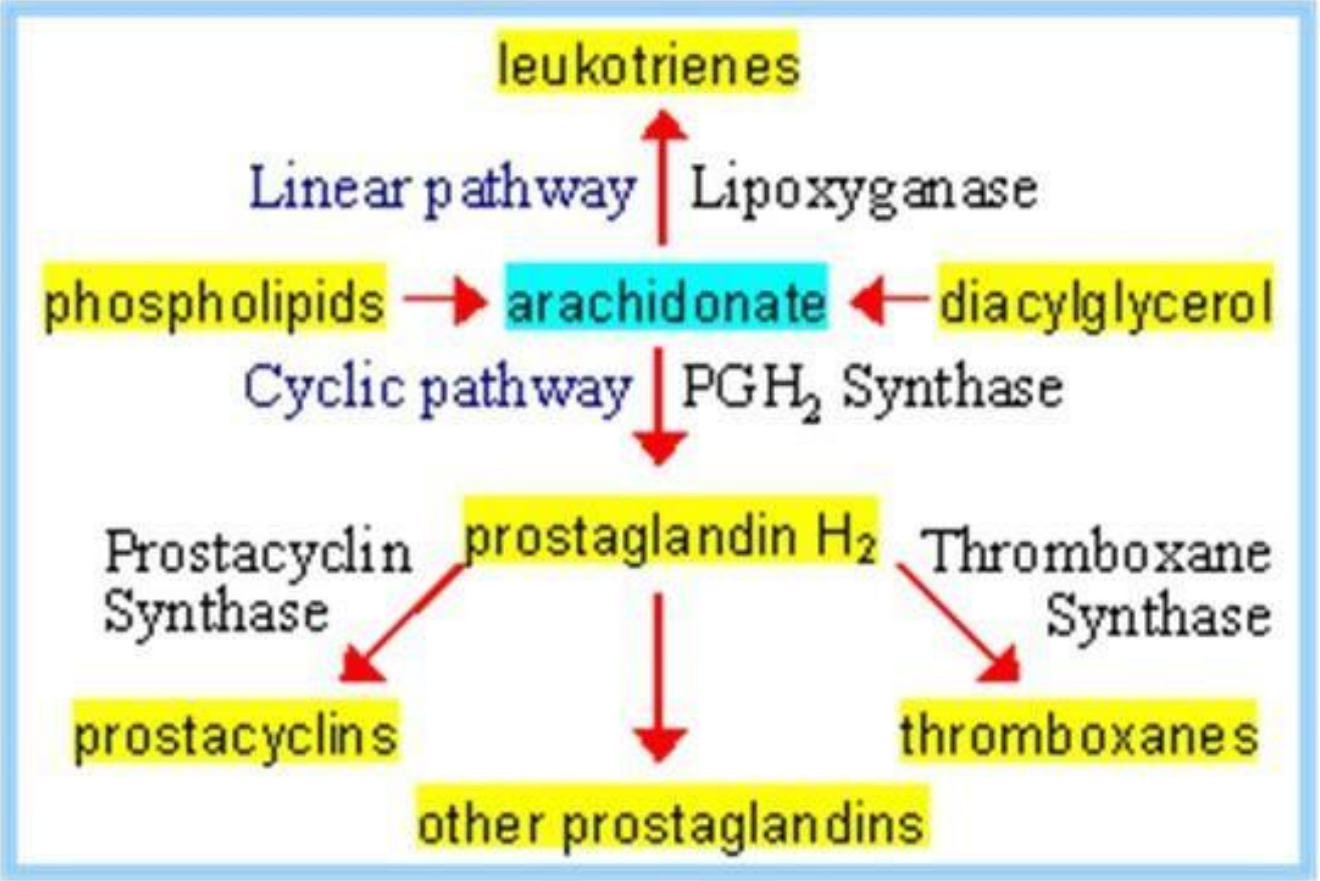
Cholesteryl esters are formed when fatty acids are attached to the cholesterol molecule.

Vitamin D is also synthesized from cholesterol. The transformation begins in the skin, where ultraviolet (UV) light causes the opening of ring B in the cholesterol structure. This intermediate is then transported to the liver, where it undergoes hydroxylation. It then travels to the kidney, where it is hydroxylated again at a different site, resulting in the fully active form of vitamin D.

Derived fatty acids: Eicosanoids (icosanoids)



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



Eicosanoids

- **Eicosanoids are lipid-derived signaling molecules synthesized from fatty acids, specifically from** *arachidonic acid* (also called arachidonate). The prefix "eicosa" refers to the 20-carbon structure of the molecule.
- **Arachidonic Acid:**
  Arachidonic acid is a 20-carbon polyunsaturated fatty acid with four double bonds, typically esterified at the second carbon of membrane phospholipids.
- **Release of Phospholipase A2**
  The enzyme *phospholipase A2* cleaves the ester bond at the carbon number 2 of phospholipids, releasing free arachidonic acid. Once liberated, arachidonic acid serves as a precursor for various types of eicosanoids.
- **Hormones**
  Hormones are signaling molecules released by ductless glands, and they reach their target via the **bloodstream**. They have **specific receptors** and affect distant sites to regulate **body homeostasis**.
- **Autocrine** signaling is when a cell produces a substance that affects **itself** or **nearby cells of the same type**.
  Paracrine signaling is when the substance affects **nearby cells of a different type**.
  Both autocrine and paracrine signals **do not enter the bloodstream**.
- **Eicosanoids** are substances that act in **autocrine** or **paracrine** ways and regulate **local homeostasis**.
  Hormones regulate **body homeostasis from a distance**.

Functions

Prostaglandins

- Inhibition of platelet aggregation
- Blood clotting

Leukotrienes

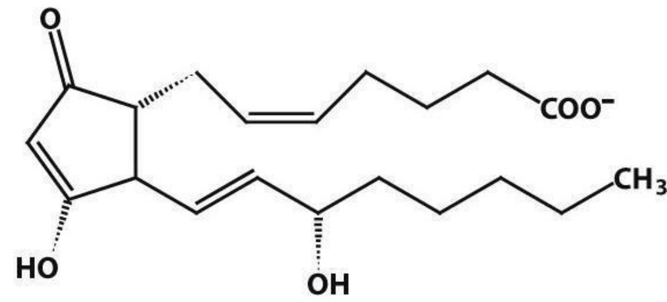
- Constriction of smooth muscles
- Asthma

Thromboxanes

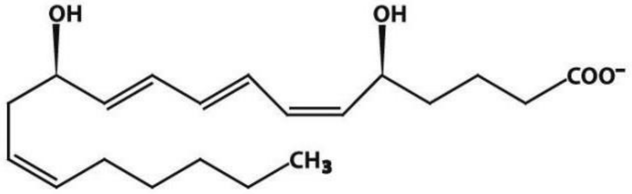
- Constriction of smooth muscles
- Platelet aggregation

Prostacyclins

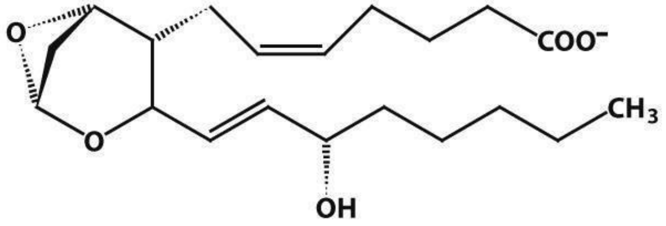
- An inhibitor of platelet aggregation
- A vasodilator



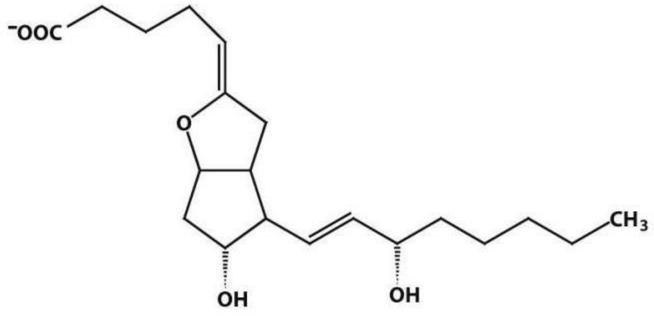
Prostaglandin E_2



Leukotriene B_4



Thromboxane A_2 (TXA_2)



Prostacyclin (PGI_2)

Functions of Eicosanoids

- **Prostaglandins**, **leukotrienes**, **thromboxanes**, and **prostacyclins** are all derived from **arachidonates** through different enzymatic actions.
- These enzymes can either **make it cyclic** or **non-cyclic**
- If the enzyme makes it cyclic and introduces oxygen, it is called **cyclooxygenase** (**COX** for short).

  There are two variants of COX: **COX-1** and **COX-2**.
- Examples of cyclic eicosanoids are: **Prostaglandins, Thromboxanes, and Prostacyclins**
- We also have **lipoxygenases**, which produce **lipoxins** and **leukotrienes.**
- **Leukotrienes** do **not** form a cyclic structure.

  The name **triene** refers to:

  "**tri**" meaning **three**,

  "**ene**" referring to double bonds in arachidonate.

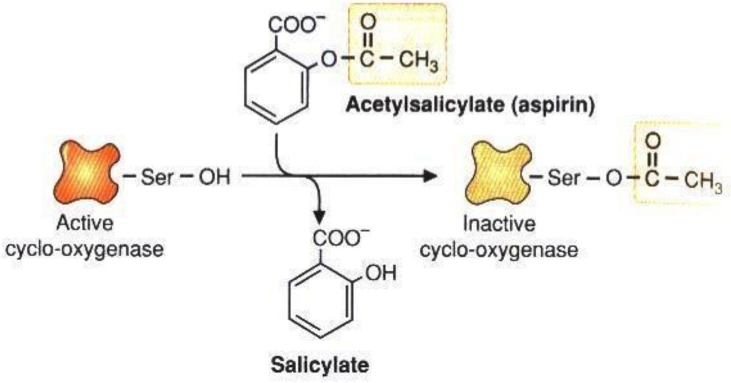
  While leukotrienes have **four** double bonds, only **three** of them are **conjugated.**
- **COX enzymes** are targeted by many drugs like:
- **Aspirin**,
- **Ibuprofen**,
- **Diclofenac, (Voltaren;** brand name for diclofenac).
- These drugs **inhibit COX enzymes without distinguishing** between **COX-1** and **COX-2**, affecting **both**.

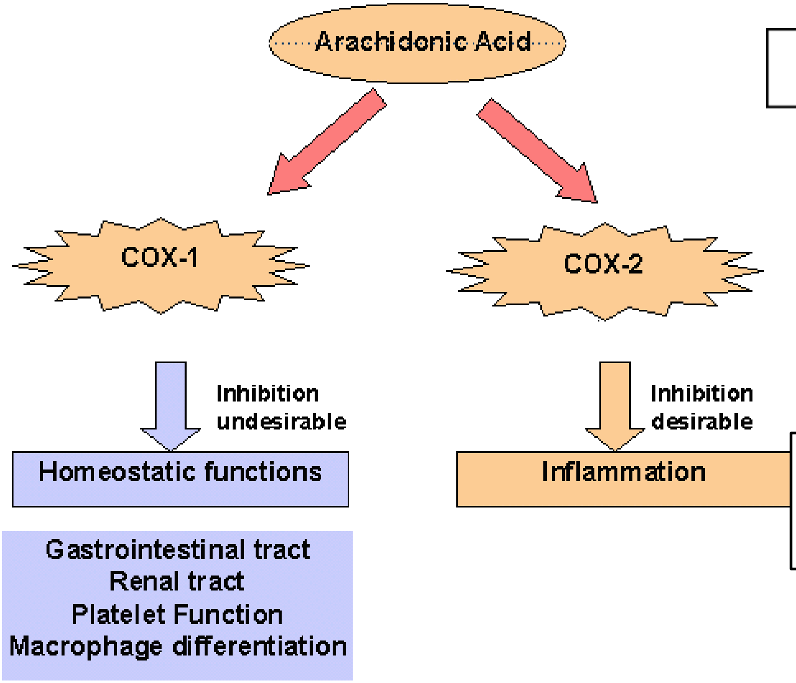
COX-2 is responsible for the inflammatory process in glands by producing prostaglandins and thromboxanes. The signs of inflammation include redness, heat, pain, and swelling. Anti-inflammatory drugs are taken to reduce these symptoms by inhibiting COX-2. However, they also inhibit COX-1.

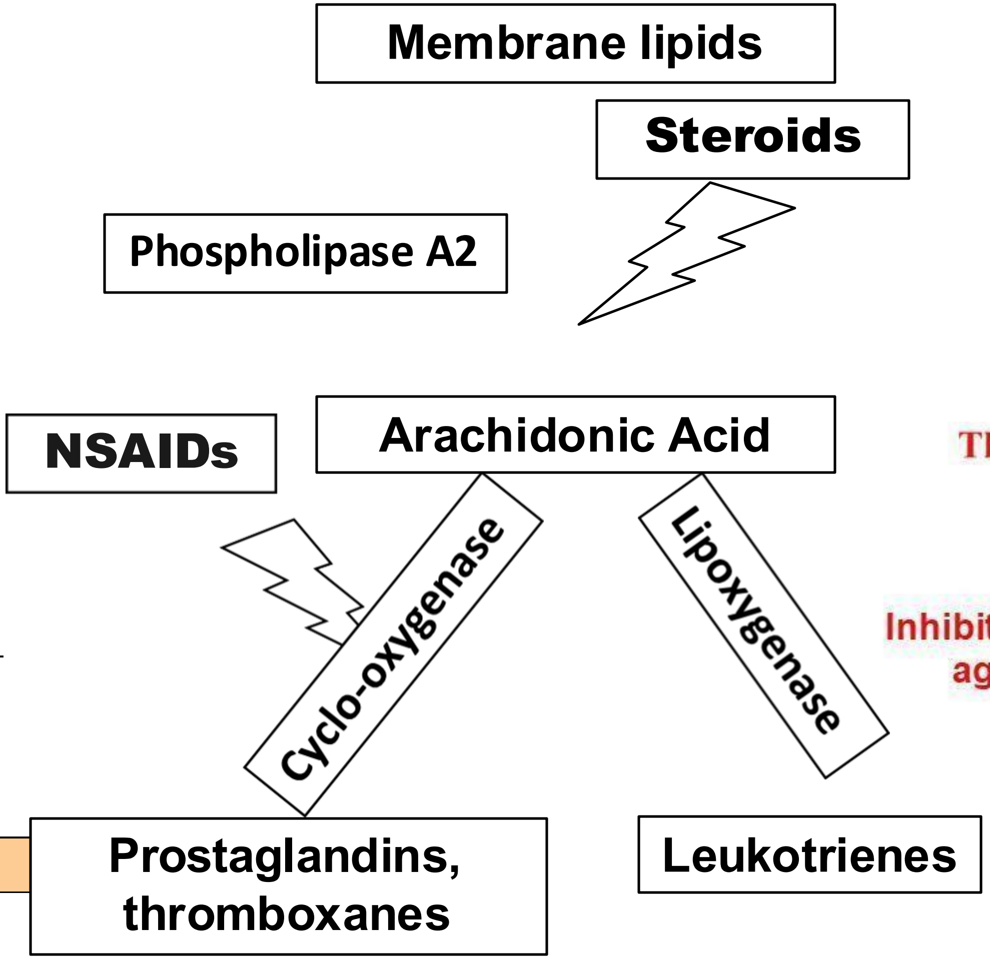
COX-1 is involved in blood clotting and stomach protection. It has a role related to hydrochloric acid in the stomach – this is why these drugs are taken with full stomach. Taking them on a full stomach helps prevent gastric irritation, since the drugs may interfere with stomach protection.

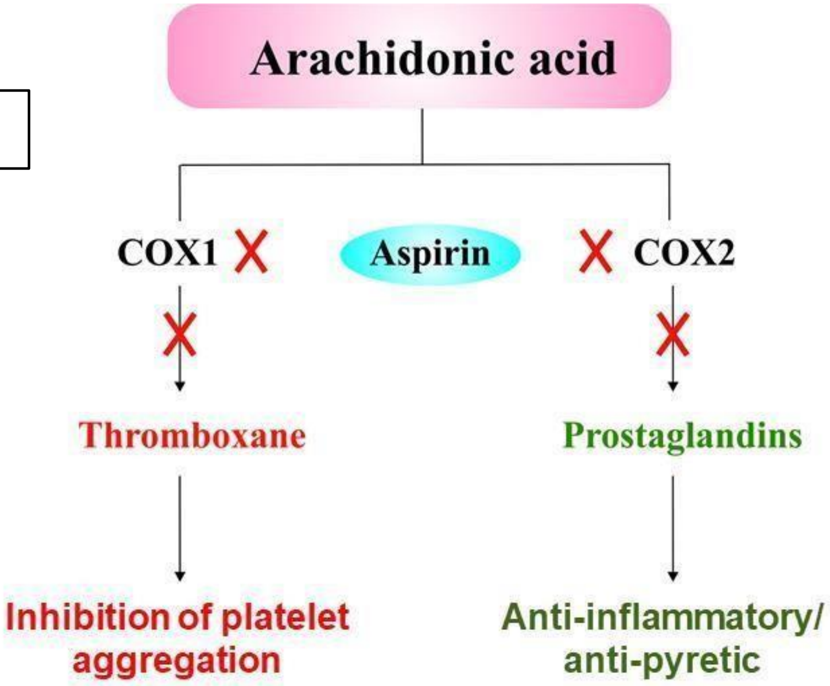
Aspirin and NSAIDS

That’s why aspirin works as a blood thinner (مُميع للدم), because it blocks COX-1 as well.









Selectives: Celebrex

Selective COX2 inhibitor without affecting COX1, but still have other side effects.

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

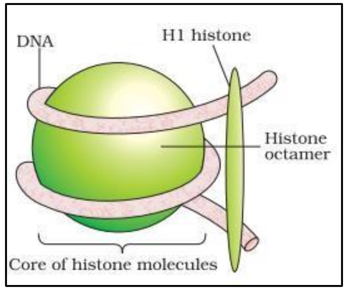
NUCLEIC ACIDS

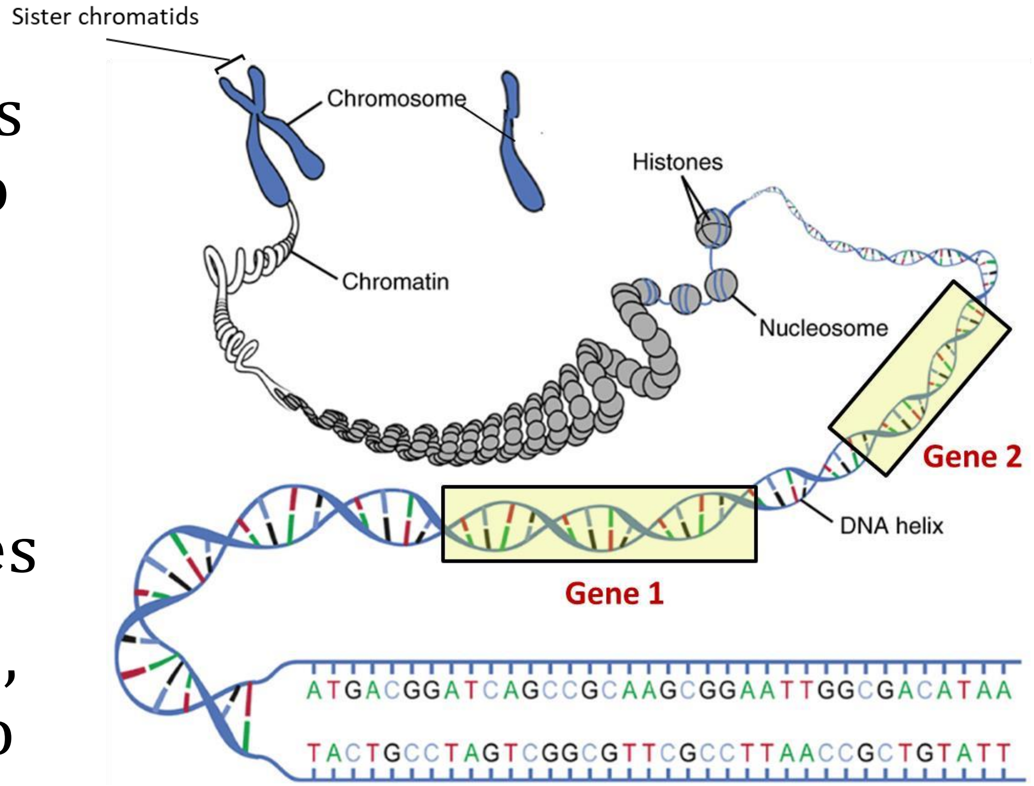
Prof. Nafez Abu Tarboush

TERMS

- DNA and RNA: nucleic acids; polymers of nucleotides
- Gene: continuous sequence of nucleotides that is transcribed (codes for or is used to make RNA)
- A nucleosome: a short sequence of DNA wrapped around proteins called histones
- Chromatin is a stretch of DNA and histones
- Chromosome is a whole molecule of DNA, which can consist of one chromatid or two identical chromatids, called sister chromatids

Nucleosome





Why do we need nucleic acids?

The genome, which is a polymer made of nucleotide monomers, is extremely large. Yet only a very small percentage of these nucleotides are actually transcribed and then translated into proteins. Most of the human genome is still not fully understood, and its function remains undiscovered. The main reason we have DNA in the nucleus is because it carries specific sequences of DNA called genes. These genes are transcribed into RNA and then translated into proteins, which are what give our bodies their structure and functions. This is also how human beings differ from one another – by having variations in these proteins.

DNA also plays a role in the production of RNA molecules, and not every RNA is used for protein synthesis. We have a massive number of RNAs; some of them have known, relatively simple functions, while others still have no known role. So again, a large portion of our DNA is still uncharacterized, and its purpose remains unclear.

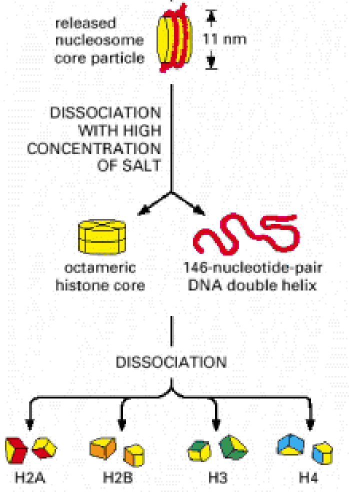
A **gene** is a continuous sequence of nucleotides that will be transcribed into an RNA molecule. A **nucleosome** is a segment of DNA wrapped around an octamer of histone proteins. The structure also includes histone H1, which binds from the outside, and a stretch of **linker DNA** that connects one nucleosome to the next. So, when we refer to a nucleosome, we are referring to the wrapped DNA, the core histone proteins, histone H1 on the outside, and the linker DNA.

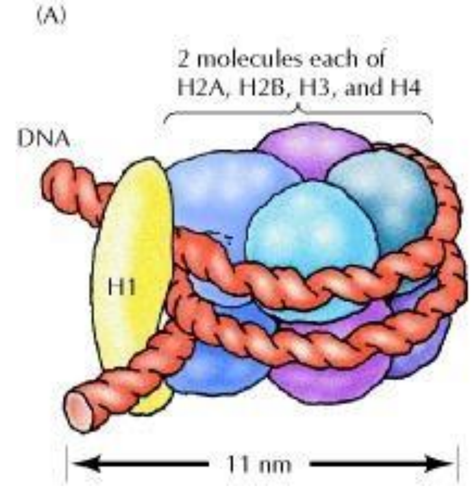
Chromatin is genetic material in its uncondensed, spaghetti-like form, while a **chromosome** is the condensed version of chromatin with a distinct shape, typically seen during cell division. If the linker DNA is removed and only the nucleosome with histone H1 remains, the structure is called a **chromatosome**.

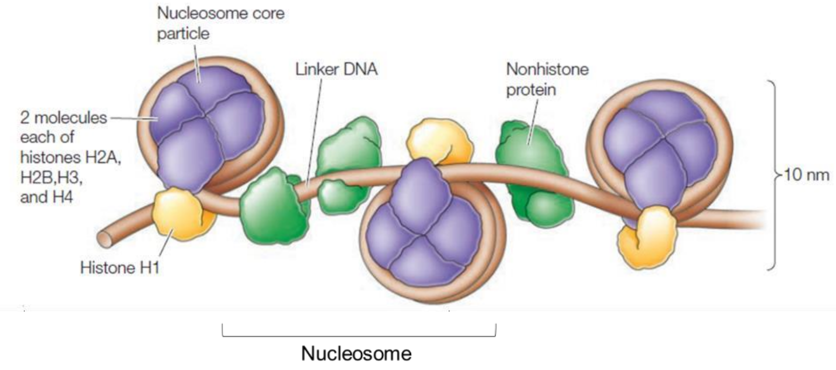
NUCLEOSOMES

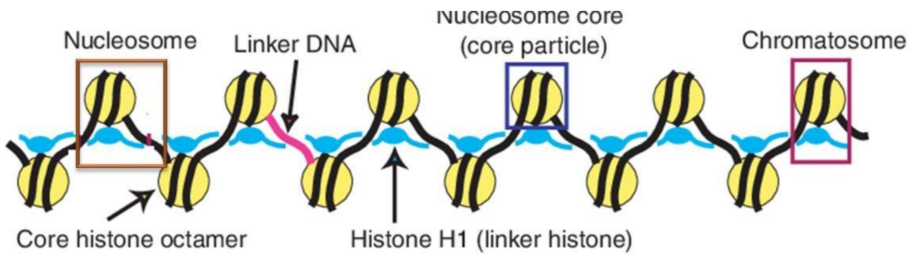
- DNA wrapped around a core particle, linker DNA, and histone H1.
- The histone core particle is an octamer (two molecules of histones H2A, H2B, H3, and H4) and the DNA wrapped around it
- A linker DNA connects two nucleosome core particles
- Histone H1 is bound to the octamer and wrapped DNA (a chromatosome)
- **Histones are positively charged facilitating DNA interaction and charge neutralization**

because DNA is negatively charged (composed of phosphate group)









DNA is made up of a nitrogenous base that connects to a ribose sugar through its nitrogen atom. This nitrogen binds to the anomeric carbon of the ribose. The ribose has a hydroxyl group (–OH) in the beta orientation. During a substitution reaction, the –OH group is displaced and replaced by the nitrogen from the nitrogenous base, forming what's called an **N-glycosidic bond**.

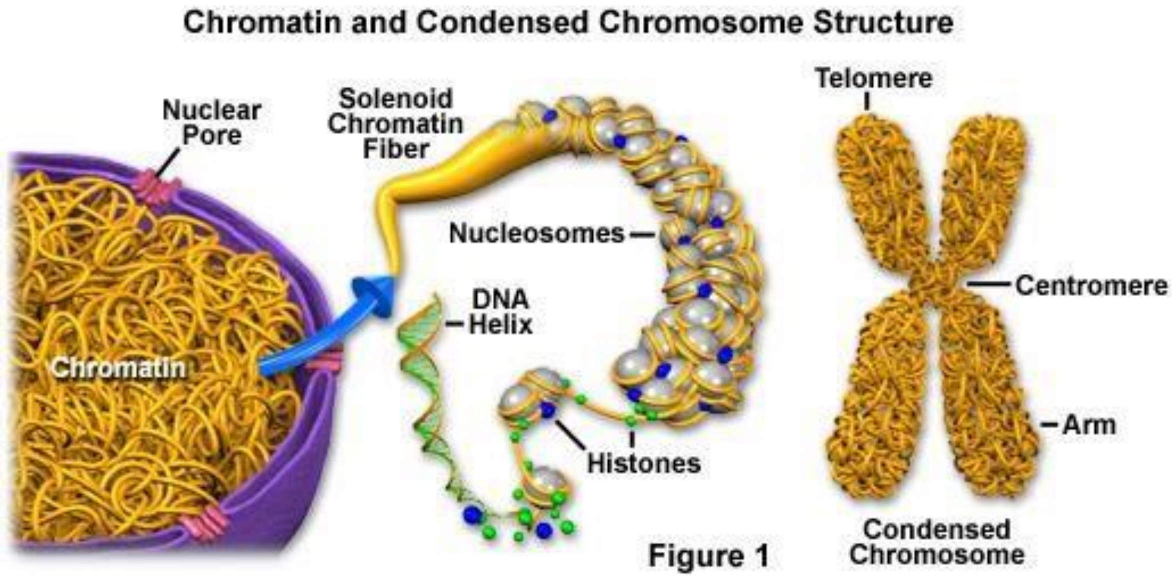
On the other side, at carbon 5 of the ribose, a **phosphorylation reaction** occurs where a phosphate group binds to C5, completing the structure of the nucleotide. The phosphate group originates as **phosphoric acid** before it binds to anything. As you may recall, phosphoric acid can donate up to three protons to the solution. This gives the nucleotide an inherently acidic nature. Simply having the phosphate group makes the structure strongly acidic.

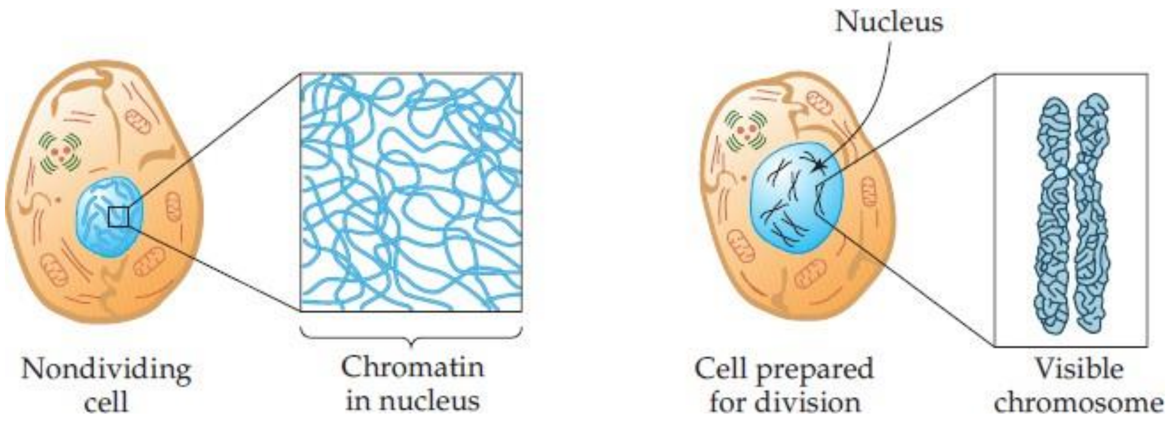
So why do we need histones to be positively charged?

Because the negatively charged DNA needs to bind to something positively charged to neutralize the charge as much as possible. This reduces the repulsion between adjacent phosphate groups. In addition to histones, positively charged ions like **Mg^{2+}** and **Ca^{2+}** are also present to help decrease the repulsion.

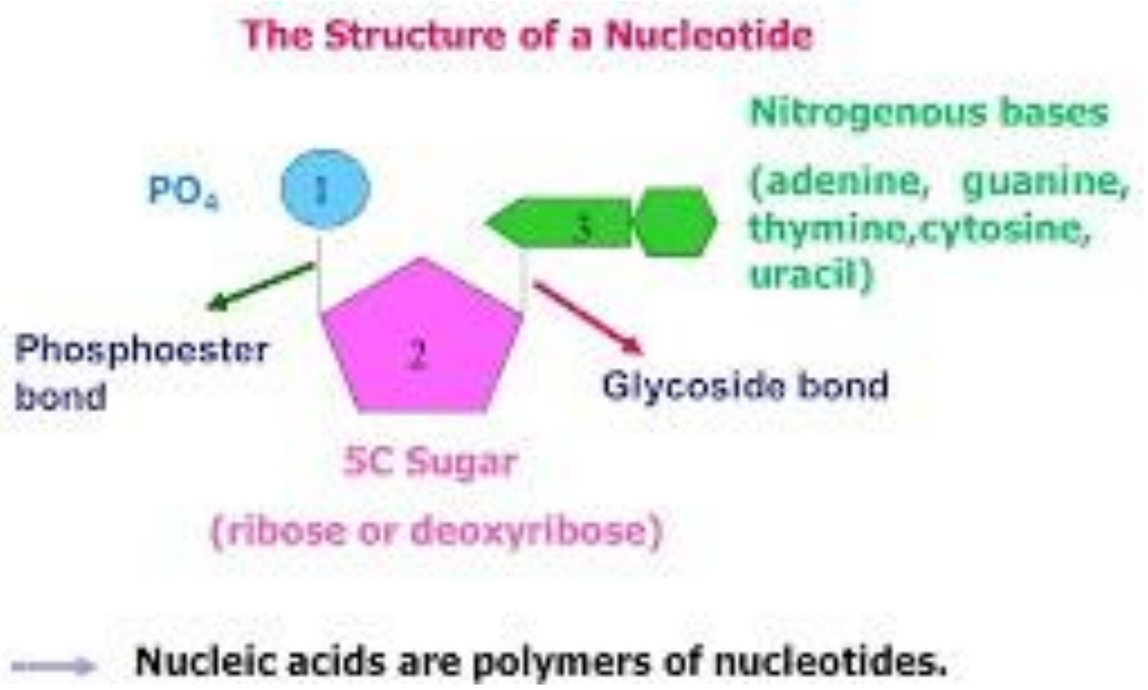
CHROMOSOME VS. CHROMATIN

- In non-dividing cells, the chromatin of chromosomes is not condensed (uncoiled) and cannot be distinguished from each other before cell division (like a spaghetti plate).
- At cell division, chromosomes become condensed (coiled) DNA molecules that can be distinguished from other chromosomes.

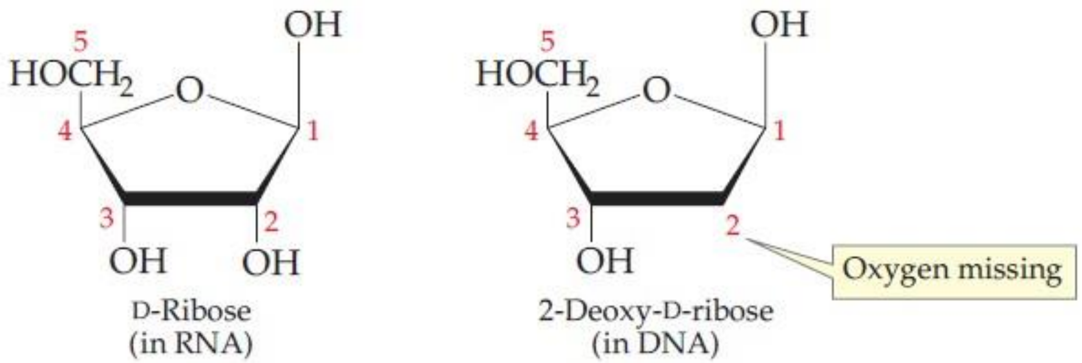




NUCLEOTIDES IN DNA AND RNA



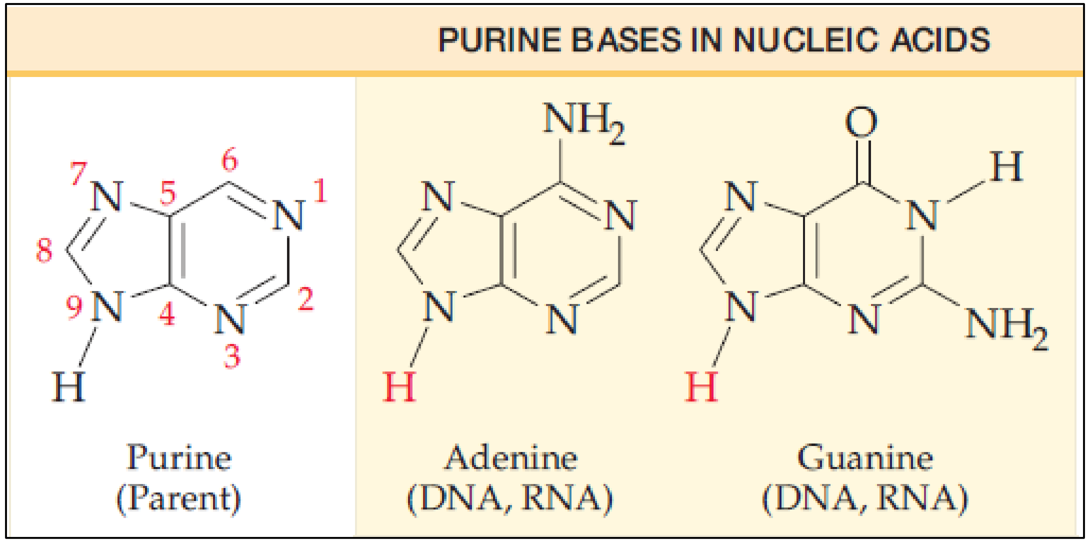
- All nucleotides have a common structure:
  1. a phosphate group linked by a phosphoester bond to a pentose.
  2. The pentose is linked to a nitrogenous base via a glycosidic bond.
  3. A nucleotide can have one, two, or three phosphate groups linked to each.

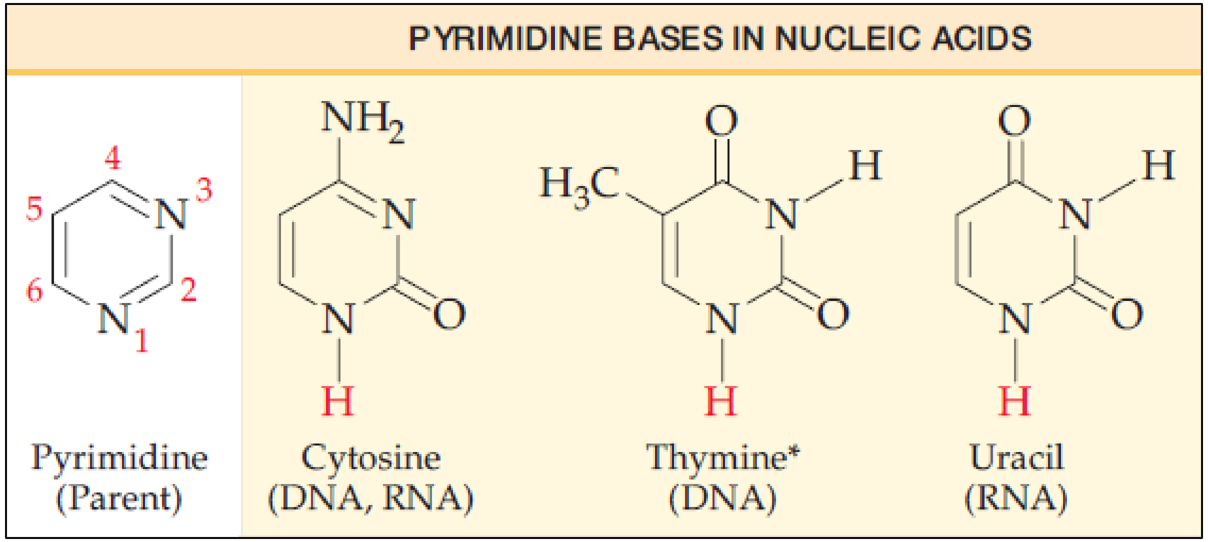


NITROGENOUS BASES

They are the bigger structure

- DNA and RNA consist of only four different nucleotides of two classes: purines and pyrimidines.
- Purines are adenine and guanine, and pyrimidines are cytosine, thymine (DNA), and uracil (RNA).
- The bases are abbreviated A, G, C, T, and U, respectively





Guanine differs from adenine by having a **keto group**, whereas adenine has an **amine group** in its place. Pyrimidines have a **single six-membered ring** structure, while purines consist of **two fused rings**: one six-membered and one five-membered. Uracil differs from cytosine by having a **keto group** where cytosine has an **amino group**. Uracil is different from thymine by lacking a **methyl group** — it is structurally the same except for that.

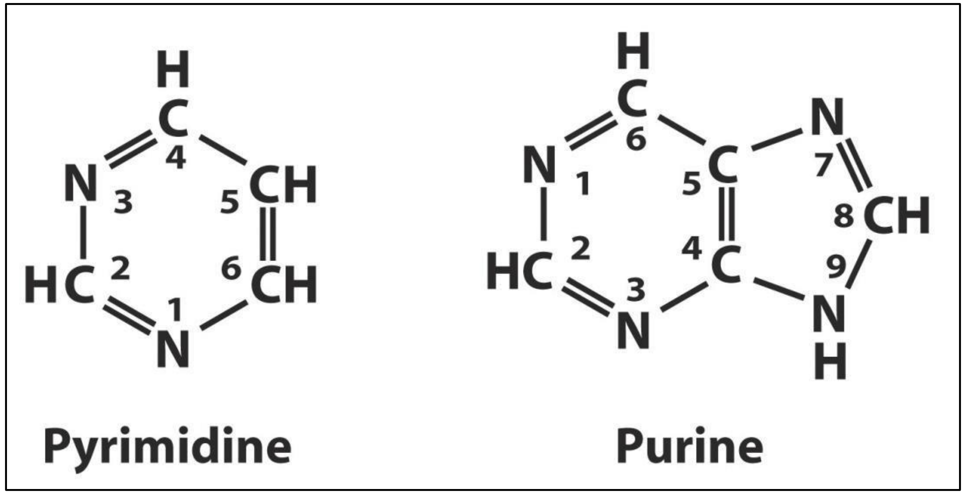
It is essential to be able to **recognize and identify the chemical structures** of these nitrogenous bases.

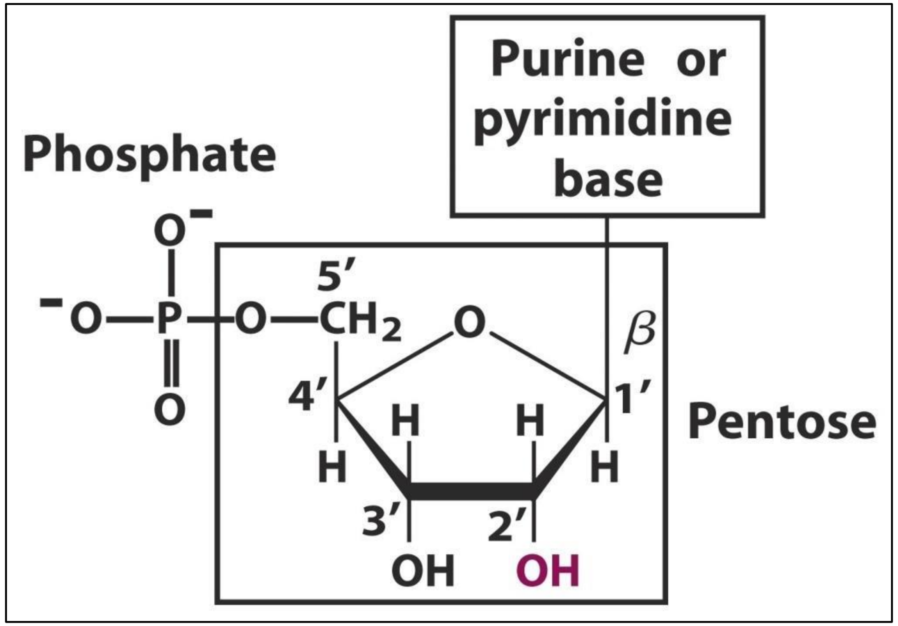
As for how these bases are connected to each other — they pair via **hydrogen bonds**:

- Adenine pairs with thymine (or uracil in RNA) via **two hydrogen bonds**,
- Guanine pairs with cytosine via **three hydrogen bonds**.

HOW ARE BASES CONNECTED TO RIBOSE?

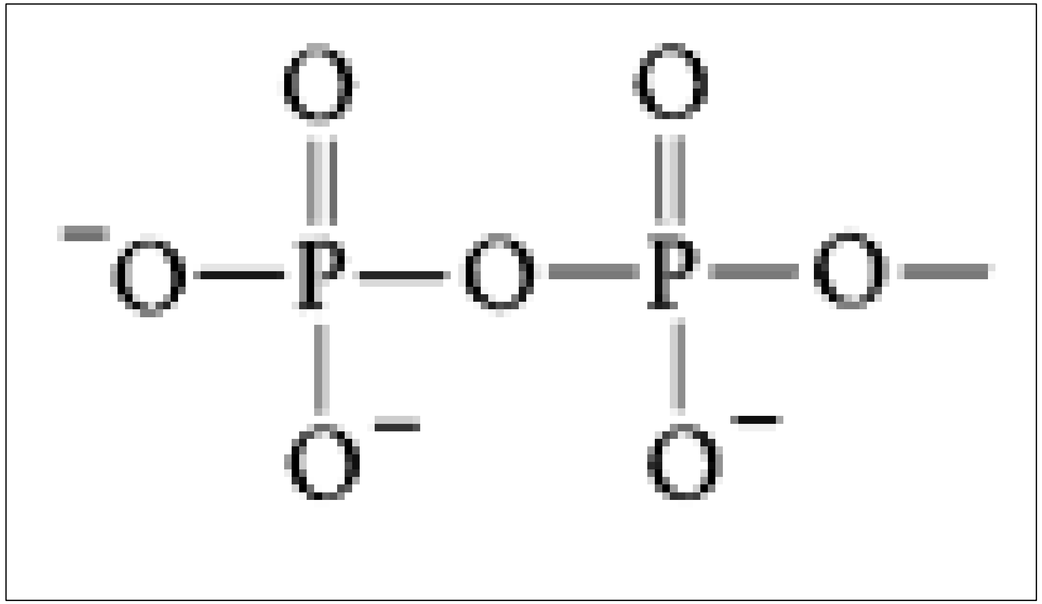
- In nucleotides, the 1 carbon atom of the sugar (ribose or deoxyribose) is attached to the nitrogen.





NUCLEOTIDES ARE ACIDIC

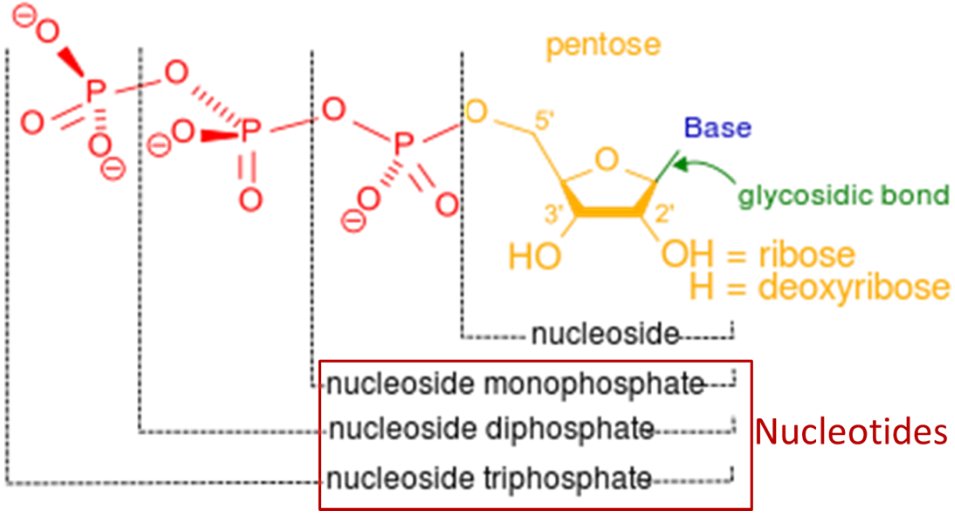
- Due to the presence of phosphate, which dissociates protons at physiological pH inside cells, freeing hydrogen ions and leaving the phosphate negatively charged



NUCLEOTIDES VS. NUCLEOSIDES

- Nucleosides are combinations of a base and a sugar without a phosphate
- Nucleotides are nucleosides that have one, two, or three phosphate groups esterified at the 5' hydroxyl
- Nucleoside monophosphates have a single esterified phosphate
  - diphosphates contain a two-phosphate group
  - triphosphates have three phosphates

Molecules like ATP, ADP, AMP, GTP, GDP, and GMP are **not exclusive components of DNA**; rather, they are found throughout the body and serve primarily as **energy carriers**. ATP, in particular, is the main energy currency of the cell, providing energy for many biochemical reactions. While these nucleotides can be incorporated into nucleic acids, their primary function outside of DNA and RNA is to supply and regulate cellular energy.



In mitochondria, ATP is used in energy metabolism. During carbohydrate metabolism, both UTP and ATP are present. In lipid biosynthesis, CTP is the dominant nucleotide. Protein biosynthesis utilizes GTP. All these nucleotides are involved in regulatory processes, and they produce the same amount of energy.

Nucleotides are connected to each other through bonds between the 3’ carbon of one nucleotide and the 5’ carbon of the next. This bond forms between the hydroxyl (–OH) group attached to carbon 3 and the phosphate group attached to carbon 5. Therefore, the direction of the bond is from 3’ to 5’.

At one end of the first nucleotide, there is a phosphate group at the 5’ carbon, while the last nucleotide has a free hydroxyl group at the 3’ carbon. Thus, the overall direction of the nucleotide chain is from 5’ to 3’.

Because the bond forms from 3’ to 5’ and the molecule extends from 5’ to 3’, new nucleotides can be continuously added at the 3’ end, allowing the chain to elongate. Accordingly, nucleotide sequences are always read from 5’ to 3’.

If numbering is absent, sequences are conventionally read from left to right.

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:

قال رسول الله ﷺ:

«اتَّقِ اللهَ حيثما كنتَ وأتبعِ السَّيِّئةَ الحسنةَ تمْحُها وخالِقِ النَّاسَ بخُلقٍ حَسنٍ»

في هذا الحَديثِ يقولُ الرَّسولُ صلَّى اللهُ علَيه وسلَّم: "اتَّقِ اللهَ"، والتَّقوى هي الخوفُ مِن اللهِ ومُراقبتُه وأنْ تَجعَلَ بينَك وبينَ عَذابِ اللهِ وِقايةً، وتَكونُ بالإتيانِ بالواجباتِ، والامتِناعِ عَن المُحرَّماتِ "حيث ما كُنتَ"، أي: في كلِّ مكانٍ وجِهَةٍ، وفي سِرِّك وعَلانِيَتِك، وفي بَلائِك ورَخائِك، وفي كلِّ أحوالِك، "وأَتبِعِ السَّيِّئةَ الحسَنةَ تَمحُها"، أي: إن وقَعتَ في سيِّئةٍ، فافعَلْ وَراءَها حسَنةً مِن صلاةٍ وصَدقةٍ، وسائرِ ما يُوصَفُ بالحسَنةِ؛ فإنَّ ذلك يَرفَعُ، ويَمْحو تلك السَّيِّئةَ، "وخالِقِ النَّاسَ بخُلقٍ حسَنٍ"، أي:خالِطِ النَّاسَ بأخلاقٍ حسَنةٍ، فأحسِنْ مُعامَلاتِهم، مِن تَبسُّمٍ في وُجوهِهم، ورِفقٍ ولينٍ في التَّعامُلِ معَهم؛ فمَن فعَلَ ذلك حازَ الدُّنيا والآخِرةَ.