Sheet
no.1

Molecular biology

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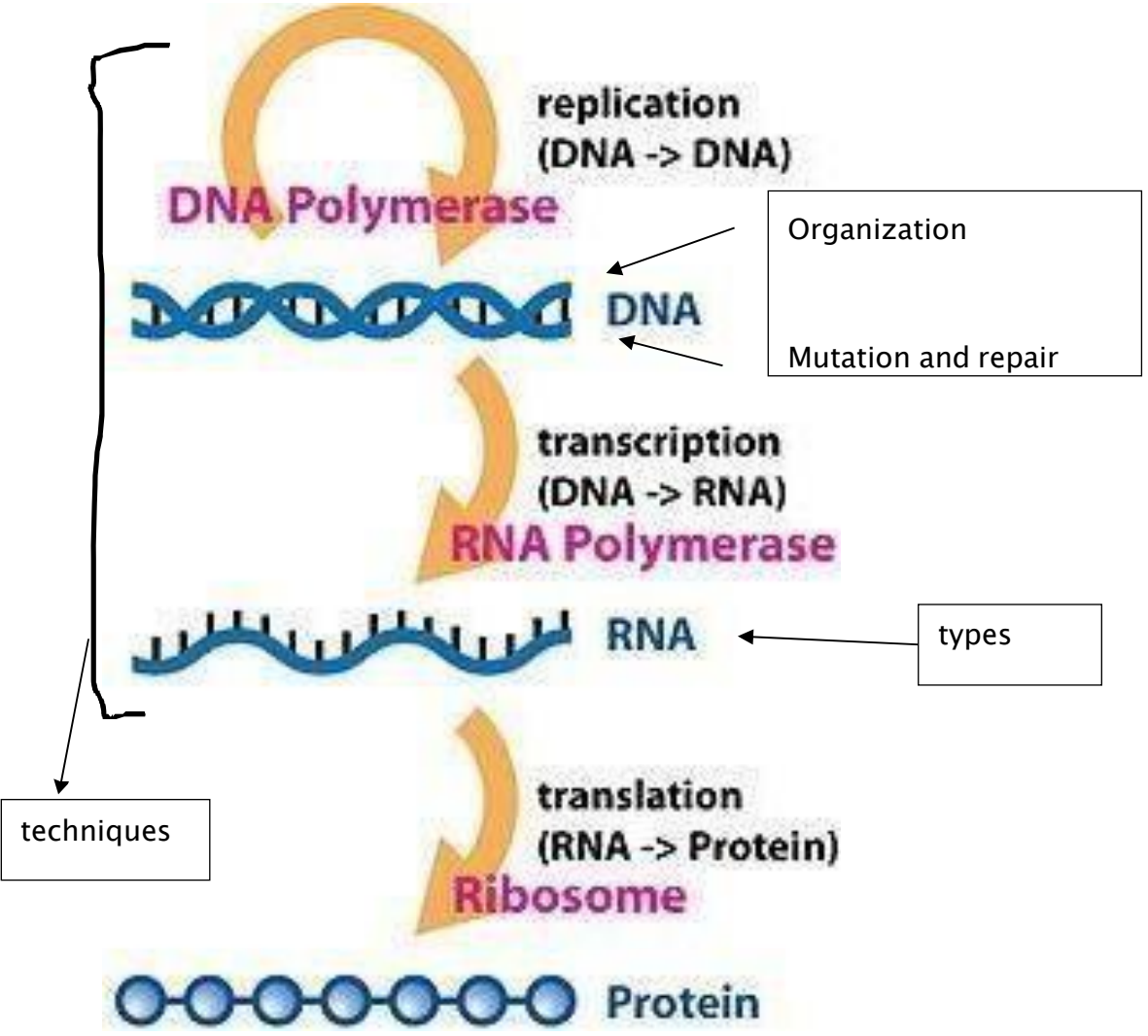
*What is Molecular Biology?

The study of biochemical reactions and structures of nucleic acids (DNA,RNA)

**it differs from GENETICS that studies the patterns of inheritance about phenotypes (physical appearance) or genotypes.

Central dogma about molecular biology (the main philosophy)



The central dogma is around

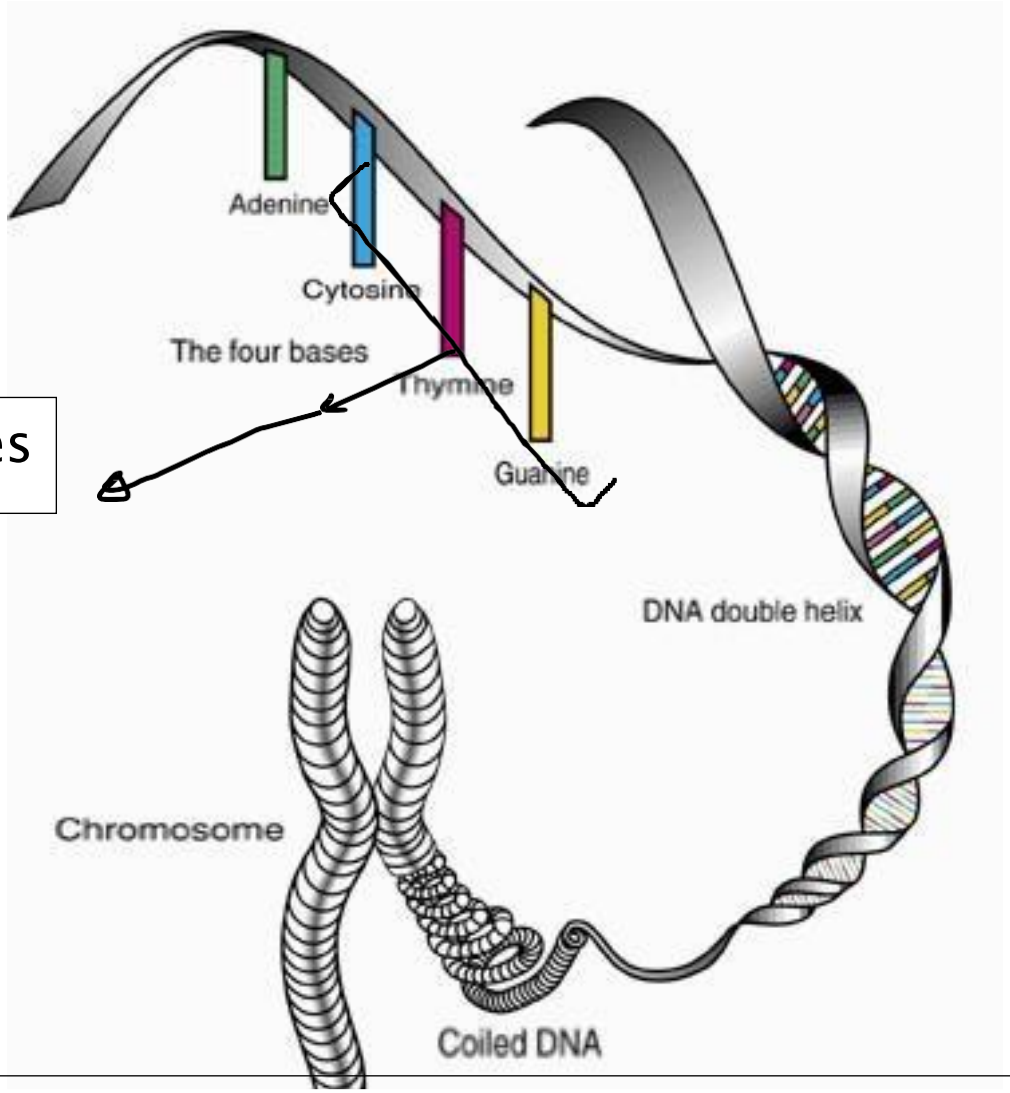
1. converting DNA to RNA (transcription)-the enzyme:RNA polymerase
2. transforming RNA to protein(translation) - by ribosomes
3. regenerating DNA from itself by DNA polymerase

Recent researches show that DNA could be synthesized by RNA and RNA can regenerate itself

DNA<--RNA→RNA

Nucleic Acids

nucleotides



Monomers-→ repetitive units→ large polymer

Nucleotides→will repeat as basic structure→ DNA

**There are types of nucleic acids:

1. Deoxyribonucleic acid (DNA)
2. Ribonucleic acid (RNA)

*The primary structure of nucleic acids is linear polymers of nucleotides (monomers) bound to each other via phosphodiester bonds.

DNA is coiled and can be associated with proteins forming chromosomes.

nucleotides → (Phosphodiester bond) → DNA → (coiling) → chromosomes

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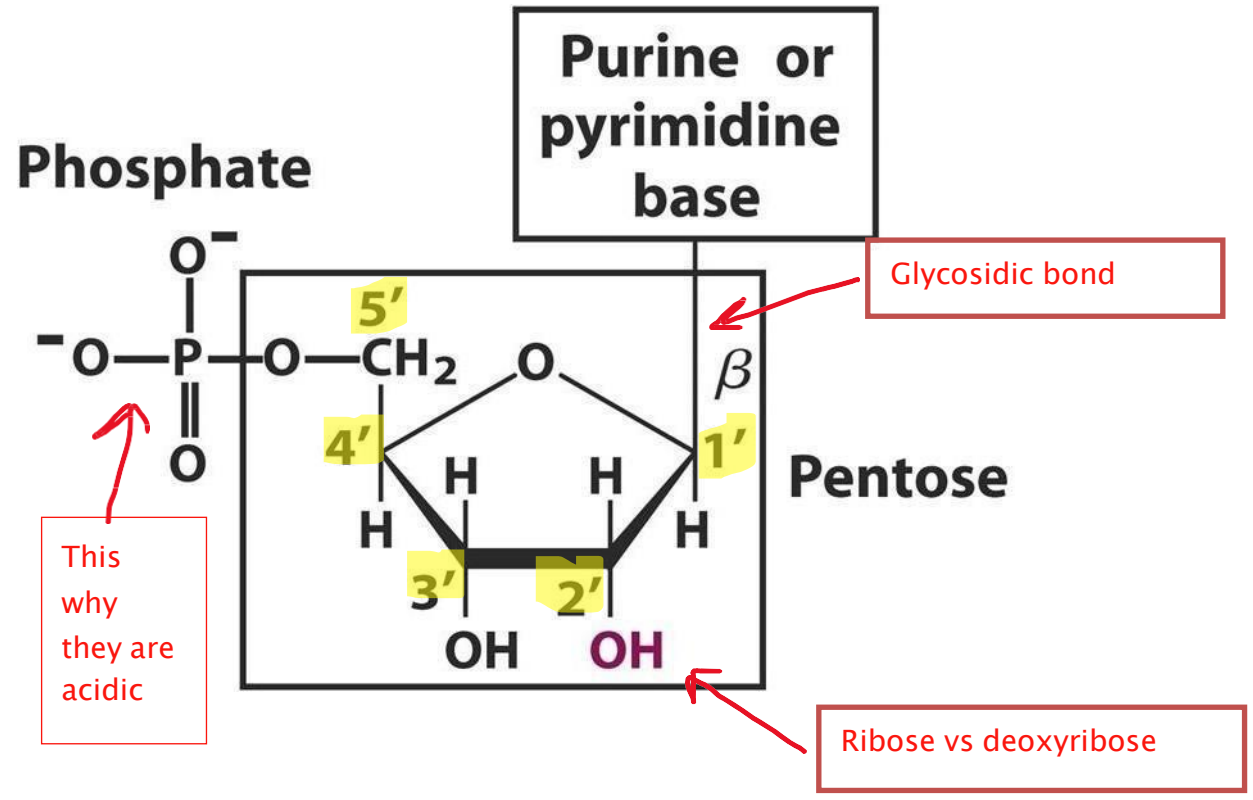
Chemical composition and bonds



The numbers on carbon atoms of sugar are very important:

For example

Carbon no.1: connects with nitrogenic bases (pyrimidines or purines) through glycosidic bond

carbon no.2: determines whether the pentose is ribose(if it is connected with OH) or it is deoxyribose (if carbon 2 is connected with H)

Carbon no .5: connects with phosphate group that gives nucleic acids their acidity)

**note: pentose means a sugar with 5 carbons(penta :5,,ose: sugar)

We use `prime on the carbons of sugar to differentiate them from the carbons in bases

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Nitrogenous bases

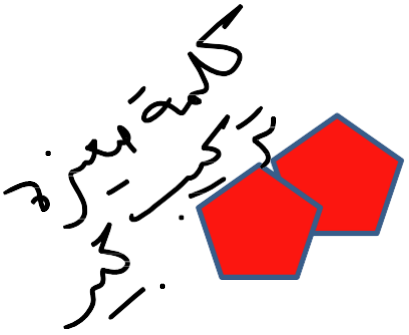
Pyrimidine

Cytosine

Thymine

Uracil

Single ring structure



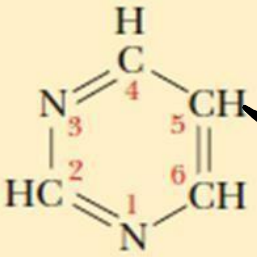
purine

Guanine

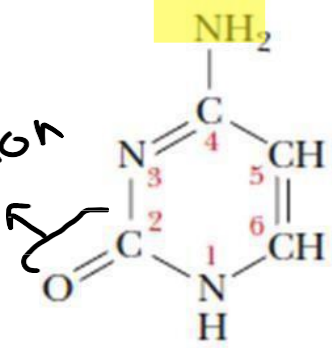
Adenine

double ring structure

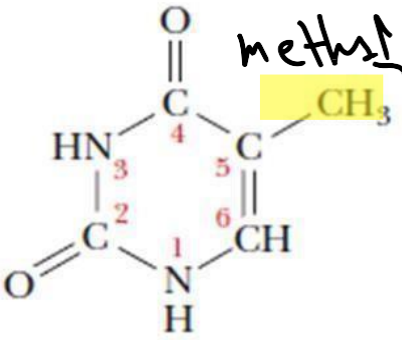
* We need to memorize which of them are pyrimidines and which are purines .we don't need to know the difference in structures between the purines alone or pyrimidines alone*



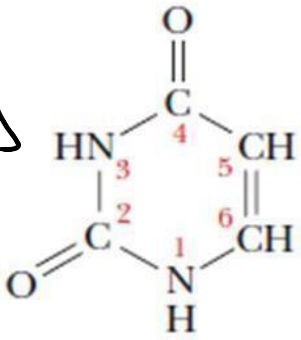
Pyrimidine



Cytosine
(in DNA & RNA)

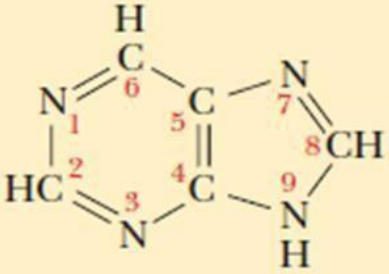


Thymine
(in DNA & some RNA)

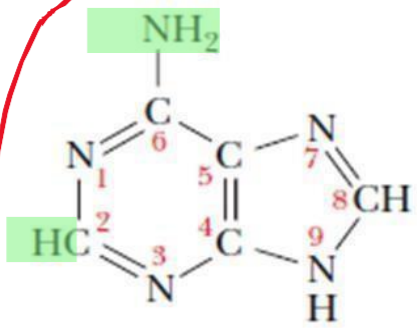


Uracil
(in RNA)

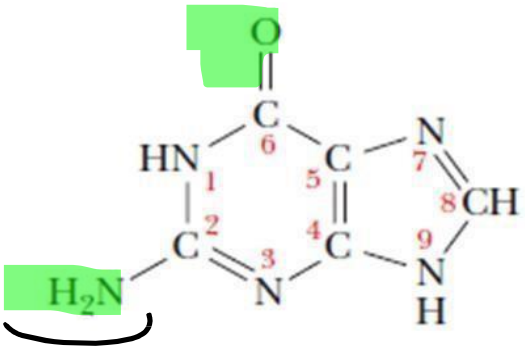
Glycosidic bond



Purine



Adenine
(in DNA & RNA)

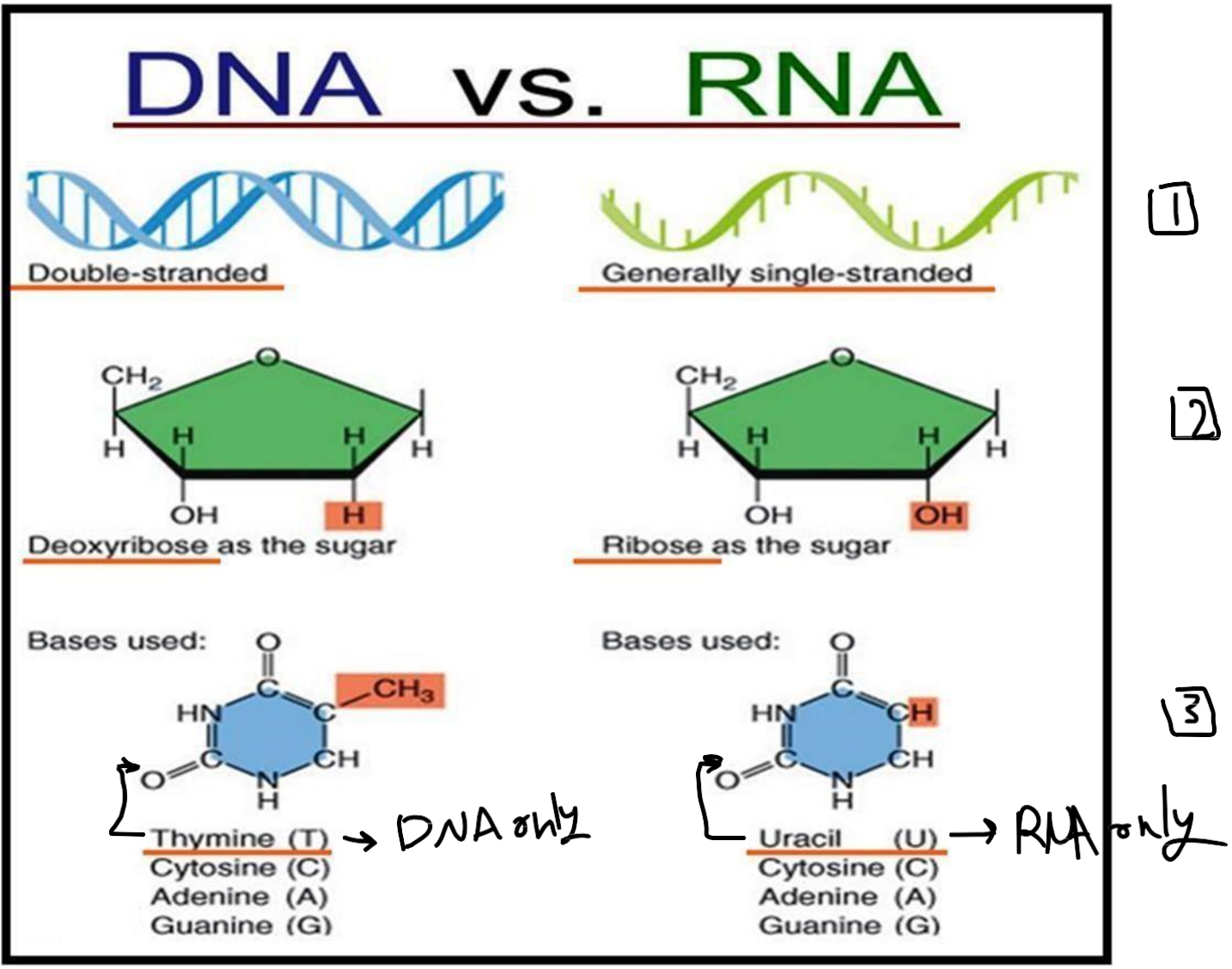


Guanine
(in DNA & RNA)

In small cases like in bacteria but we have to memorize that they are in DNA only

G , A, C→ DNA
U→ RNA
T→DNA

In prokaryotes and eukaryotes not viruses



The image shows the main differences between DNA,RNA

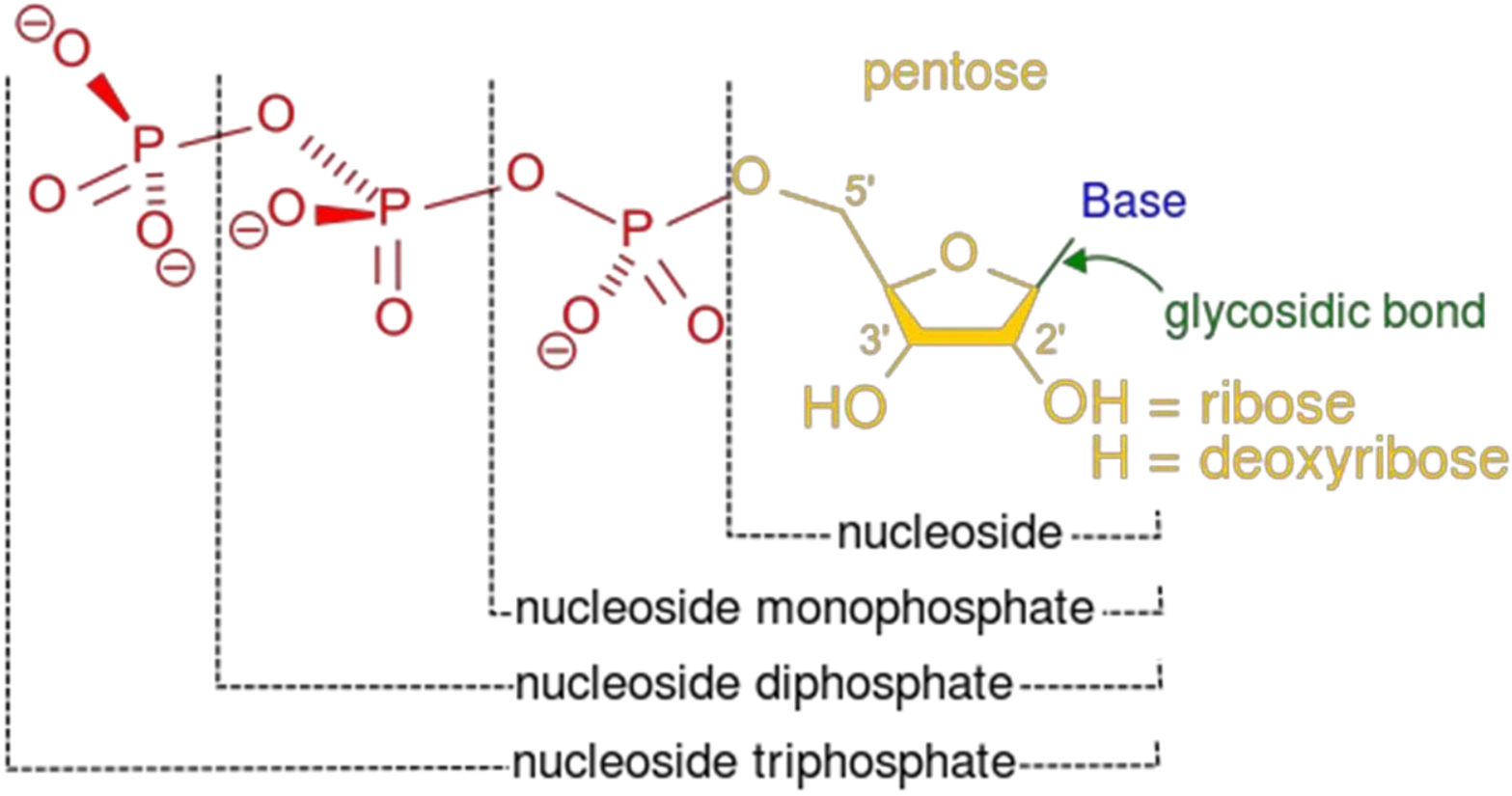
DNA	RNA
Double stranded	Single stranded
Carbon no. 2 in sugar has H ONLY	Carbon no.2 has hydroxyl group OH
Thymine only exists in DNA	Uracil only exists in RNA

- Some exceptions:

  RNA may be found as double stranded so the judge is the type of pentose

  Uracil may be found in DNA if there is a mutation but thymine wont be found in RNA even if there is a mutation

Nucleotides vs. Nucleosides



Nucleoside is sugar with a nitrogen base(no P)

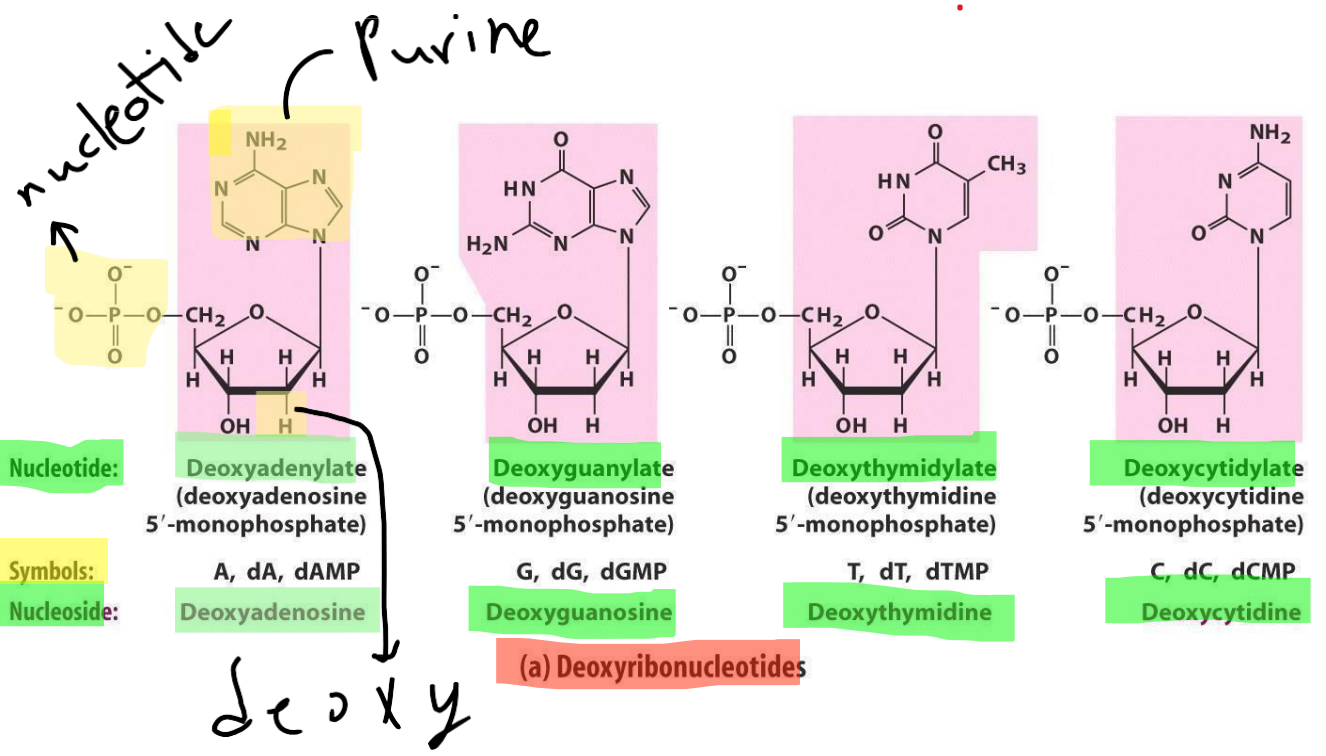
Nucleotide is nucleoside (sugar + nitrogen base) + phosphate

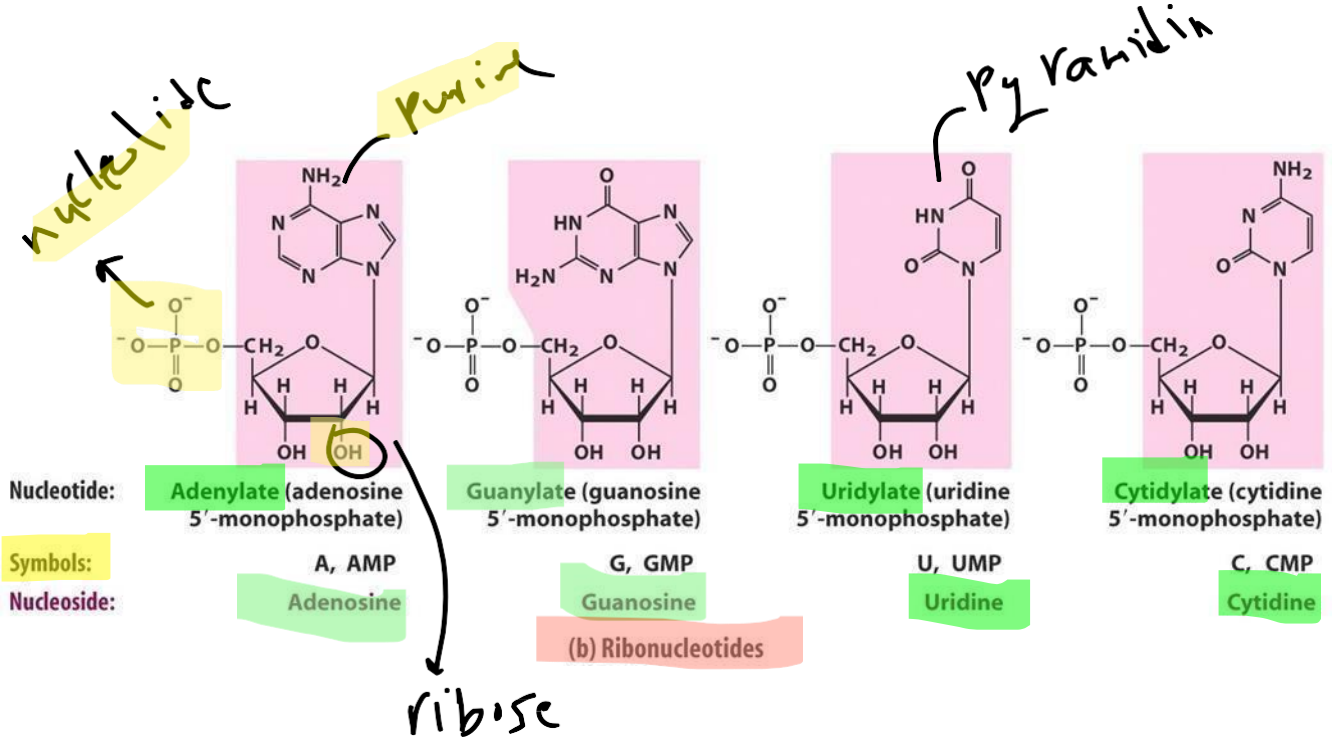
If we add one phosphate to the nucleoside it becomes nucleoside monophosphate

Two phosphates-→ nucleoside diphosphate…etc

We say for example nucleoside monophosphate to specify the name , cause if we say nucleotide we wont know the number of P

Nucleotides vs. Nucleosides





The doctor will ask about the names for the above, so we have to decide:

1. If there is a phosphate it is nucleotide….if there isn't it is nucleoside
2. On carbon 2 of the pentose if there is H it is deoxyribose… there is OH it is ribose

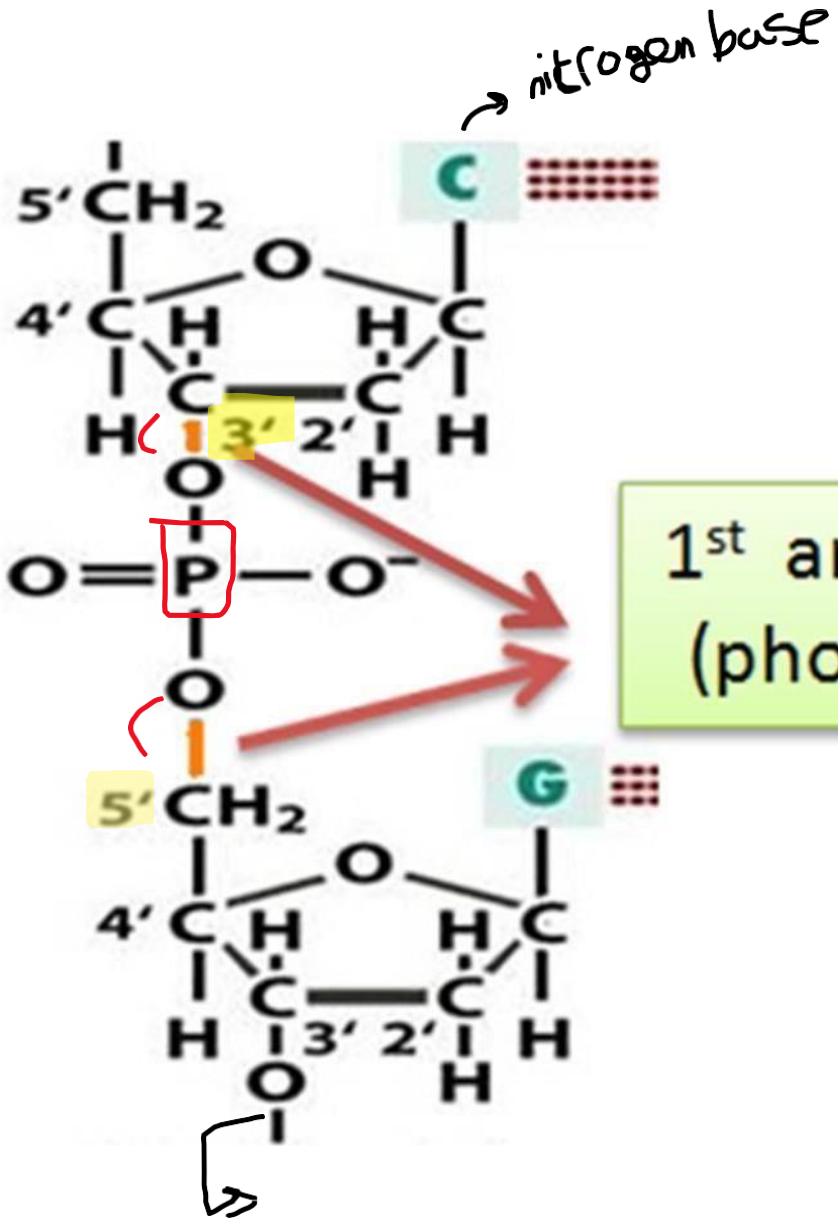
3. About the nitrogen base if it is double ring it is purine…it is single ring it is pyrimidine

He wont ask if it is cytidine or uridine for example cause both are pyrimidines

About symbol when we say dATP : d for deoxy…A for adenine..T: tri…

Formation of a nucleic acid polymer

To get a nucleic acid , nucleotides will connect together by phosphodiester linkage



1st and 2nd ester linkage (phosphodiester bond)

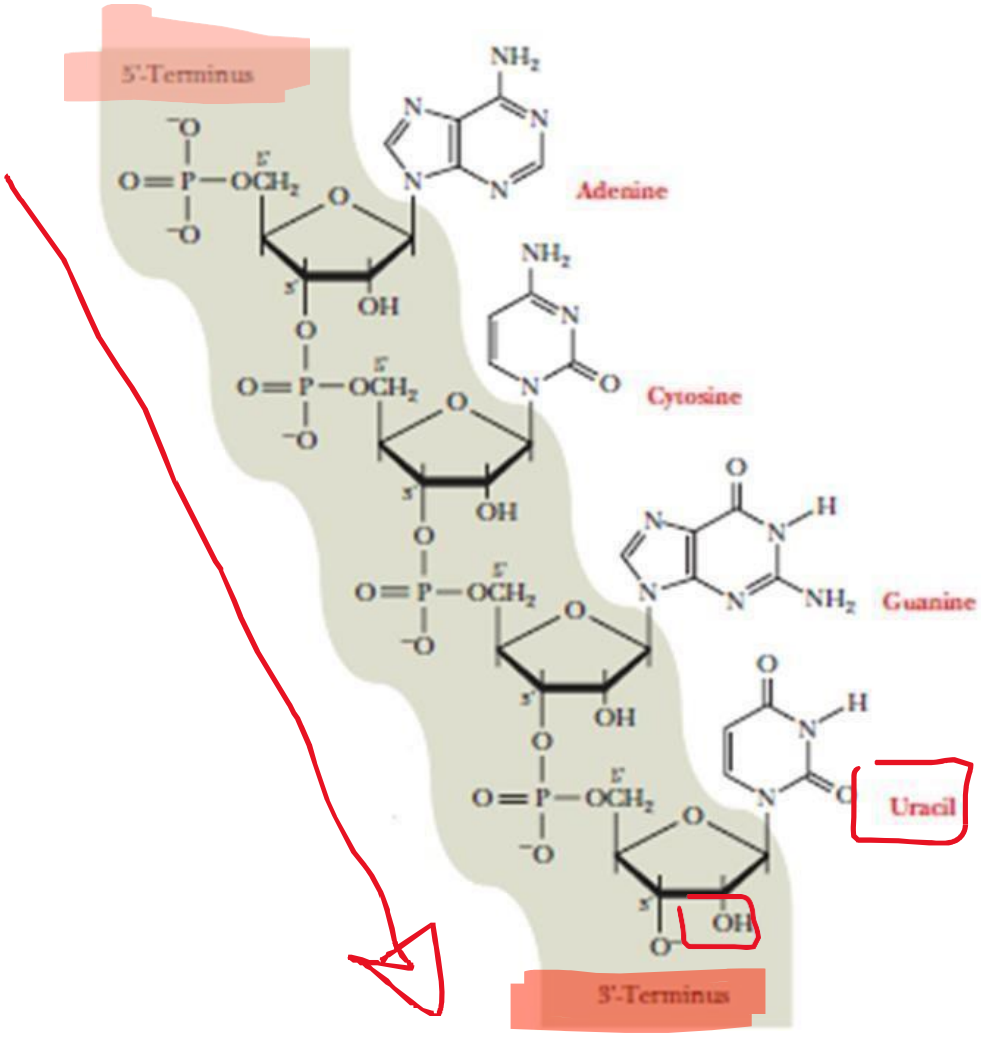
2 esters are mediated by phosphate so the bond is phosphodiester

We can elongate the nucleotide by adding More phosphodiester linkages

Here it is between 3` and 5` mediated by P

Nucleic acid polymers

DNAisapolarmoleculethathasdifferentends(3`and5`)



it is RNA:

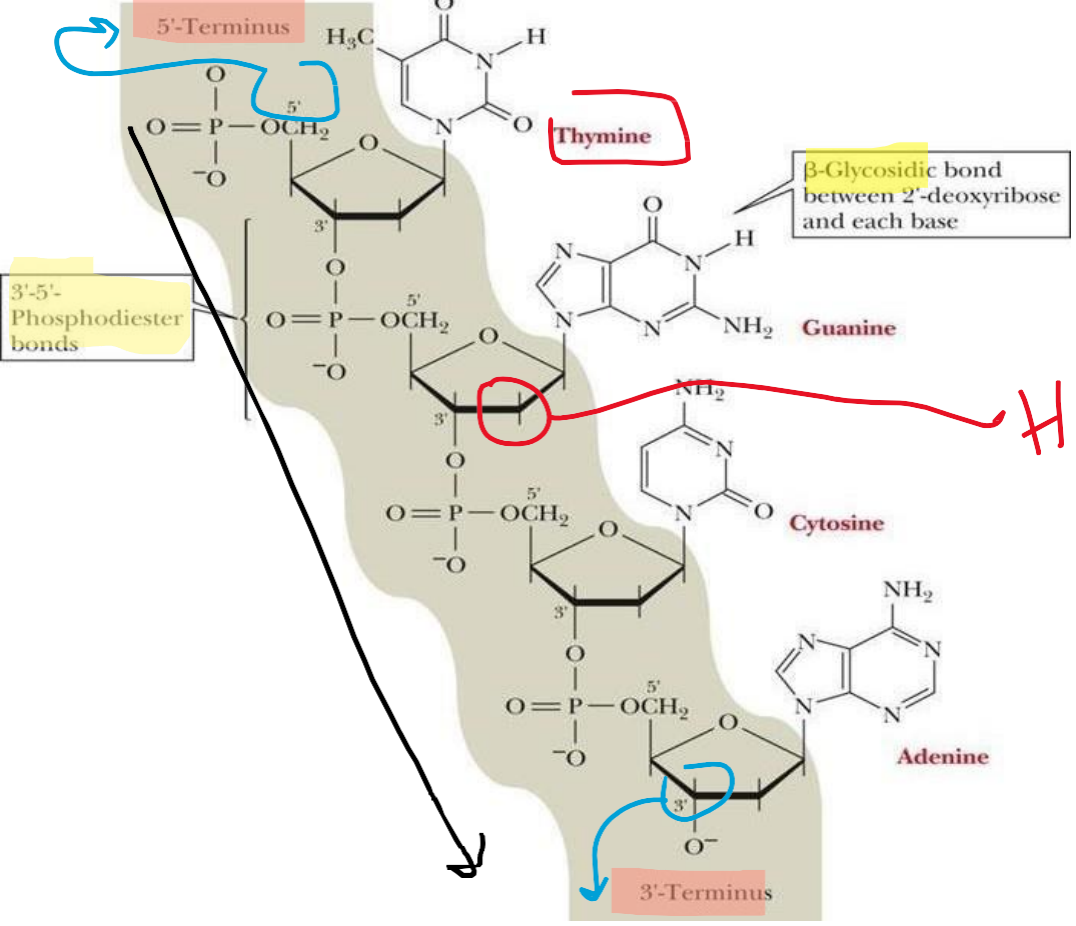
1. Carbon no 2 attaches with OH

It is ribose

2. Carbon no 1 on 3 terminus attaches with Uracil

**the sequence of the nucleotides in this strand is:

ACGU (we read and write from 5`to 3` and the addition is on 3`)



3 2 bonds in this sheet:

1- Glycosidic between pentose and nitrogen base And

2- Phosphodiester in the backbone

3- Hydrogen bonds Between bases

it is DNA

1. The first nitrogen base is Thymine
2. The C no 2 attaches with H only (we don't write it in structural formula) it is deoxyribose

The sequence or order of nitrogen bases is (TGCA)

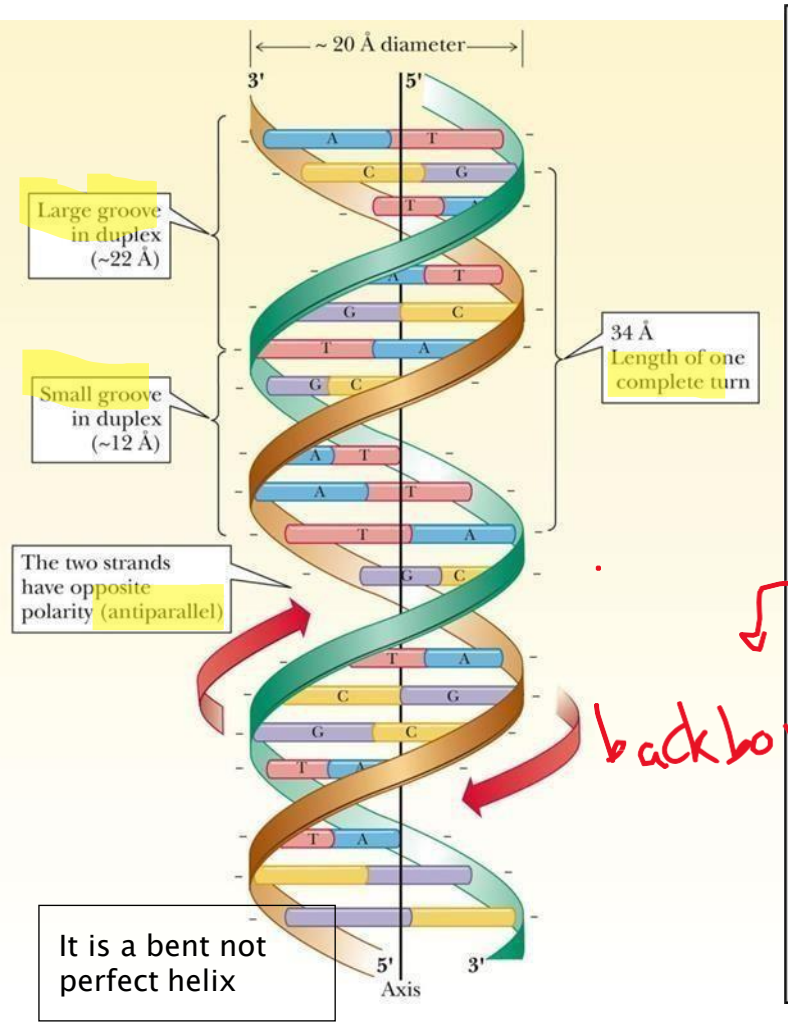
*to know if the terminus is 3` or 5` we look on the C no 3 if it is 3` so the terminus is 3` and the same for 5`

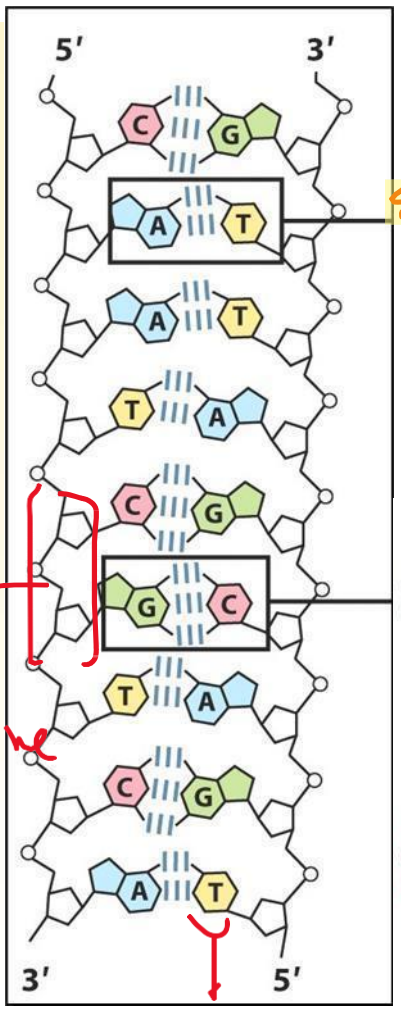
*A letter d can be added to indicate a deoxyribonucleotide residue. If we say TGA it means DeoxyT,dG,dA

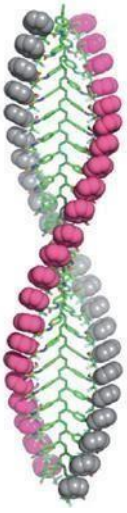
*for example, dG is substituted for G(Guanine).

*The deoxy analogue of a ribooligonucleotide would be d(GACAT).

DNA structure







it is a uniform perfect helix

DNA characteristics:

1*DNA is A double helix

2*Specific base-pairing

A = T; G = C; Pur = pyr

3*Complementary

4*Backbone vs. side chains

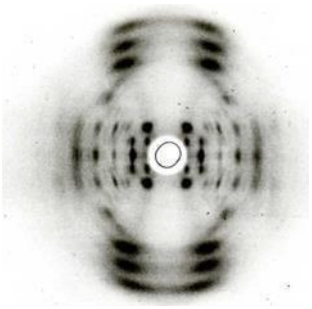
Backbone : phosphate +pentose

Side chain: nitrogen bases(T,A,..)

5*Antiparallel

6*Stability vs. flexibility

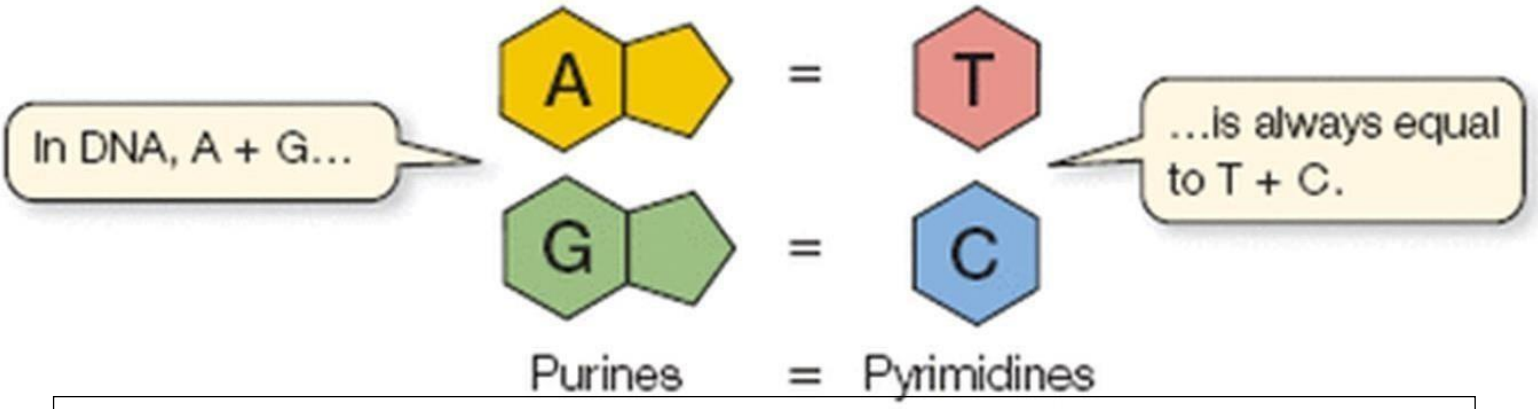
7*Groovings



a crystallographic image

James Watson and Francis Crick were the first who describe that DNA is a double helical structure

Chargaff's rules



#the number of T=THE number of A

#the number of G=THE number of C

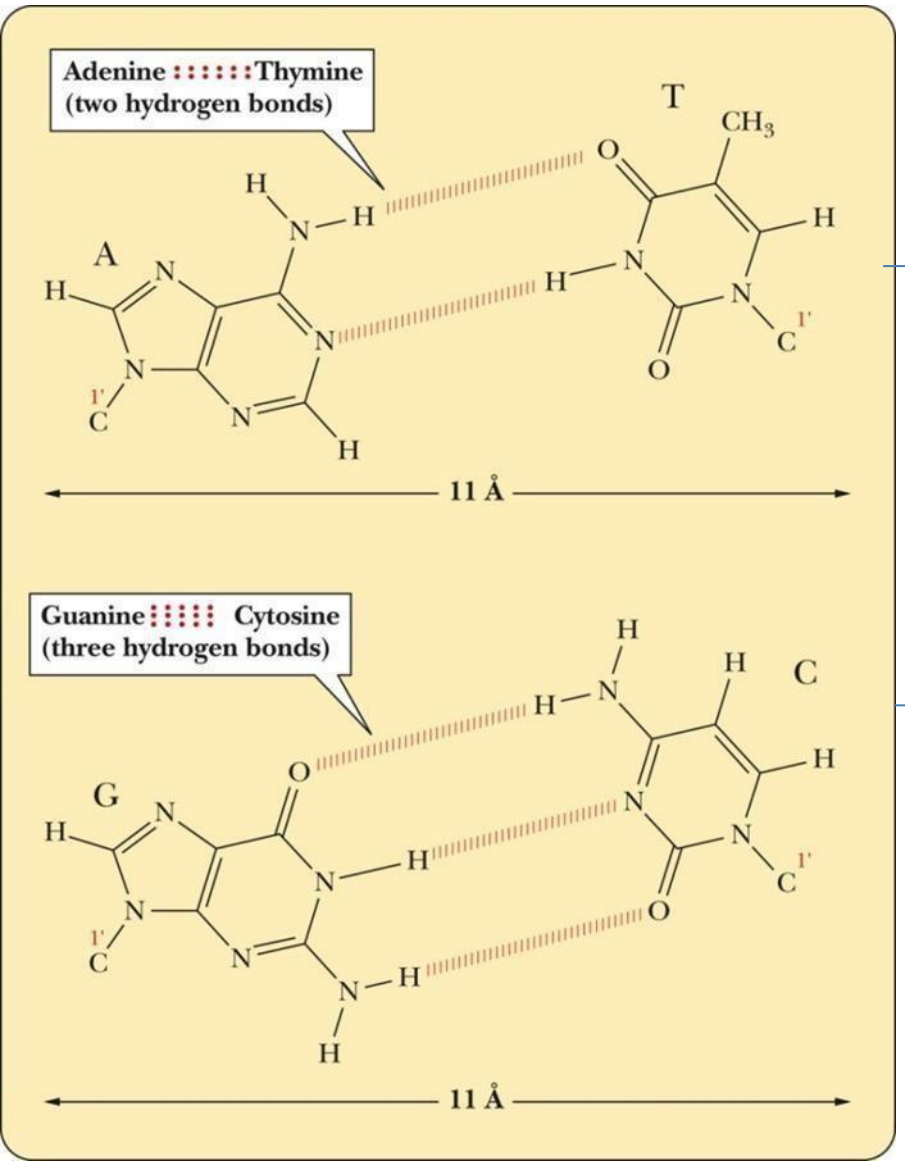
#G+C+A+T+100%

#G+C ≠A+T...(it depends on DNA)

#A+G=T+C

PURINES=PYRAMIDINES

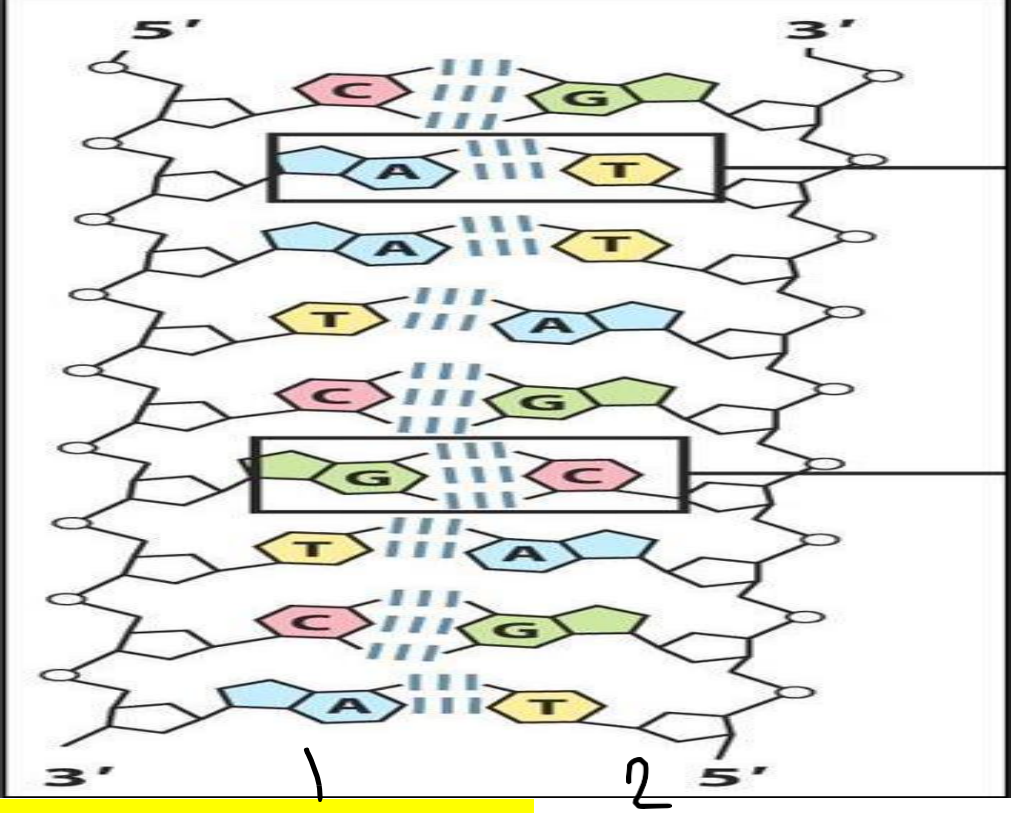
Base pairing



A connects with T
NON COVALENTLY
By 2 hydrogen bonds

G connects with C
NON COVALENTLY
By 3 hydrogen bonds

non covalent bonds help in stability of DNA



DNA is complementary: is a property shared between two nucleic acid sequences, such that when they are aligned antiparallel to each other, the nucleotide bases at each position will be complementary.:A with T

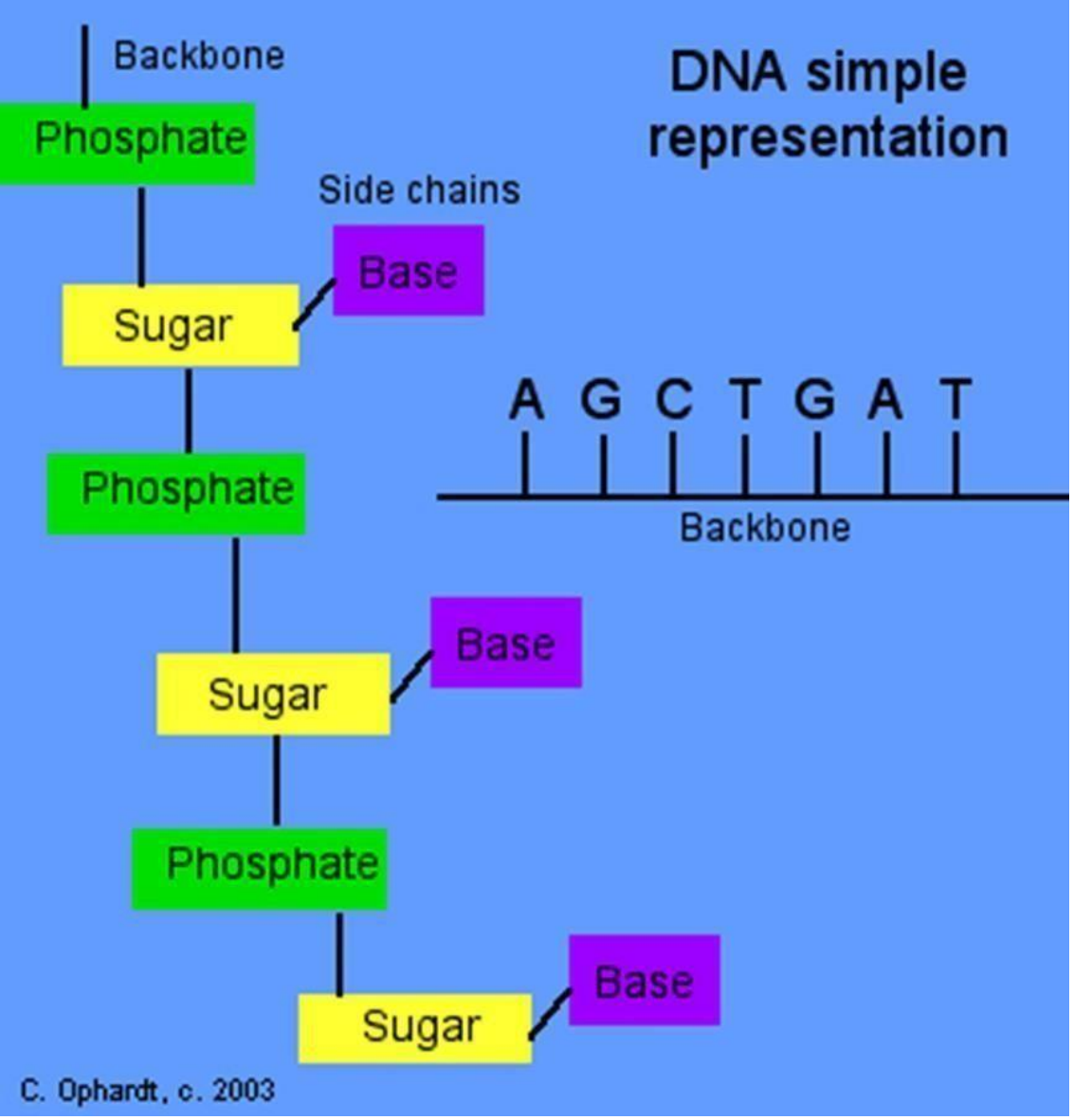
G with C

The sequence for 1 is : 5' CAATCGTCA 3'

The sequence for 2 is : 3' GTTAGCAGT 5'

CAATCGTCA

GTTAGCAGT

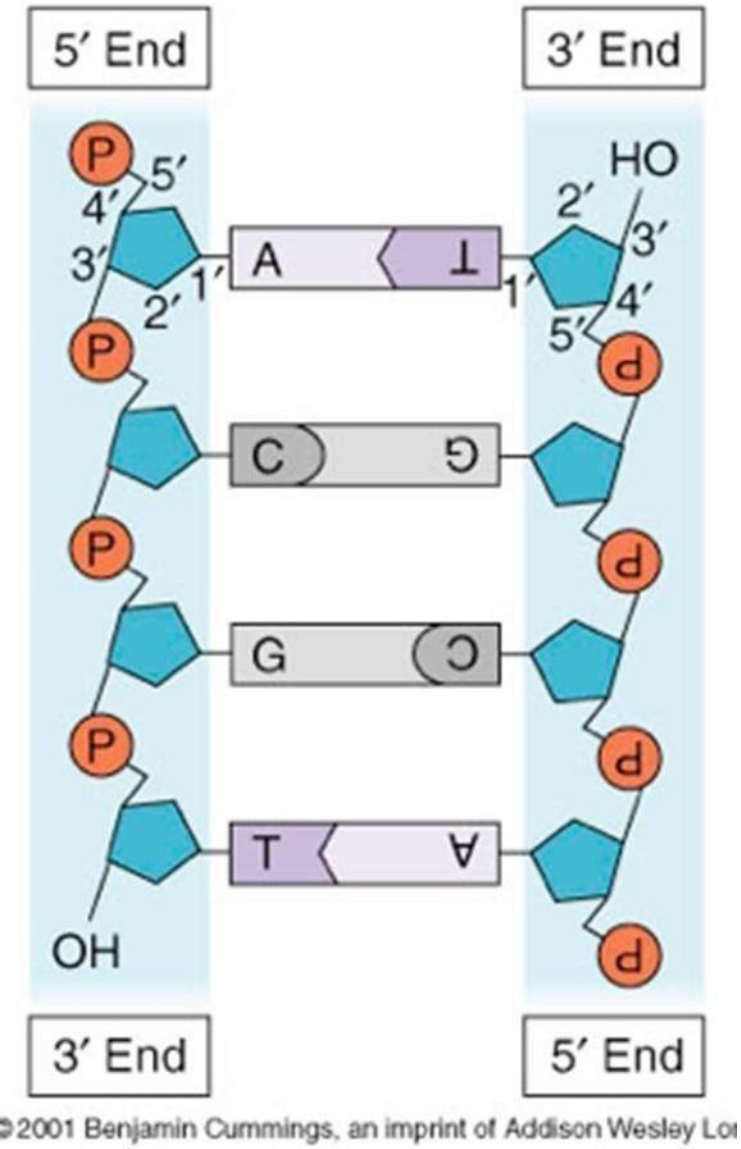


Backbone vs. side chains

P + sugar

A/T/C/G

The base is usually perpendicular on the backbone



DNA is Antiparallel

The 2 strands are side by side but run in opposite directions.

3`faces 5` in the complement strand

5` faces 3` in the complement strand

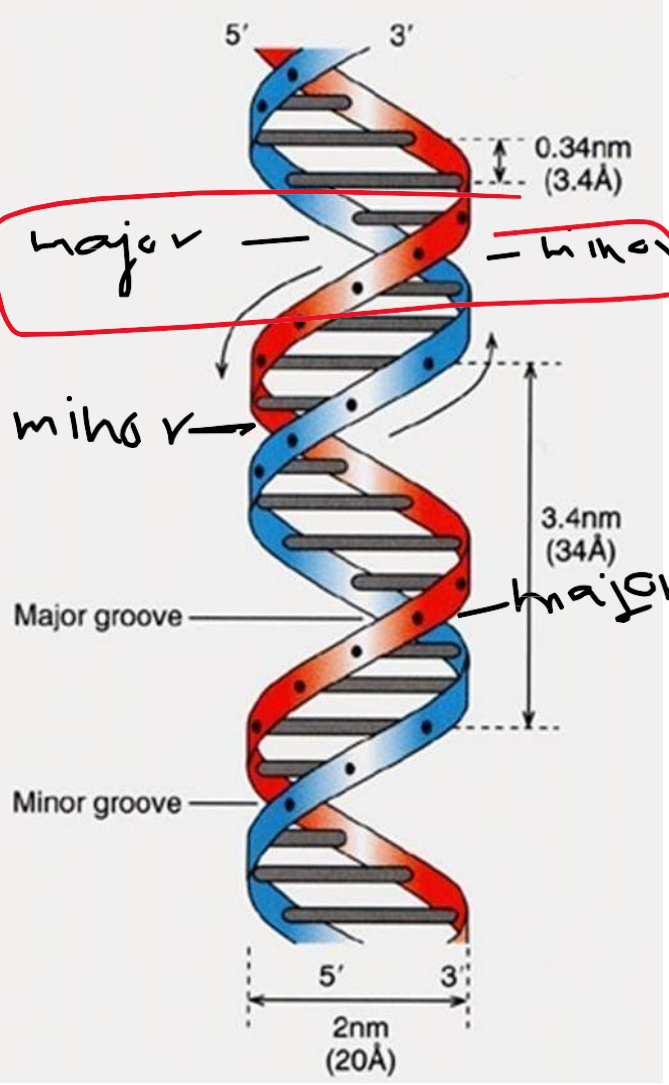
DNA is flexible, yet stable

DNA is not perfect .There are irregular angles on its sides which make it flexible and stable(can be bent to interact with proteins)

DNA grooves

:because DNA isn't perfect so it has grooves the irregular angles on its sides:

Minor groove (the small groove) and Major groove(its space is larger than minor, it allows DNA to interact with proteins)

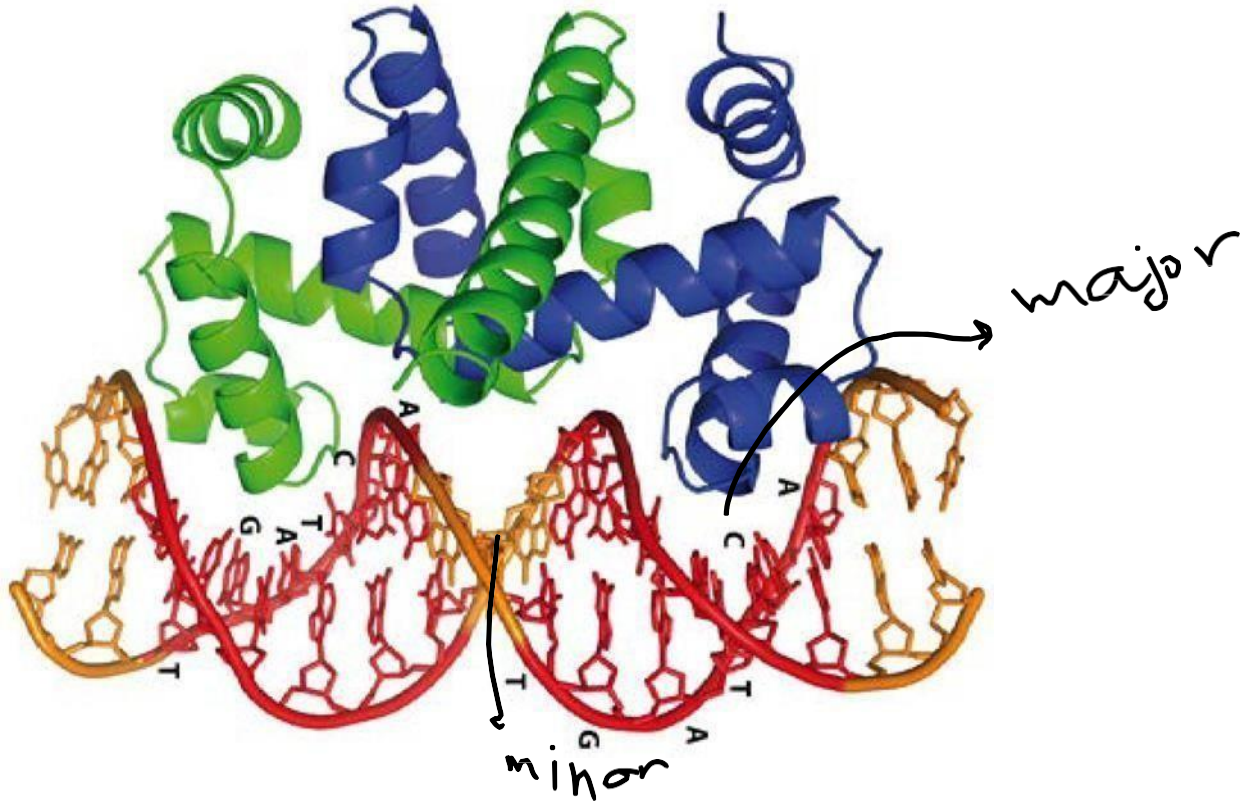


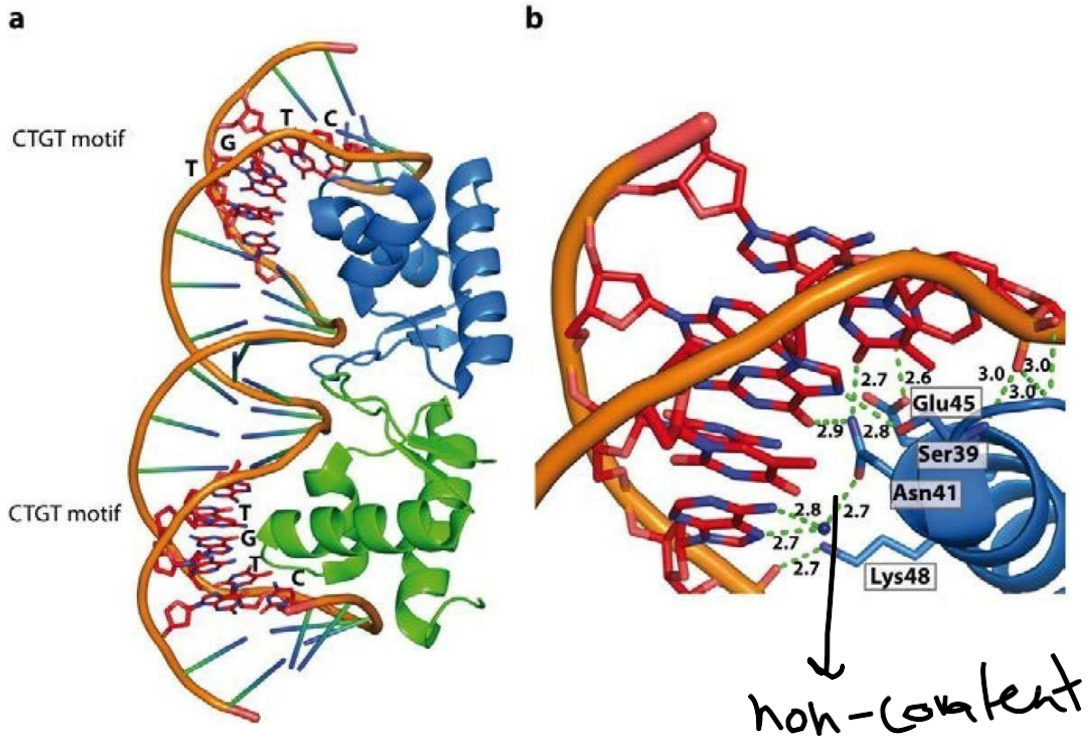
the importance for this groove is to facilitate the ineraction between proteins and DNA

proteins insert themselves in the major groove and interact with exposed nucleotides ,some of small part can insert themselves in minor

** that is why specific proteins interact with specific AA that will insert in specific grooves

Amino Acids





Biochemistry is about non covalent bond
They are 4 forces:
Van der waals (London)
Hydrophobic
Electrostatic
H bonds

Writing the sequence of nucleic acids

DNA

5' ...A T G G C C T G G A C T T C A... 3'
3' ...T A C C G G A C C T G A A G T... 5'

OR

A T G G C C T G G A C T T C A

We write from 5` to 3`

DNA has 2 strands

DNA has T which is not found in RNA

*when we write the sequence we don't have to write where 5` is , it is known that it is the beginning
And if we write the complementary below we don't need to write that 3` is opposite to 5` it is known
But if we write the complementary alone we have to write from 5` terminus

RNA

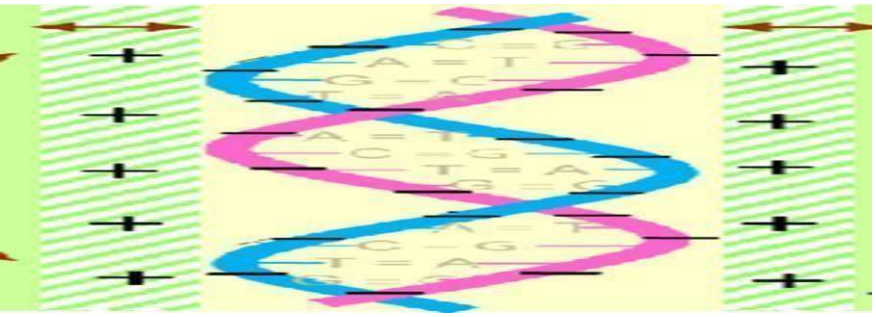
5' ...A U G G C C U G G A C U U C A... 3'

One strand...has U

Ions stabilize DNA

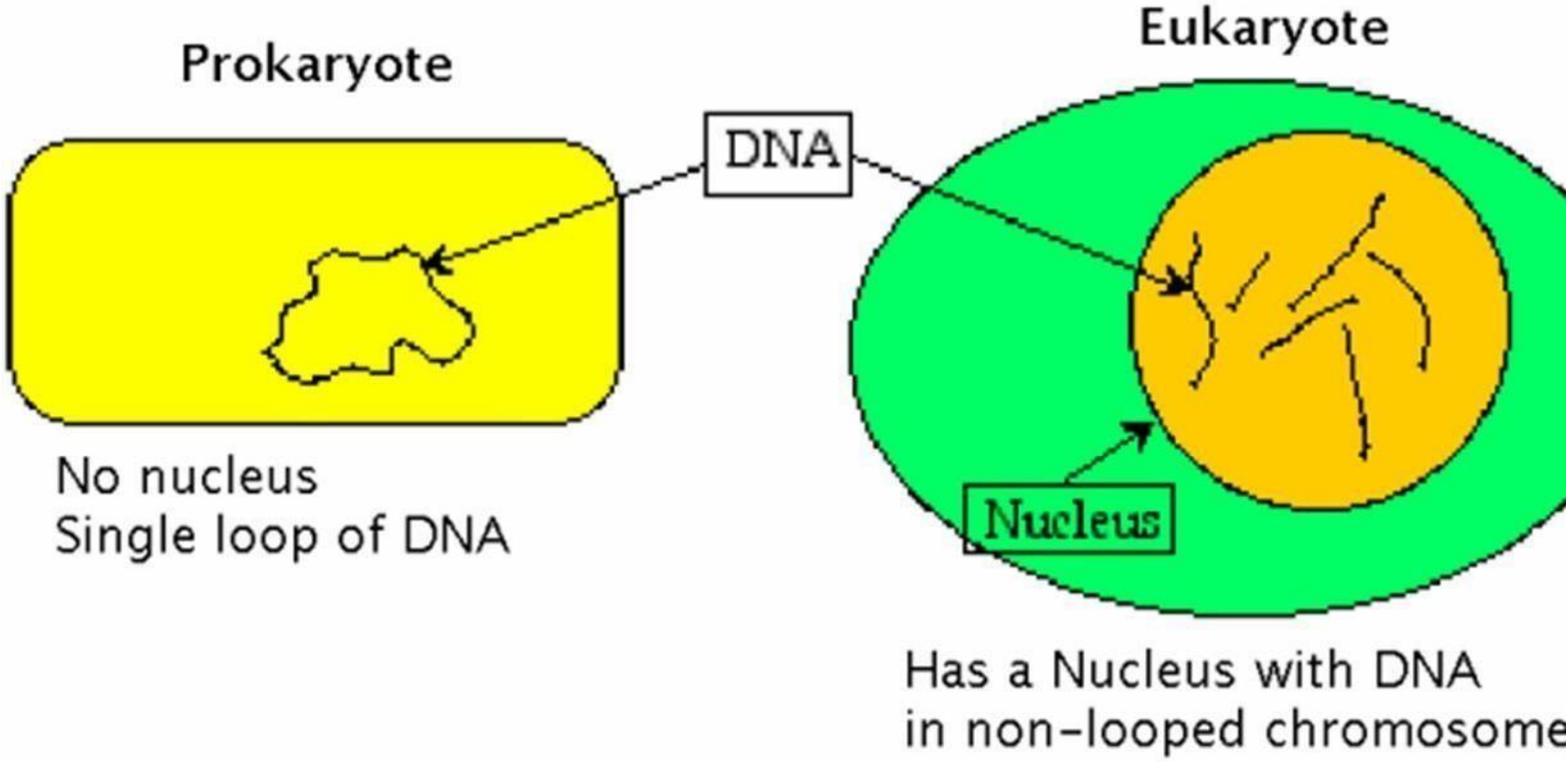
There is so much repulsion among the negative charges of the phosphates, so the -ve charges will attract Positively charged ions (Na+ or Mg2+) associate with the phosphate groups.

Example: histones(which is highly +ve protein because it has +ve amino acids like Lysin)



Prokaryotes versus eukaryotes

↳true



DNA in prokaryotes is circular

DNA in Eukaryotes is linear (individual units) enclosed inside nucleus

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In eukaryotes…

*In eukaryotes, DNA is coiled to package the large DNA.

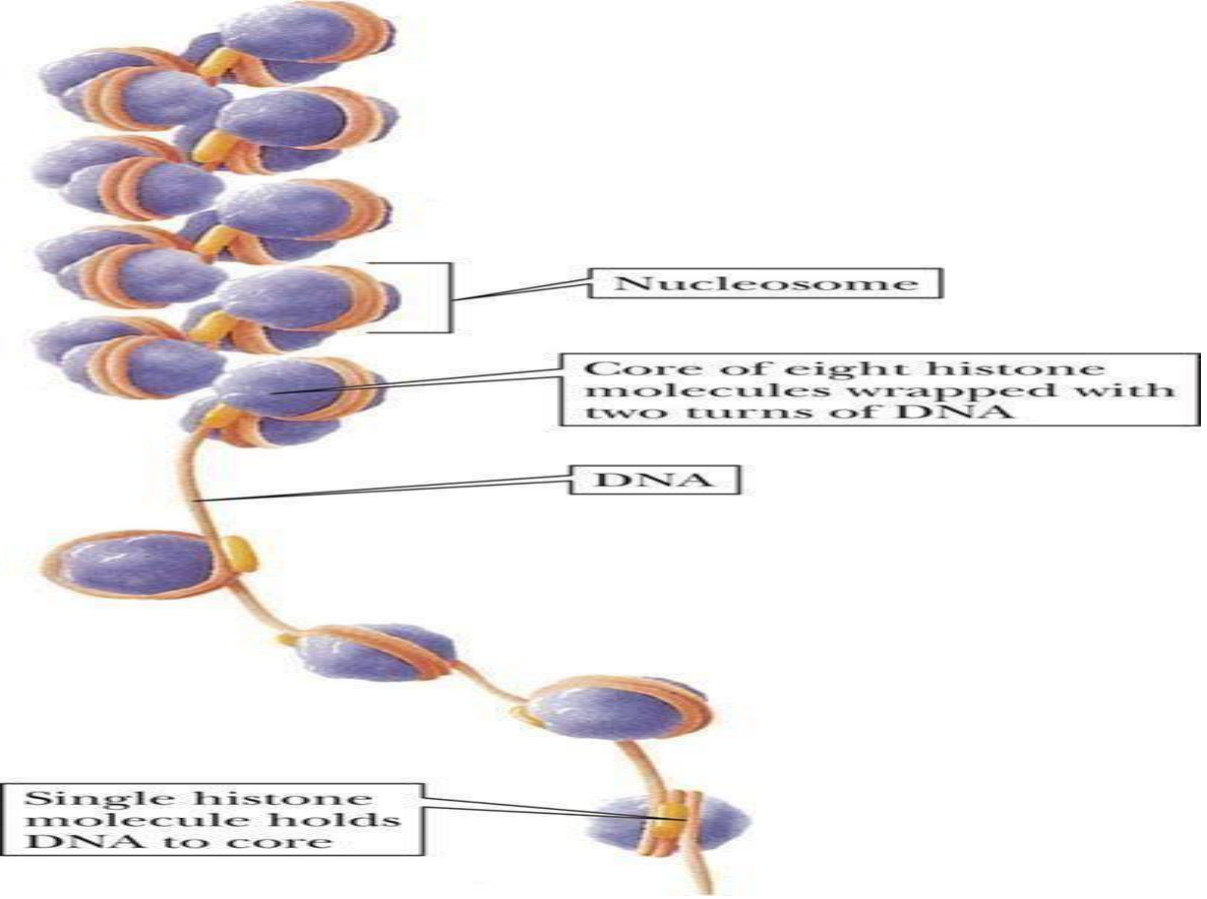
*Eukaryotic DNA is complexed with a number of proteins, principally histones, which package DNA.

*Chromatin = DNA molecule + proteins.

*The basic structural unit of chromatin is known as a nucleosome.(many nucleosomes give chromatine)

*there are 5 types of histone , 4 of them are used in octamer (H2A,H3,H4,H2B)….2 molecules of each

H1 is used to steal the interaction between DNA and octamer



Nucleosomes

*A nucleosome consists of DNA wrapped around a nucleosome 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.it is the free part , remaining part of DNA after wrapping

Histone H1 is bound to the octamer and wrapped DNA (a chromatosome).

**Histones are positively charged facilitating DNA interaction

and charge neutralization.

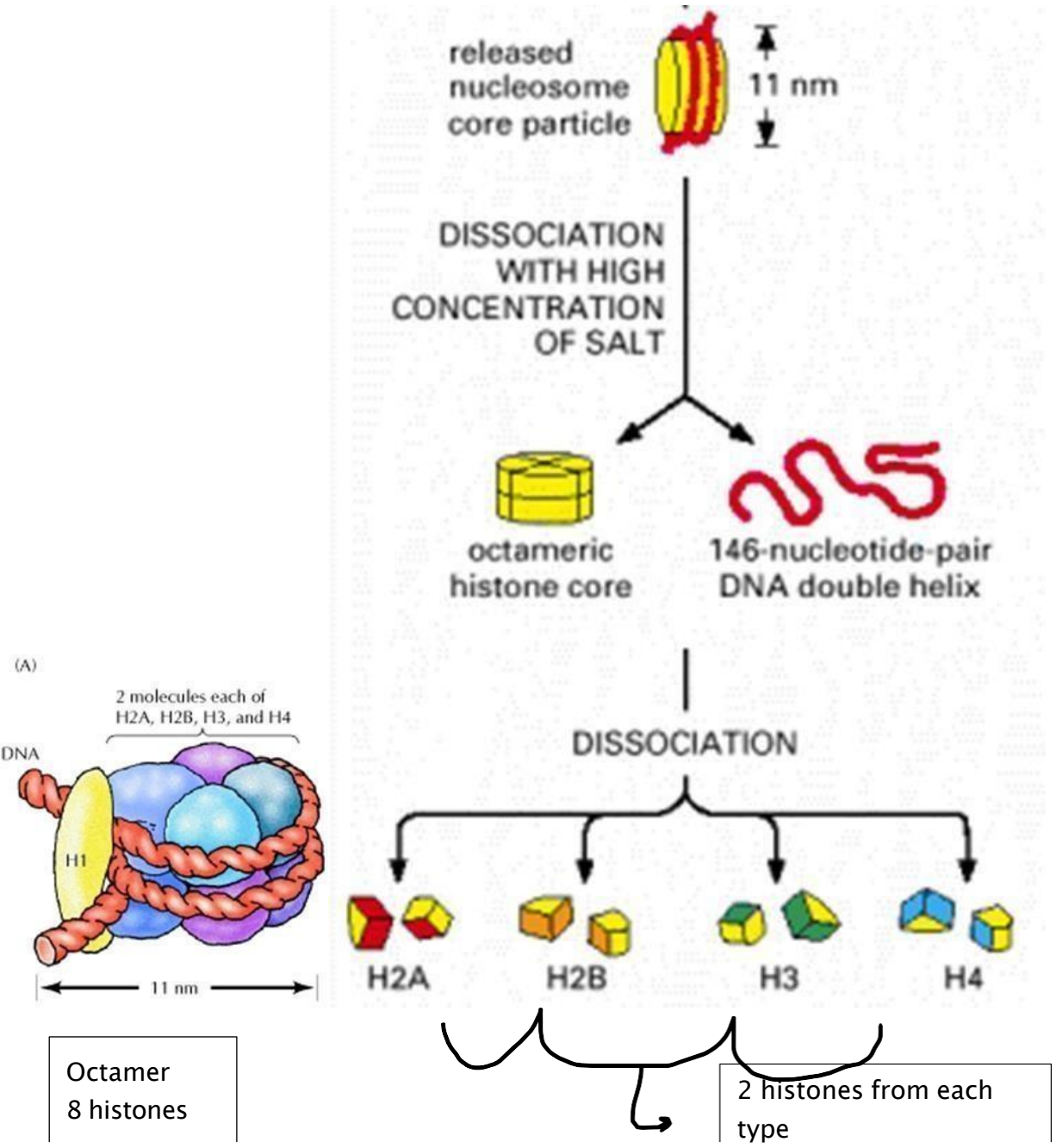
Octamer(means 8 histones)+DNA=nucleosome core particle

Nucleosome core particle+H1=chromatosome

Chromatosome +free DNA(DNA linker)= nucleosome

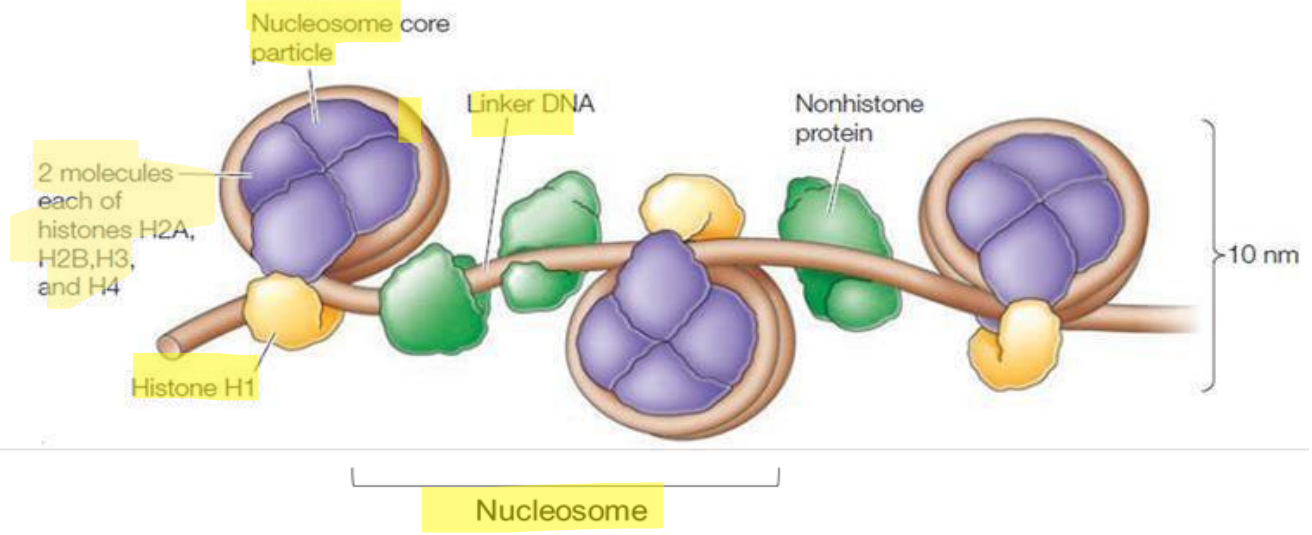
Many nucleosomes give chromatin(Compact DNA with proteins)

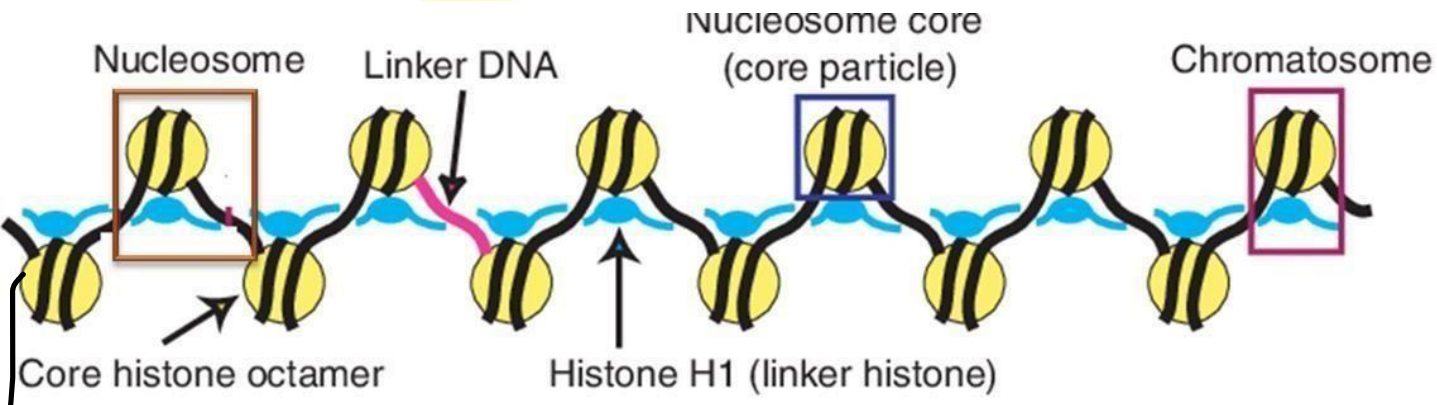
Chromatin will pack to give chromosome



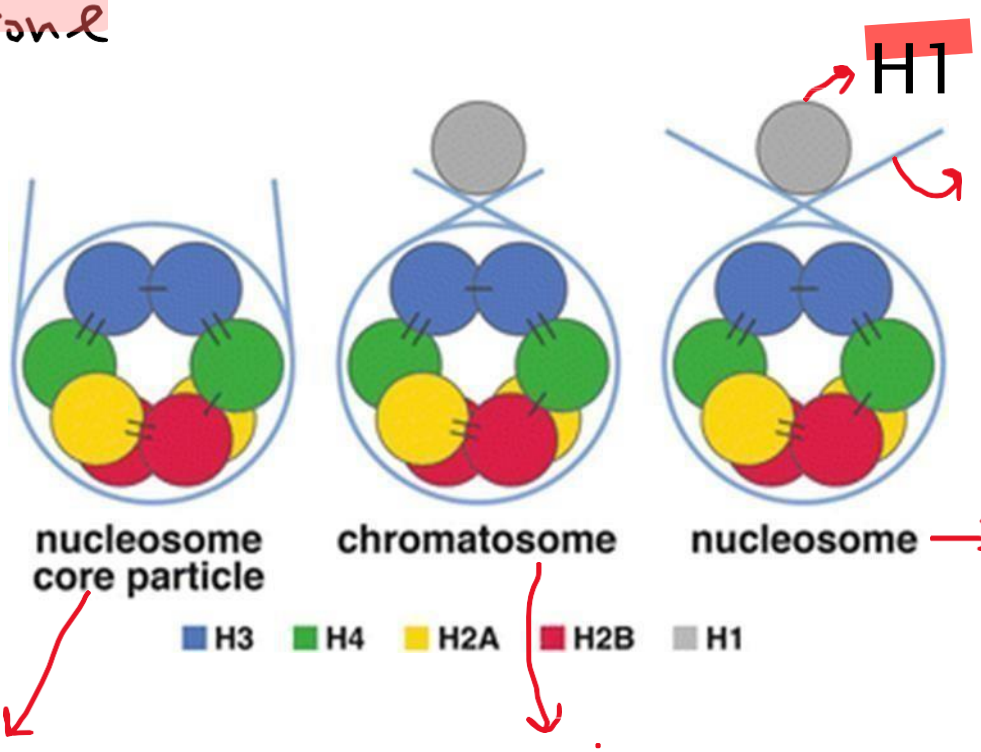
Octamer
8 histones

2 histones from each type





histone



Not always exist

DNA linker

Chromatosome+DNA linker

Octamer+DNA

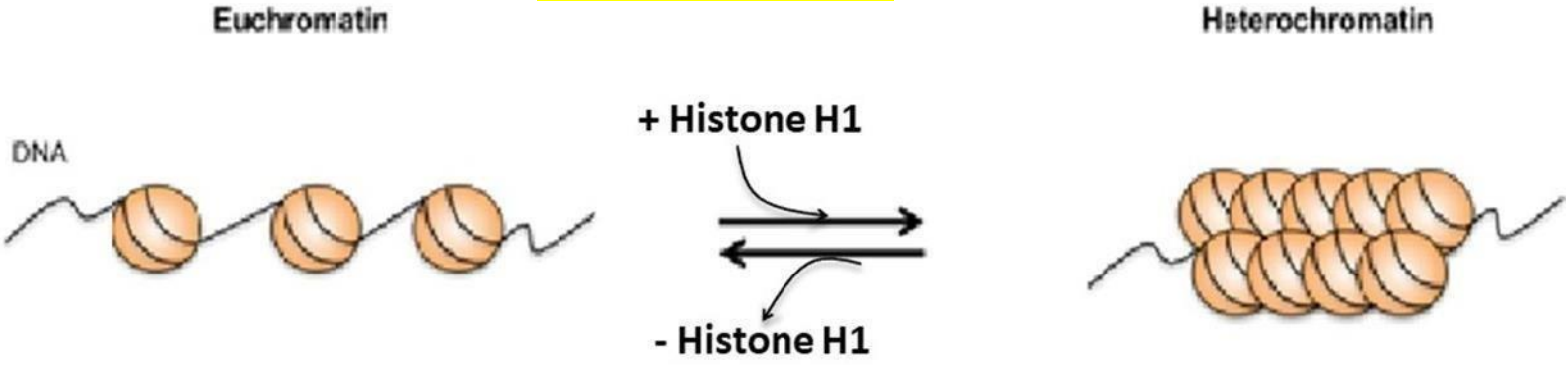
nucleosome core particle+H1

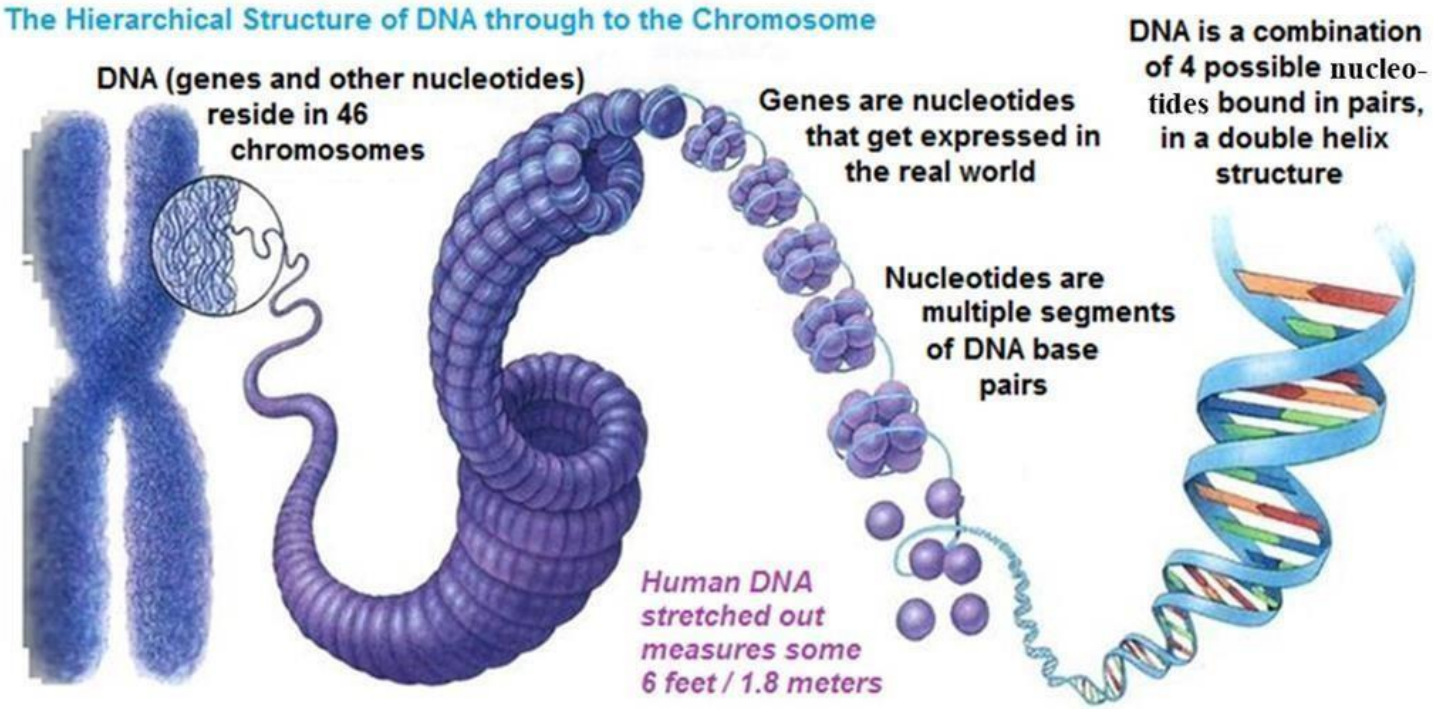
Histones package chromosomes

*the importance of H1 is to make the DNA highly packed forms what we call heterochromatin(compact)

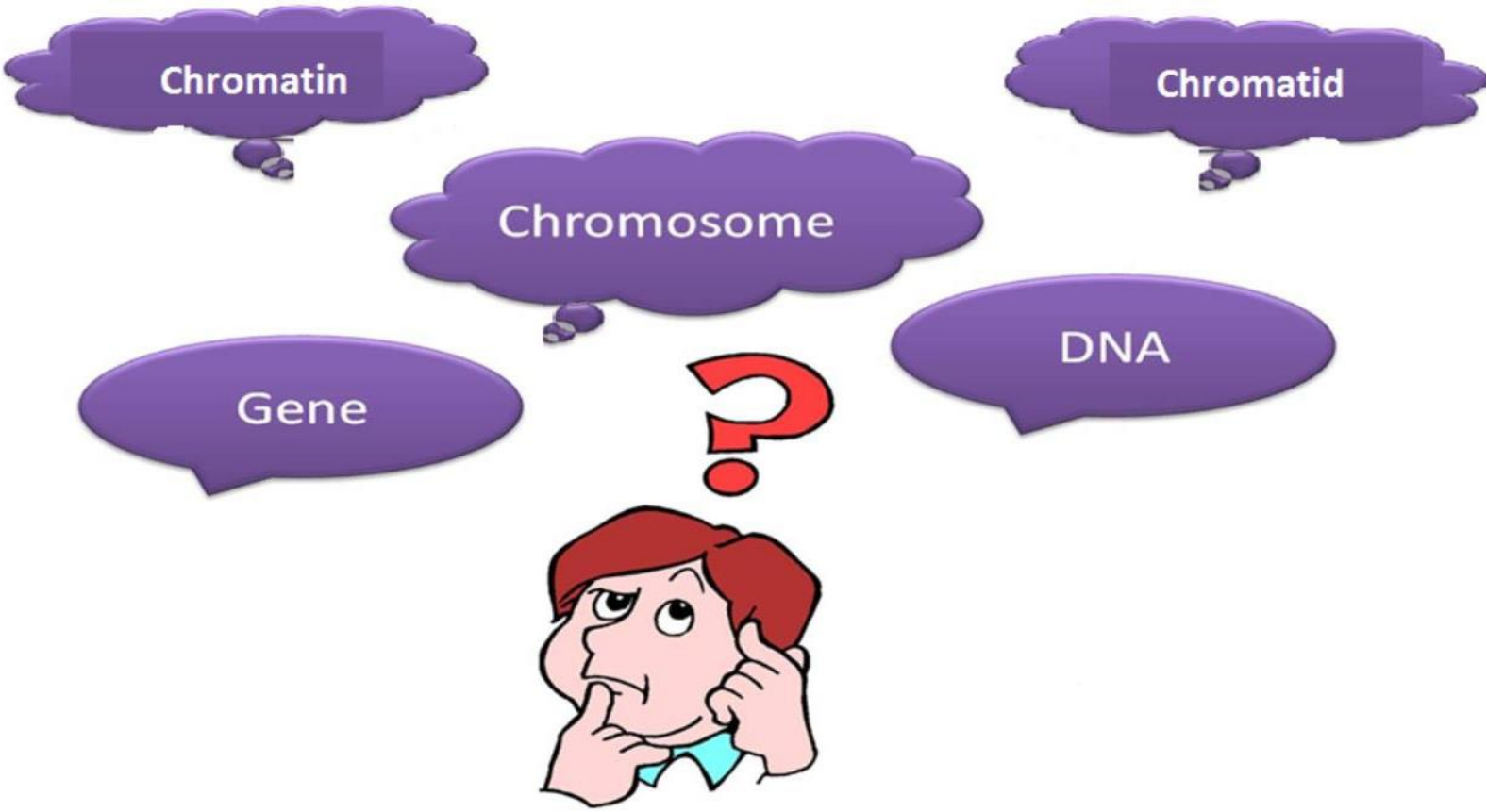
If H1 is removed then the DNA will be flexible

Forms what we call euchromatin(loose)



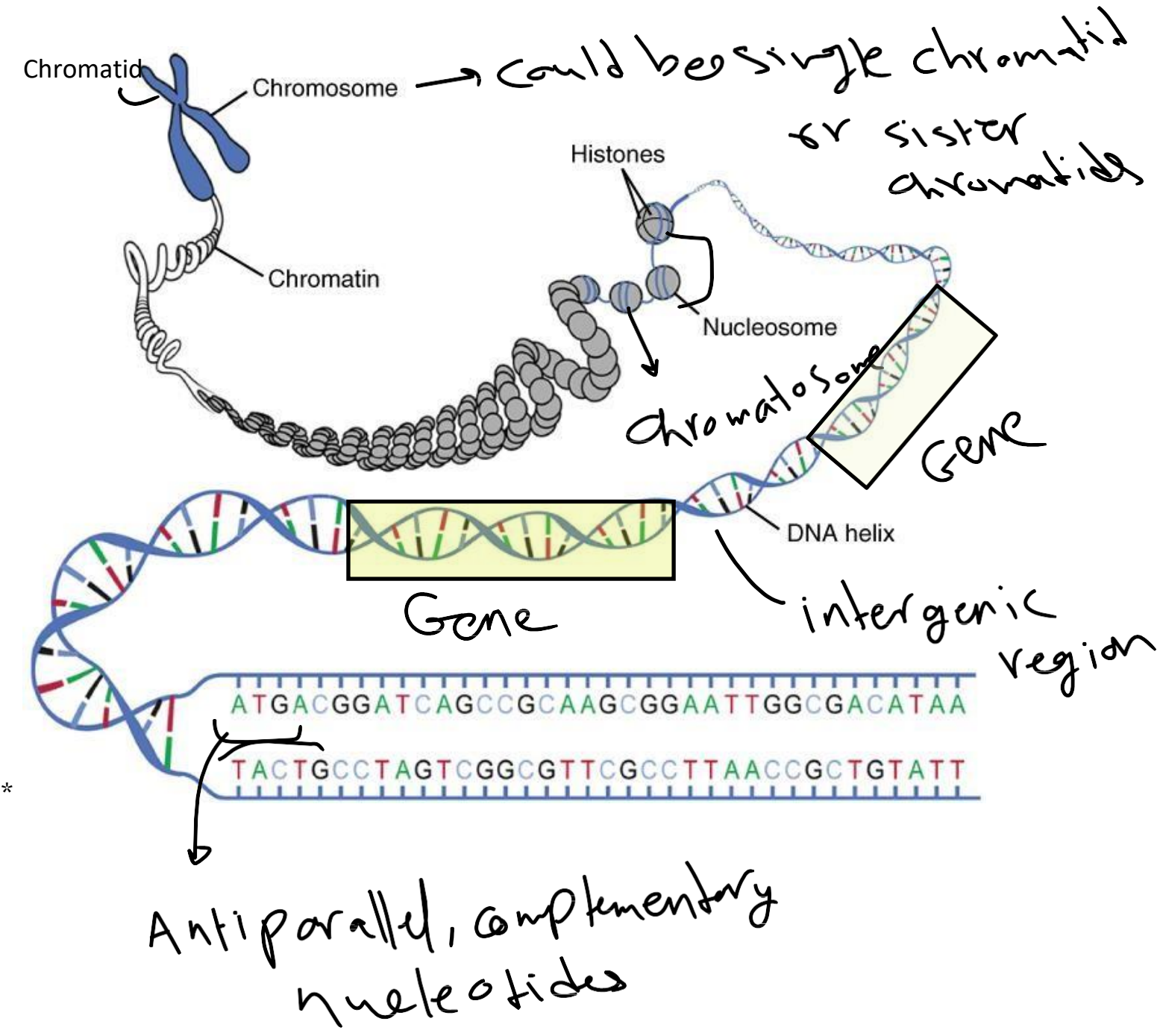


Terms to know



* chromosome:chromo: means color,,,some: boby
They discovered a body that can be colored so they called it colored body(chromosome) and the same to chromatid , chromatin and so on
*chromosome: is a complete structure of DNA molecule (in our cells we have one arm of chromosome that is called chromatid)
*when cells undergo miosis , chromosome duplicates its chromatid so we get 2 chromatids called sister chromatids that form chromosome.
If we zoom the chromosome: we see DNA+ proteins(chromatin)
-if they are highly packed …. heterochromatin
- if they are loosely packed ….euchromatin
Another more zoom:
Free DNA linker+ chromatosome(histones+ DNA)=nucleosome
*zoom:
We get DNA: double stranded helical molecule
Each strand has nucleotide
They are complementary and antiparallel to each other
*gene:certain sequence of nucleotides….another sequence will encode(not code,,code is ACG for example) another gene

The region between genes is intergenic region



*

Nucleotide→gene→ DNA→nucleosome→chromatin→chromatid→ chromosome

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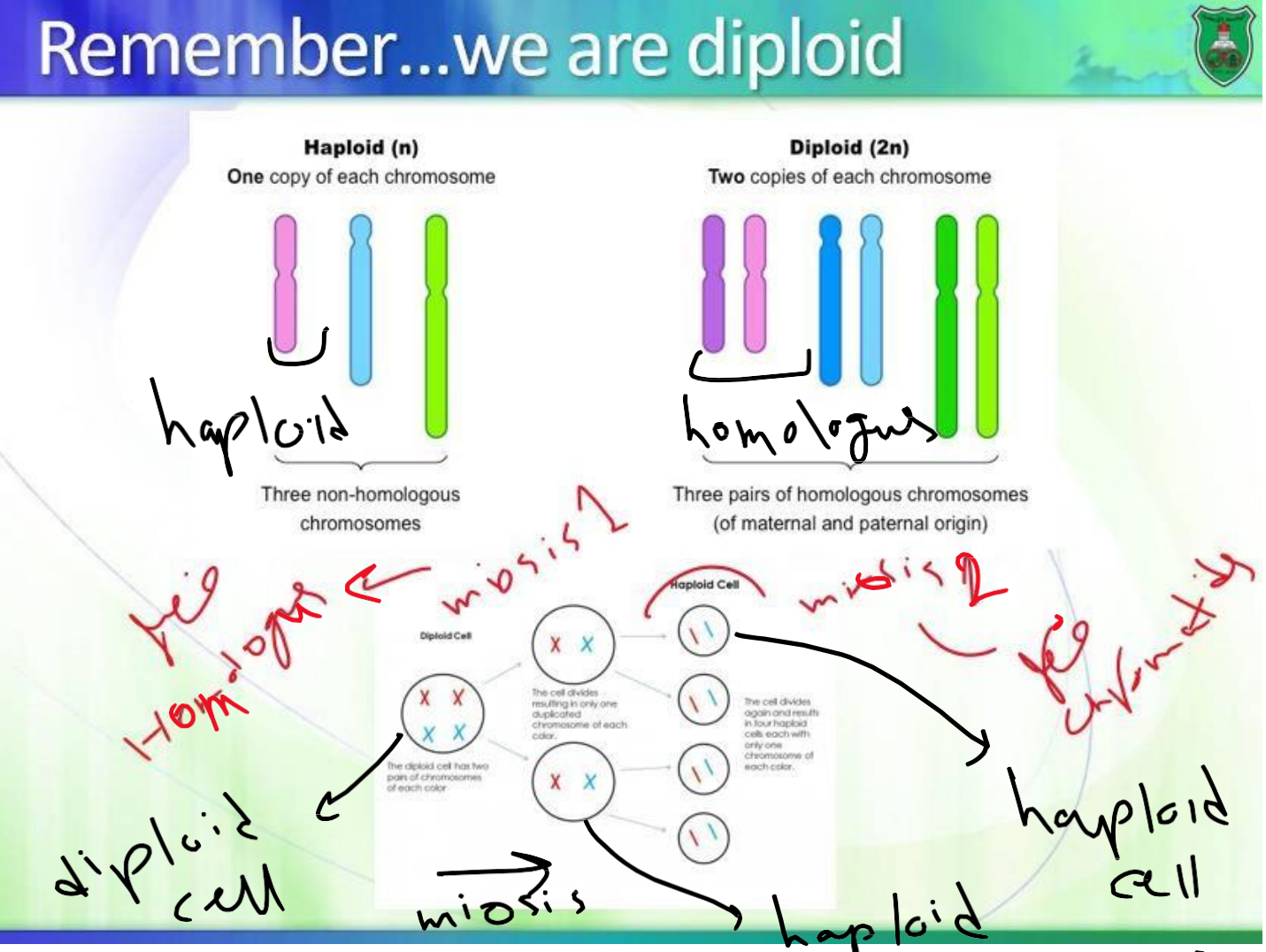
*Our cells are diploid

*one full chromosome it is haploid

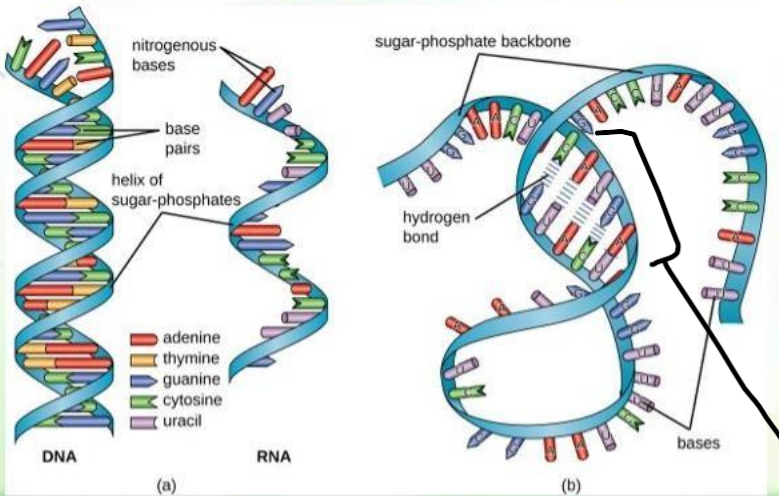
* 2 copies of chromosome(maternal and paternal) it is diploid we call them homologus chromosomes



RNA

* has no branches
*usually DNA is double helical strand and RNA is single stranded but there are always some exceptions
*RNA can form different structures within these structure we have the formation of hydrogen bonds

- It consists of long, unbranched chains of nucleotides joined by phosphodiester bonds between the 3'-OH of one pentose and the 5'-PO_4^- of the next.
- The pentose unit is a ribose (it is 2-deoxyribose in DNA).
- The pyrimidine bases include uracil and cytosine (thymine and cytosine in DNA).
- In general, RNA is single stranded (DNA is double stranded).



RNA does not have a precise structure, but it can fold on itself forming hydrogen bonds within the same molecule.

Bases are complementary to each other
They can form among RNA bases themselves by looping of RNA

Different molecule …different dimensional structures (like DNA and RNA)

*when we write RNA sequence we have to illustrate if we start writing from 3 terminus or 5 terminus

Types of RNA

The common 3 types are(mRNA, tRNA, rRNA)

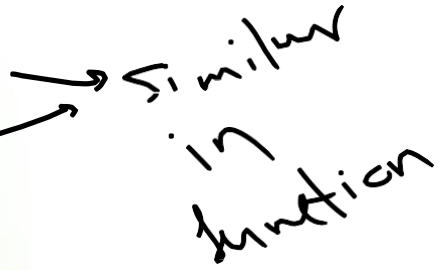
But scientists have discovered different RNA molecules in number , structure ….

*the table below will be discussed with details later on

the starred RNAs are the required

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



Past paper:

1. What is the maximum number of phosphate groups that can be attached to pentose sugars in nucleotides?

A) 1
B) 2
C) 3
D) 4
E) there is no specific max number.

Answer: C

2. Nitrogenous bases are attached to each other by:

A) hydrogen bonds
B) ionic bonds
C) glycosidic linkages
D) phosphodiester bonds
E) disulfide bridges

Answer: A

3. Each nucleotide is attached to the other nucleotide by:

A) ionic bonds
B) phosphodiester bonds
C) hydrogen bonds
D) glycosidic linkages
E) disulfide bridges

Answer: B

4. Nitrogenous bases are attached to sugar molecules by:

A) hydrogen bonds
B) ionic bonds
C) glycosidic linkage
D) disulfide bridges
E) phosphodiester bonds
Answer: C

5. The lowest level of DNA packaging:
A) 30 nm fiber
B) naked DNA molecule
C) chromosomes
D) nucleosomes
E) more than one of the above
Answer: D

6. RNA molecules contain an additional oxygen atom compared to DNA molecules located on which carbon atom of the pentose sugar:
A) 1
B) 2
C) 3
D) 4
E) 5

Answer: B

7. The glycosidic bond that exists in nucleosides is between:

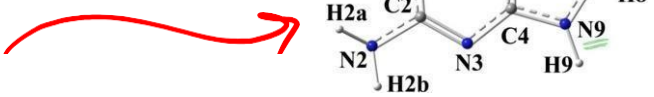
A) 3’ carbon of sugar and N9 of adenine

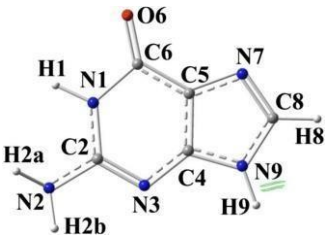
B) 1’ carbon of sugar and N1 of guanine

C) 5’ carbon of sugar and N1 of cytosine

D) 1’ carbon of sugar and N9 of guanine

E) 5’ carbon of sugar and N1 of thymine





C1: it is the C of sugar where nitrogen base attaches

purines attach at N9

pyrimidines attach at N1

Answer: D

8. Which one of these statements about nitrogenous bases is TRUE

A) Adenine and thymine are purines.

B) cytosine and guanine are pyrimidines.

C) guanine is a purine and Adenine is a pyrimidine.

D) Adenine is a purine and uracil is a pyrimidine.

Answer: D