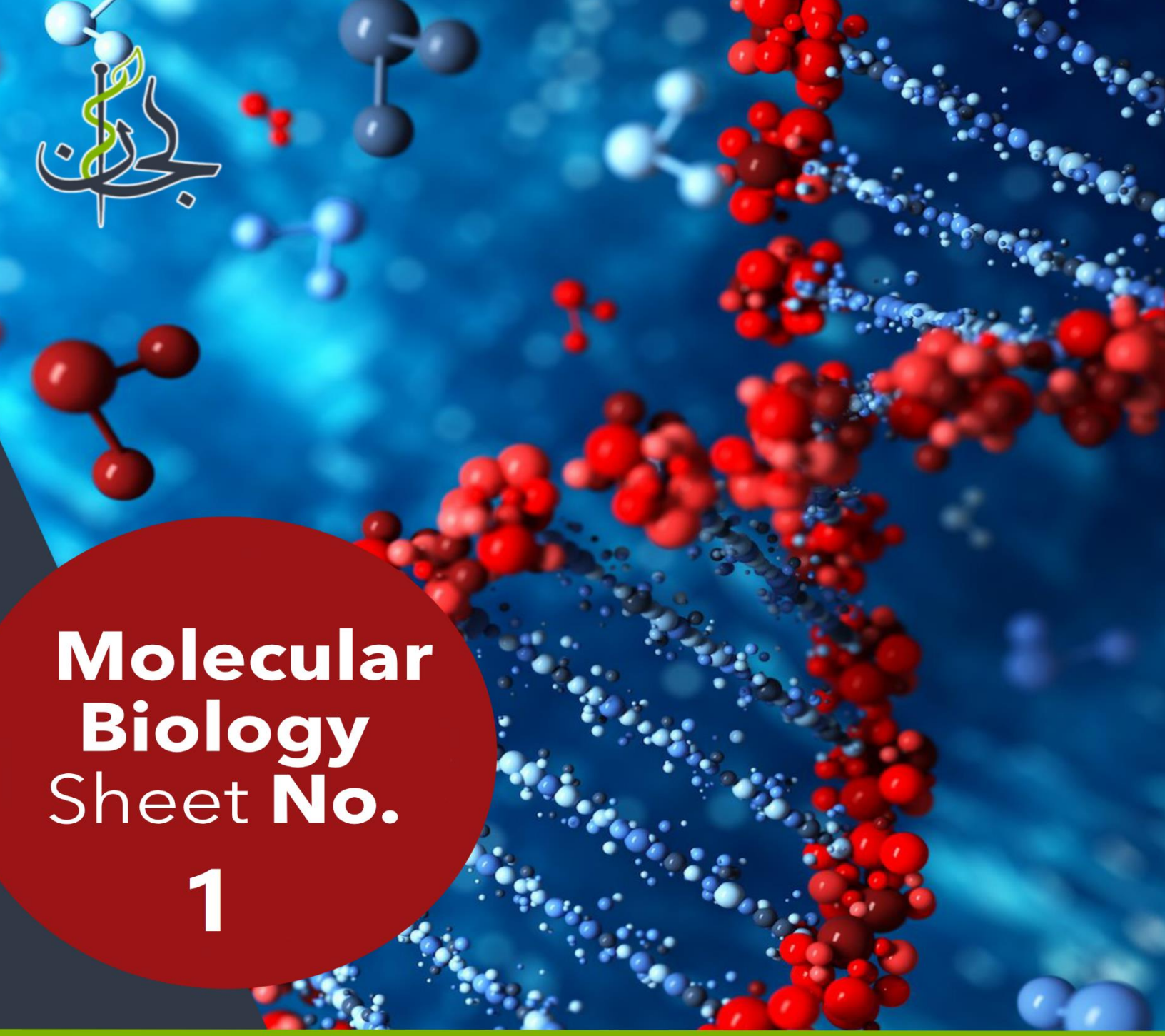


Molecular Biology Sheet No. 1

Writer Naiera Alsaadi & Sumayah Alkasaji

Scientific correction Ahmad Qatawneh

Grammatical correction Ahmad Qatawneh

Doctor Dr. Maamoun Ahram

WHAT IS MOLECULAR BIOLOGY?

- It is a biochemistry, talking about the different reactions, biochemical structures, information of these molecules, but it is specifically related to (DNA & RNA). molecular biology is not genetics; there is an overlap between genetics and molecular biology. So, genetics deal with patterns of inheritance of phenotypes and genotypes and it deals with chromosomal structures rather than small molecules like DNA and RNA.

- Now there is something known as **the central dogma of molecular biology** and is basically the following:

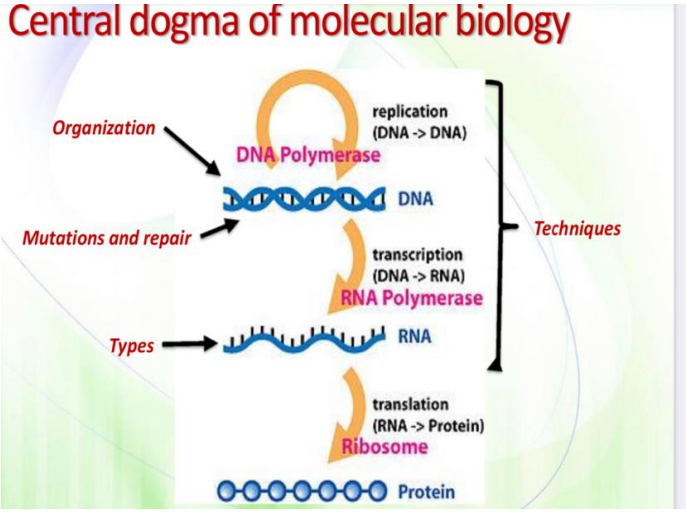
A It is the way in which DNA Molecules are used to make RNA, and this is done via the process known as (transcription), and it is catalyzed by an enzyme known as (RNA POLYMERASE).

B Then RNA is used to synthesize proteins in process known as (translation)

And this involves Ribosomes .

Also, DNA can make a copy of itself via (replication) and it is Catalyzed by (DNA POLYMERASE).

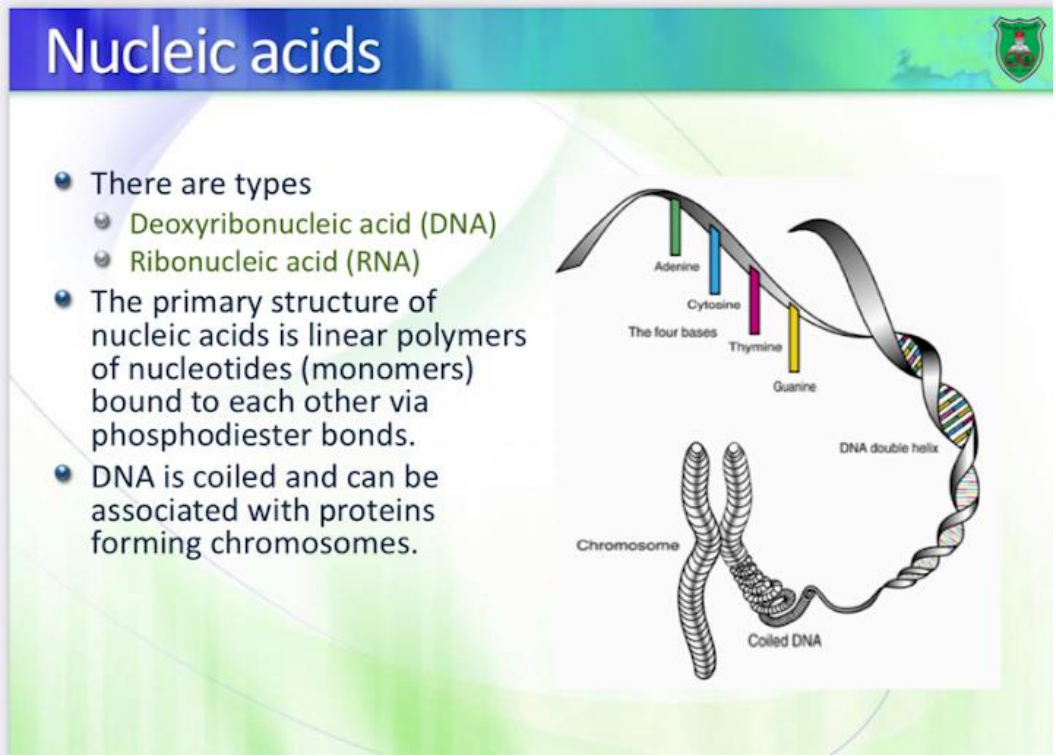
SO (DNA – RNA – PROTEINS)



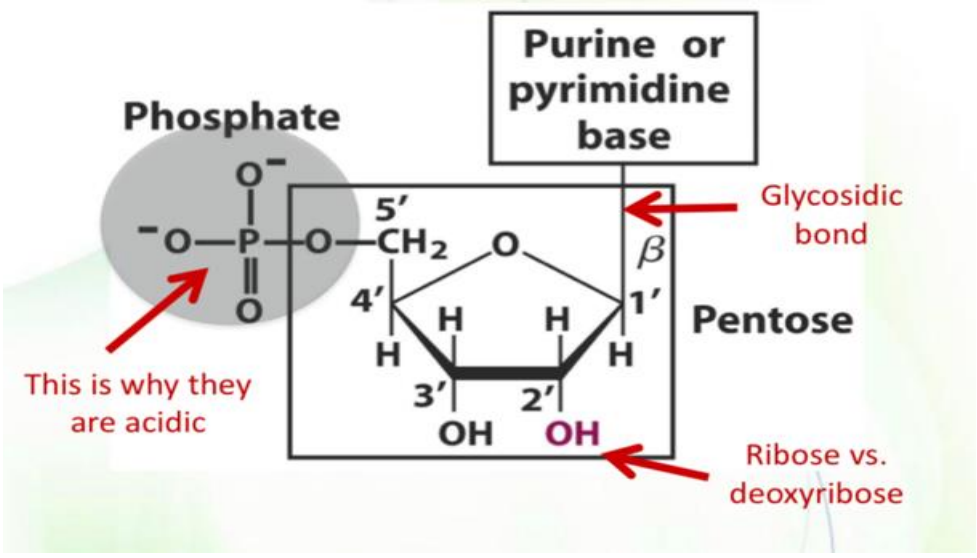
There are 2 types of nucleic acids:

- **DNA (Deoxyribonucleic)**
- **RNA (Ribonucleic acid)**

- The structure of DNA has nucleotides known as (monomers) connected to form (DNA polymer). So, the polymer is made of repetitive units known as (nucleotides) organized in large structures known as **Nucleic Acids** .



WHAT ARE NUCLEOTIDES? molecules that are made of three components:



1- Pentose Sugar molecule: linked to a nitrogenous base on one carbon and on another one it is linked to a phosphate group.

- The sugar molecule is a 5-carbon (a pentose) known as -**ribose- RNA**; **deoxy ribose -DNA-.**
- In normal way (**RNA**), carbon number **2** carries a hydroxyl group. In deoxy (**DNA**), it replaced by a hydrogen (so DNA has less O than RNA).

That is why it is called DNA:

D: deoxyribo-

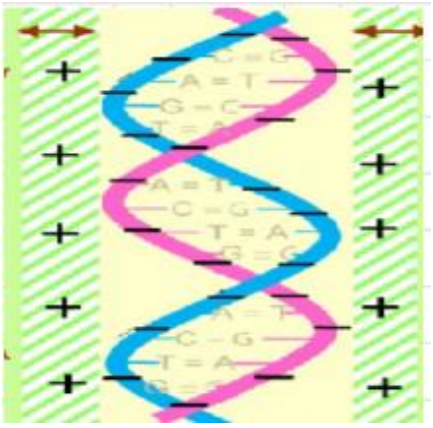
N: nucleic

A: acid

الحمض النووي الرايبوزي منقوص الأكسجين

2- phosphate: attached to the sugar at carbon 5, and negatively charged.

- Deoxy means that it does not have oxygen.
- DNA & RNA are negatively charged (**acidic**) because of these high negative charged groups.



Positively charged ions (Na+ or Mg2+) associate with the phosphate groups to stabilize the DNA.

• Example: histones

3- Nitrogenous bases:

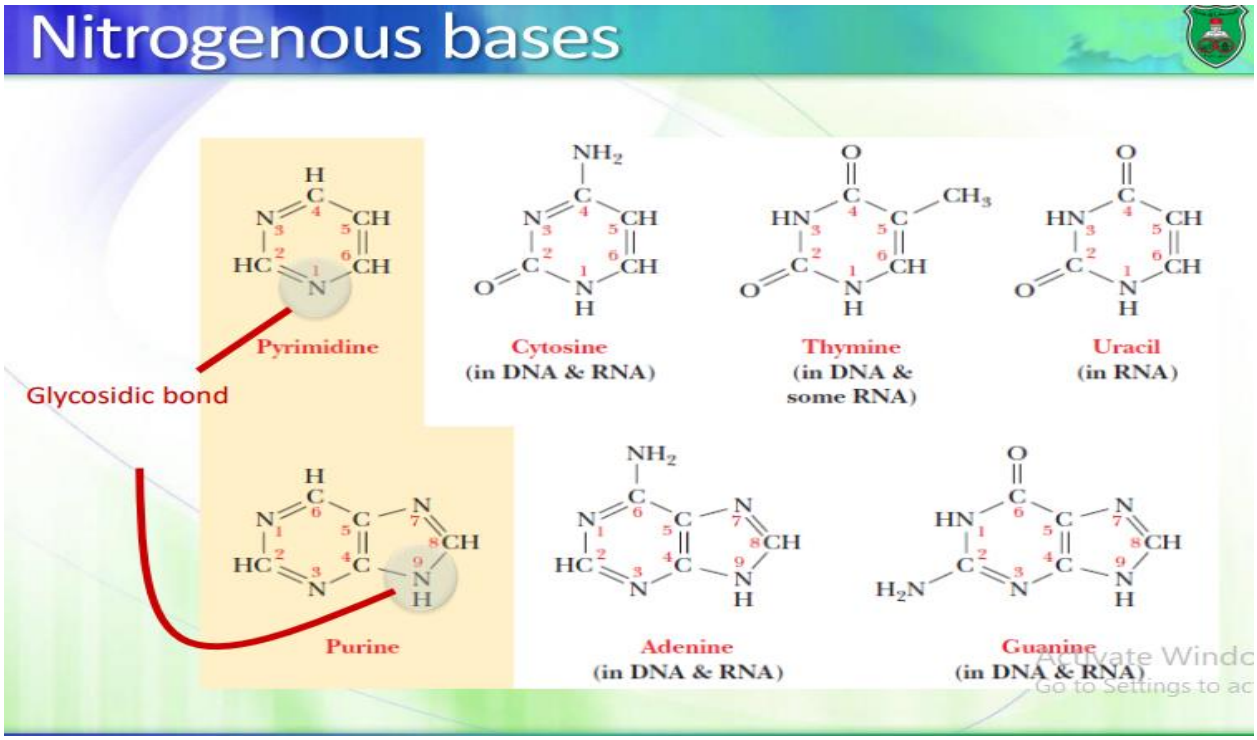
- There are 2 types of bases: (pyrimidine & purine).
- **Purine**: the little word, related to the large structure (Double ring structure). **Pyrimidine**: the large word, related to the small structure (single ring structure).

Purine: **adenine & guanine** Pyrimidine: **cytosine, thymine & uracil**	الكلمة الطويلة مع التركيب القصير والكلمة القصيرة مع التركيب الطويل

- Numbers of carbons in sugar VS in nitrogenous bases:

- sugar numbers have a sign above them (**'**), (**prime**).

So, 1' indicates carbon number 1 in the sugar ring, whereas 1 indicates carbon number 1 in the base.

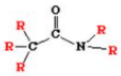


- Note: the sugar forms glycosidic bond with **Nitrogen 1** of the **pyrimidine**, and with **Nitrogen 9** of the **purine**.

Note on the following slide, thymine exists in DNA and some RNA (that is, viral RNA), **but for the purpose of the course** and talking about human DNA, there is not thymine in RNA . This is a direct quote from Dr. Mamoun

How to distinguish between nitrogenous bases?

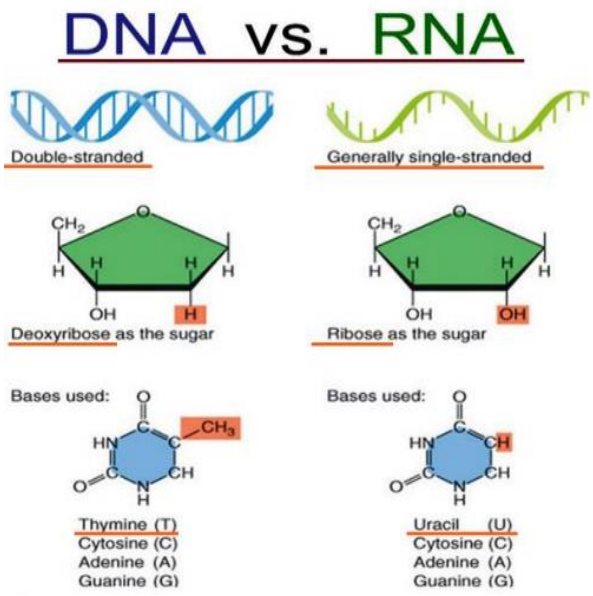
	Carbon 6	Found in
Adenine	Carbon number 6 connected to 2 nitrogens	DNA & RNA
Guanine	Amide group	DNA & RNA

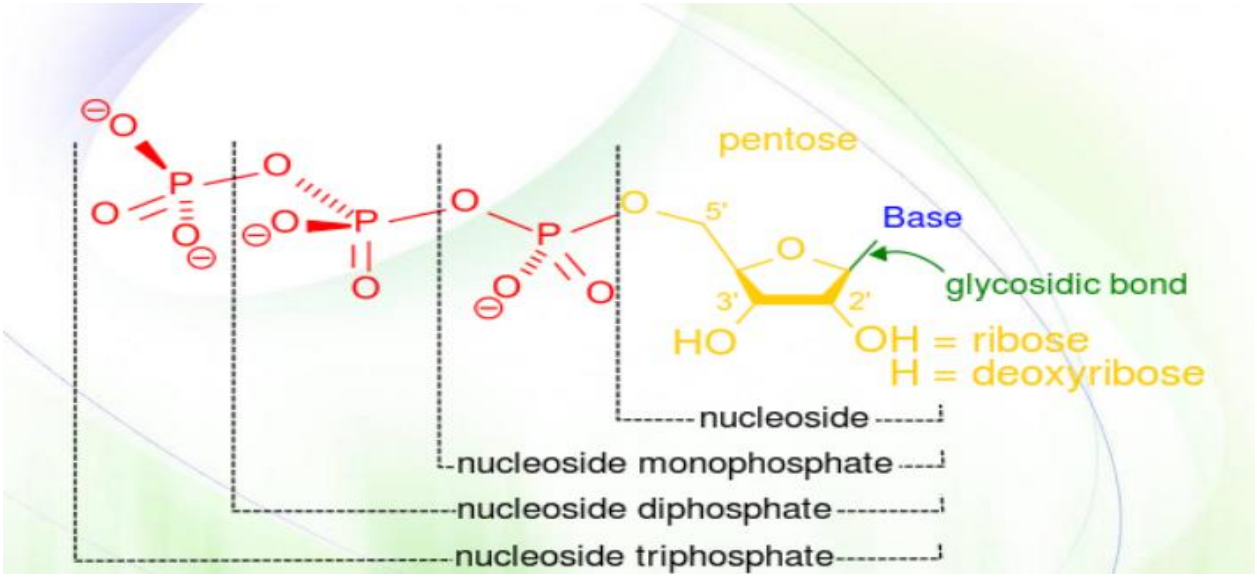


Amide

	Carbon 4	Found in
Cytosine	Carbon 4 connected two 2 nitrogens	DNA & RNA
Uracil	Amide group	RNA only
Thymine	Amide group but with additional -CH3 (methyl group) linked to Carbon 5	DNA and some RNA

Differences between DNA and RNA: (in prokaryotes and eukaryotes, not viruses)





Nucleoside: a molecule that is made of sugar (ribose or deoxyribose) and a base (no phosphate).

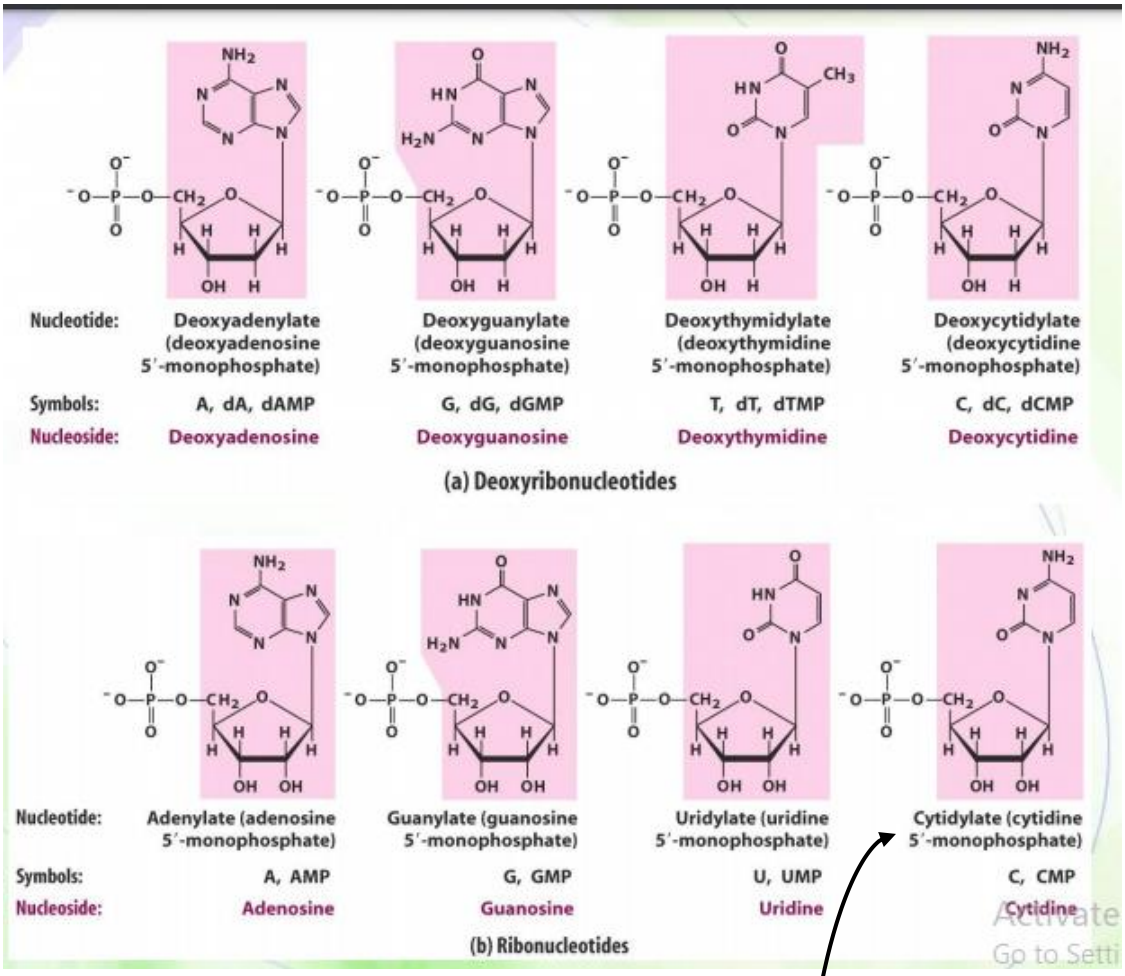
Nucleotide: a molecule that is made of sugar, base and one, two, or three phosphate groups.

- Nucleoside **mono**phosphate: nucleoside (sugar+ base) +**one** phosphate group.
- Nucleoside **di**phosphate: nucleoside+ **two** phosphate groups.
- Nucleoside **tri**phosphate: nucleoside+ **three** phosphate groups. (ATP: Adenosine triphosphate)

Special naming for monophosphates:

DNA

RNA



Note: symbols are required, memorize them!

(**RNA**): Nucleoside + (mono-di-tri)-phosphate

OR Nucleoside+ **-ylate**

(**DNA**): Deoxy- Nucleoside + (mono-di-tri)-phosphate

OR deoxy-nucleoside+ **-ylate**

To deepen our understanding, let us take this structure as an example:

* It has one phosphate group (**monophosphate**).
* There is a single-ring-structure nitrogenous base with amino group (**cytosine**).
* Carbon 2' (of the sugar) has hydroxyl group (**ribose- RNA**).

Cytidine monophosphate – cytidylate – CMP- C

In RNA:

Adenosine monophosphate, Adenylate, A or AMP.

Guanosine monophosphate, Guanylate, G or GMP.

Uridine monophosphate, Uridylate, U or UMP.

Cytidine monophosphate, Cytidylate, C or CMP.

In DNA:

Deoxyadenosine monophosphate, DeoxyAdenylate, A or dAMP.

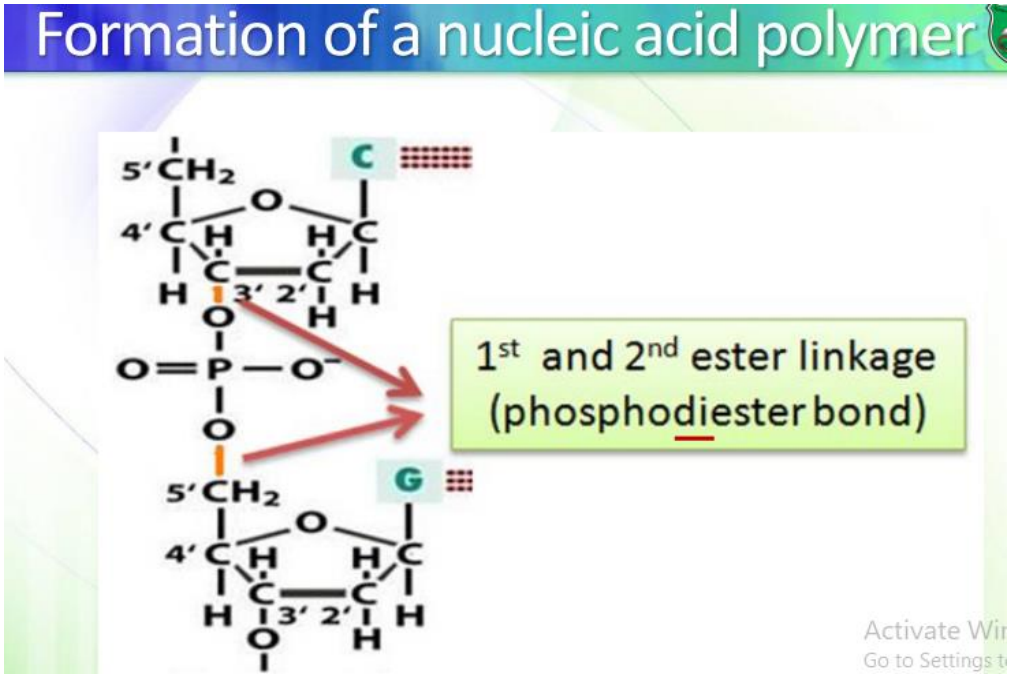
Deoxyguanosine monophosphate, DeoxyGuanylate, G or dGMP.

Deoxythymidine monophosphate, Deoxythymidylate, T or dTMP.

Deoxycytidine monophosphate, DeoxyCytidylate, C or dCMP.

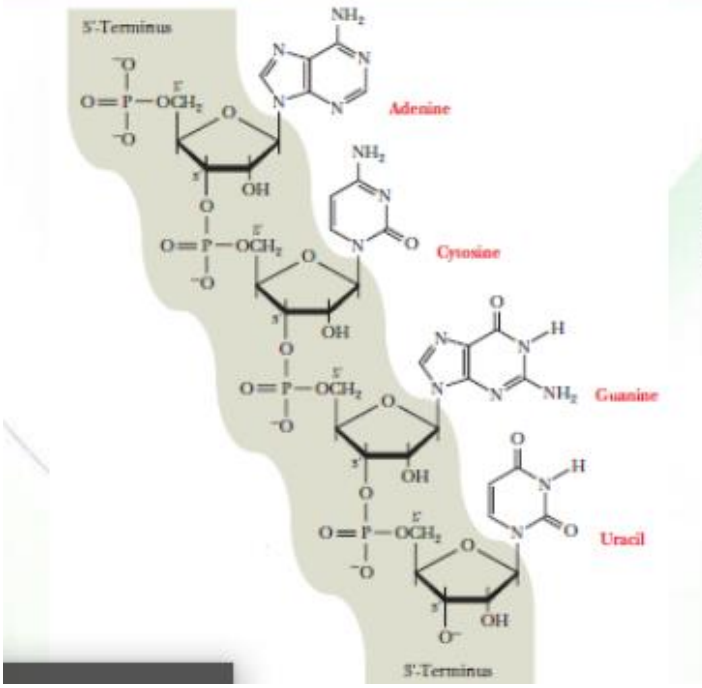
(The letter **d** can be added to indicate a deoxyribonucleotide residue. For example, **dG** is substituted for **G**. The deoxy analogue of a ribooligonucleotide would be **d(GACAT)**)

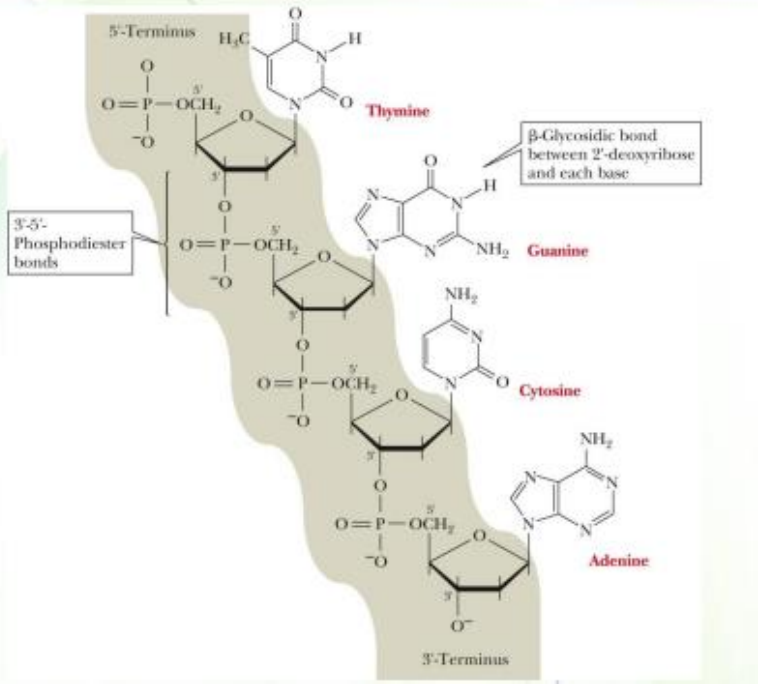
Nucleotides are attached to each other by phosphodiester bonds between **carbon 3'** of the first nucleotide and **carbon 5'** of the next nucleotide mediated by a phosphate group.



- We add nucleotides to the **3'** end forming a phosphodiester bond. The phosphate group on the **5'**carbon of the first nucleotide remains untouched.

Nucleic acid polymers





Sequence is A- C-G-U **5' TO 3'** Sequence is T- G- C- A

(Not U-G-C-A) (Not A-C-G-T)

RNA **DNA**

- We should depend on **sugar** (not on Uracil & Thymine) to distinguish between **DNA & RNA**; in certain mutations we can find Uracil in DNA)!
- Both DNA & RNA are polar structures composed of 2 different ends (terminals).

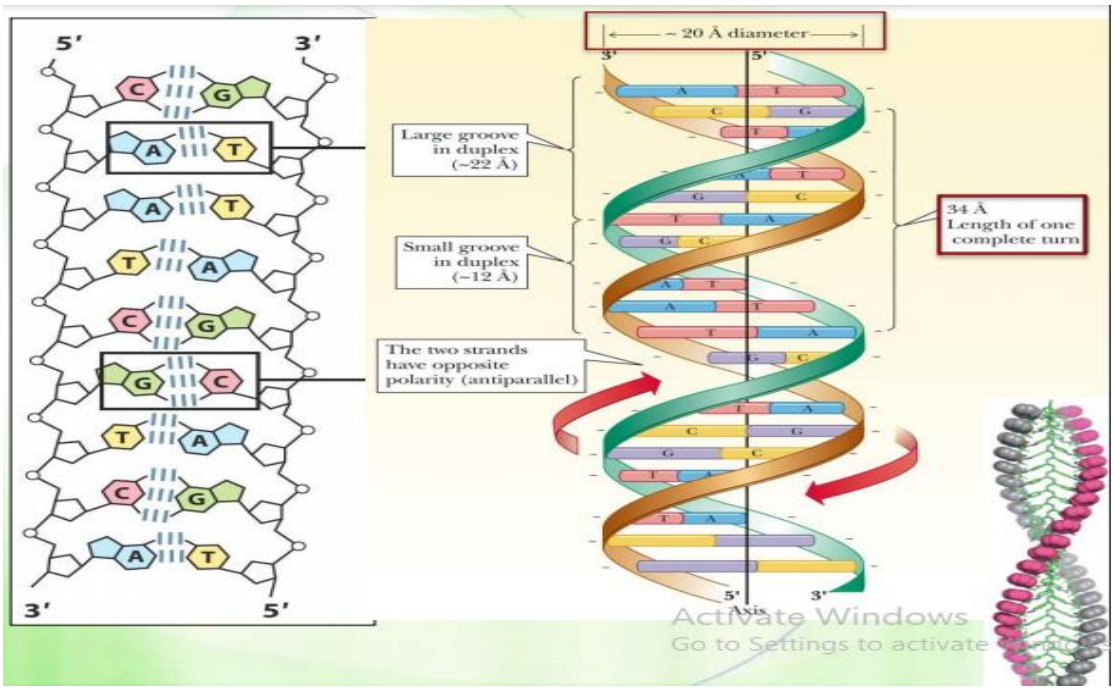
DNA structure: DNA structure has been identified by Watson and Crick.

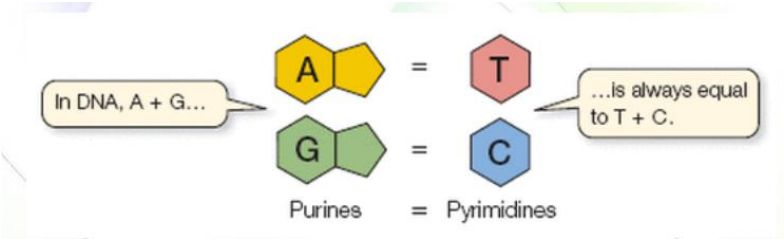
- Double helix: DNA is a double stranded molecule, composed of two strands intertwining around each other. (**DNA's helical structure is not perfect**)
- Specific base pairing:

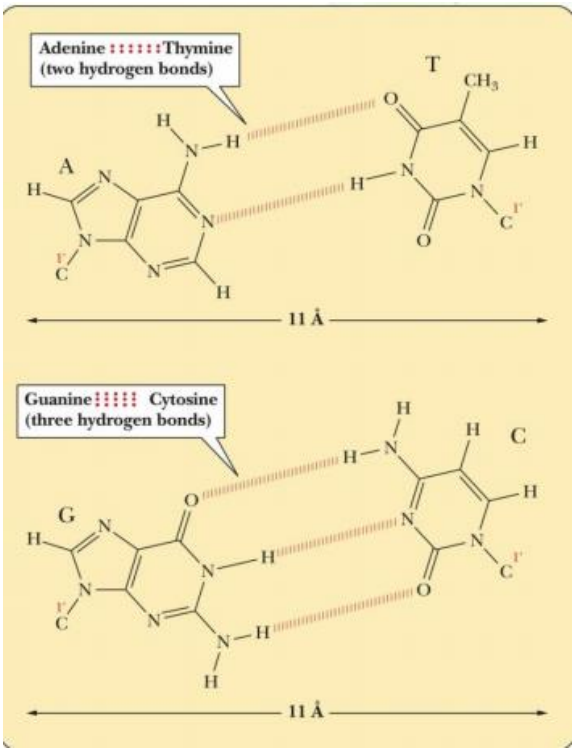
- Nitrogenous bases of the 2 strands pair together by specific H-bonds.

- Chargaff (scientist) found that the number of T= A and number of C= G, which means that if a strand has **Adenine**, the opposite base of the complementary strand must be **Thymine**.

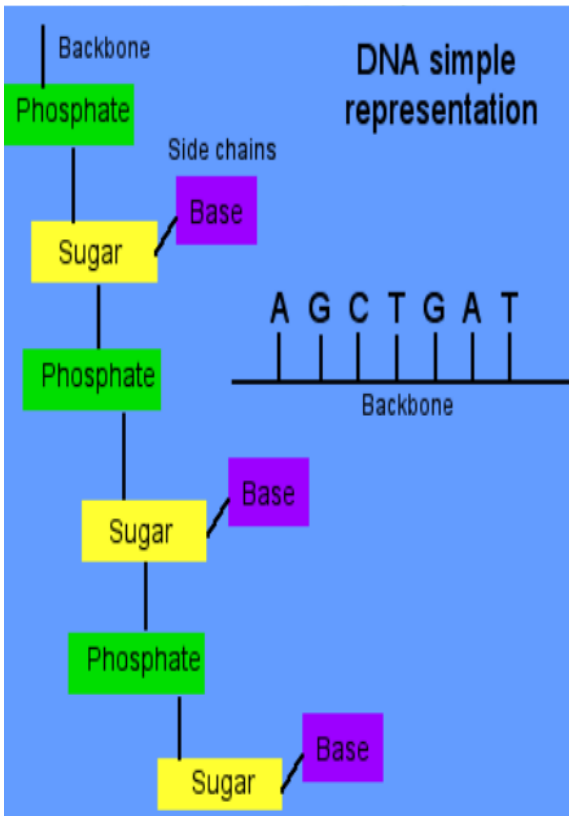
- In other words, **C** always pairs with **G** Forming **3** hydrogen bonds, and **A** always pairs with **T** = Forming **2** hydrogen bonds. **(pyrimidine pairs to purine دائمًا:)**







- **Backbone VS Side chains:**



- Back bone is phosphate, sugar, phosphate, sugar…

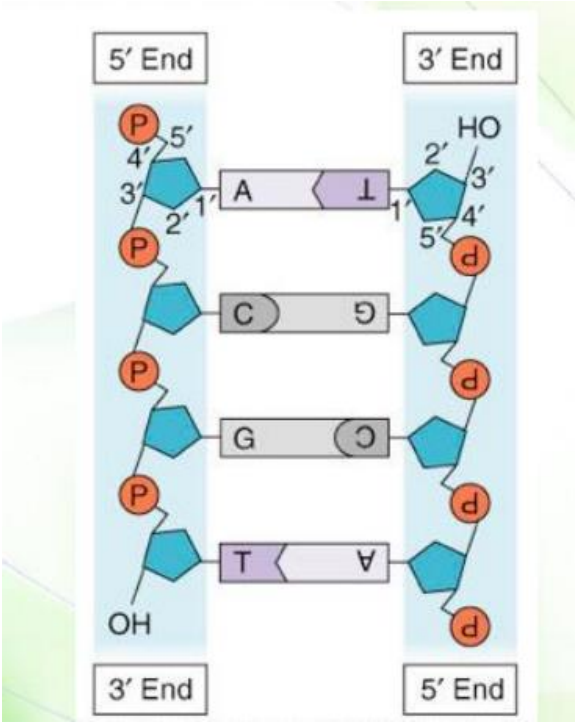
(connected to each other by phosphodiester bonds).

- Side chains are the nitrogenous bases.

(connected to the sugar by glycosidic linkages).

- Bases are oriented inward (hidden inside the helix).

- **DNA is antiparallel:**



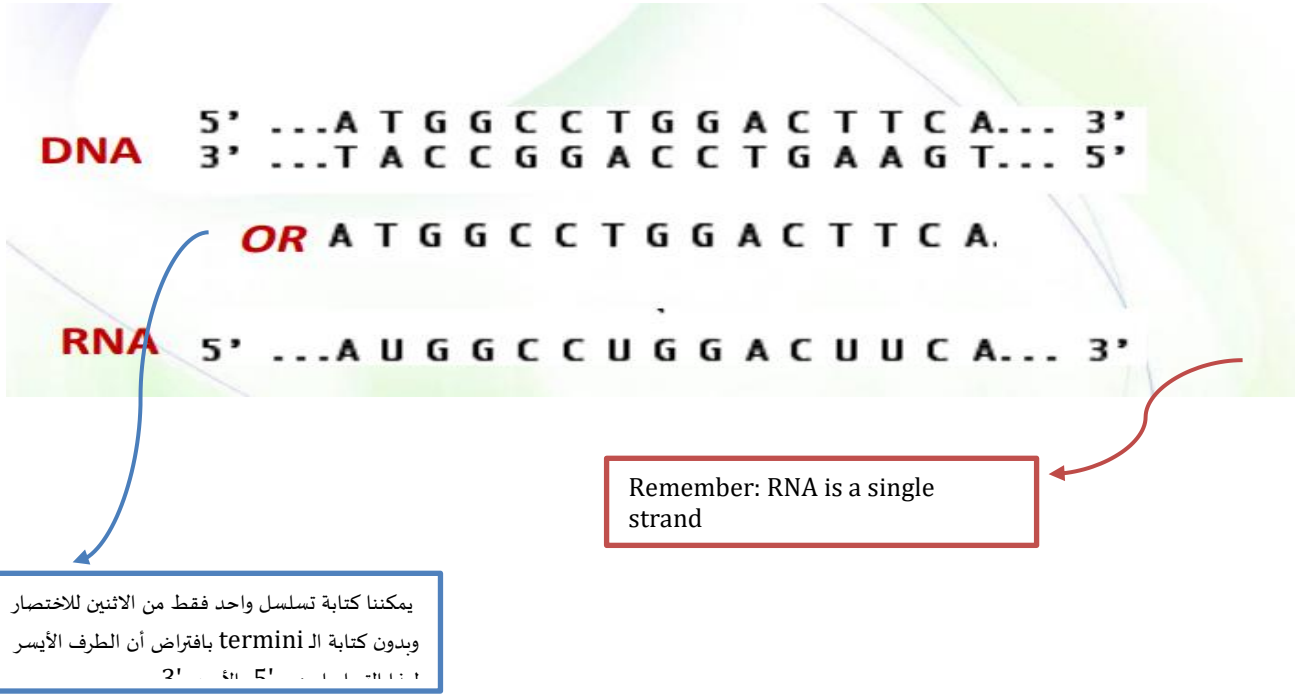
- The two ends are **opposite** to each other.

(3' of the first strand is opposite to 5' of the second strand as shown)

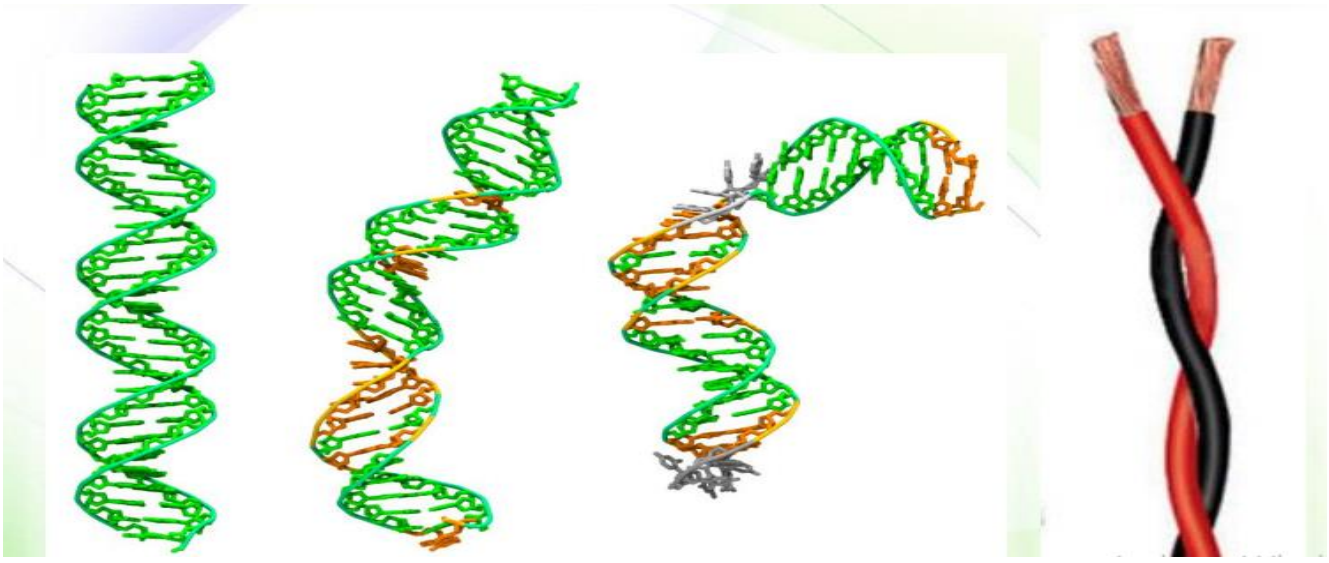
- The sequence of the left strand is **ACGT**.
  The sequence of the right strand is **TGCA**.

- *Remember: sequence is always **(5' to 3').***

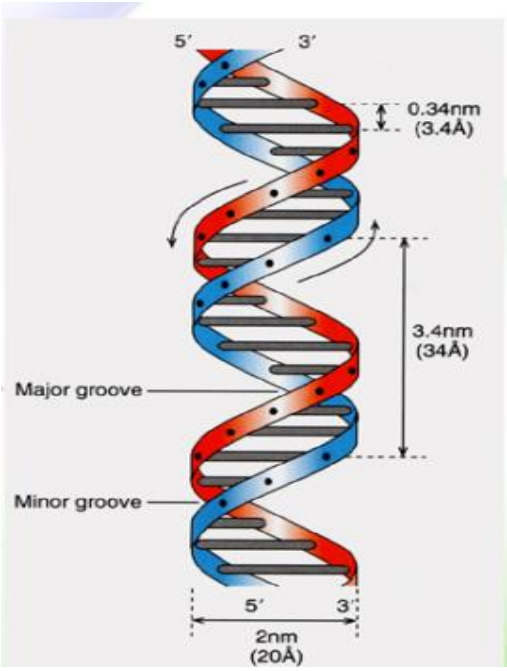
- You may be given a particular sequence and asked to write the complementary one:



- **DNA is flexible, yet stable:** It is like an electrical wire, so you can bend it BUT it cannot be easily broken. (This property fits DNA's functions and helps allows it to coil and interact with proteins).



- **DNA grooves:**

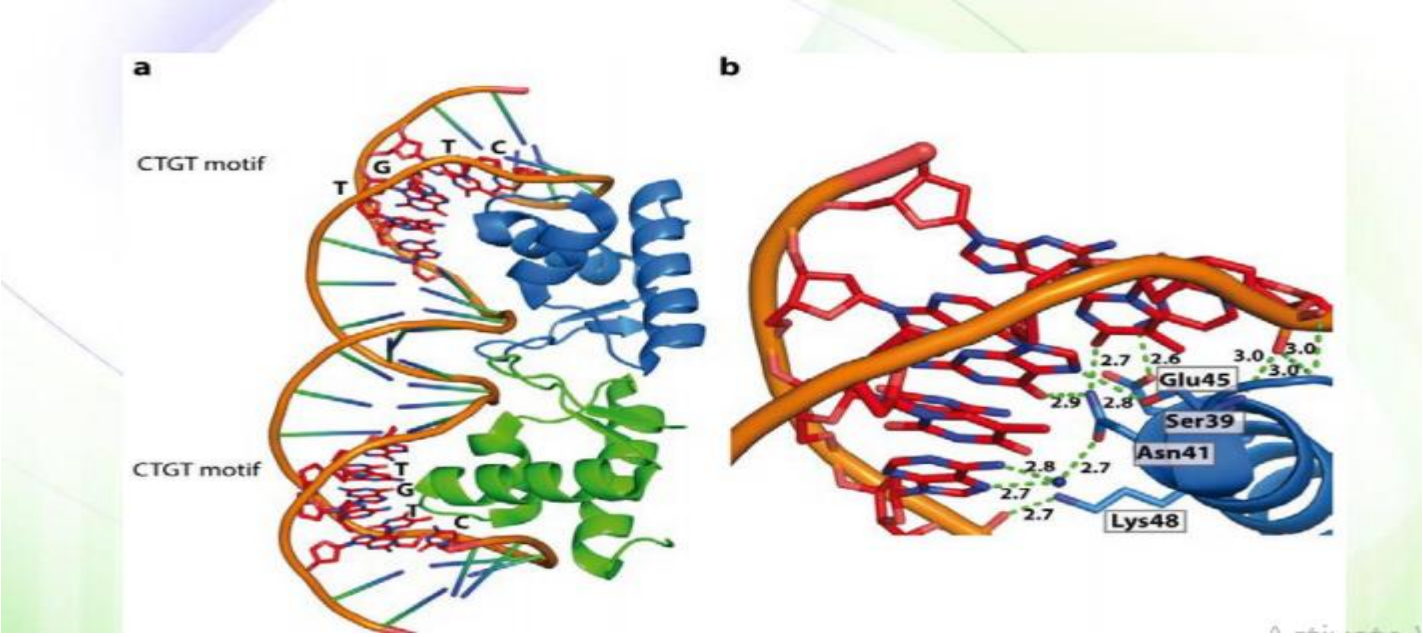


- **DNA is not a perfect double helix, due to this imperfection, DNA has two structures:**

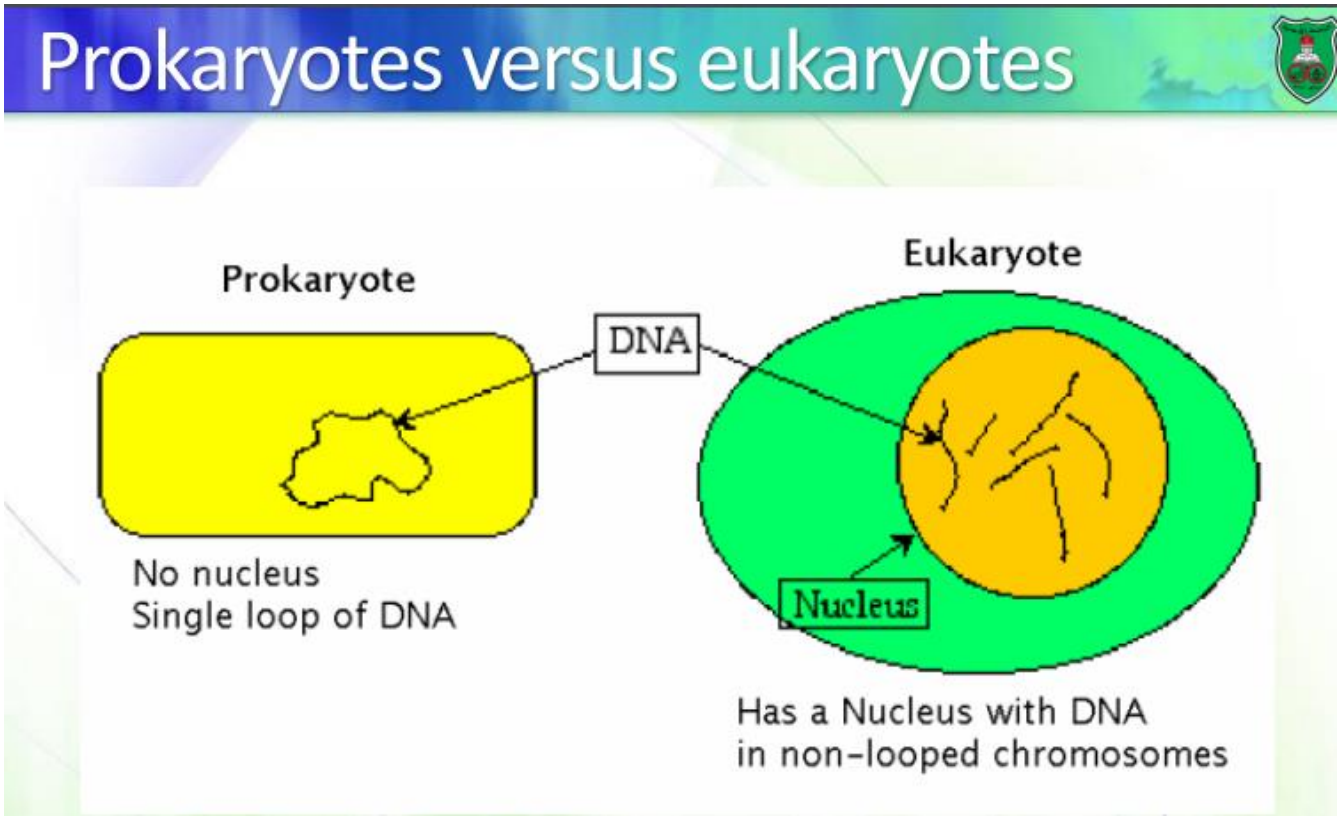
- major groove : **larger** than minor groove with **bigger** space.

- minor groove : **smaller** than major groove with **smaller** space.

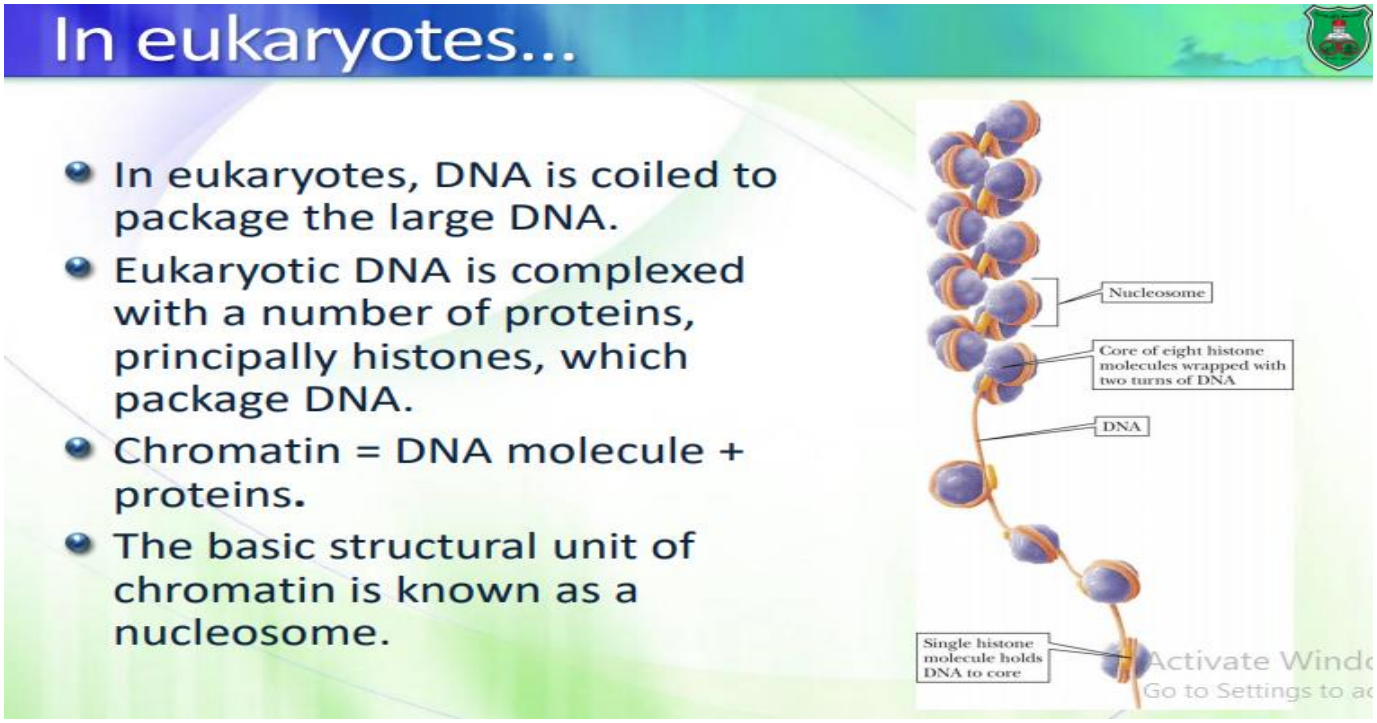
- Proteins prefer to interact with DNA at the **major grooves**, to have enough space to insert themselves inside the DNA**.**
- Interactions can take place in **minor grooves**, but primarily, they take place in major grooves.
- The interaction occurs between **amino acids** of proteins with the **bases** of the DNA molecule via **noncovalent** bonds. (Hydrogen bond, electrostatic interactions, Van Dear Waals interactions and hydrophobic interactions).



- Some of nitrogenous bases are exposed (**not all are oriented inward).**
- These exposed bases determine the types of proteins that will interact with the DNA sequence.
- In other words, **the sequence of DNA is important in determining the types of proteins it interacts with.**



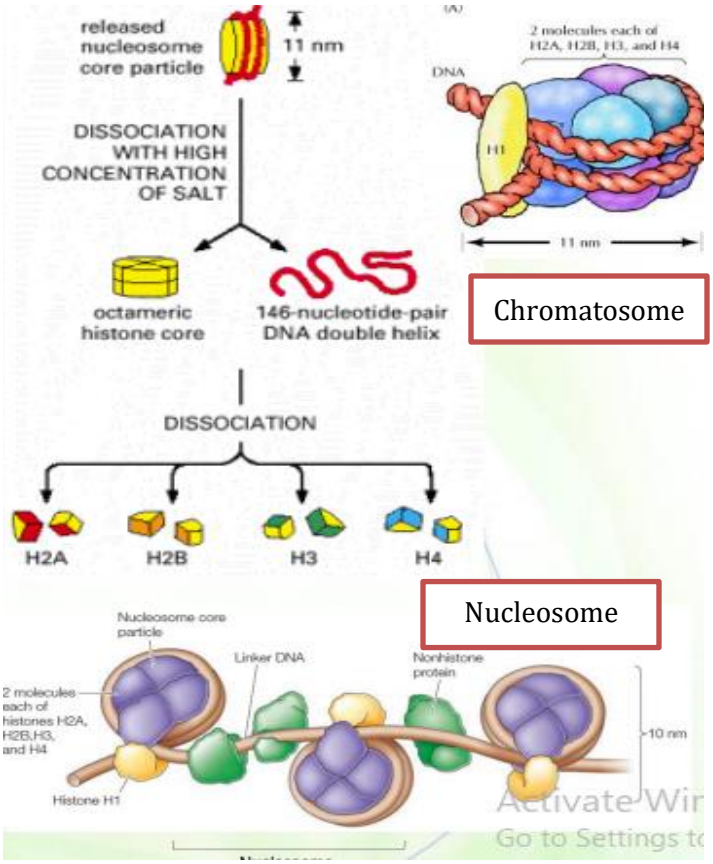
- **Eu** means **TRUE** (eukaryotes have true membrane bound nucleus).
- Eukaryotes have **linear multiple chromosomes**, whereas Prokaryotes have **single circular one**.



In a single eukaryotic cell, the length of DNA is **2 meters**, it must be packed inside a nucleus by wrapping around histones(positively charged proteins) that interact with the phosphate groups (negatively charged) of the nucleotides to make neutralization. (DNA is coiled to package the large DNA).

- Basic units of chromatin are nucleosomes:

- **Nucleosome**: the structure that is composed of DNA wrapping around histones+ linker DNA (histone-free DNA)+H1.
- **The histone protein core**: an octamer (made of 8 histone molecules, two of each type: H2A, H2B H3 and H4).



Chromatosome

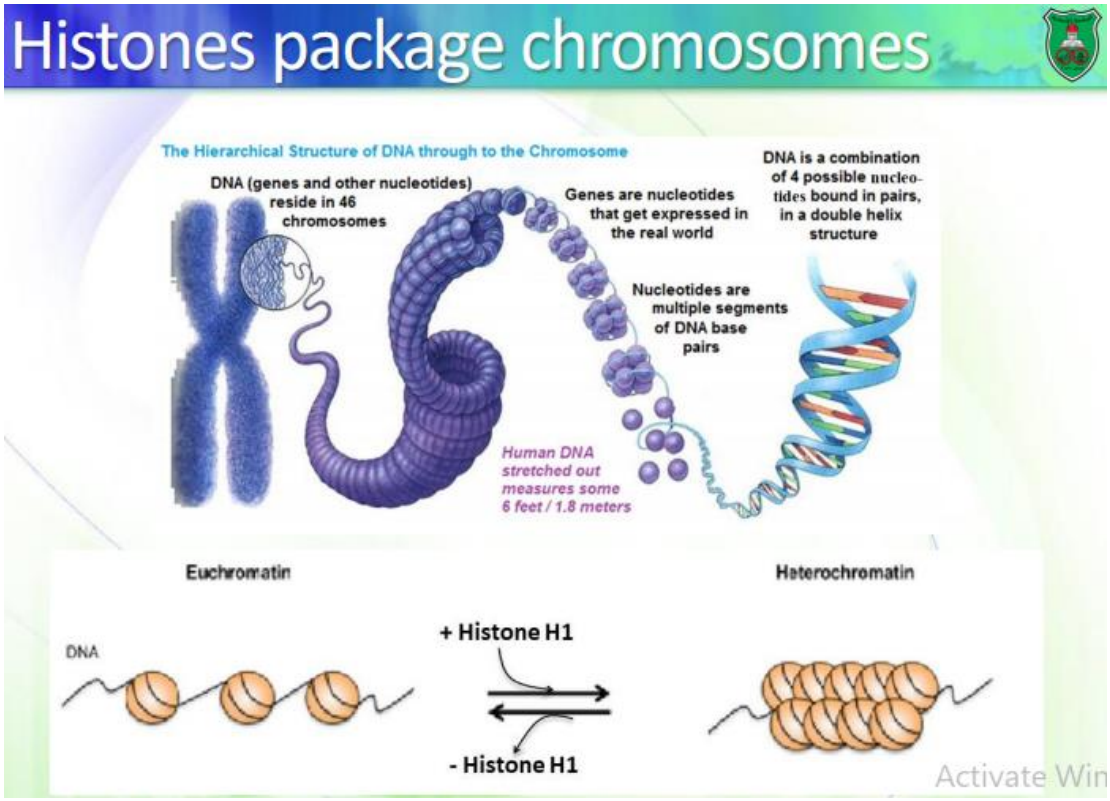
Nucleosome

Chromatosome: the structure that is composed of DNA wrapping around Histones and H1 histone protein.

(linker DNA قبل إضافة الـ).

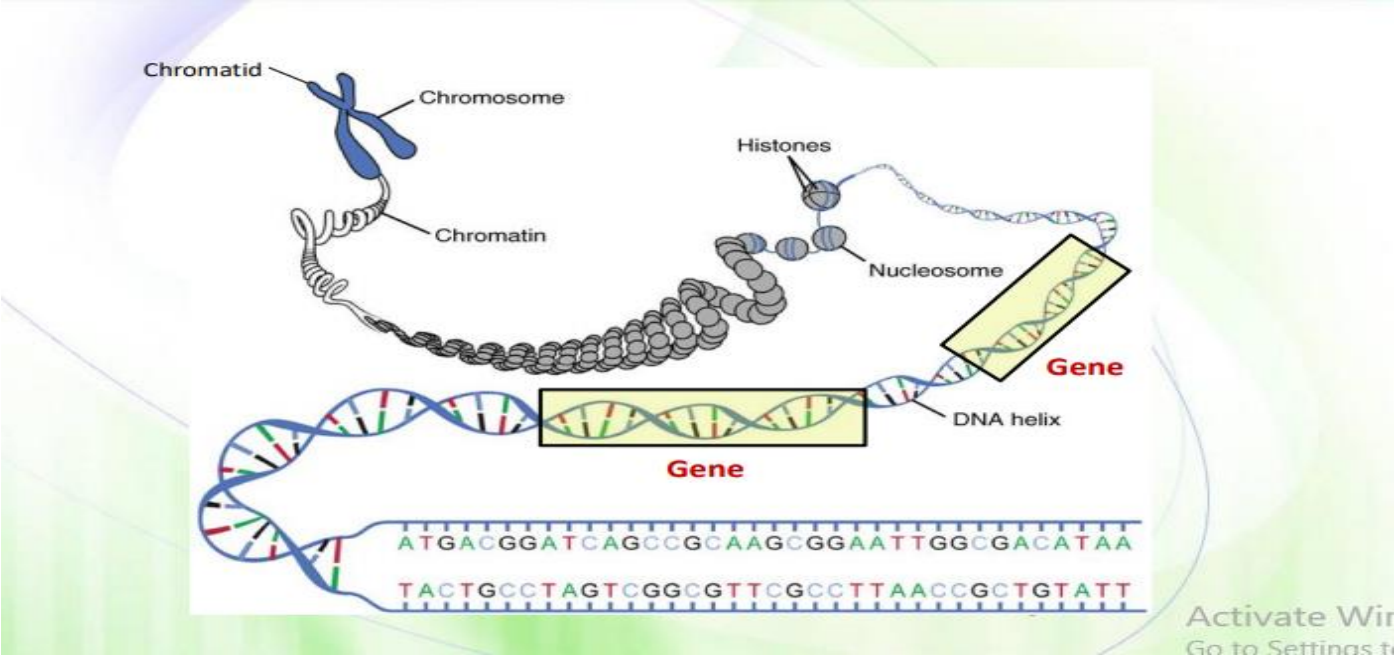
H1 acts as a lock that seals the octamer and DNA wrapped around it.

Chromatosome + linker DNA = Nucleosome

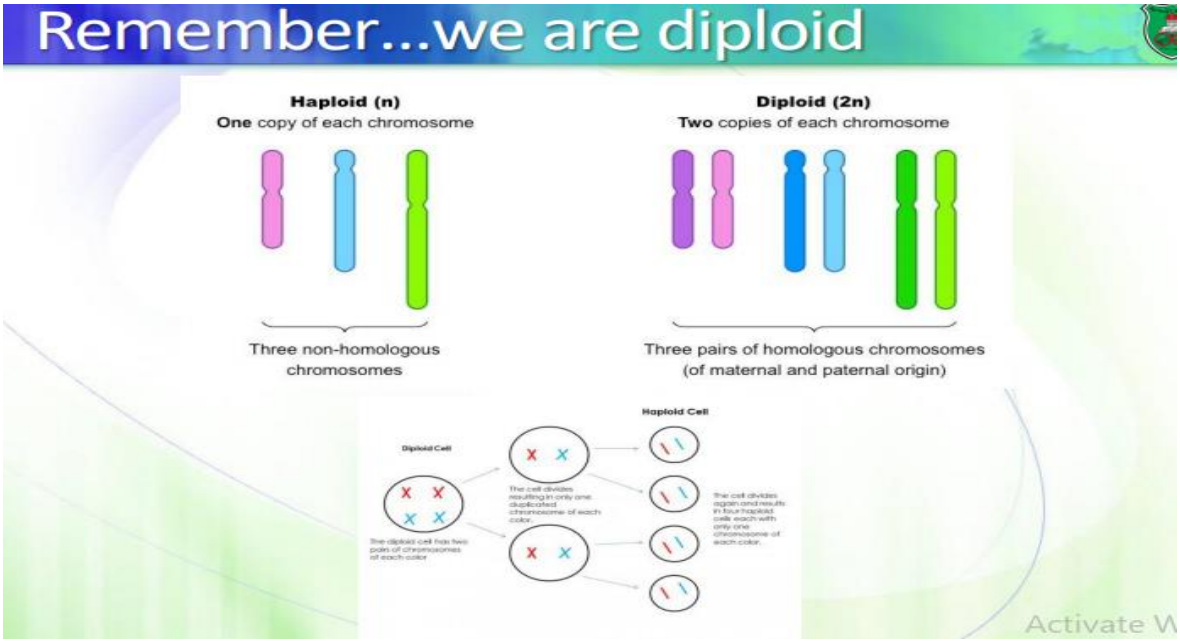


Euchromatin= loose chromatin (no H1)
Heterochromatin = packed chromatin (with H1)

Important terms to know:



- **Chromatin**: DNA + proteins, (a part of chromosomes).
- **Chromosome**: DNA wrapped around histones into a large unit, (2 sister chromatids if it is undergoing meiosis or mitosis). In the case of non-dividing cells, the DNA molecule is composed of single chromatid .
- Chromosomes are usually portrayed as X-shaped structures, however this is not the case for **non-dividing cells** .
- **Gene**: A region in DNA, (sequence of nucleotides that RNA & proteins are made from)



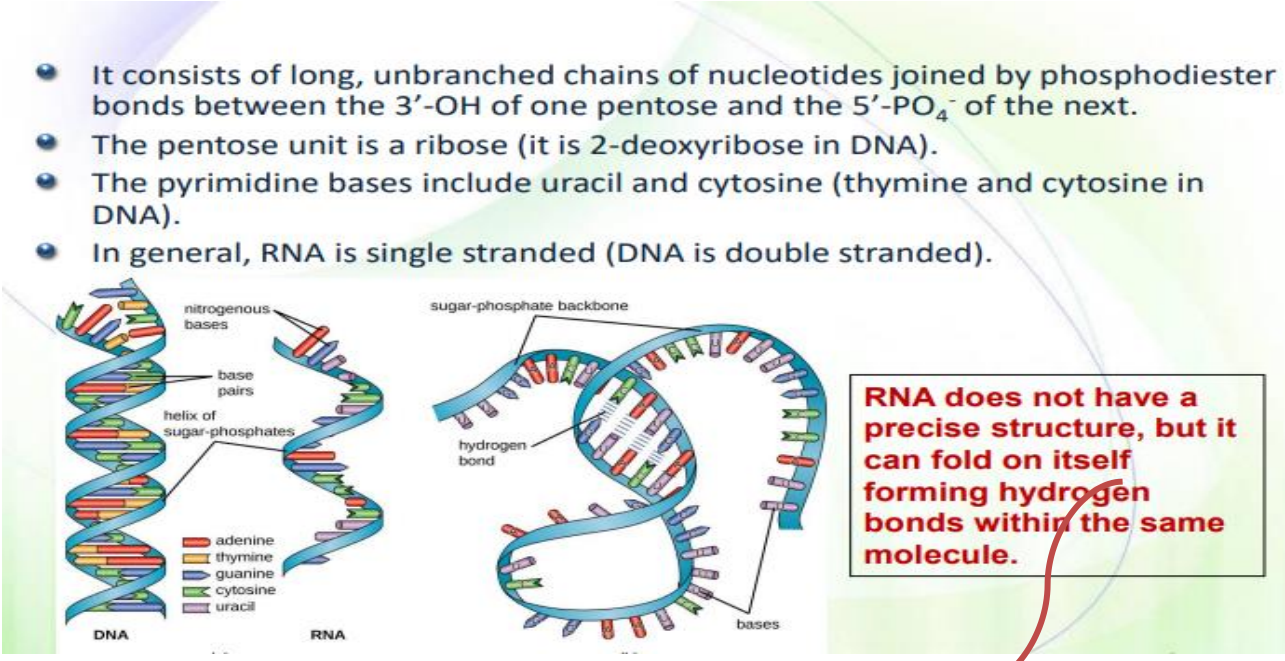
- **Diploid**: every cell contains 2 copies of every chromosome (homologous chromosomes). one comes from father (paternal) and one comes from mother (maternal).
- **Homologous chromosomes**: the order of genes in the 2 chromosomes is exactly the same.
- **Haploid** (1n): contains one copy of chromosome, only in germ cells (sperm and egg).

- As shown in the figure above:

  a diploid cell (**double structured chromosomes** **2 sister chromatids**) undergoes meiosis to produce 4 haploid cells (**single structured chromosome** a single chromatid in each daughter cell).

RNA:

RNA does not have a particular structure like DNA, in some cases, RNA can be found as double structure!



RNA molecules can have hydrogen bonding between bases if they are **complementary** to each other.

Types of RNA

Symbol	Non-Coding RNAs	Functions
* tRNA	Transfer RNA	mRNA translation (structural)
* rRNA	Ribosomal RNA	mRNA translation (structural)
* miRNA	micro RNAs	Post-transcriptional transposon repression
piRNA	Piwi-interacting RNA	DNA methylation, transposon repression
* siRNA	Short interfering RNA	RNA interference
snoRNA	Small nucleolar RNAs	RNA modification, rRNA processing
PROMPT's	Promoter upstream transcripts	Associated with chromatin changes
tiRNAs	Transcripton initation RNAs	Epigenetic regulation
lincRNAs	Long intergenic ncRNA	Epigenetic regulators of transcription
rasiRNA	Repeat associated small interfering RNA	Involved in the RNA interference (RNAi) pathway
eRNA	Enhancer-like ncRNA	Transcriptional gene activation
T-UCRs	Transcribed ultraconserved regions	Regulation of miRNA and mRNA levels
NATs	Natural antisense transcripts	mRNA stability
PALRs	Promoter-associated long RNAs	Chromatin changes
tasiRNA	Trans-acting siRNA	Represses gene expression
* lncRNA	Long noncoding RNA	Regulation of gene transcription

- In this course we will study 5 types only (marked with *).
- There is another type of RNA not written here called Messenger RNA (mRNA).

DONE.