*Advances in molecular biology have led to significant discoveries concerning the mechanisms of the embryonic development, disease and immunologic response.

Introduction

- Molecular biology is the study of biological molecules and the molecular basis of structure and function in living organisms.
- The field of molecular biology arose from the meeting point of work of geneticists, biochemists, physicists, and structural chemists on a common problem: (the structure and function of the gene.)
- The goal of molecular biology is to understand the cell growth (1), division (2), specialization (3), movement (4), and interaction (5) in terms of various molecules that are responsible for them. So we understand why the cell behaves like this?!

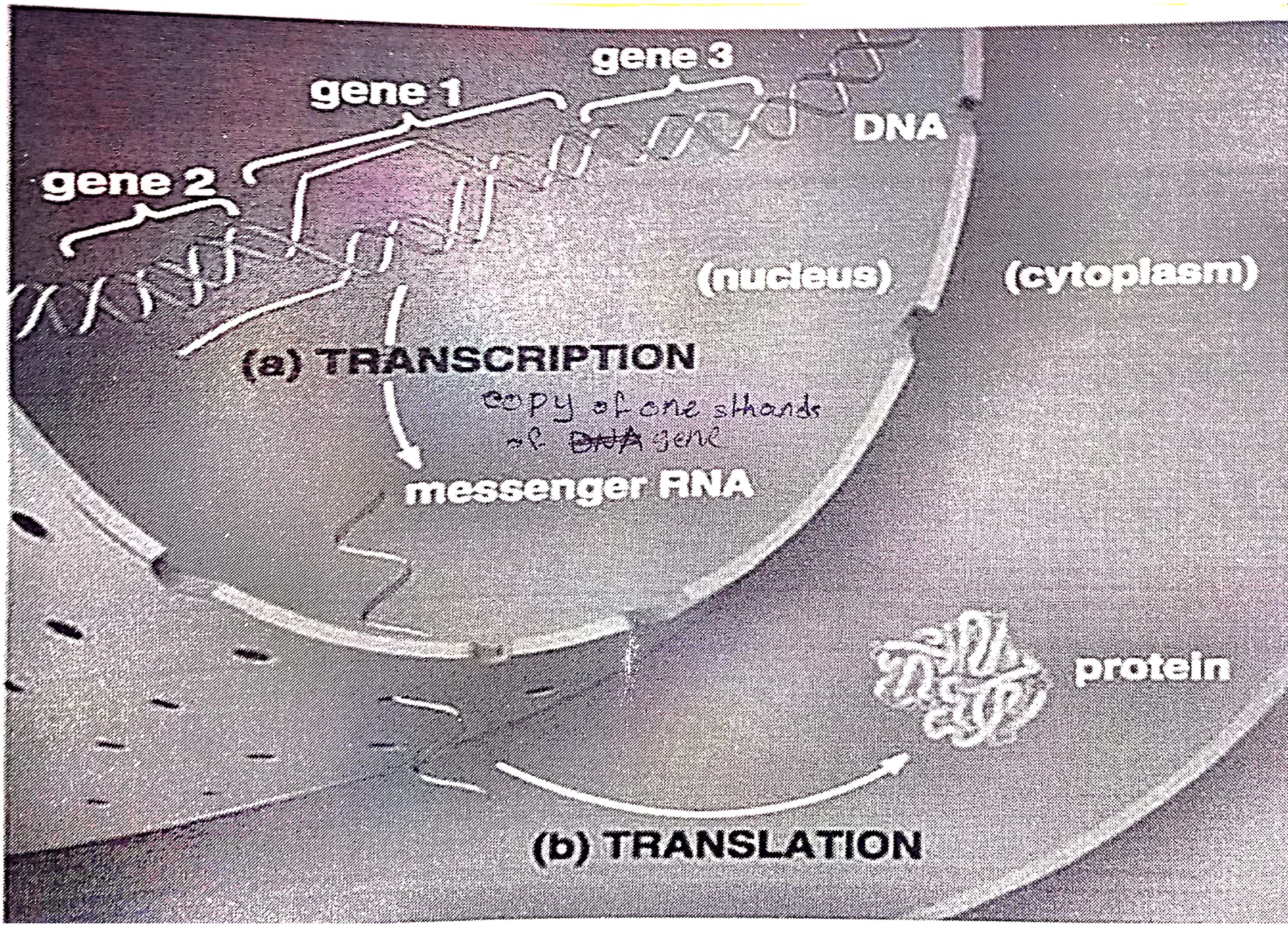
to understand
cell movement
cell interaction
cell replicate
communication

* knowledge needed to help in understanding "molecular biology":
Physics, microbiology, mathematics, biochemistry, genetics, cell biology ... etc
Recombinant DNA technologies, genetic engineering, molecular medicine, bio technology

1

* DNA is the genetic material in the cell and it regules the function of the cell by regulating the activity of genes except sometimes (only some viruses) their genetic material is RNA 1

49%


gene 3
gene 1
gene 2
DNA
(nucleus)
(cytoplasm)
(a) TRANSCRIPTION
copy of one strands
of ~~DNA~~ gene
messenger RNA
protein
(b) TRANSLATION

* What do we mean by gene regulation?

gene activity: when the gene is active or silent or not active

* All our cells have the same set of chromosomes genes, they all have growth hormone gene... they all have insulin hormone gene...
* Trascription: copy of one strand of DNA
* mRNA —travels→ from cytoblasm ⟶ nucleus (بالعكس), mRNA fits itself on ribosomes where transulation occurs
    * silent: always not active as insulin hormone in bone but the active gene can get ~~nonactive~~ nonactive untill need
* Transulation: convertins the message of the mRNA to produce a polypeptide

- So, what is responsible for the control of proding polypeptides?

the genes

what produces RNA?

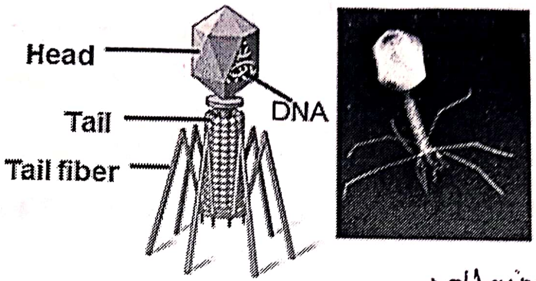
DNA

* DNA is coppied to make mRNA which is used as the template to make proteins
    - the formation of mRNA is called transcription
    - " " " proteins " " transulation
* DNA regulation determains what type and amount of mRNA should be transcribed and this subsequently detemines the type and amount of proteins, this process is the fundamental control mechanism for growth and development.

Models of biological system

- **Viruses**

  the most simple



99% the genetic material is DNA but in viruses ~~not~~ some

genome: the total of all genitic materia

- **Bacteria** prokaryote, agar (Agar is a complex polysaccharide derived from red algae), cell division, prototroph, auxotroph

  → obtained from seaweed (it is resistant to the action of bacterial enzyme)

- **Yeast** eukaryotes

  More developed

- **Animal cells** cell culture, cancer cell culture, stem cells

  (growing animal cells in the lab)

  difficult
  - high nutrition requirement
  - sensitive to the temperature (environmental changes)

  highly contaminant → cuz of nutrition rish media

- **Plant cells**

  we can in the lab grow a whole plant from a simple cell but the animal is more sensitive so they growed organs

Scanned by CamScanner

* if u want to test the activity of Antibiotic which cells will u choose?
  Bacteria

* what about Anti-cancer drugs
  Animal cells

treatments, antiviral drugs
viruses

<< it depends on what u study >>

☆ Viruses :

- the simplest cells, they are totally inactive outside the host cells
- made of only DNA surrounded by Protein coat
- the study of it's cells helped in proving that DNA and not protein is the genetic material by separating the protein from DNA And then injecting them in other cells and see which cells are affecting, the virus began to replicate where the DNA was injected.
  which means the nucleic acids in viruses controlled the host cell and forced it to produce other viruses.

☆ Bacteria :

- Unicellular (has a single chromosome)
- Prokaryote cells (lack membrane bounded organelles and mitochondria, has a cell wall and divide by binary fission).
- It is easy to plant, we usually grow it in Agar (Jell-like substance) we place it in a small dish an add Agar and we plant bacteria within few hours, thousand of bacteria will grow so high cell devision of bacteria very easy to grow, has a single chromosome (easy to multiply)
- if the bacteria require only the basic nutrition (prototroph)
- if it needs extra supplement of nutrition like vitamins (auxotroph)
- example: Escherichia coli (E.coli) which divide every 20 minutes at optimal conditions
  - they also can be grown in Liquid (browth)

If the liquid is complex extract of bioligical material it's called (browth)
If the growth medium is simple mixture contains no organic compounds other than a carbon source such as sugar such as glucose, glycerol, lactate + ions it's called (Minimal medium)

Minimal medium: bacteria that can grow in it Prototroph
browth: " " " " " " auxotroph
↳ أو
أحماض أمينية، فيتامينات،

* Metabolism in bacteria is precisely regulated, they rarely synthesis substances that aren't needed
  ex: if tryptophan is present in growth medium, bacteria won't make it, but once used up synthesizing enzyme activates

☆ Yeast :

very easy and fast to grow
mutant strains of yeast were often used to discover the genes that control growth, division, cell behavior patterns, they also are used to produce large number of human genes

(*) Animal cells :

- Primary cell culture represent normal animal tissue.
- Animal cells grow well intitially but eventually die off. (very sensitive)
- Tumour cells grow indefinitely and are easier to propagate in culture.
- Embryonal stem cells holds a great promise as starting point for the production of tissues and organs as human replacement parts.
- molecular biologist has succeeded in injecting foreign genes into animal eggs and thus generating transgenic animals.
- in some animal cases improved agriculture productivity such as enhanced milk production from animal cows
- Attempts will be made to inject foreign genes into human cells to correct genetic defect (gene therapy)

* Plant cells:

to learn about gene function in plants

* Ultra-violet rays and some chemicals cause mutations
* we can minimize the symptoms of the disorder by treatment of symptoms

Genetics and Medicine

- Most disease result from environmental influences interacting with the individual genetic makeup {**genetic predisposition** (sometimes also called **genetic** susceptibility)}.
- e.g., high blood pressure, diabetes mellitus, psychiatric disorders sickle-cell anemia gout / hyperlipidemia
- More than 3000 defined human genetic diseases are known.

- Genetically determined diseases are not a marginal group.
- The total estimated frequency of genetically determined diseases of different categories in the general population is about 3.5–5.0%.

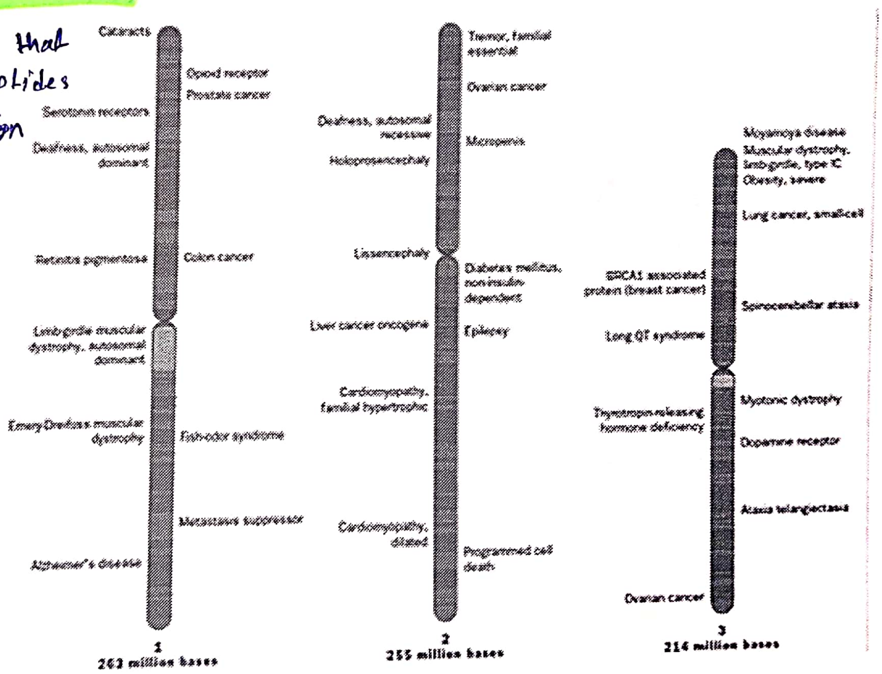
(to avoid)

- Genetic counselling is generally offered prior to marriage or conception, in order to predict the likelihood of conceiving an affected child, during pregnancy. (mi
- Gene therapy is used to correct defective genes that cause disease not yet an active current therapy. however cloning has a high potential for curing many diseases but it is still under investigation.

Introduction

polypeptide: protein hormones & Enzymes

- **Genome**
- **Chromosome** : genetic hereditary material, found in nucleus
- **DNA** (Watson-Crick model)
- **Gene** active parts of DNA that produces polypeptides
- protection **RNA** function: production a polypeptide
- **Proteins**



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master blueprint DNA for all cellular structures

* Genome: total of all genetic material (nucleic acid) containing the genetic instruction for making an organism
* chromosome: made of DNA & genetic heridatry material (found in nuclears) + protein
* gene: the active part of DNA and can produce polypeptide
* polypeptide: protein, hormones, enzymes
* RNA: protection of the polypeptide
* many hormones are protein

* mutation at a single gene locus (monogenic disease) → Mendelian mode of inheritance.
  - ↳ an inheritance pattern.
  - ↳ it is causes by errors made by the cells when it copies DNA & DNA Damage resulting from chemicals and radiation among other causes

Nucleic Acids

- **Nucleic acids** occur in two forms:

taking one from ribose nucleic acid

1- **DeoxyriboNucleic Acid (DNA)**

2- **RiboNucleic Acid (RNA).**

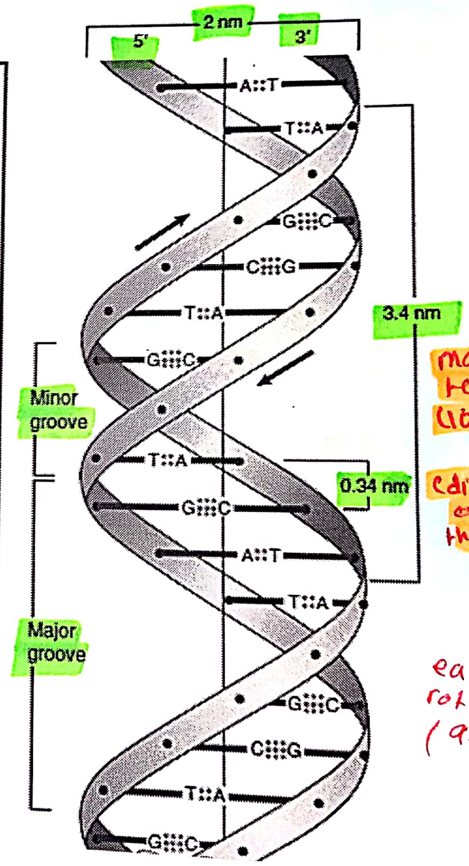
- Both DNA and RNA are polymers of **nucleotides**.
- DNA is the molecule of heredity in all cells except some viruses where RNA is the molecule of heredity.
- RNA molecules are synthesized on DNA templates and participate in protein synthesis in the cytoplasm.

- made of 2 strands
- they run opposite to each other (anti parallel)

if they start with 5 it will end in 3 and viceversa

DNA

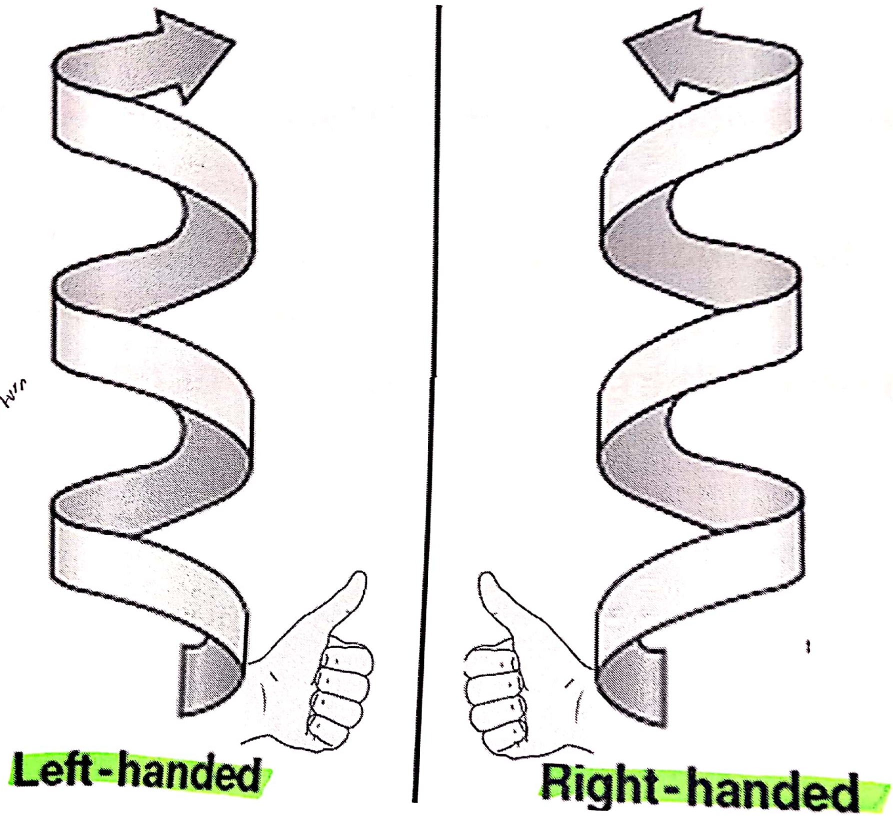
- Right-handed antiparallel double-stranded helix (spiral structure).
- Has a diameter of about 20 A^0 (2 nm).
- Makes complete turn every 34A^0 (3.4 nm)
- The distance between adjacent nucleotide is 3.4 A^0.
- The bases of DNA are flat and stacked above one another.



makes a complete term (10nucleotides)

(distance between one nucleotide & the next one)

360° turn
each base pair is rotated about 36° (about)



Z-DNA
11 each turn

11-10 pairs each turn

A-DNA
B-DNA → more abundant

clockwise
away from the observer

7

* each strand is a linear arrangement of repeating units called nucleotides
* the particular order of the bases arraned along the sugar-phosphate backbone is called the DNA sequence
* the sequence specifies the exact genetic instructions required to create a particular organism with it's own unique traits
* Prokaryotic genes are more closely packed and are usually arranged alone one circular chromosome than Eukaryotic genes

* the two strands of DNA are coailed, which maximizes the exposure the of the negatively charged phosphate backbone to water and shields the hydrophobic bases in the middle from water

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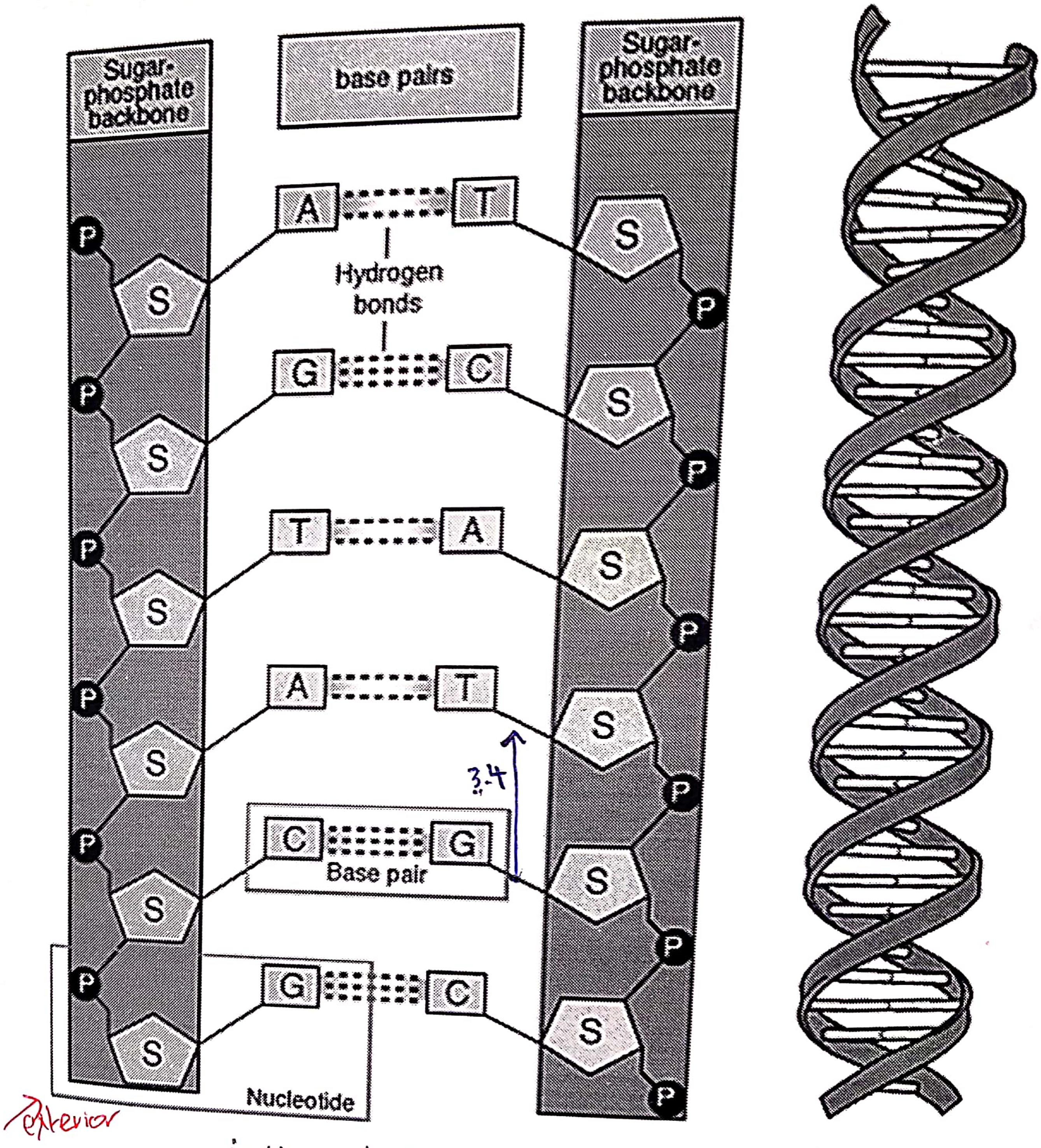

in the center is nitrogenios bases

* the most important thing in the DNA is the sequence of the bases cuz they are the genetic code, any chance will lead to a mutation which may lead to death
that why I have to maintain the DNA stable and non-active

RNA

helps in the protection of polypeptides ♡

- Single strand of nucleotides
- There are three classes of RNA based on their functions:
- 1) transfer RNA (tRNA); transfer the A.A during transulation
- 2) messenger RNA (mRNA); copy of one strand of gene
- 3) ribosomal RNA (rRNA). it enters in the structure of rRNA

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- Chemically RNA differs from DNA in two respects:
- 1- It contains ribose sugar instead of deoxyribose.
- 2- It has uracil (U) instead of thymine (T).

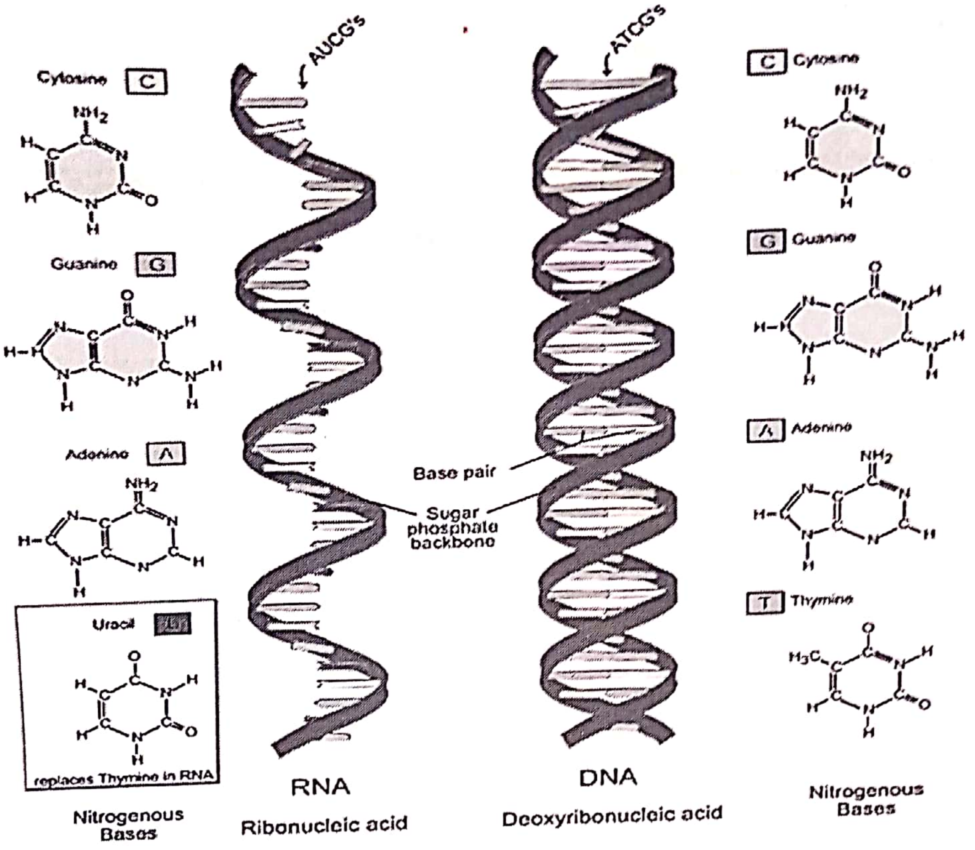
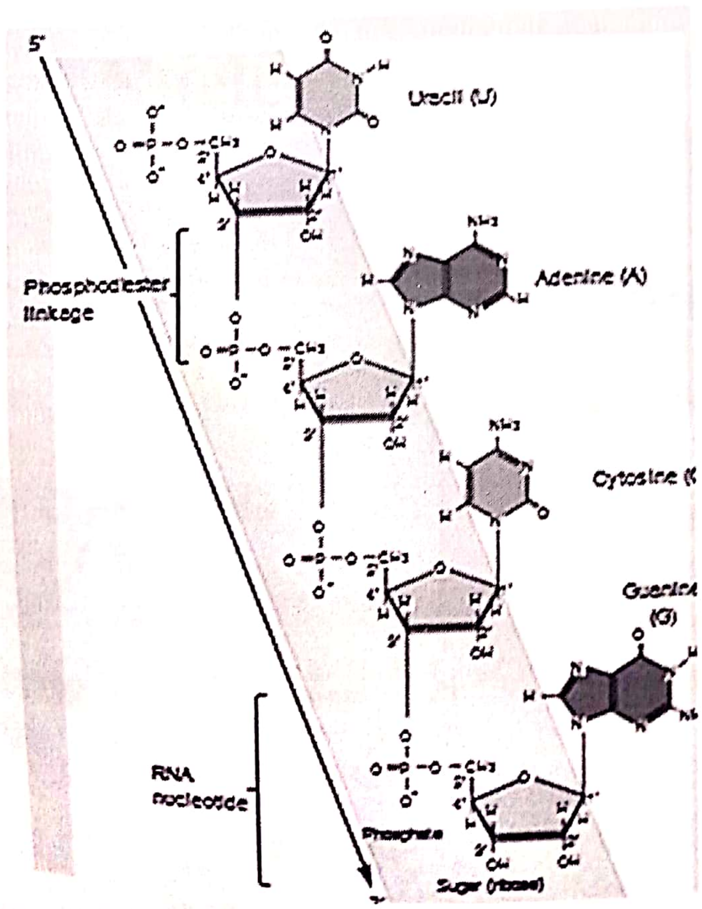


Image adapted from: National Human Genome Research Institute. Talking Glossary of Genetic Terms. Available at: www.genome.gov/ Pages/Hyperion//DIR/VIP/Glossary/Illustration/rna.shtml.



RNA ✓
one strand

A.A → proteins
Monosaccar → polysaccarides

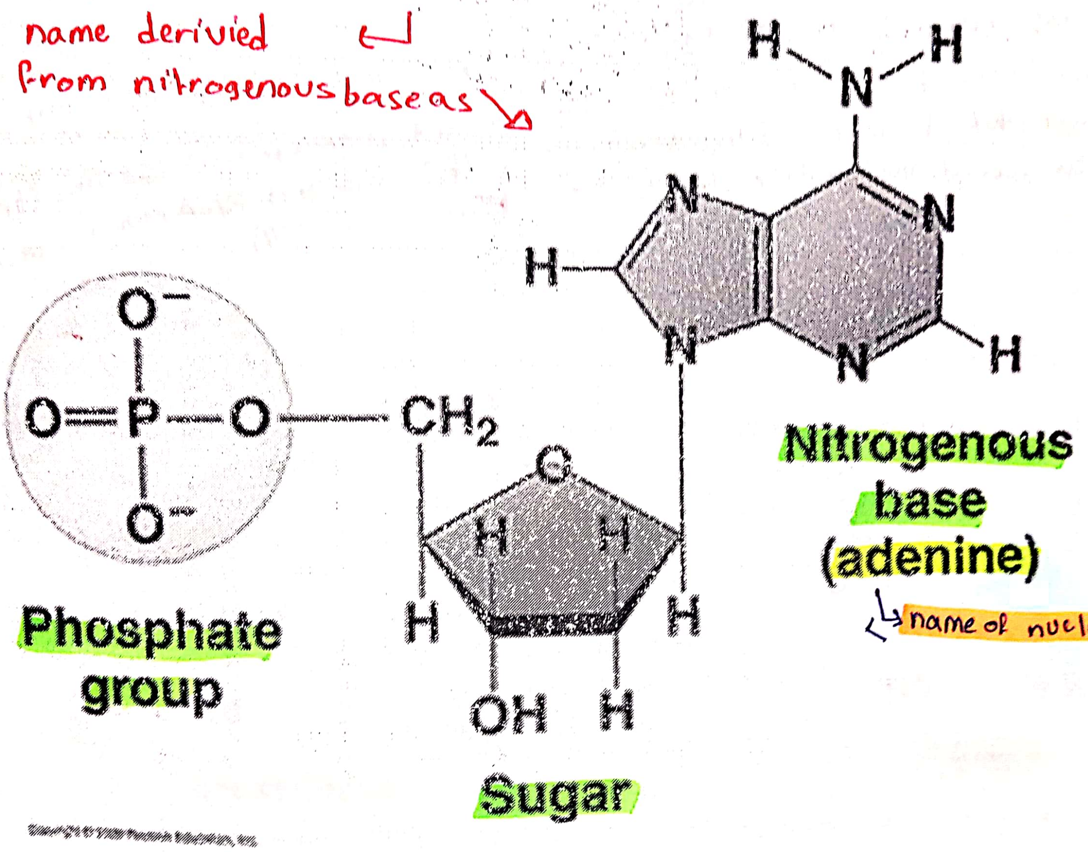
Nucleotides

→ building block for nucleic acids

- DNA and RNA are long, unbranched polymer of nucleotides
- **A nucleotide is made up of:**
- 1- Sugar (deoxyribose in DNA and ribose in RNA)
- 2- Phosphate
- 3- Nitrogen base.
- In DNA nitrogen bases are adenine (A), guanine (G), cytosine (C), and thymine (T), while in RNA adenine (A), guanine (G), cytosine (C), and uracil (U)).
- Nucleotides are named after the nitrogen bases present,
- The genetic information is stored in the sequence of bases
- Nucleosides are formed by joining a nitrogenous base to a sugar

Nucleotide

name derivied ↵
from nitrogenous base as ↘



Sugar + Base ⟶ Nucleoside

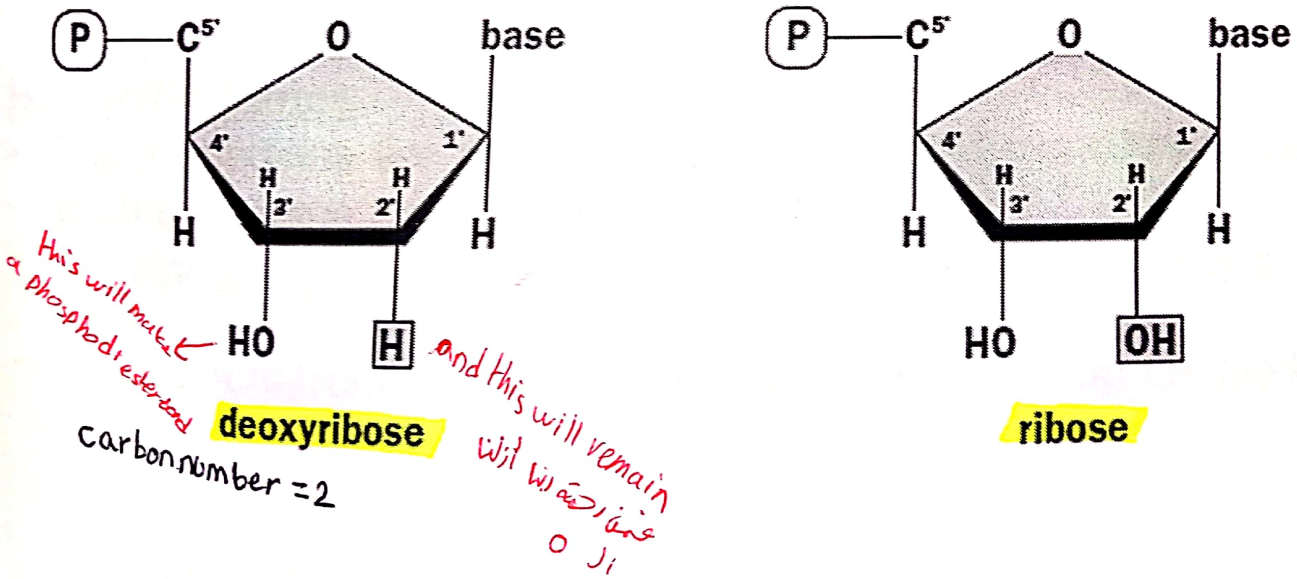
Nucleoside + Phosphate ⟶ Nucleotide

Base	Nucleosides	Nucleotides
RNA		prime: carbon number in the sugar
Adenine	Adenosine	Adenosine-5′-monophosphate (AMP)
Guanine	Guanosine	Guanosine-5′-monophosphate (GMP)
Cytosine	Cytidine	Cytidine-5′-monophosphate (CMP)
Uracil	Uridine	Uridine-5′-monophosphate (UMP)
DNA		
Adenine	Deoxyadenosine	Deoxyadenosine-5′-monophosphate (dAMP)
Guanine	Deoxyguanosine	Deoxyguanosine-5′-monophosphate (dGMP)
Cytosine	Deoxycytidine	Deoxycytidine-5′-monophosphate (dCMP)
Thymine	Deoxythymidine	Deoxythymidine-5′-monophosphate (dTMP)

note: could be 3′

• 1- Ribose & Deoxyribose Sugar

- The carbon atoms on the sugar ring are numbered 1’ (one prime) to 5’ to distinguish them from atoms in the bases. The ribose in DNA differs from that of RNA by the absence of oxygen at the carbon atom number 2 and is thus 2-deoxy-β-D-ribose in DNA while in RNA β-D-ribose.



deoxyribose

ribose

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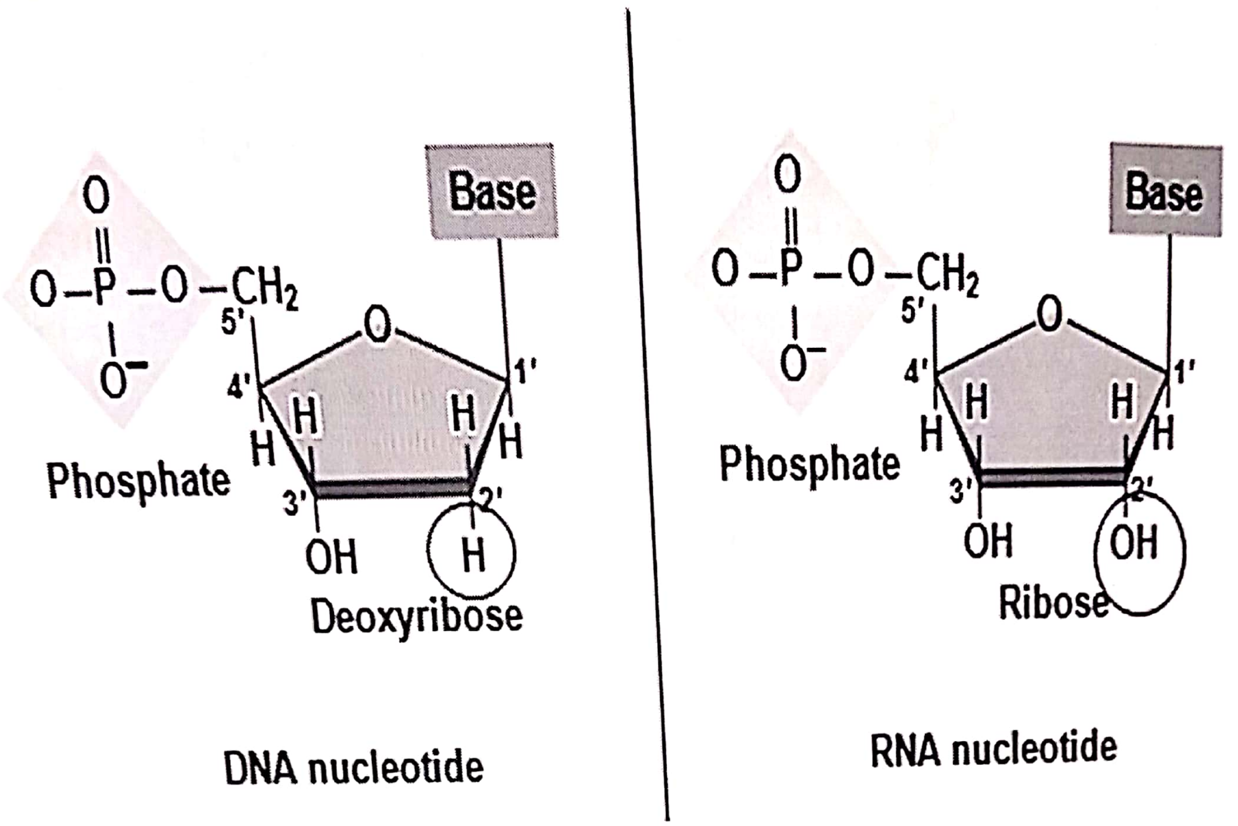
* why do we remove one oxygen from DNA? Why is it so important?

the OH group is a highly reactive functional group and H group isn't reactive (inert)

we need to keep DNA stable (not changed) cuz we use it forever but RNA remains in our cells for few seconds and then is destroyed cuz DNA بتصنع RNA

Nucleotides of DNA and RNA



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- **2- Nitrogen bases**
  - Because of their nitrogen content and basic qualities (hydrophobic) they are known as **nitrogenous bases.** not reactive
  - The organic bases are of two general types: **purines** and **pyrimidines**.

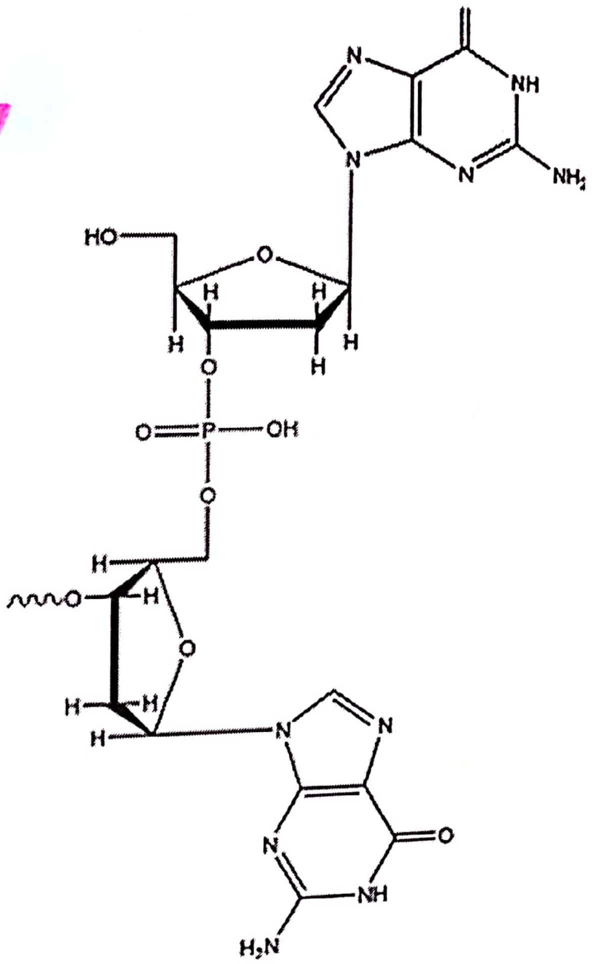
A. Purines

- The purines are **adenine** (A) and **guanine** (G).
- Each purine consists of a six-sided ring attached to a five-sided ring fused with

B. Pyrimidines

- The pyrimidines are **cytosine** (C), **thymine** (T), and **uracil** (U).
- Each pyrimidine consists of a six-sided ring only.
- Thymine is found primarily in DNA and uracil is found only in RNA.
- Uracil differs from thymine by lacking a methyl group on its C 5

The plane of the nitrogen base is oriented perpendicular to the plane of the pentose group



alway purines interact with Pyrimidines

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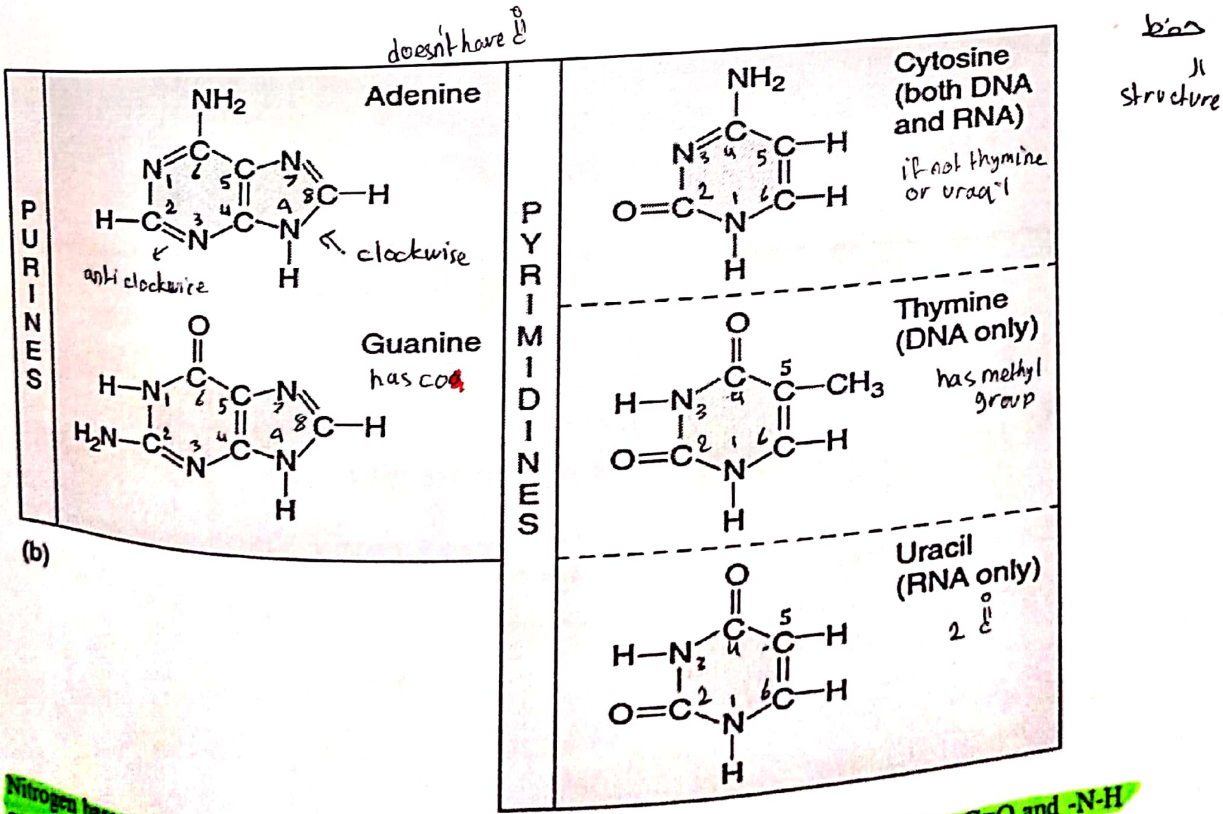
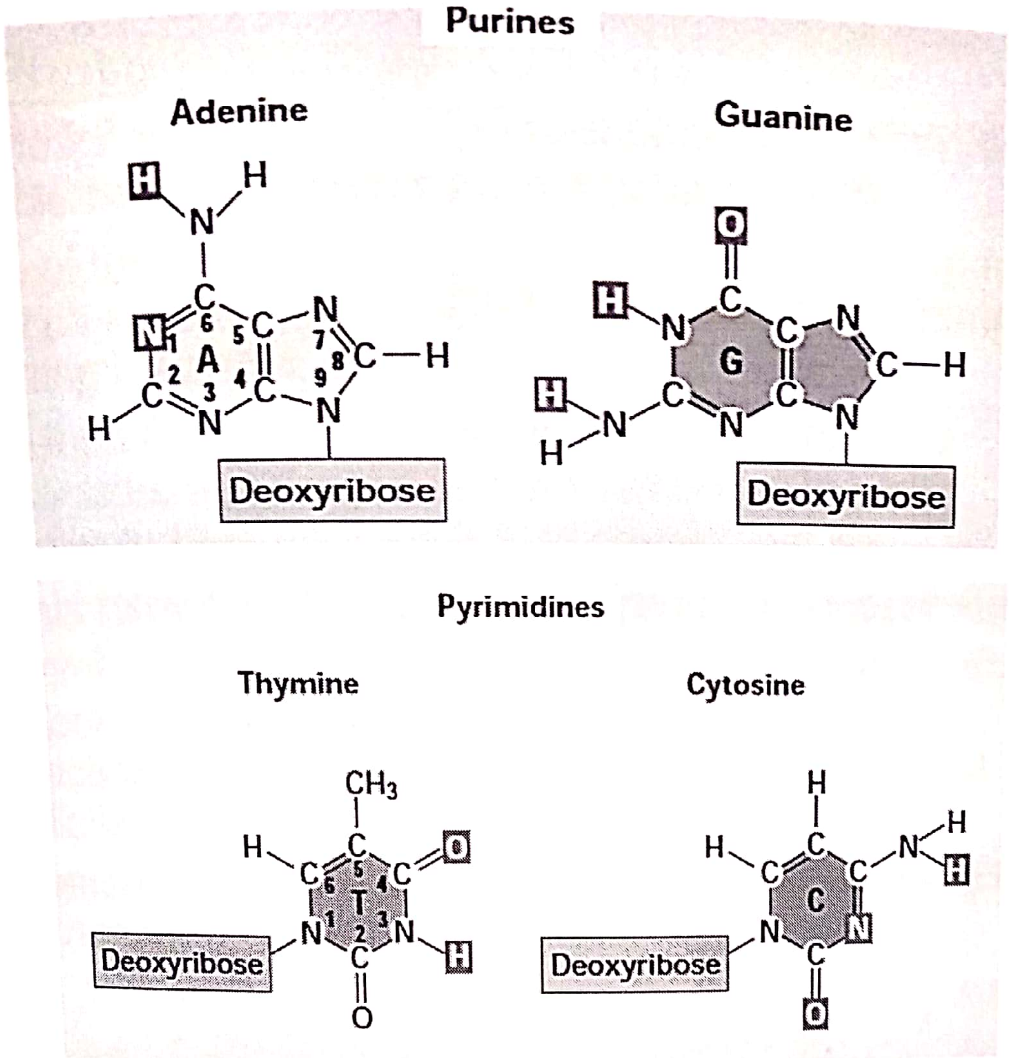


(b)

Nitrogen bases are hydrophobic with a hydrophilic edge. These hydrophilic edges are the -C=O and -N-H groups that can act as H-bond acceptors and donors. The hydrophilic edges of the bases interact in a very specific way A=T and G≡C, and thus this will leave the nitrogen bases as pure hydrophobic in the centre of the DNA.



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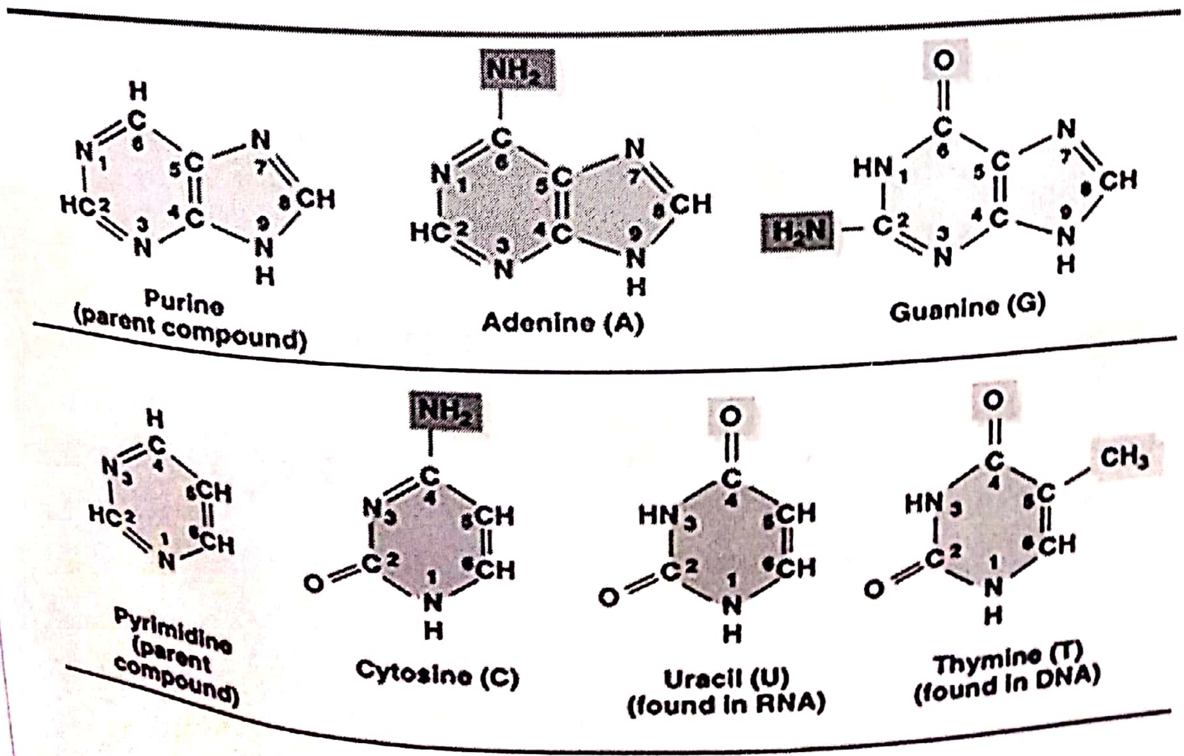
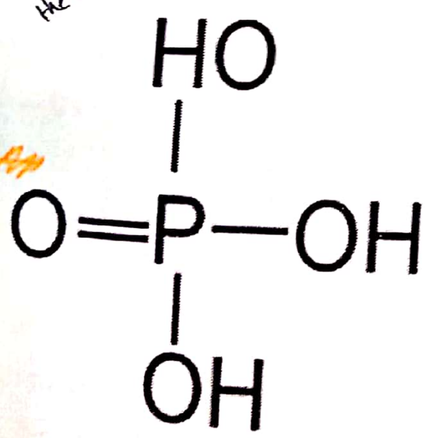
Nitrogenous bases of DNA and RNA



- **3- Phosphate group**
- A phosphoric acid (H_3PO_4) is bounded to one oxygen by a double bond and three hydroxyl groups (–OH).
- Two of the hydroxyl groups can form covalent bonds, phosphodiester bonds, with the sugar hydroxyl groups by splitting out water.
- The third -OH group on the phosphate is free and dissociates a hydrogen ion (H+ ions) and leaving negatively charged oxygens at physiologic pH.
- In this form, the structure is referred to as phosphate.
- Therefore, phosphate is a negatively charged which gives the polymer its acidic property and promoting their attraction to positively charged histone proteins that partially neutralized this negative charges
- because of the phosphate charges both DNA and RNA are negatively charged.

Phosphoric acid

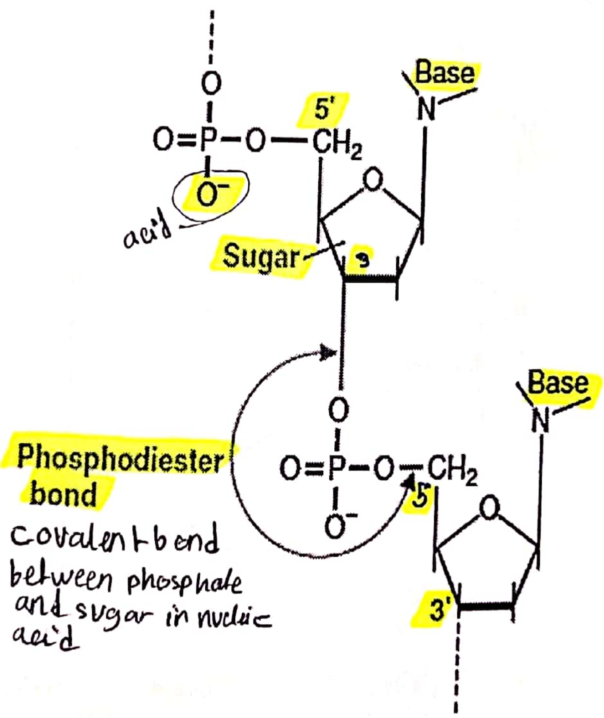
(nucleic acid) releases H+ so it is an acid which will give the phosphate group the negative charge
this is why DNA and RNA are negative
↑ electrophoresis



H_3PO_4

they 3OH are highly reactive

Phosphate always bond to sugar only
no direct interaction between phosphate and nitrogenious bases



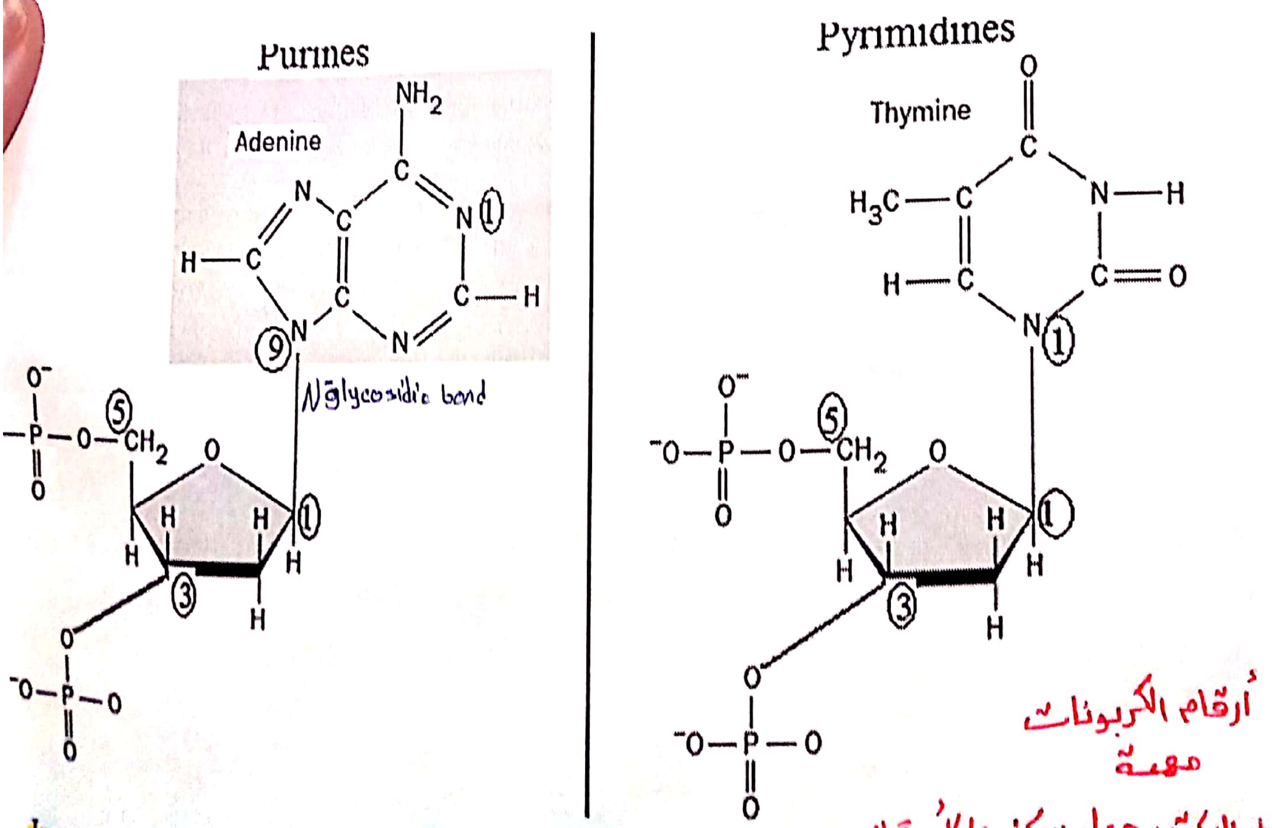
The nitrogen atom in position 9 of a purine or in position 1 of a pyrimidine is bound by N-glycosidic bond to the carbon number 1 of the sugar.

On the other hand, the phosphate group links the 3' end of one nucleotide to the 5' end of the next nucleotide through phosphodiester bonds.

- This gives the sugar-phosphate backbone directionality a 5' end and 3' end.

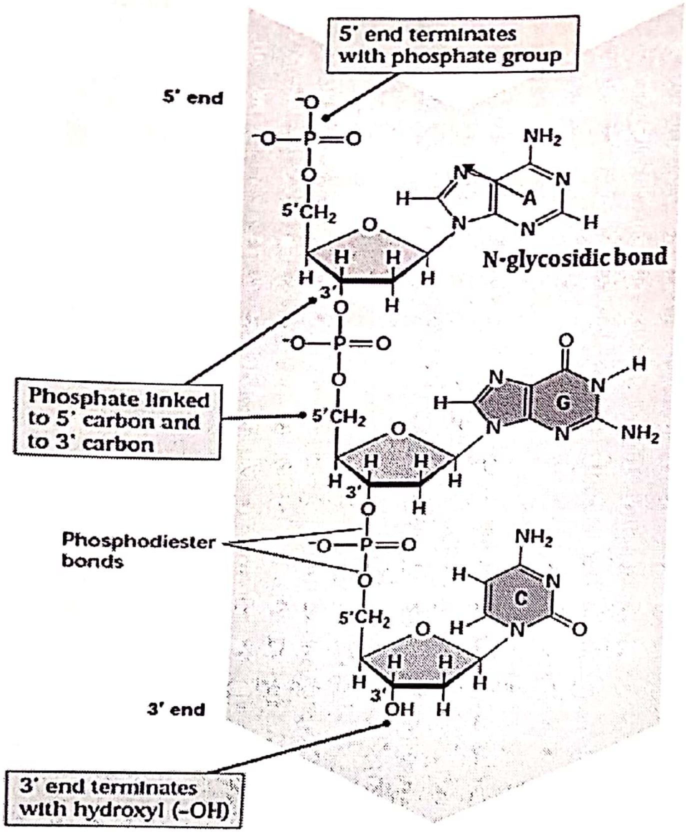
- In DNA the direction of the nucleotides in one strand is opposite to their direction in the other strand and thus called antiparallel.
- The 5' end has a terminal phosphate group and the 3' end has a terminal hydroxyl group.

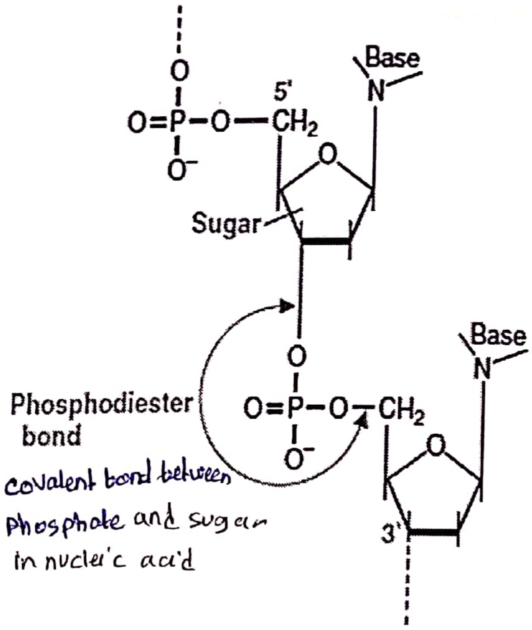
- **Sequences are written and read in the 5' to 3' direction (from left to right); for example, the sequence AUG is assumed to be (5')AUG(3')**



In a nucleotide, the nitrogen atom in position 9 of a purine or in position 1 of a pyrimidine is bound to the carbon number 1 of the sugar by N-glycosidic bond.

Covalent bonds in DNA





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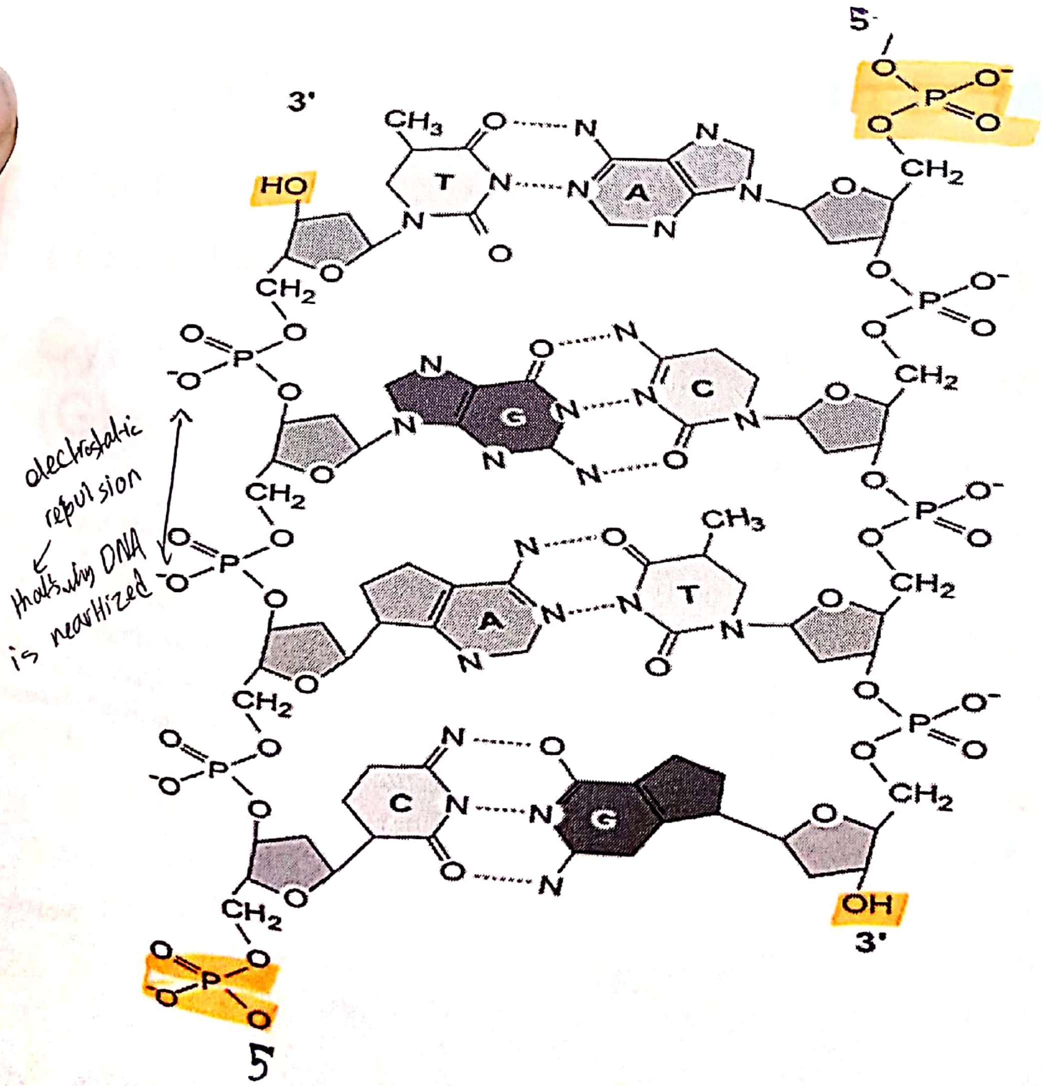
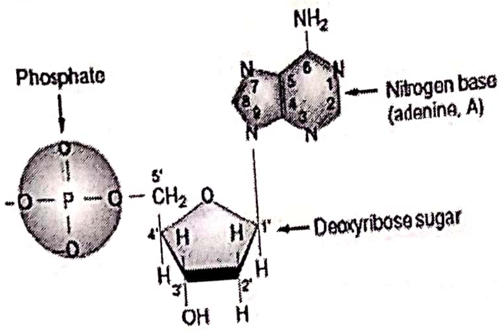
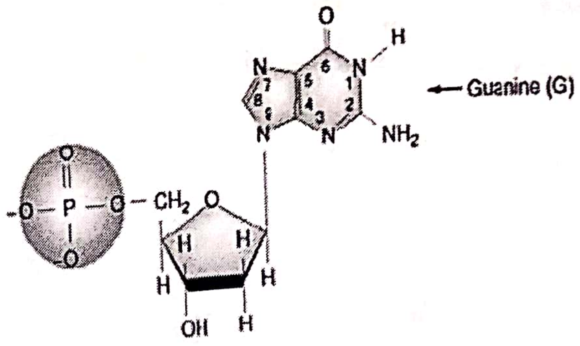


Purine nucleotides

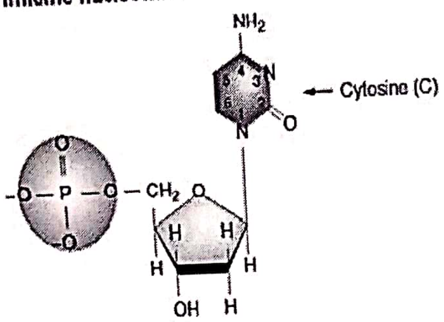


Deoxyadenosine 5'-phosphate (dAMP)

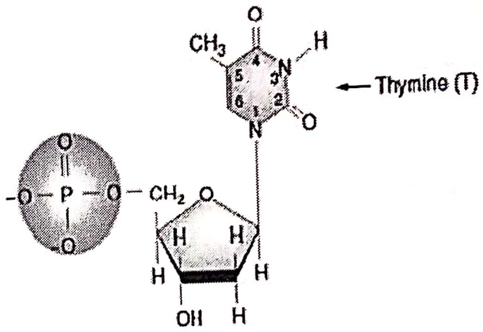


Deoxyguanosine 5'-phosphate (dGMP)

Pyrimidine nucleotides



Deoxycytidine 5'-phosphate (dCMP)



Deoxythymidine 5'-phosphate (dTMP)

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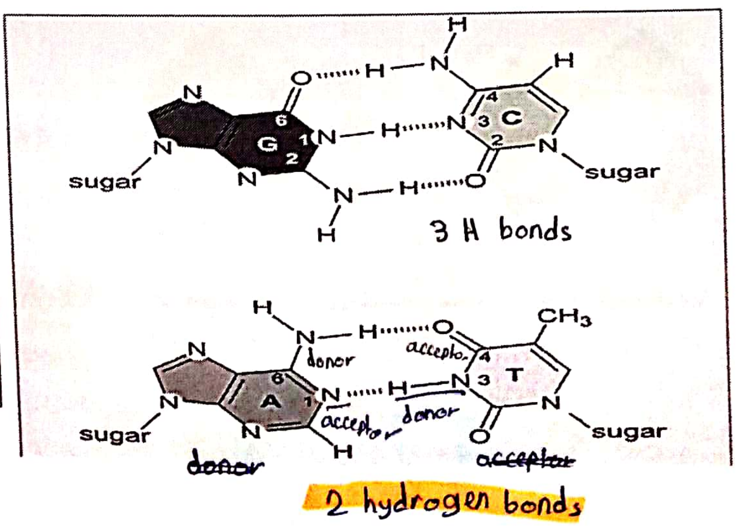
Base Pairs and bonds in DNA

- Adenine (A) specifically binds to thymine (T) by two hydrogen bonds (A=T) and
- Cytosine (C) specifically binds to guanine (G) by three hydrogen bonds (C≡G)

Chargaff's Rule: in any sample of double-stranded DNA, the amount of adenine equals the amount of thymine, the amount of guanine equals the amount of cytosine, and the total amount of purines equals the total amount of pyrimidines.

A + G = T + C

C=O carbonyl



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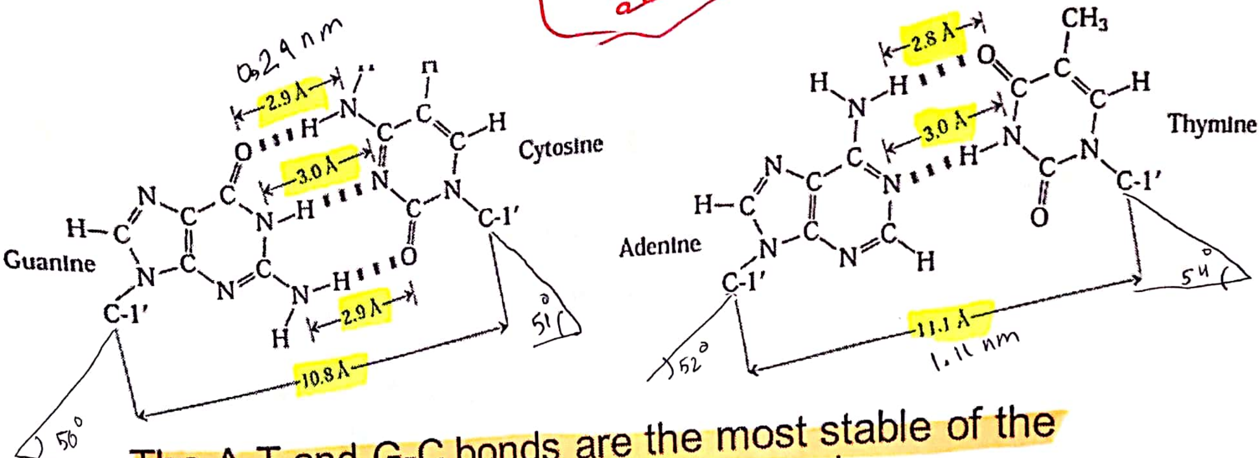
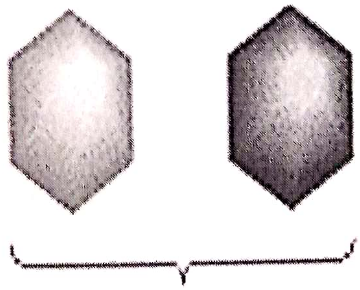


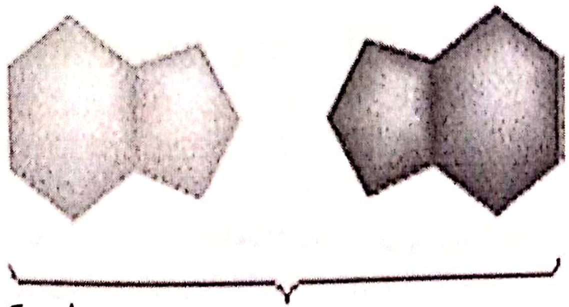
- The A-T and G-C bonds are the most stable of the various base-pairs on energetic grounds.
- These two base pairs have essentially identical dimensions within the double helix structure of DNA and thus avoiding partnership of purine-purine which will be too wide or pyrimidine-pyrimidine which is too narrow. This means that these are also the only two base pairs which will properly fit into the double helix that is the outside diameter of the double helix will be uniform over its length
- Hydrogen bonds are weak they can be broken and rejoined relatively easily which is essention in biological function

the most stable bond is the bond that reqvires the least amount of energy and the least is
A=T C≡G

Pyrimidine + pyrimidine: DNA too thin



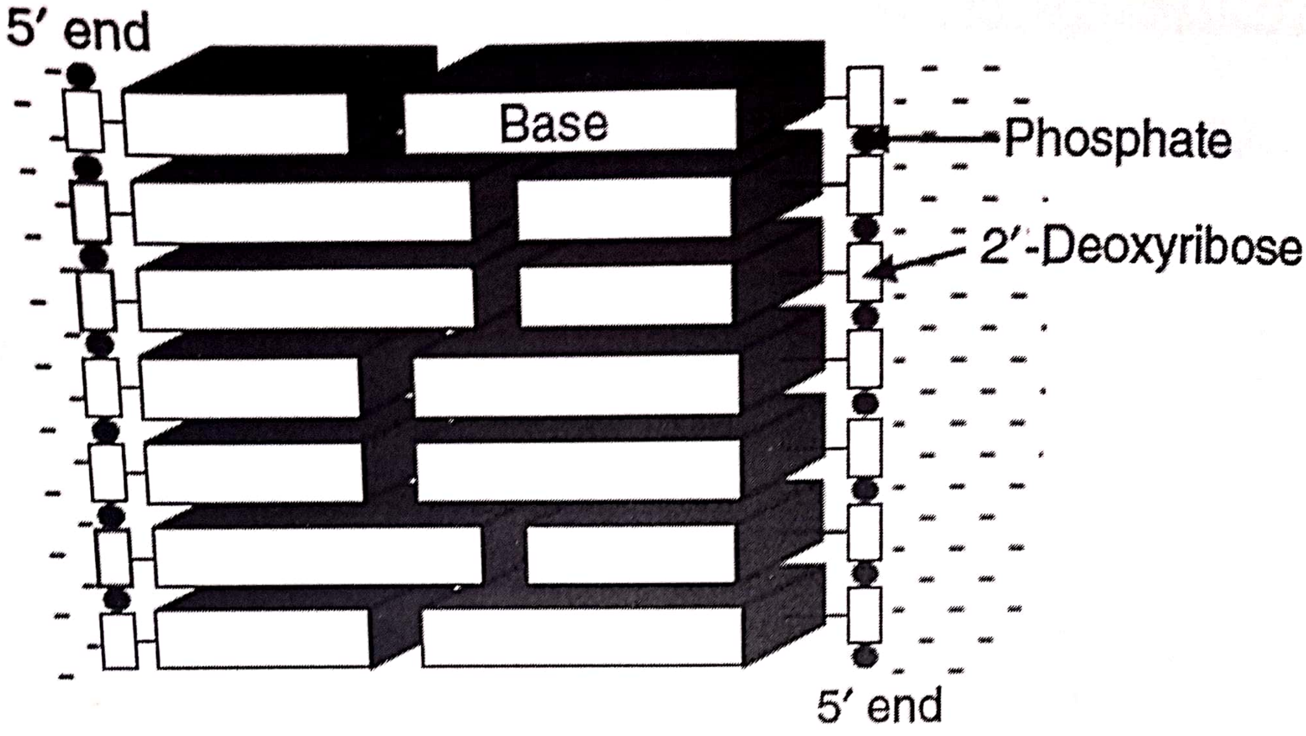
Purine + purine: DNA too thick



occupy large space

So large

diameter is 2 nanometer but this isn't ↑
no identical pairs of DNA



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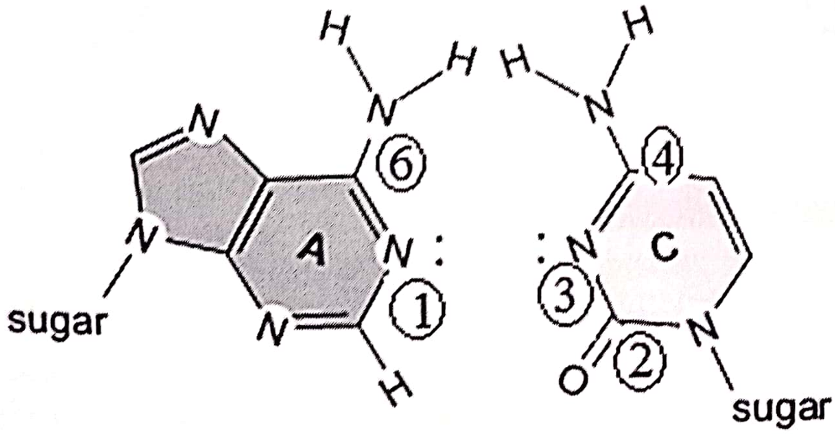

Suppose we tried to pair an adenine with a cytosine.

1- Then we would have a hydrogen bond acceptor (N1 of adenine) lying opposite a hydrogen bond acceptor (N3 of cytosine).

2- Likewise, two hydrogen bond donors, the NH2 groups at C6 of adenine and C4 of cytosine, would lie opposite each other.

•Thus, an A:C base pair would be unstable

The DNA Double Helix Is a Stable Structure

First, Hydrogen bond

- The two strands of DNA are held together by H-bonds
- Polar atoms in the sugar–phosphate backbone form external H bonds with surrounding water molecules.

Second, the negatively charged phosphate groups are all situated on the exterior surface of the helix in such a way that they have minimal effect on one another and the phosphates interact with positively charged (magnesium, potassium, or sodium) ions and with positively charged histone proteins.

Third, Stacking interactions which involve hydrophobic interaction and Van der Waals forces in the core of the helix. Base stacking helps to minimize contact of the bases with water, and base-stacking interactions are very important in stabilizing the three-dimensional structure of nucleic acids.