DNA & RNA Structure

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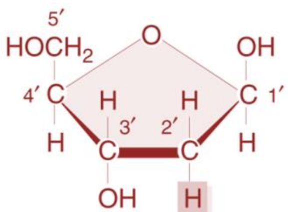
- **DNA**, ***Deoxyribonucleic acid***, is a *nucleic acid*, which makes *one of the major macromolecules* present in a biological cell.
- DNA is the hereditary (genetic) material that is present in the cells or living systems of all the living organisms. It codes the *information for all of the biological processes* taking place in a living cell (such as metabolism, growth and reproduction, etc).
- This genetic information present in the DNA is transferred from generation to generation in living organisms.
- Some of the viruses (viruses are considered living when inside their host cell) do not contain DNA as their genetic material.
- Some cells such as RBCs in animals and sieve cells in plants do not contain DNA.

- In **eukaryotic** cells, DNA is found in a cell's nucleus. Also, some DNA is present in mitochondria and chloroplasts organelles.
- In **prokaryotic** cells, DNA lies freely in the cell cytosol (without any membranous structure around it) in a discreet region referred to as nucleoid. Also, small extra-chromosomal forms called plasmid (carrying additional genes) may be present in some bacteria.
- DNA is *self-replicating* biomolecule.
- DNA is a biopolymer made of (deoxyribo-)nucleotides.
- The DNA stands for ***Deoxyribonucleic acid,*** where:-
  - '*deoxy*' means lacking oxygen (ribose lacking hydroxyl groups at C2),
  - '*ribo*' means ribose sugar,
  - '*nucleic*' means nuclear material of a living cell,
  - '*acid*' due to the acidic nature of DNA because of the presence of phosphate groups.

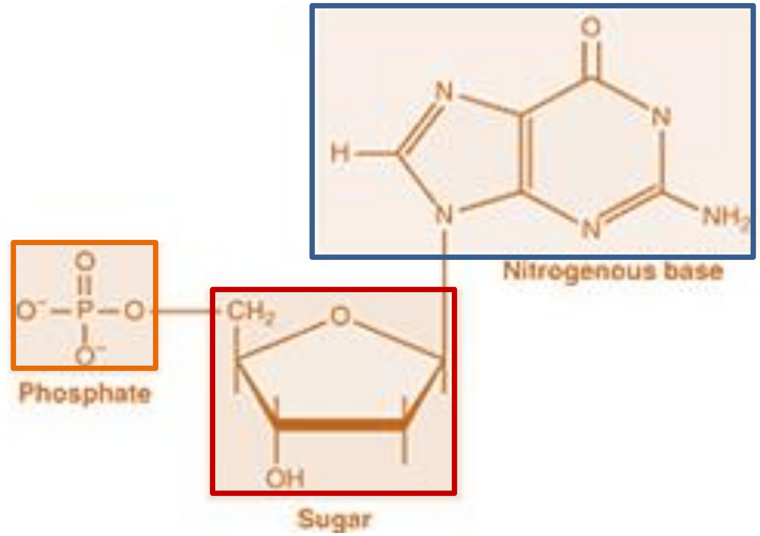
Nucleotides

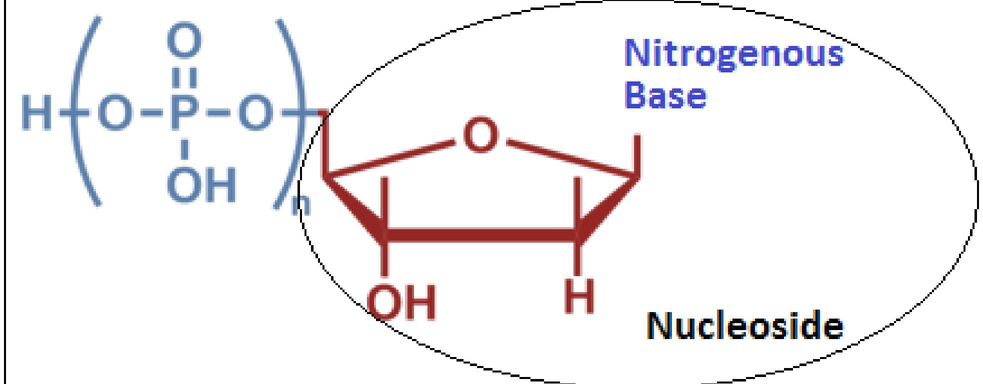
- Every ***nucleotide*** contains *3 components*:

1. a phosphate group,
2. a sugar (deoxyribose), and
3. nitrogenous bases.



Deoxyribose





Nucleoside + Phosphate = Nucleotide

n = 1 - nucleoside monophosphate
2 - nucleoside diphosphate
3 - nucleoside triphosphate

Nucleosides in DNA

Base	Sugar	Nucleoside	Common name
Adenine	Deoxy Ribose	Adenine deoxyribonucleoside	DeoxyAdenosine
Guanine	Deoxy Ribose	Guanine deoxyribonucleoside	DeoxyGuanosine
Cytosine	Deoxy Ribose	Cytosine deoxyribonucleoside	DeoxyCytidine
Thymine	Deoxy Ribose	Thymine deoxyribonucleoside	DeoxyThymidine

- There are *5 types of nitrogen bases* in biological systems:-

  1. **adenine** (A),
  2. **guanine** (G),
  3. **thymine** (T) in the case of DNA,
  4. **cytosine** (C), and
  5. **uracil** (U) in the case of RNA.

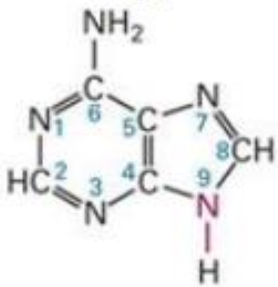
  Purines (1–2)

  Pyrimidines (3–5)

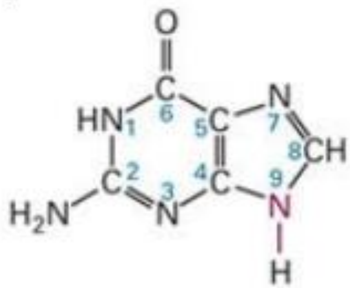
- The specific sequence of nucleotide bases makes up the *hereditary code* of DNA.
- The nitrogenous bases are divided into two groups; Purines (G and A), and pyrimidines (C, U, and T).

- *All of these biomolecules are named 'nitrogenous bases' because*
  - nitrogen atoms in their structure,
  - lone pair of electrons on one of the nitrogen atoms behaves as a base, i.e., can donate a pair of electrons.

Nitrogenous Bases

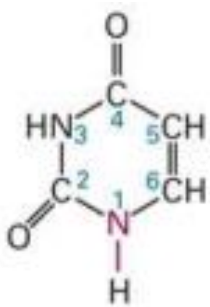


Adenine (A)

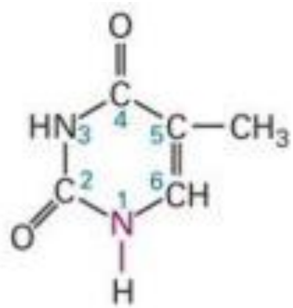


Guanine (G)

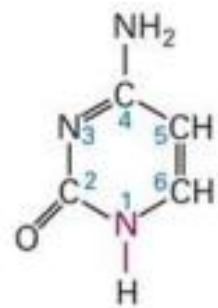
Purines (adenine and guanine) have a 2-ringed structure (nine-membered) with 4 nitrogen atoms.



Uracil (U)



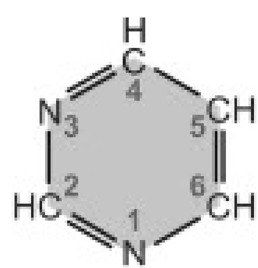
Thymine (T)



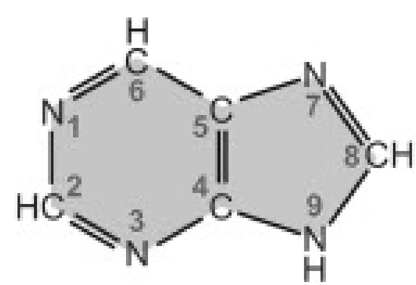
Cytosine (C)

Pyrimidines (cytosine, uracil, and thymine) have only 6-membered single ring, having 2 nitrogen atoms.

Numbering of elements in Nitrogenous Bases



Pyrimidine



Purine

DNA Structure

- DNA is a long polymer containing repeating units of nucleotides (A, T, G, and C). Different DNA molecules in different organisms may contain hundreds to millions of nucleotides in it.
- DNA is composed of 2 strands that are held together (by the hydrogen bonds between two complementary nitrogenous bases of opposite strands) and form a double helical structure.
- The backbone of DNA is made up of alternating units of sugar (deoxyribose) and phosphate molecules.
- The backbone units are connected together by phosphodiester bonds, in which a phosphate group makes one ester bond to the 3^{rd} carbon atom of the sugar ring at one side (the 3′-end or three prime end) and 5^{th} carbon atom of another sugar ring on the other side of the phosphate group (5′-end or five prime end).
- In this was, the DNA strands show opposite polarity, *i.e.*, if one strand has 3′-end to 5′-end polarity and the other has5′-end to 3′-end polarity.

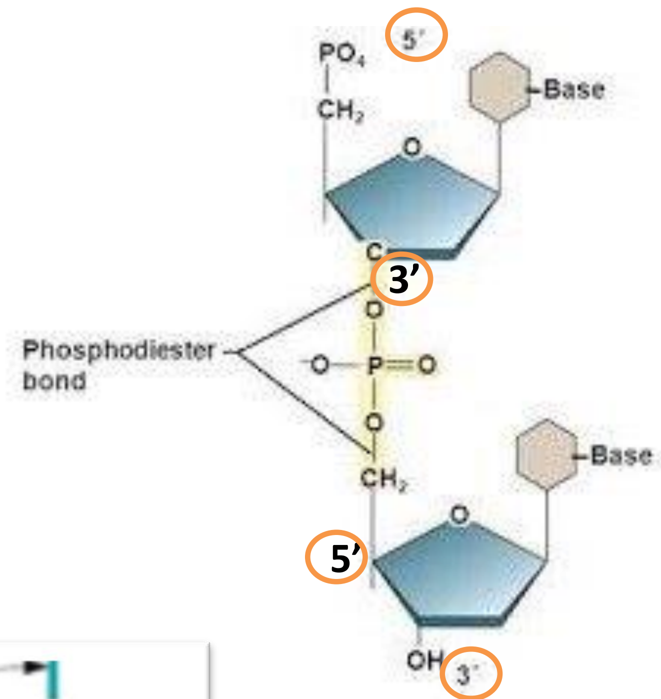
Bonds in DNA Molecule

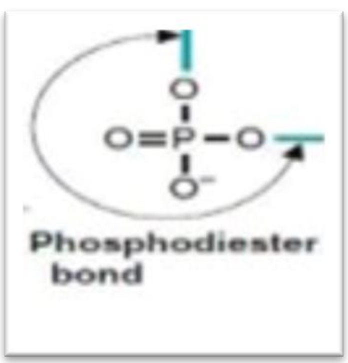
- Covalent bonds in DNA backbone.
- Hydrogen bonds (non-covalent interactions) between two strands.

1. Ester bond between phosphate and 5'OH of deoxyribose sugar.

   Diester bond between 5'phosphate of one nucleotide to 3'carbon of deoxyribose sugar of next nucleotide.

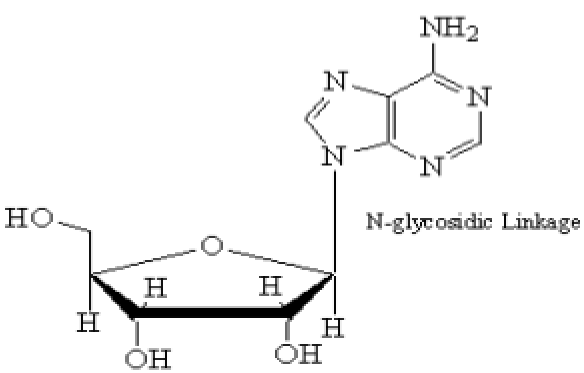
   (This is called as **Phosphodiester bond** which is formed between a phosphate molecule and 3' and 5' carbon atoms on two <u>independent</u> pentose (deoxyribose) sugars of DNA. Thus, nucleotides in a strand of DNA are held together by ***phosphodiester bonds,*** a specific type of covalent bond).

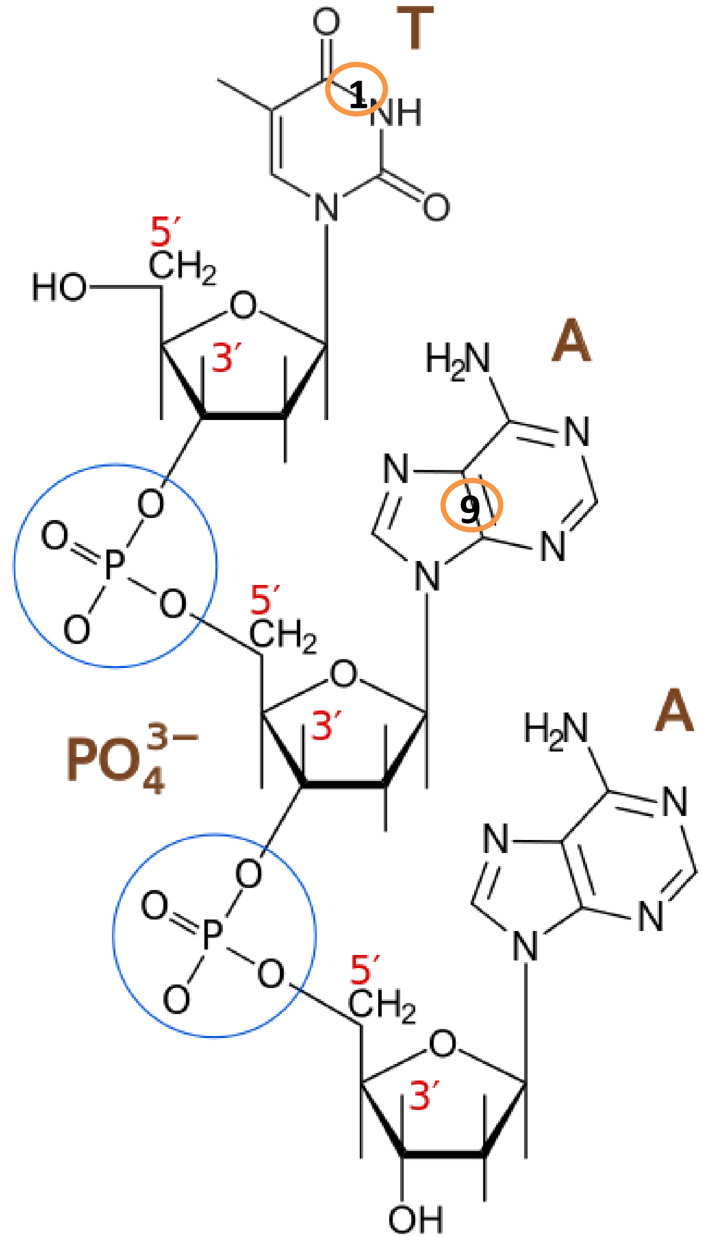




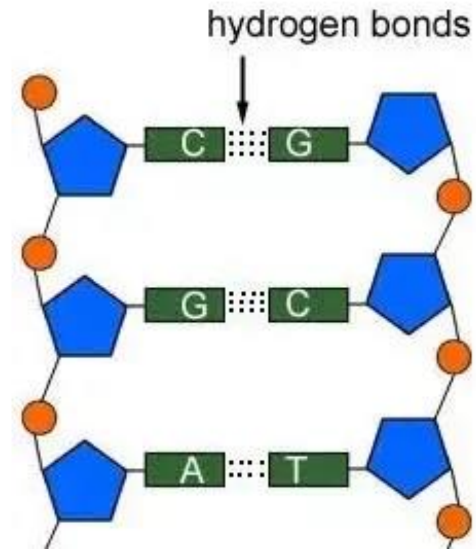
2. Glycosidic bond between deoxyribose sugar at its 1st carbon and nitrogenous Base.

- ✓ A nitrogen atom of the nitrogenous base is linked to one of the carbon (1st) atoms of sugar.
- ✓ In purines, linkage occurs between 9' nitrogen atom and C1 of sugar.
- ✓ In pyrimidine bases, 1st nitrogen of pyrimidine bases is linked to the 1' carbon of the sugar group.

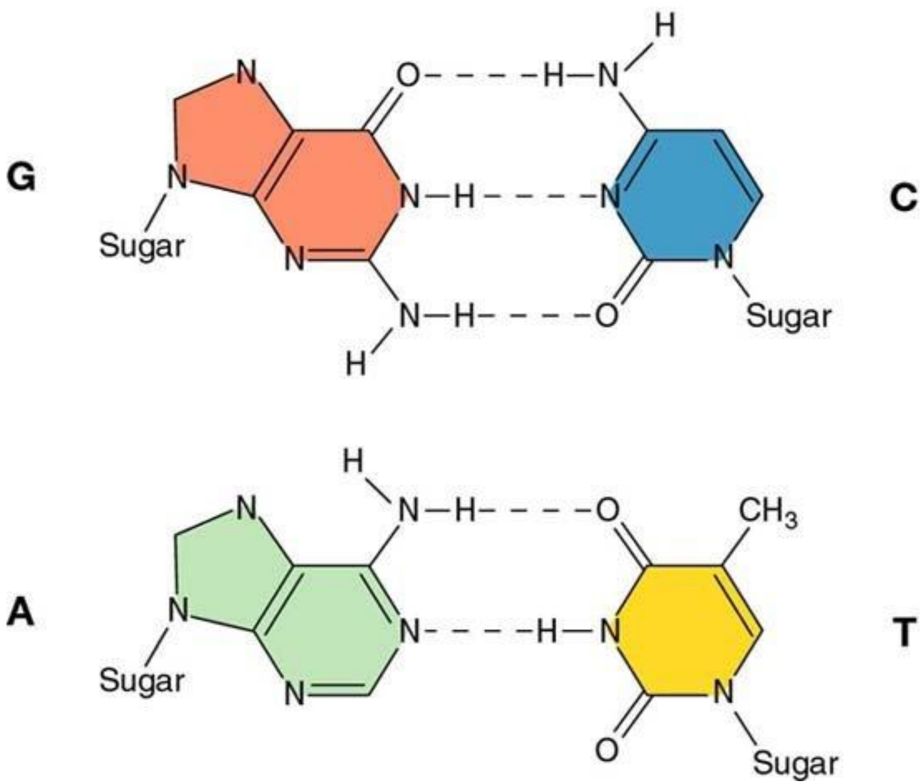




3. Double or triple hydrogen bond between nitrogenous bases of two opposite DNA strands. Thus, the two strands of DNA are held together by hydrogen bonds.



There are 2 H-bonds between Adenine and Thymine and 3 H-bonds between Cytosine and Guanine.



In a DNA double helix, the two strands are situated close enough so that the polar hydrogens (having positive charge) and polar oxygen or nitrogen (with negative charge) atoms having opposite polarization are attracted and, form a hydrogen bond.

Hydrogen bond is not strong like a covalent bond, but in aggregate is strong enough to hold the two molecules in position.

Brief History of DNA

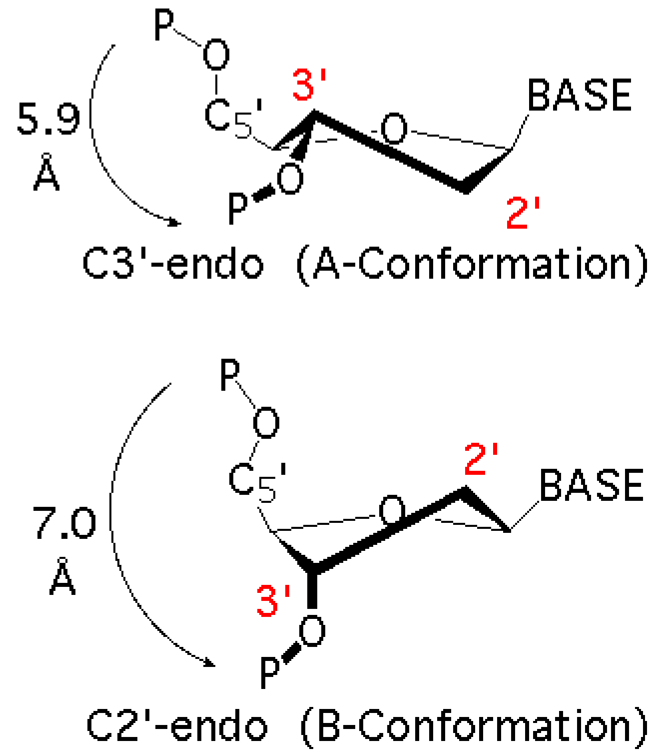
- In 1869, Friedrich Miescher identified a substance in the nuclei of human WBC which he named "nuclein".
- In 1919, based on Miescher's work, Phoebus Levene proposed the "polynucleotide" model of nucleic acid.
- Based on Levene's work, Erwin Chargaff and Oswald Avery proposed the "Chargaff's rule" for A, T, G, and C arrangement and composition.

> [Chargaff's rule states that DNA from any organism should have a 1:1 ratio (base Pair Rule) of pyrimidine and purine bases and, more specifically, that the amount of guanine purine is equal to cytosine pyrimidine and the amount of adenine purine is equal to thymine pyrimidine.1:1 stoichiometric ratio of purine and pyrimidine bases means A+G=T+C.]

- In 1953, James Watson and Francis Crick gave the double helix model of DNA with the help of X-ray crystallography done by Rosalind Franklin and Maurice Wilkins.

Sugar Puckering in DNA

- The conformation of the ribose or deoxyribose sugar rings may vary in DNA. This is termed as sugar puckering.
- The sugar ring pucker conformations affect the overall structure of RNA and DNA by maintaining a stable helical form.
- The structure in turn influences the function.
- The sugar pucker is mostly seen in DNA at positions of C2′ and C3′ atoms relative to a plane formed by the C1′, O4′, and C4′ atoms.

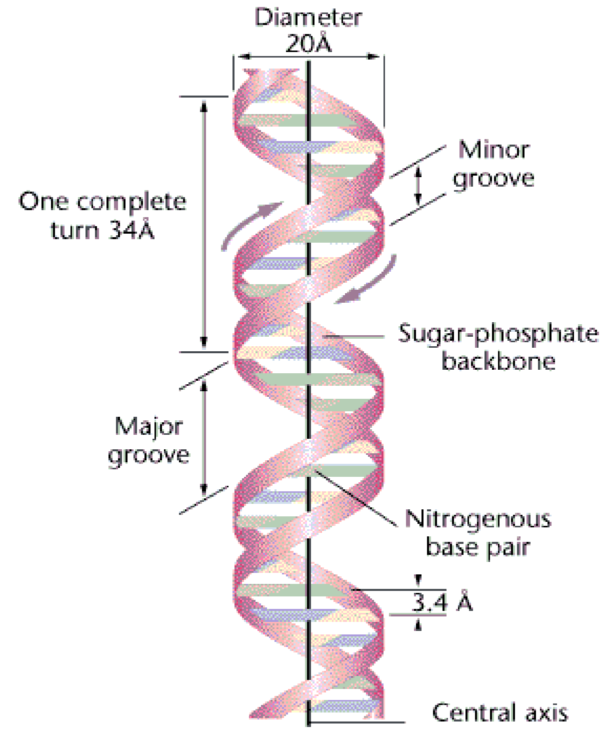


Helix Structure of DNA

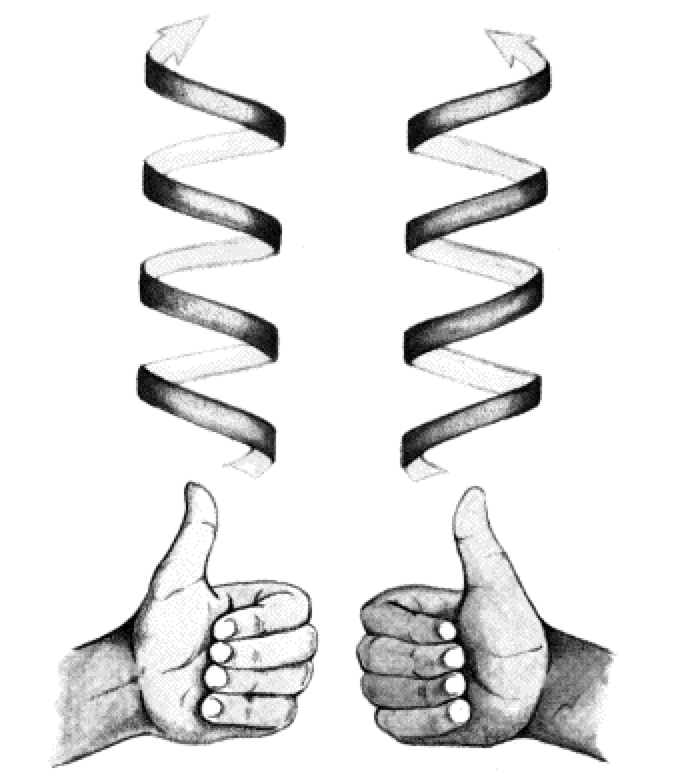
- The 3-dimensional double helix describes the appearance of double-stranded DNA, which is composed of two linear strands that run opposite to each other, or **anti-parallel**, and **twist together** (making helical structure).
- The double helical DNA has a twisted ladder like structure, where each strand comprises a backbone containing alternating groups of phosphate and sugar groups. The nitrogenous bases, attached to the sides of the ribose sugars are placed centrally in the double stranded structure, making hydrogen bonded nitrogenous base pairs. These nitrogenous base pairs hold the two strands together and appear like a ladder in dsDNA.
- The formation of nitrogenous base pairs occurs by following Chargeff's rules (number of A=G, T=C or A+G=T+C).

- Adenine forms a base pairing with thymine whereas cytosine pairs with guanine. This pairing is referred to as the base complementary rule since the DNA strands are complementary to one another.
- Thus, when the sequence of a strand is TTGGCCAA, then the complementary strand should have AACCGGTT as its sequence.
- DNA helix may have different conformations (A, B, D, Z, etc.)
- The B-form was described by James Watson and Francis Crick, and it is believed to predominate in cells.
- Other than B-DNA, about 20 other slightly different variations of the right-handed helical form of ds-DNA exists, such as A-DNA, C-DNA, and D-DNA .

B-DNA

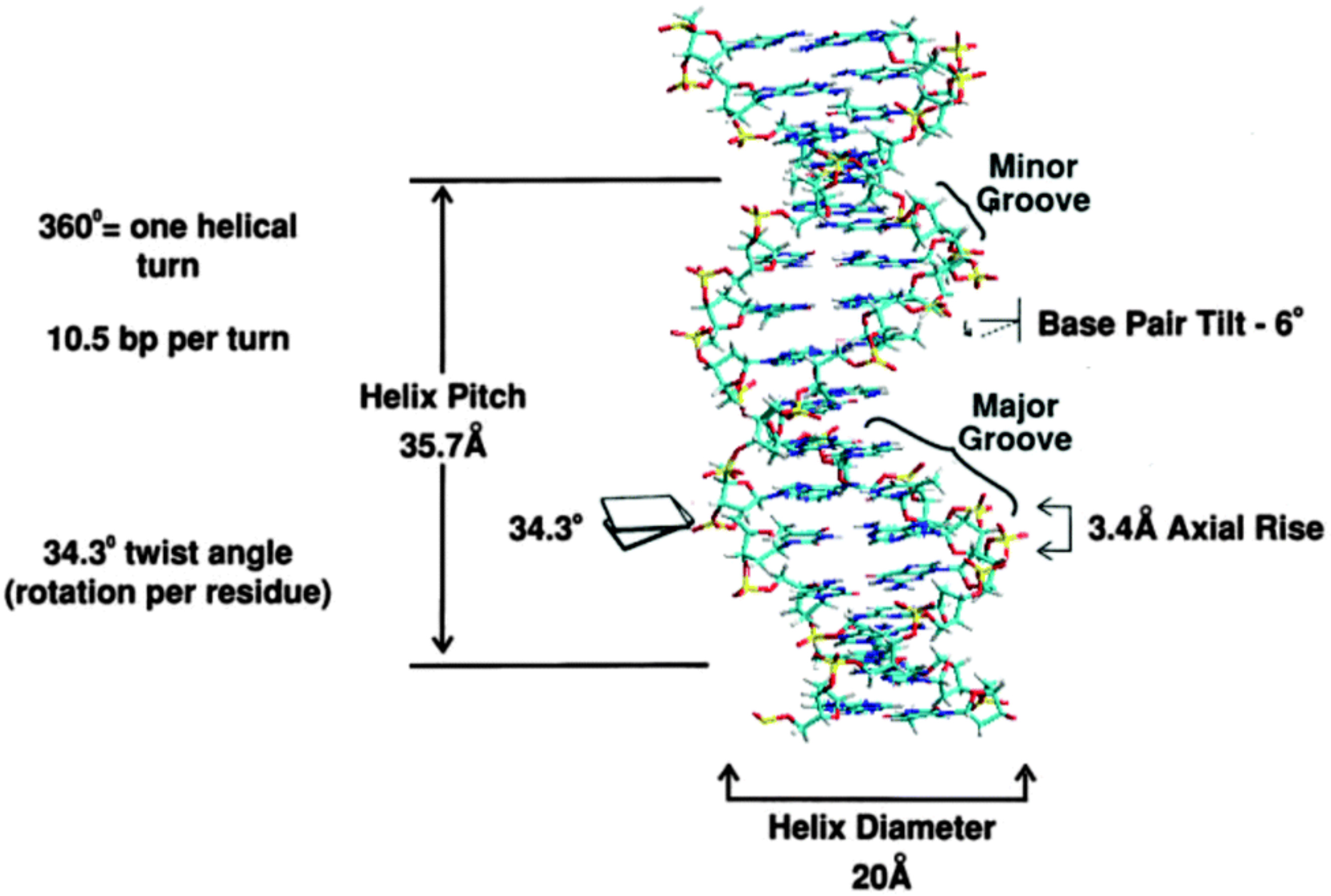


- It has a right-handed double helix, means the chains rotate counterclockwise as they approach an observer observing the longitudinal axis.
- It is the common form of DNA exists under normal physiological conditions.
- The double strands of B-DNA run in opposite directions (anti-parallel).
- The structure is asymmetrical, i.e., twisted in a way that it has alternating major grooves and minor grooves.
- The major and minor grooves are wider and narrow, respectively.
- The width and depth of the B-type major grooves are **12Å** and **8.5Å**, respectively. Oppositely, the width and depth of the B-type minor grooves are **6Å** and **7.5Å**, respectively.
- In a B-type, the sugar pucker is at **C_2 endo form**.
- In **one turn**, there are **10.5 base pairs**, with a length (pitch of helix) of 3.4nm**.**
- The distance between two adjacent deoxyribonucleotides is 0.34nm.
- The helix width of B-DNA is 2nm (20 Å). Thus, B-DNA is narrower than A-DNA.



Most DNA double helices are right-handed; that is, if you were to hold your right hand out, with your thumb pointed up and your fingers curled around your thumb, your thumb would represent the axis of the helix and your fingers would represent the sugar-phosphate backbone.

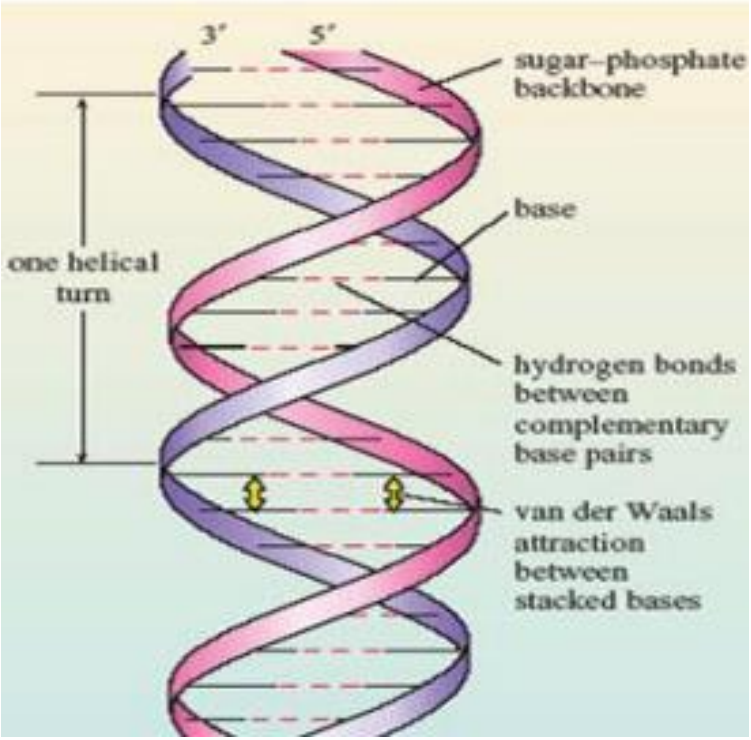
Other features:-



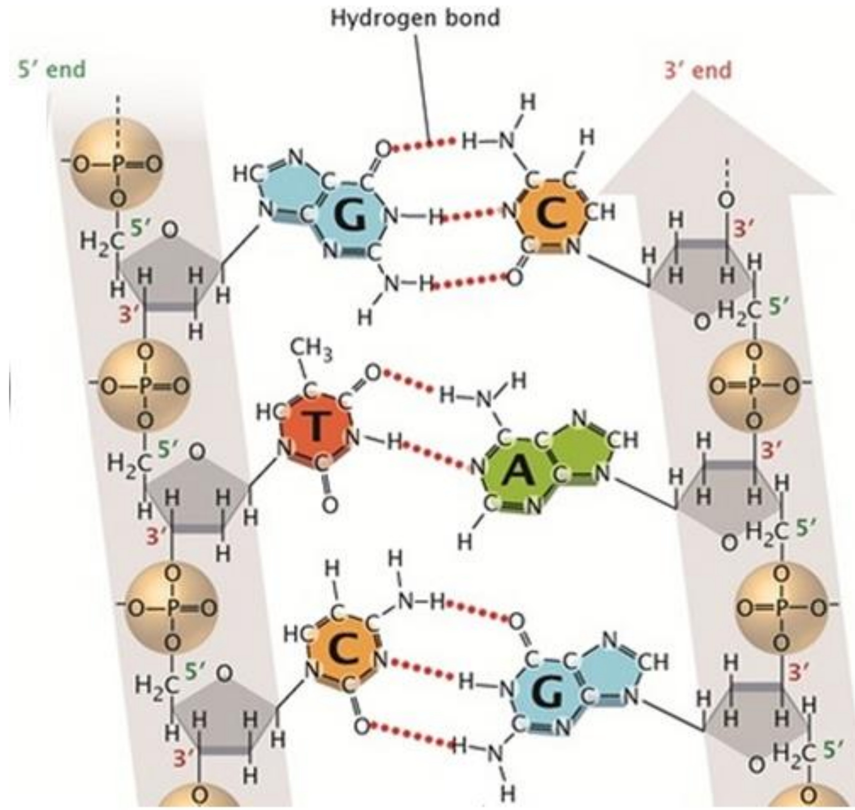
Two factors are mainly responsible for the ***stability of the DNA double helix***:

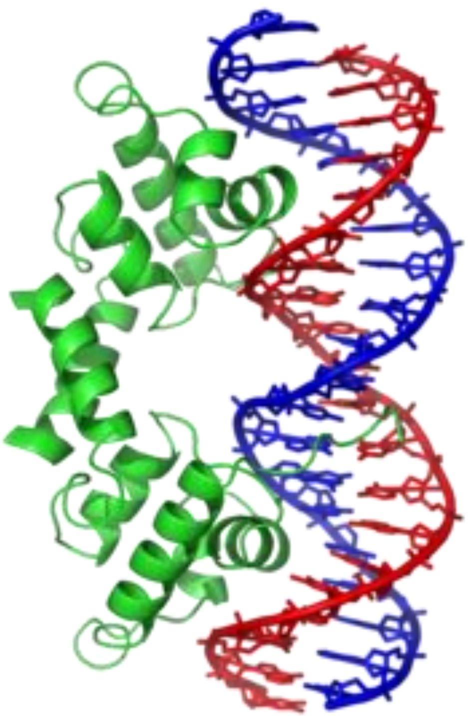
(a) Base pairing between complementary strands and
(b) Stacking between adjacent bases (Base stacking)

- Base stacking interaction is a very complex interaction that depends on Van der Waals forces, electrostatic dipole forces between bases, forces due to pi-pi interaction, etc.



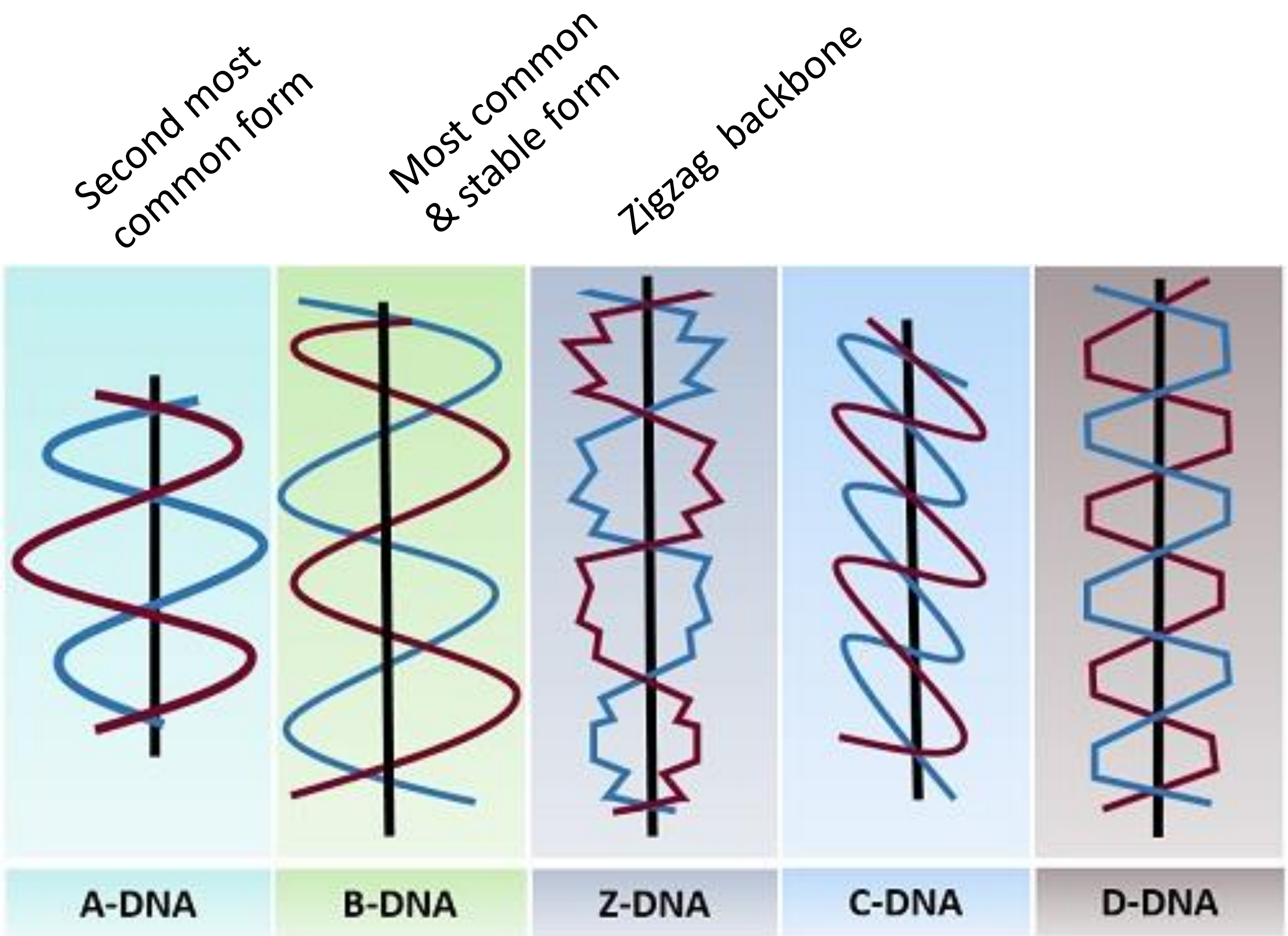
- Not only are the DNA base pairs connected via hydrogen bonding, but the outer edges of the nitrogen-containing bases are exposed and available for potential hydrogen bonding as well.





- These hydrogen bonds provide easy access to the DNA for other molecules, including the proteins that play vital roles in the replication and expression of DNA.

DNA conformations other than B- DNA



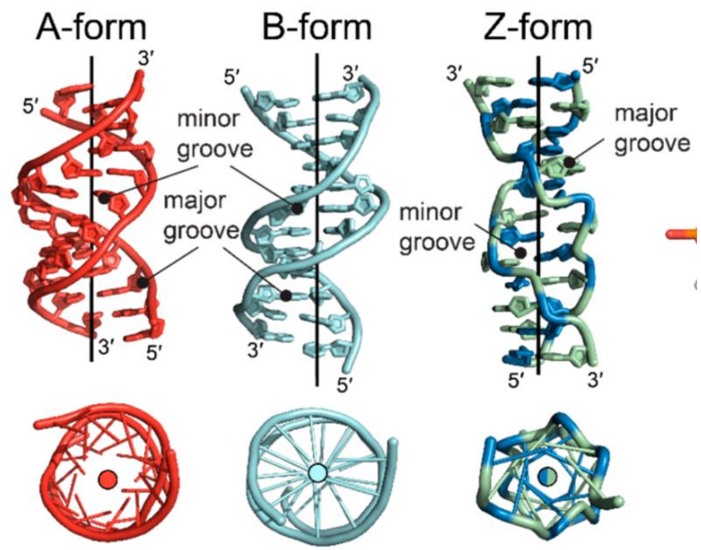
Properties	A-DNA	B-DNA	Z-DNA	C-DNA	D-DNA	E-DNA
Helical sense	Right handed coiling	Right handed coiling	Left handed coiling	Right handed coiling	Right handed coiling	-
Occurrence conditions	75% relative humidity with the presence of ions like sodium, potassium, cesium.	92% relative humidity with the low ion concentration	Occur at very high salt concentration with alternating purine and pyrimidine base sequence	66% relative humidity with the presence of lithium & magnesium ions.	-	-
Plane of the base	Perpendicular to the helical axis	Perpendicular to the helical axis	Perpendicular to the helical axis	Perpendicular to the helical axis	Perpendicular to the helical axis	-
Rotation per base pair	33 Degrees	36 Degrees	30 Degrees	38.6 Degrees	-	-
Axial rise per base pair	2.56 Å	3.38 Å	3.71 Å	3.32 Å	3.03 Å	-
Helix diameter	25.5 Å	20 Å	18 Å	19.0 Å	-	-
Base pairs per turn	11bp	10bp	12bp	9.33bp	8bp	7.5bp

Properties	A-DNA	B-DNA	Z-DNA	C-DNA	D-DNA	E-DNA
Sugar phosphate backbone	Normal	Normal	Zig-Zag	Normal	Normal	-
Base pair tilt	19 Degrees	6.3 Degrees	7 Degrees	-7.8 Degrees	-16.7 Degrees	-
Helix pitch	25.5 Å	35.5 Å	45.6 Å	30.9 Å	-	-
Major groove	Narrow and deep major groove	Wide and deep major groove	Flat major groove	-	-	-
Minor groove	Wide and deep minor groove	Narrow and deep minor groove	Narrow and deep minor groove	-	-	-
Sugar puckering	C3 – endoconformation	C2 – endoconformati on	C3 – endoconformation for purines and C2 – endoconformation for pyrimidines	-	-	-
Base pair tilt	19 Degrees	6.3 Degrees	7 Degrees	-7.8 Degrees	-16.7 Degrees	-

In the cell, E-DNA is found very rarely and having extended or **eccentric DNA**. After the X-ray crystallographic study, E-DNA is found **intermediate** between the B-DNA to A-DNA.

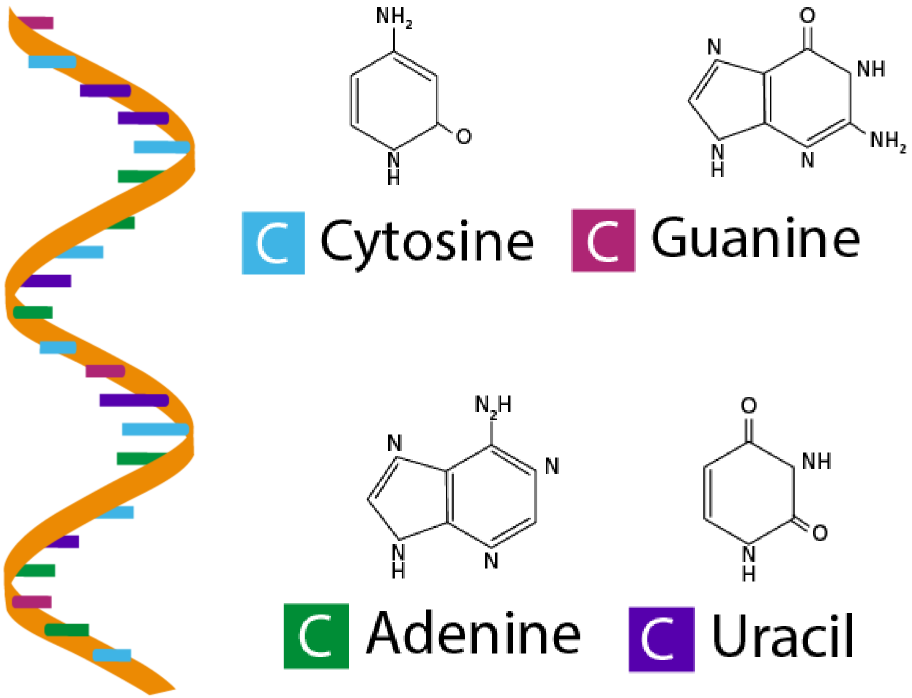
Common Forms

Property	A-DNA	B-DNA	Z-DNA
Helix handedness	RIGHT	RIGHT	LEFT
base pairs per turn	11	10.4	12
Rise per base pair along axis	0.23nm	0.34nm	0.38nm
Pitch	2.46nm	3.40nm	4.56nm
Diameter	2.55nm	2.37nm	1.84nm
Conformation of Glycosidic bond	ANTI	ANTI	ALTERNATING ANTI AND SYN
Major Groove	PRESENT	PRESENT	ABSENT
Minor Groove	PRESENT	PRESENT	DEEP CLEFT



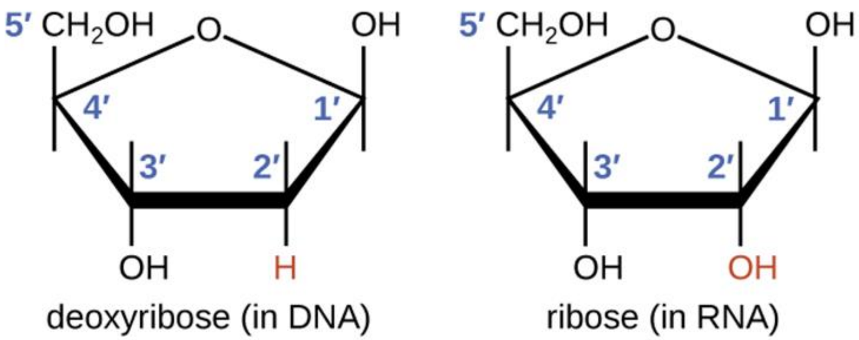
- Z-DNA is a transient form of DNA, only occasionally existing in response to certain types of biological activity. It is formed *in vivo* in DNA containing alternating purine & pyrimidine repeats.
- Z-DNA was first discovered in 1979.
- Scientists have discovered that certain proteins bind very strongly to Z-DNA.
- The Z-form DNAs are presumed to play a role in various cellular functions **such as gene expression** DNA processing events, genetic instability, e.g., Z-DNA-forming sequences have the potential to enhance the frequencies of recombination, deletion, and translocation events in cellular systems.

RNA

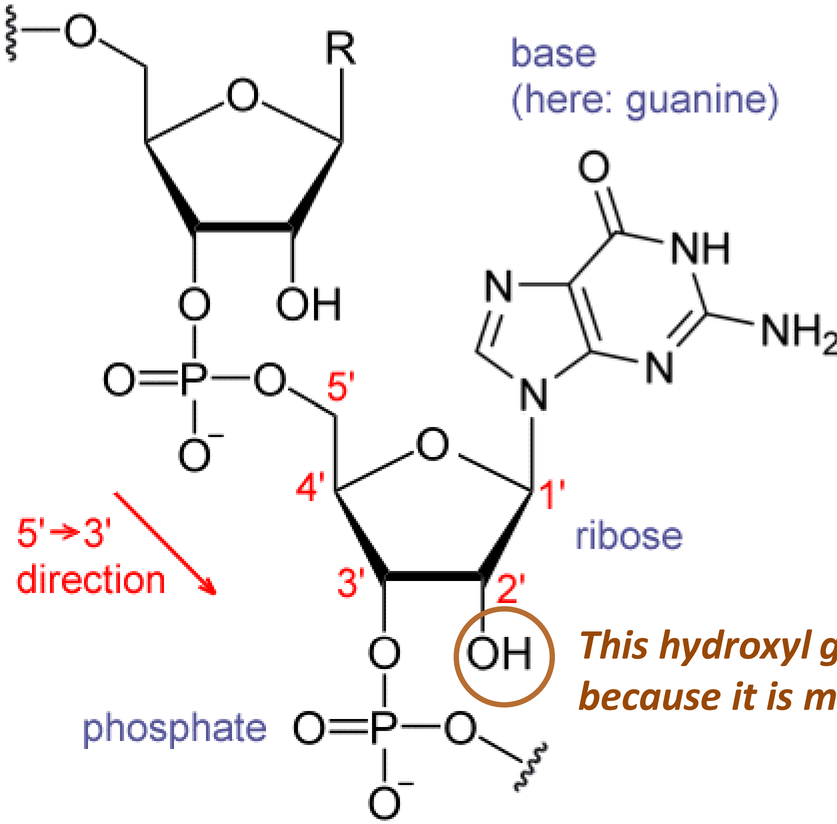


Ribonucleic acid (RNA) is a molecule that is present in the majority of living organisms and viruses.

- It is made up of ***ribonucleotides***, which are ribose sugars attached to nitrogenous bases and phosphate groups.
- Ribose sugar is a cyclical structure made up of five carbons and one oxygen atom. This sugar contains two OH-groups at 2' Carbon and 3' Carbon.



- The alternative ribose sugar and phosphate groups form the backbone of the RNA's structure, and these are linked together through ***phosphodiester bonds***.

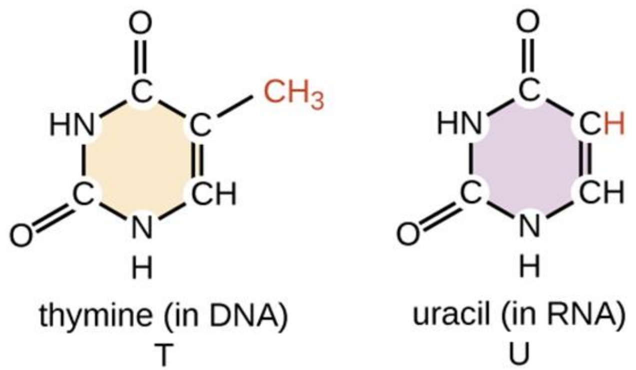


This hydroxyl group make RNA less stable than DNA because it is more susceptible to hydrolysis

Nucleosides in RNA

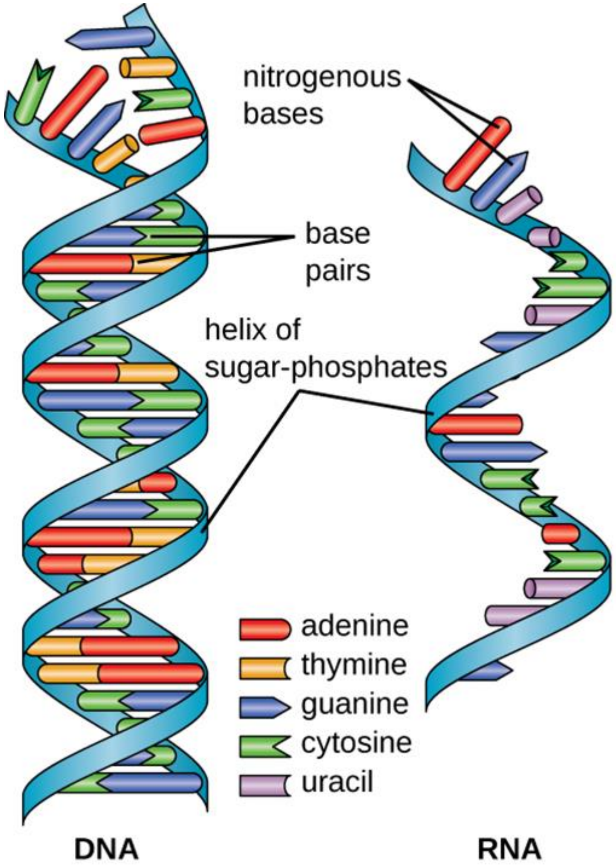
Base	Sugar	Nucleoside	Common name
Ribonucleosides			
Adenine	Ribose	Adenine ribonucleoside	Adenosine
Guanine	Ribose	Guanine ribonucleoside	Guanosine
Cytosine	Ribose	Cytosine ribonucleoside	Cytidine
Thymine	Ribose	Thymine ribonucleoside	Thymidine
Uracil	Ribose	Uracil ribonucleoside	Uridine

- The nitrogenous bases include adenine, guanine, **<u>uracil</u>**, and cytosine.
- Thymine at the place of uracil confers to additional stability because thymine has greater resistance to photochemical mutation, making the genetic material more stable.

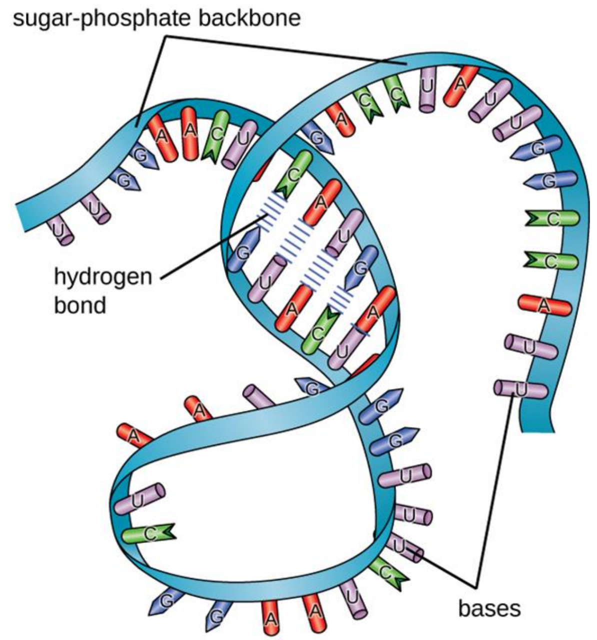


- There is no thymine in RNA because thymine is more energetically expensive to produce. This is because thymine is a methylated version of the base found in RNA called uracil, and the addition of this methyl group uses energy.
- RNA employs uracil because the instability doesn't matter as much for RNA (mRNA is relatively short-lived and any potential faults don't result in any lasting damage).

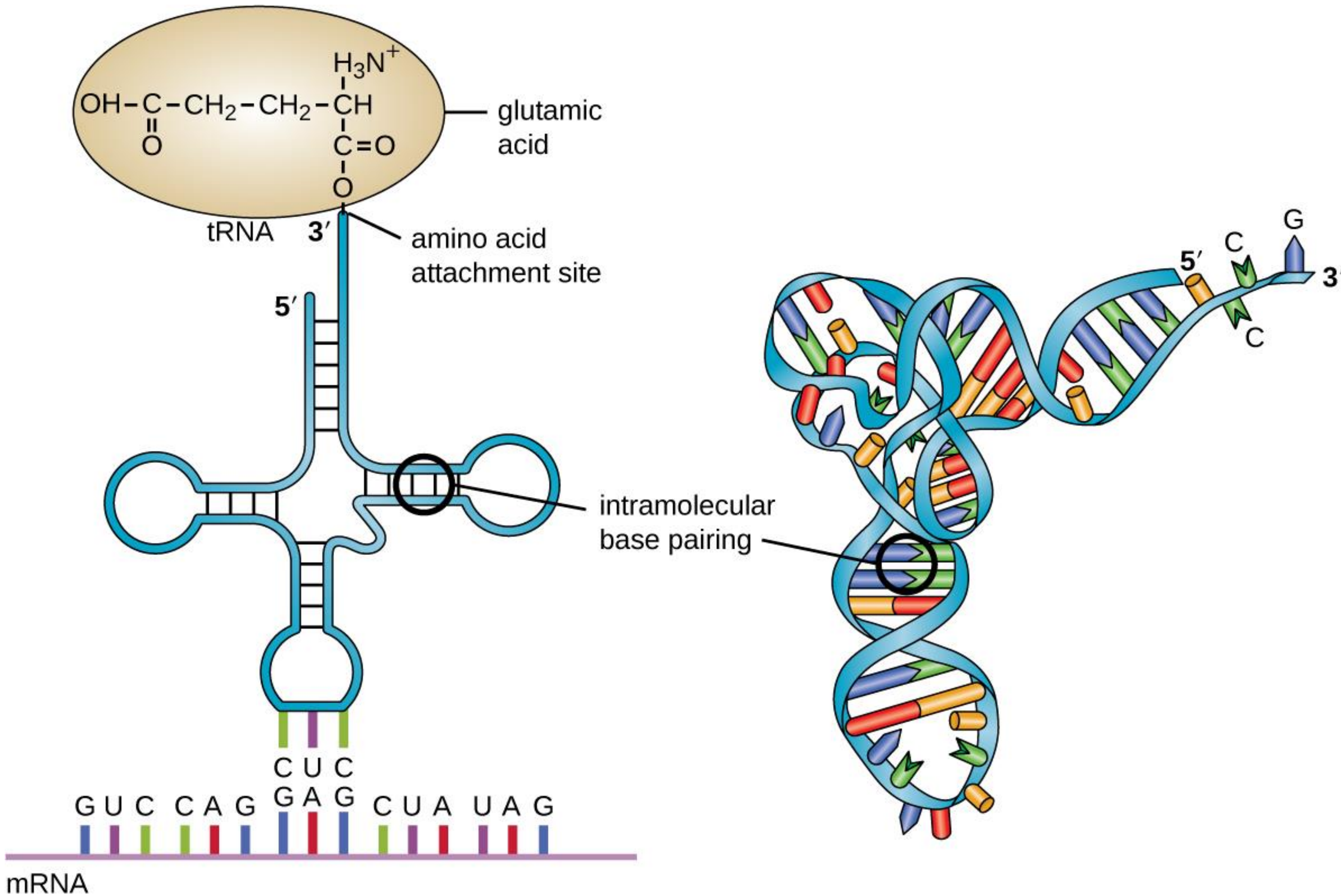
- RNA mostly exists in the single-stranded form, but there are special RNA viruses that are double-stranded.
- An RNA virus uses RNA instead of DNA as its genetic material and can cause many human diseases.
- The RNA molecule can have a variety of lengths and structures (whereas DNA molecules are typically long and double stranded).



- The structural difference (of OH at C2) between the ribose and deoxyribose sugars gives DNA added stability, making DNA more suitable for storage of genetic information.
- On the other hand, the presence of OH group in ribose sugar accounts for relative instability of RNA makes it more suitable for its more short-term functions.
- Even though RNA is single stranded, most types of RNA molecules show extensive intramolecular base pairing between complementary sequences within the RNA strand, creating a predictable three-dimensional structure essential for their function.



RNA can fold upon itself, with the folds stabilized by short areas of complementary base pairing within the molecule, forming a three-dimensional structure.

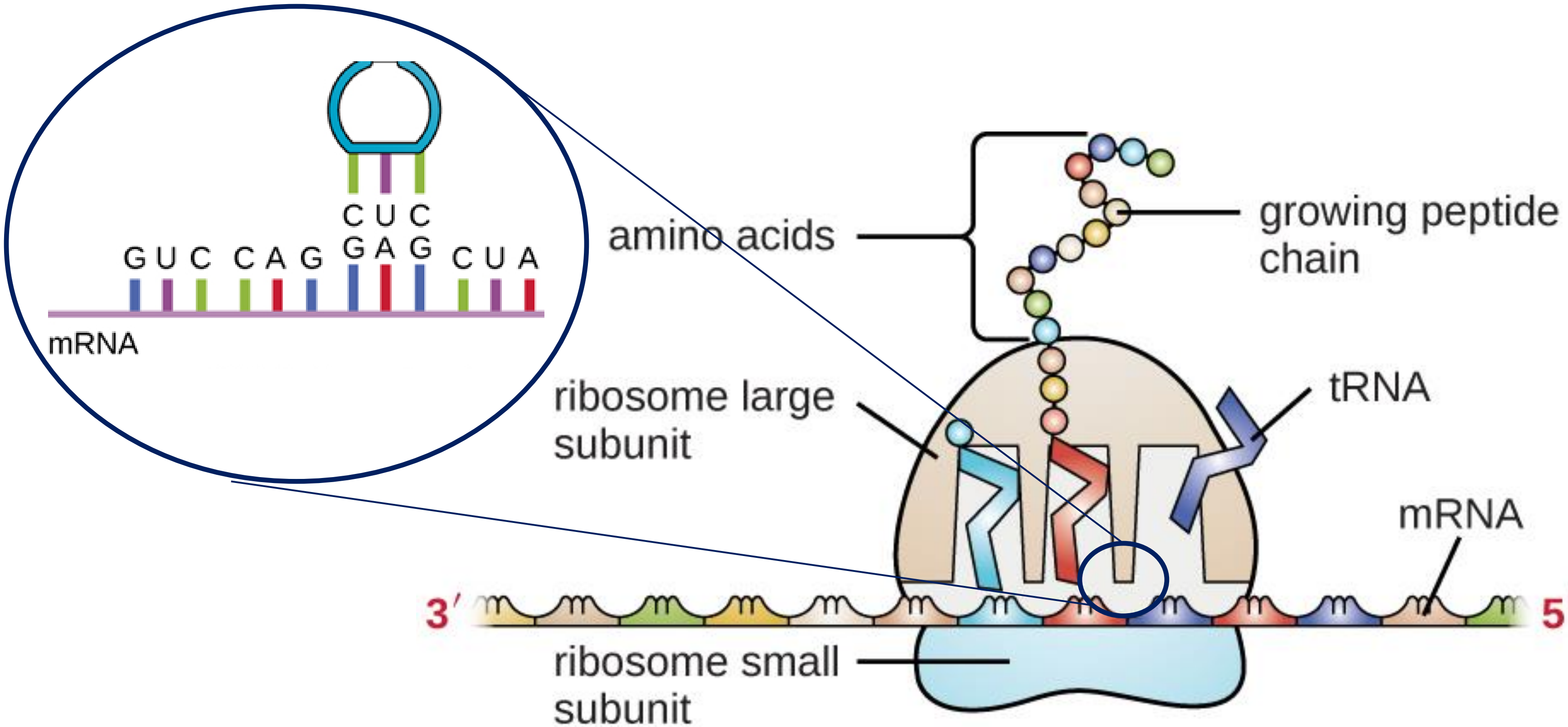


tRNA 2-dimensional structure

tRNA 3-dimensional structure

Common RNA Types in a Cell for Protein Synthesis

	mRNA	rRNA	tRNA
Structure	Short, unstable, single-stranded RNA corresponding to a gene encoded within DNA	Longer, stable RNA molecules composing 60% of ribosome's mass	Short (70-90 nucleotides), stable RNA with extensive intramolecular base pairing; contains an amino acid binding site and an mRNA binding site
Function	Serves as intermediary between DNA and protein; used by ribosome to direct synthesis of protein it encodes	Ensures the proper alignment of mRNA, tRNA, and ribosome during protein synthesis; catalyzes peptide bond formation between amino acids	Carries the correct amino acid to the site of protein synthesis in the ribosome



A generalized illustration of how mRNA and tRNA are used in protein synthesis within a cell

THANK YOU