Chapter 7

Nucleic acids

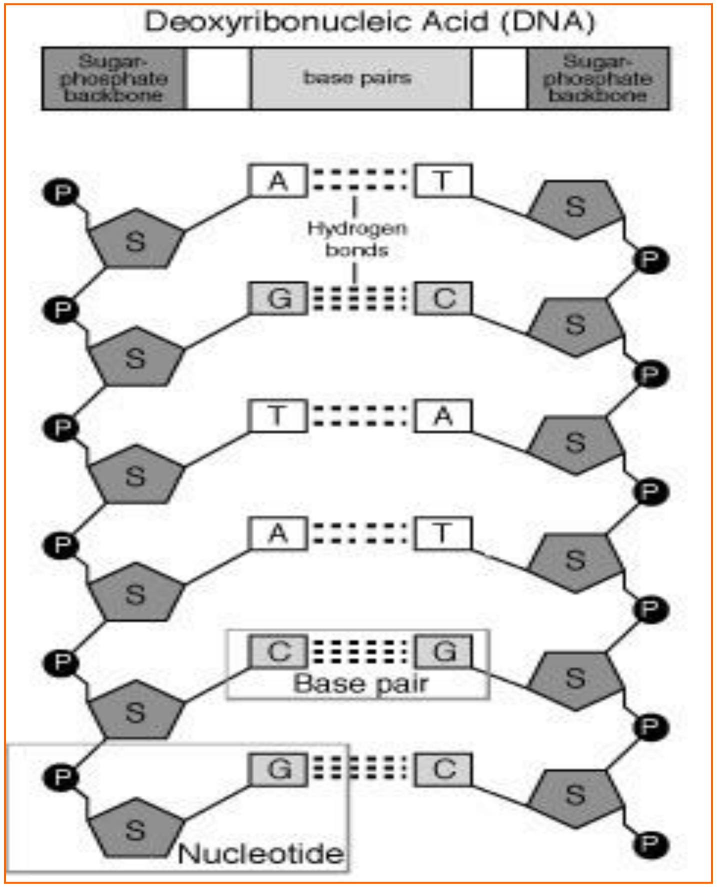
Introduction

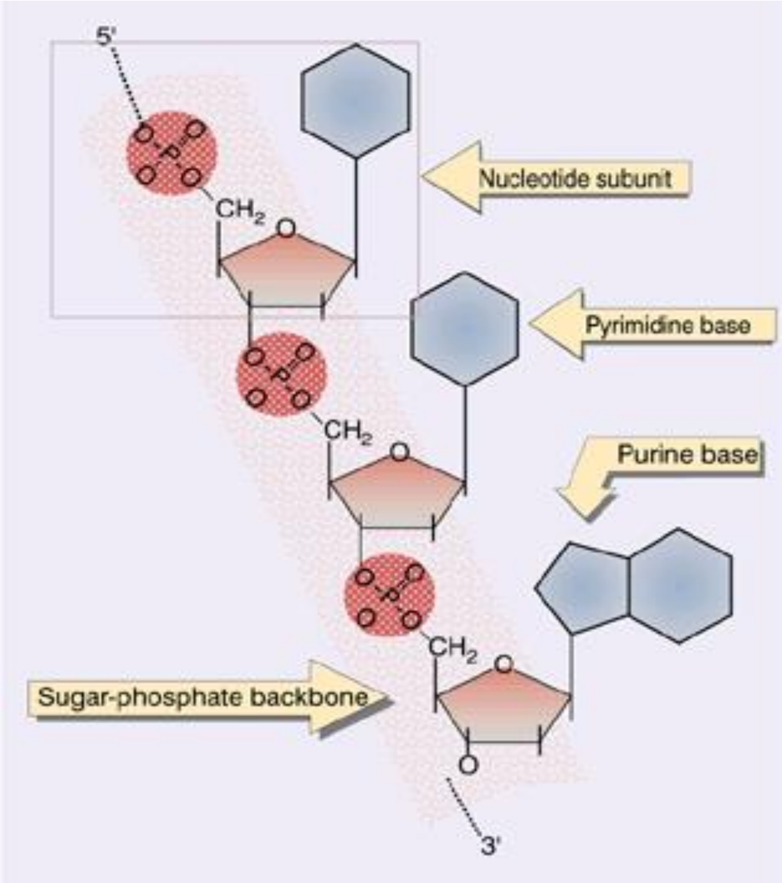
- Typical living cells in organisms contain mechanism to undergo
  - Cell replication-i.e for the organism to construct a replica of itself and
  - Protein synthesis
- These processes requires set of instructions to specify every step required
- Genes/genomes (genetic material) are sources of these information required
- A typical genome is composed of Deoxyribonucleic acid (DNA) in living organisms
- Synthesis of specific protein is also directed by Ribonucleic acids (RNA’s) derived from genes

Introduction

- ❖ Some viral genomes are composed of Ribonucleic acid (RNA)

- ❖ The DNA and RNA are called **Nucleic acids (or polynucleotides** b/c they are composed of nucleotide units**)**





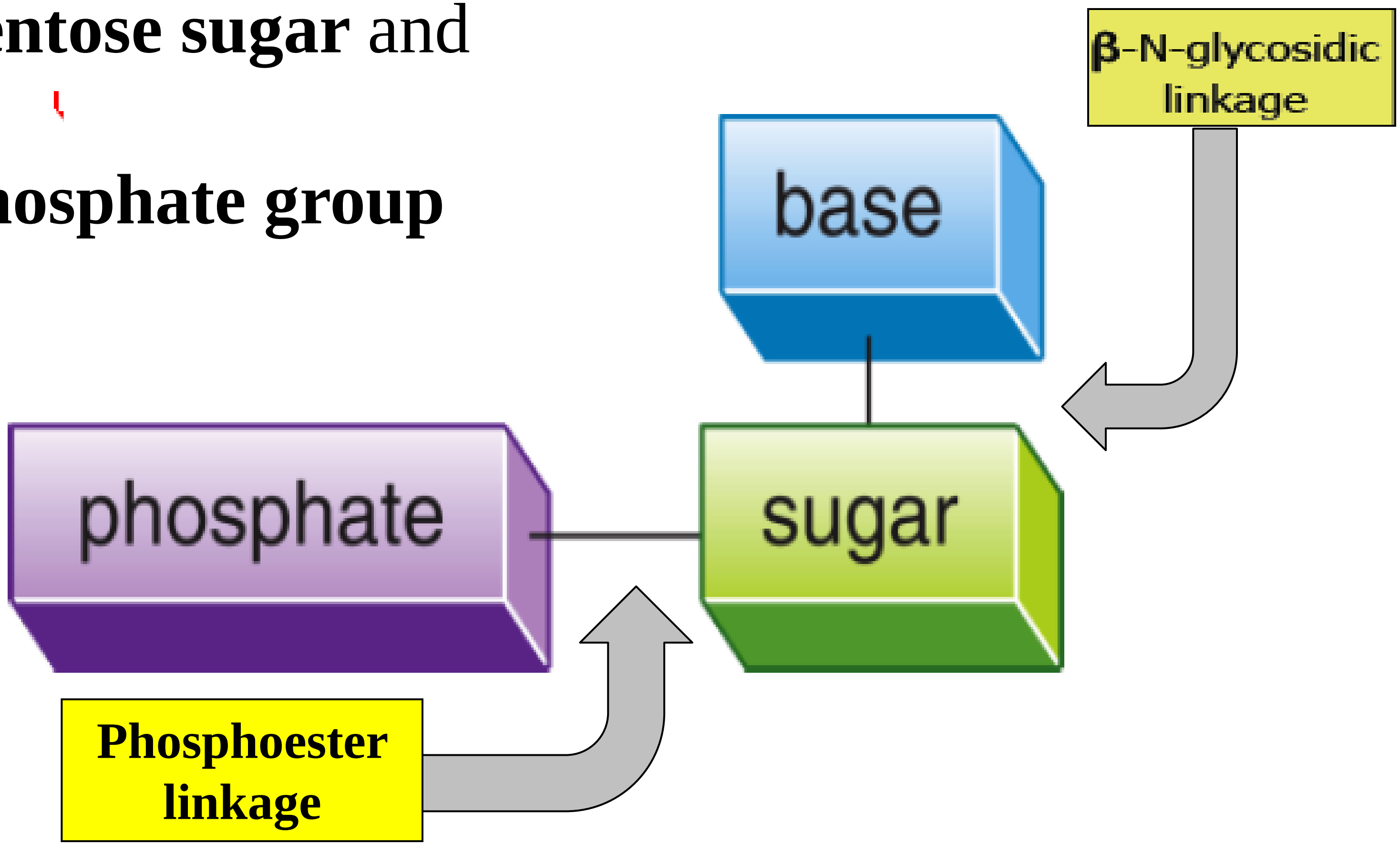
Nucleotides

❖ Nucleotides are composed of three components

➢ **A nitrogen base** – heterocyclic ring containing nitrogen

➢ **Pentose sugar** and

➢ **Phosphate group**



Nucleotide components

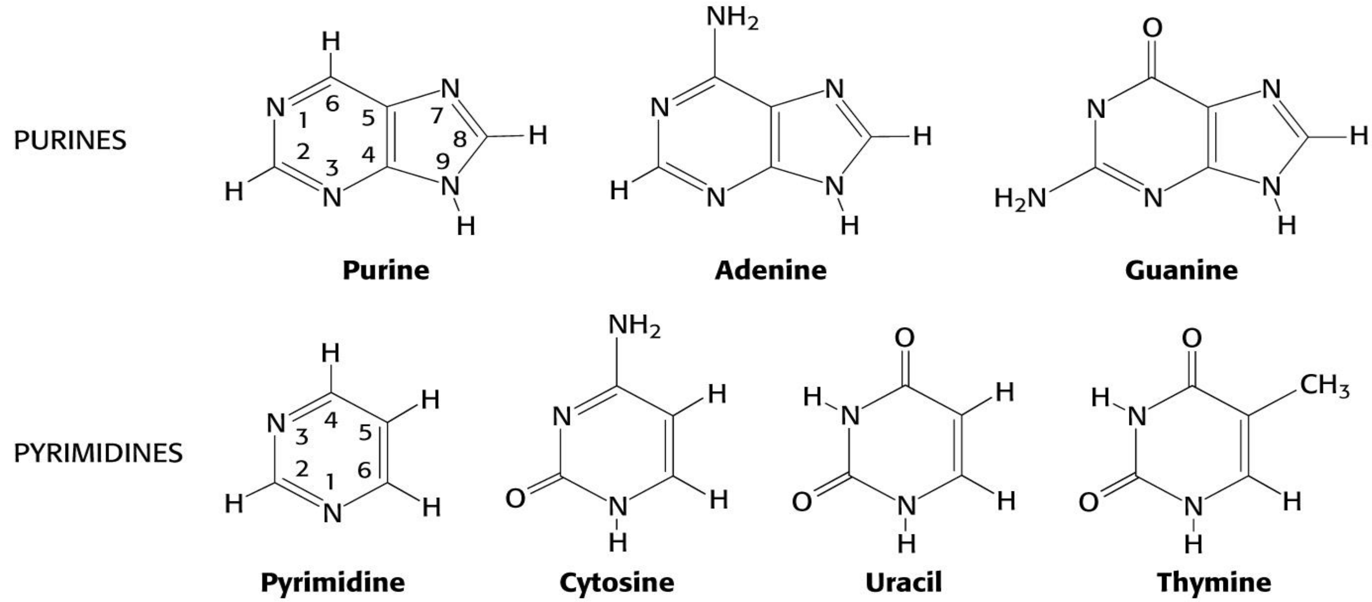
❑ Nitrogen bases

❖ Heterocyclic nitrogenous compounds associated with nucleotides

❖ They are responsible for chemical basicity of the nucleotides

❖ Are placed into two major classes

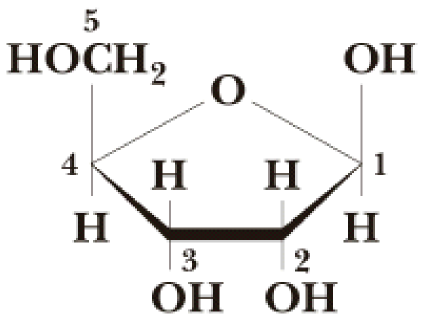
- ➢ **Purines** :- Including **adenine (A)** and **guanine(G)** and
- ➢ **Pyrimidines**:- Inncluding **thymine(T)** , **cytosine(C)** and **uracil (U)**



Nucleotide components

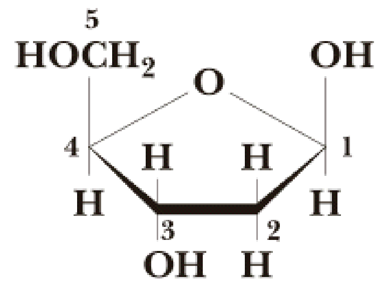
- ❑ **<u>Pentose sugars</u>**

  ❖ Two common types are used D-ribose & 2-deoxy-D-ribose



Furanose form of
D-Ribose

β-D-Ribofuranose



Furanose form of
D-2-Deoxyribose

β-D-2-Deoxyribofuranose

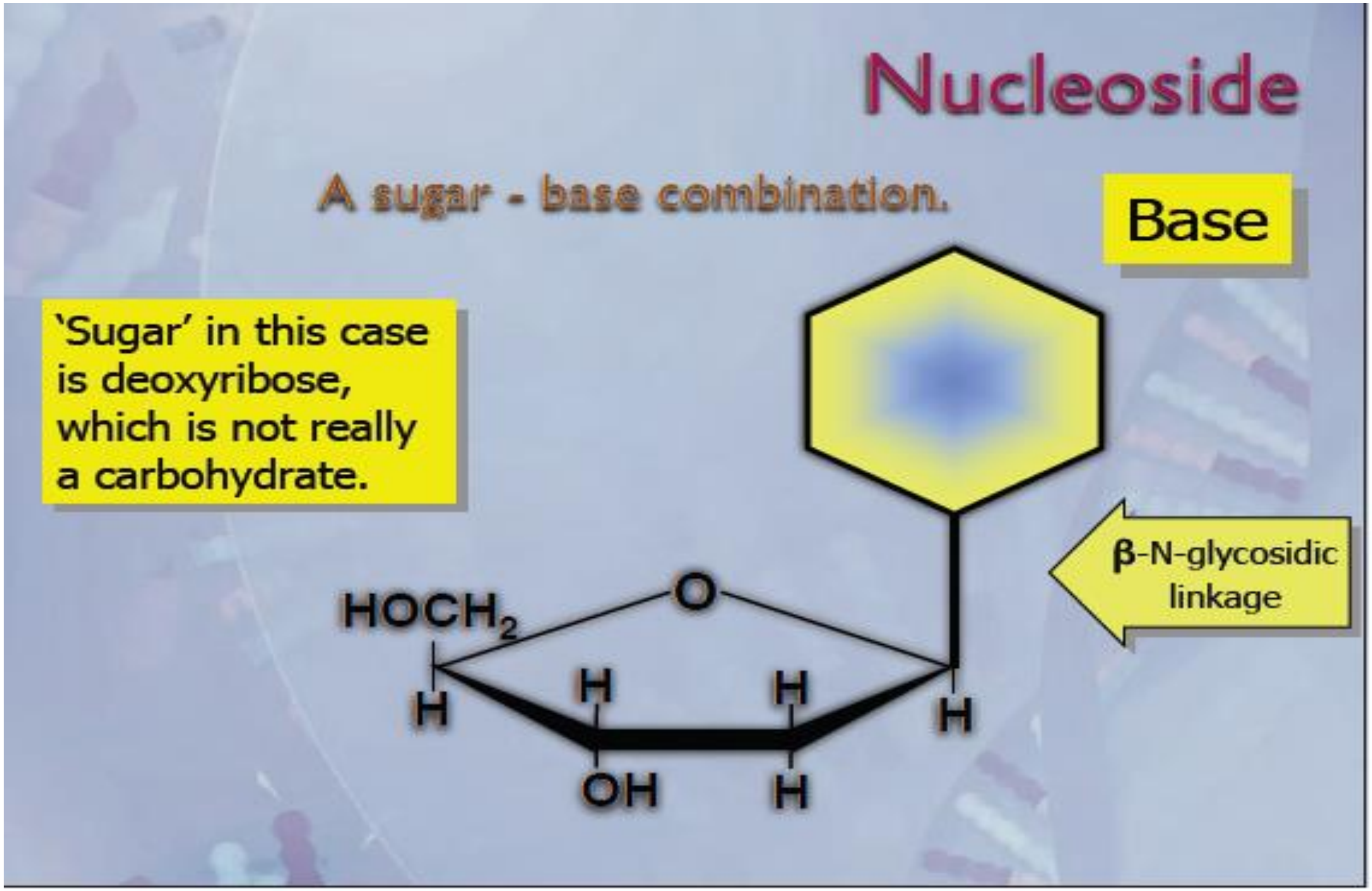
- ❑ **<u>Phosphate groups</u>**

  ❖ One or more phosphate groups may also be incorporated

  ❖ They are responsible for chemical acidity of the nucleotides

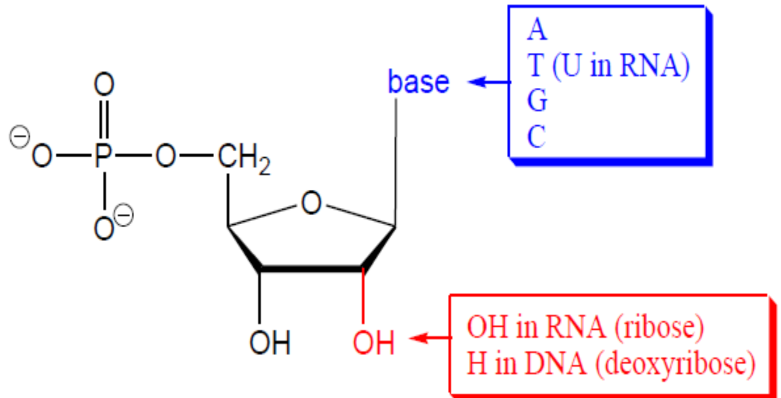
Nucleotide construction

❖ The N-bases (at N-1 or N-9) and pentose sugars (C-1) are linked through N-glycoside to give a **nucleoside**



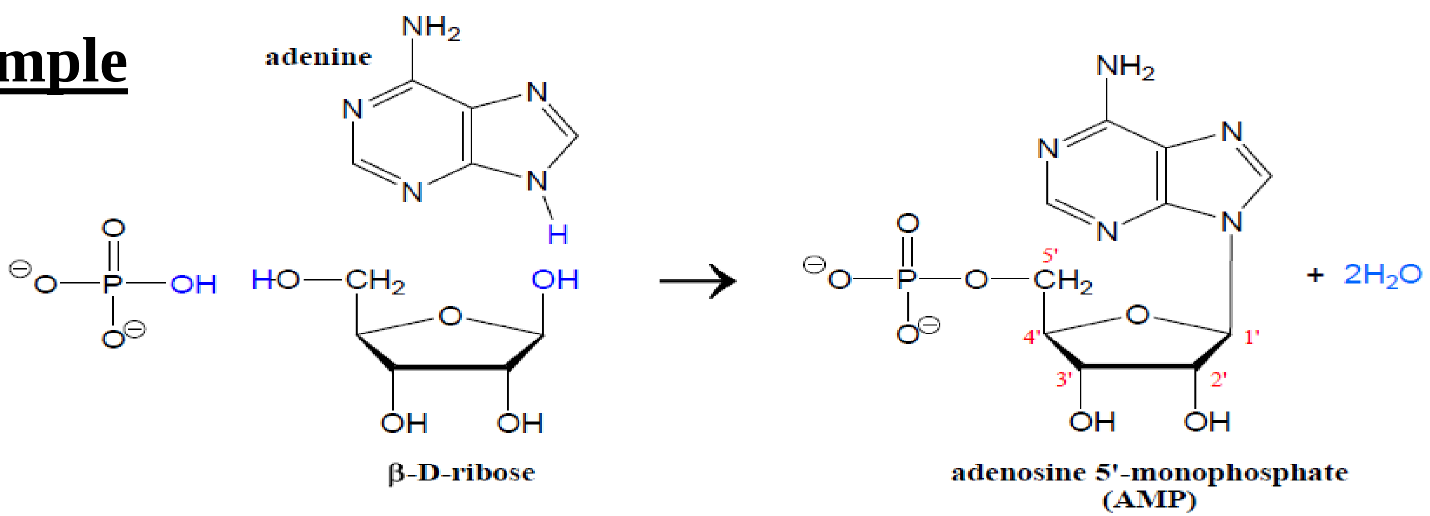
Nucleotide construction

❖ The phosphate group forms phosphester bond with hydroxy group of pentose sugars (at C-5) to give a **<u>nucleotide</u>**

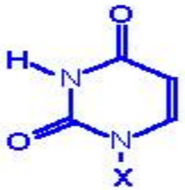
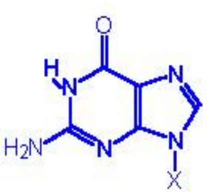


a nucleotide

<u>Example</u>



Nucleotide Nomenclature

Base Formula	Base (X=H)	Nucleoside X=ribose/deoxyribose	Nucleotide	Example
	Cytosine, C	Cytidine, A Deoxycytidine, dC	Cytidylate Deoxycytidylate	Cytidine monophosphate (CMP) Cytidine diphosphate (CDP) Cytidine triphosphate (CTP)
	Uracil, U	Uridine, U	Uridylate	Uridine monophosphate (UMP) Uridine diphosphate (UDP) Uridine triphosphate (UTP)
	Thymine, T	Thymidine, T Deoxythymidine, dT	Thymidylate Deoxythymidylate	Thymidine monophosphate (TMP) Thymidine diphosphate (TDP) Thymidine triphosphate (TTP)
	Adenine, A	Adenosine, A Deoxyadenosine, dA	Adenylate Deoxyadenylate	Adenosine monophosphate (AMP) Adenosine diphosphate (ADP) Adenosine triphosphate (ATP)
	Guanine, G	Guanosine, G Deoxyguanosine, dG	Guanylate Deoxyguanylate	Guanosine monophosphate (GMP) Guanosine diphosphate (GDP) Guanosine triphosphate (GTP)

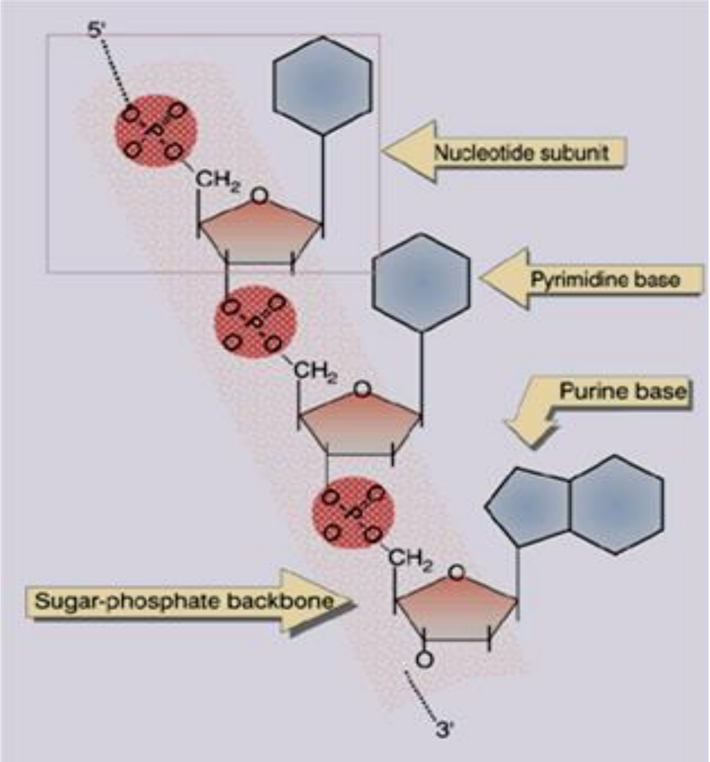
Comparison of DNA and RNA

- DNA and RNA generally differ in the following regard

Parameters	DNA	RNA
Sugar units	2'-deoxyribose	Ribose
N-bases	Uracil is absent Thymine is exclusively found	Thymine is not found except in tRNAs
Helix structure	Double stranded	Single stranded
Molecular size	Larger	Smaller
Mobility	Basically immobile	Highly mobile
Life span	Long-lived	Broken down soon after their job

DNA Structure

- DNA structure is created by joining nucleotide monomers using phosphodiester linkage with 3' ends of pentose sugar



- This creates the backbone

- N-bases/residues are extended outside the backbone

- DNA/RNA have defined sequence of N- bases that always refer to arrangement in 5' to 3' direction

DNA Structure

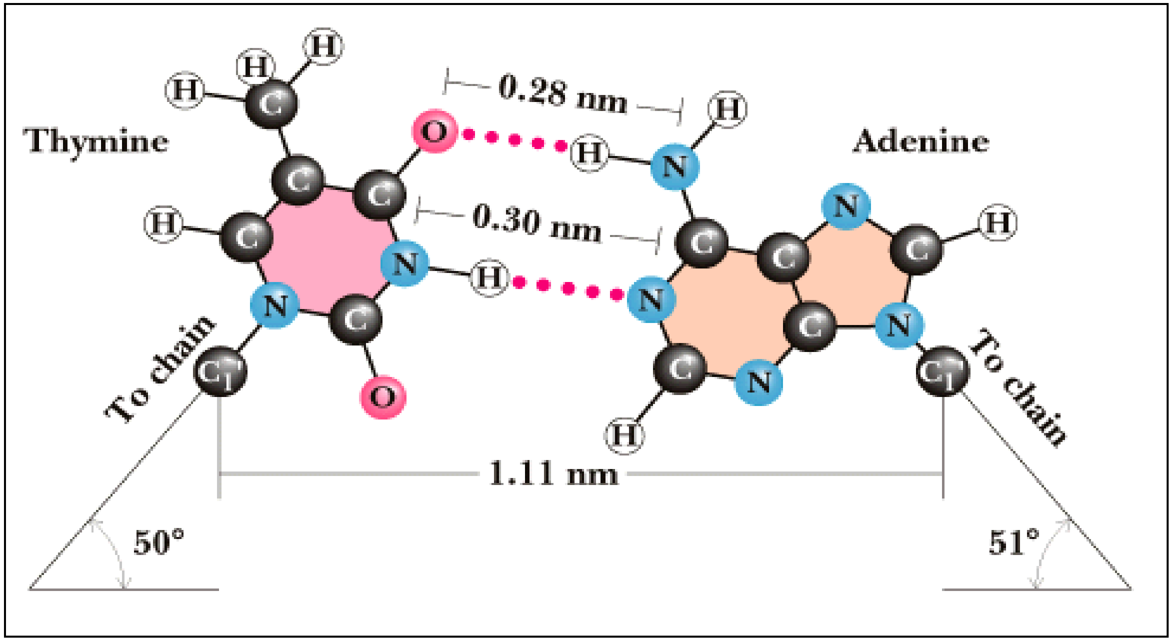
- ❖ DNA has a double helical structure
  - ➢ First proposed by James Watson and Francis Crick (1953)

- ❖ This structure is formed due to
  - ➢ Base pairing b/n two adjacent strands and
  - ➢ Aqueous environment

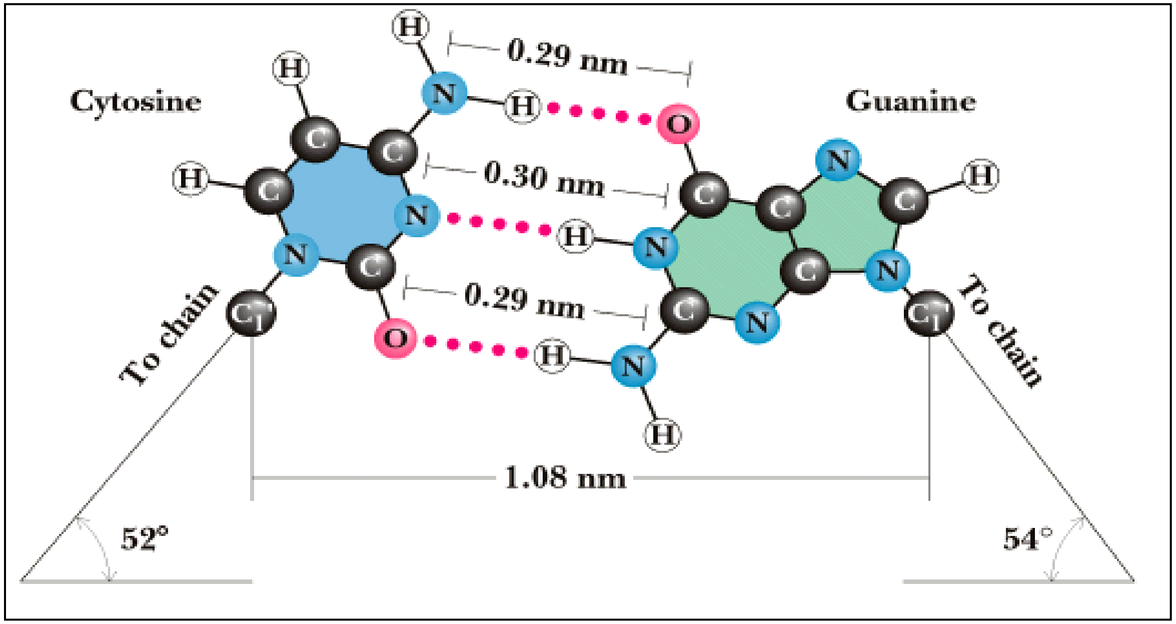
- ❖ Base pairing always occur through hydrogen bonds b/n a purine and a pyrimidine i.e G=C & A=T

DNA Structure

A-T pairing



G-C pairing



DNA Structure

Properties of DNA helix

❖ The helix stems of individual strands are antiparallel

✓ i.e oriented in opposite direction 5' ---> 3‘ & 3' ---> 5'

❖ Distance between the backbones is always the same giving DNA molecule a regular shape.

❖ Plane of bases are oriented perpendicular to backbone

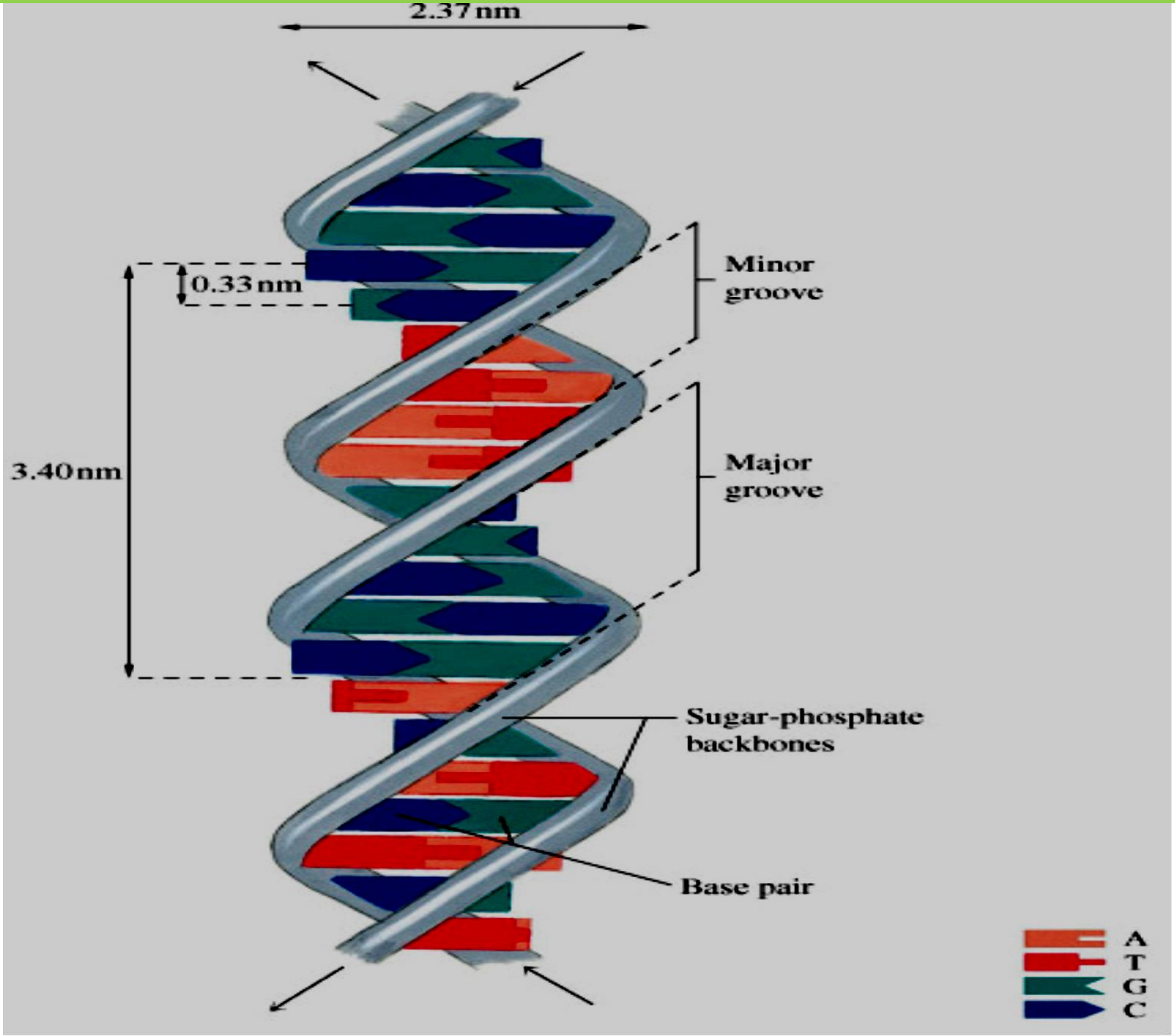
❖ Twisting lead to the formation of two groves (major and minor) with different rise and pitch

❖ High temperature breaks H-bonds between bases pair

➢ This cause the strands of the helix separate

✓ This process is called thermal denaturation

DNA structure



Classes of RNA

- **Three major classes exist**

i) **Ribosomal RNA (rRNA)**

- an integral part of ribosomes (sites for protein synthesis)
- most abundant class (accounts for 80% of the total cellular RNA)

ii) **Transfer RNA (tRNA)**

- carry activated aa's to the ribosomes during protein synthesis

iii) **Messenger RNA (mRNA**

- are products of DNA transcription
- serve as messengers to carry info. from DNA to the ribosomes
- encode the sequence of aa in proteins

Functional role of Nucleic acids

❑ Biological role

- ❖ **Carriers of genetic information :- DNA**
- ❖ **Carriers of energy** :-Nucleoside 5'-triphosphates (e.g ATP)
- ❖ **Biological recognition units**:- N-Bases serve this function
  - ➢ **Component of coenzymes**:- e.g NAD^+, $NADP^+$, FAD and coenzyme A.
  - ➢ **Mediators of important cellular processes** (e.g 2^0 signal transduction pathways).
    - ➢ cAMP –control phosphorylation of a number of proteins
    - ➢ cGMP –involve in photoreception (rhodopsin (rods) or opsins (cones)
- ❖ **Controlling enzymatic reactions through allosteric effects on enzyme activity**.
    - ➢ ATP is central to energy metabolism
    - ➢ GTP drives protein synthesis
    - ➢ CTP drives lipid synthesis
    - ➢ UTP drives carbohydrate metabolism

Functional role of Nucleic acid

- **As activated intermediates in numerous biosynthetic reactions.**
  - S-adenosylmethionine (S-AdoMet) involved in
    - Methyl transfer reactions (methylation reactions)
    - Synthesis of polyamines (as a source of propylamine)
  - Many sugar coupled nucleotides involved in glycogen and glycoprotein synthesis

- **Therapeutic** :-
  - Many synthetic nucleotide analogues are used for their therapeutic potential.

    e.g anti-tumor agents, anti-viral agents, drugs used for treatment of gauty etc..