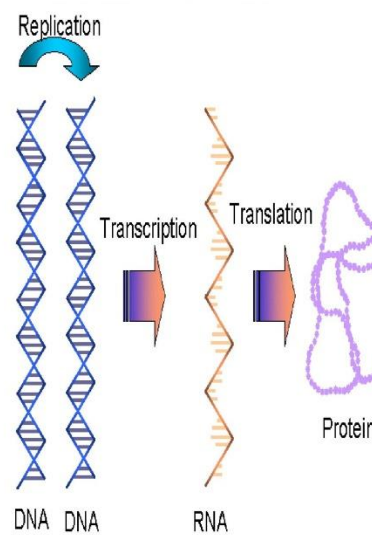
DNA:- "GENETIC MATERIAL"

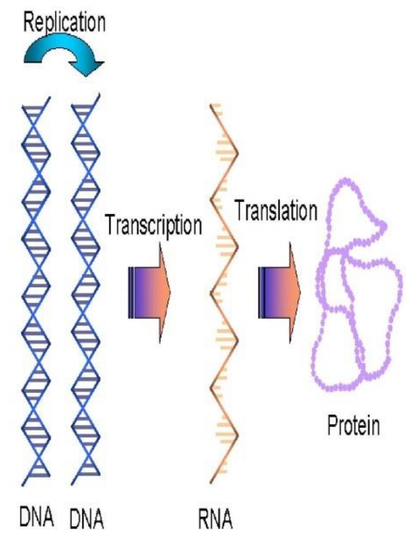
What is DNA needed for?

- Genetic information is transferred from DNA and converted to protein. RNA work as messenger. Proteins are the biological workers.
- Information of the DNA is copied to a RNA molecule in transcription
- The process by which DNA is copied to RNA is called transcription.



What is DNA needed for?

- RNA directs the protein synthesis in a translation.
- By which RNA is used to produce protein is called translation.
- Protein's 3D structure determines its function. Information transfer only in one direction.



What is DNA genetic material & its role?

- DNA, deoxyribonucleic acid, is the genetic material in our cells which was passed on to us from our parents and determines our characteristics.
- DNA serves two important cellular functions:

  a) It is the genetic material passed from parent to offspring .

  b)It serves as the information to direct and regulate the construction of the proteins necessary for the cell to perform all of its functions.

Why DNA is called the genetic material?

- Genetic material is that substance which controls the formation and expression of traits (a genetically determined characteristic) in an organism.
- It can replicate and pass on from a cell to its daughter cell and from one generation to the next.

Requirements for a genetic material?

- Must be stable.
- Must be capable of being expressed when needed.
- Must be capable of accurate replication.
- Must be transmitted from parent to progeny (a descendant)without change.

Characteristics for a genetic material

- Following are the 4 main characteristics:-

  a) Replication

  b) Storage of information

  c) Expression of information

  d) Variation by mutation.

Genetic Information

- It includes information of genetic tests of individual's and individual's family members. It also contain information about family medical history.
- Chromosomes are contained inside the cell's nucleus which are long, thin, threadlike structures made from molecules of DNA that store genetic information.
- They are found in the nucleus of body cells in pairs – one is inherited from the mother and one is inherited from the father.

What part of DNA is genetic information located?

- The genetic information is stored in the chemical structure of the DNA.
- There is a backbone that consists of a sugar and phosphate. Connecting the two backbones are the bases.
- The bases are adenine (A), thymine (T), guanine (G), and cytosine (C).

Direct evidences

- Frederick Griffith's (1928) experiment on Bacterial Transformation
- Oswald Avery, Colin Macleod and Maclyn McCarty's (1944) experiment on Transformation
- Alfred D. Hershey and Martha Chase (1952) experiment on T- Even (2,4) Bacteriophage (a virus which parasitizes a bacterium by infecting it and reproducing inside it).

Transforming Principle

- **Transformation** occurs when one bacterium (microscopic, single-celled creatures) picks up free-floating DNA and incorporates it into its own genome.
- The idea of the **transforming principle** was discovered during an experiment by Frederick Griffith.

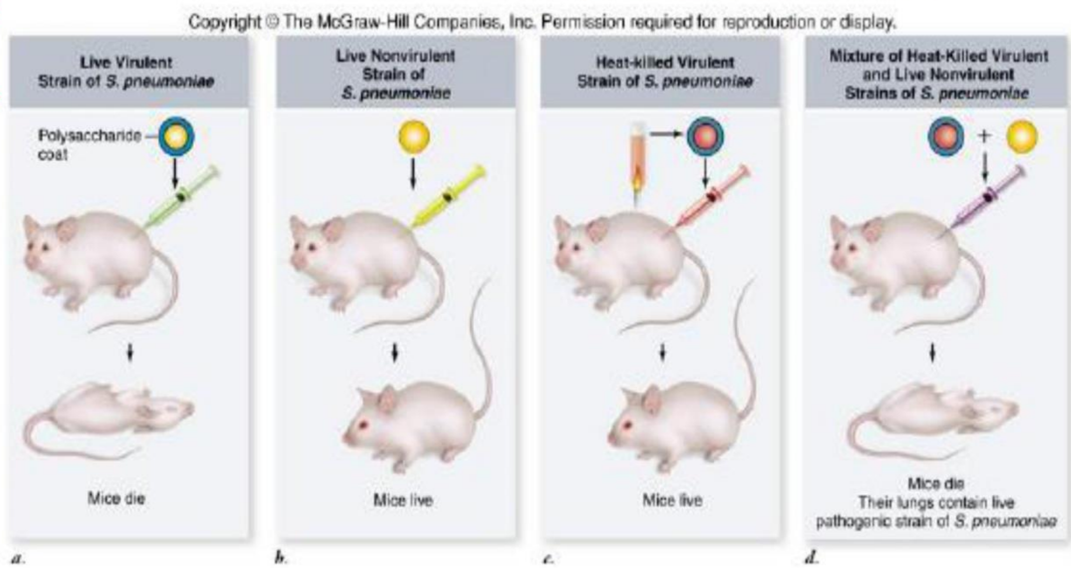
Transformation Experiment

- In 1928 Frederick Griffith (Griffith effect), suggested that bacteria are capable of transferring genetic information through a process known as transformation.
- Based on it, he concluded that R strain bacteria had been transformed by S strain bacteria. The R strain inherited some 'transforming principle' from the heat-killed S strain bacteria which made them virulent.
- This transforming principle was considered as genetic material.

Experiment on Diplococcus pneumoniae

- Griffith performed experiment on bacteria (Diplococcus pneumoniae) having Two strains.
- SIII strain was virulent(harmful in effect), possessed a lipopolysaccharide capsule and could kill mice by causing disease Pneumonia and made round colonies on a culture plate
- RII strain was a virulent and lacked a Lipopolysaccharide (LPS) capsule, growing in rough–shaped colonies on a culture plate.

STEPS IN THE EXPERIMENT

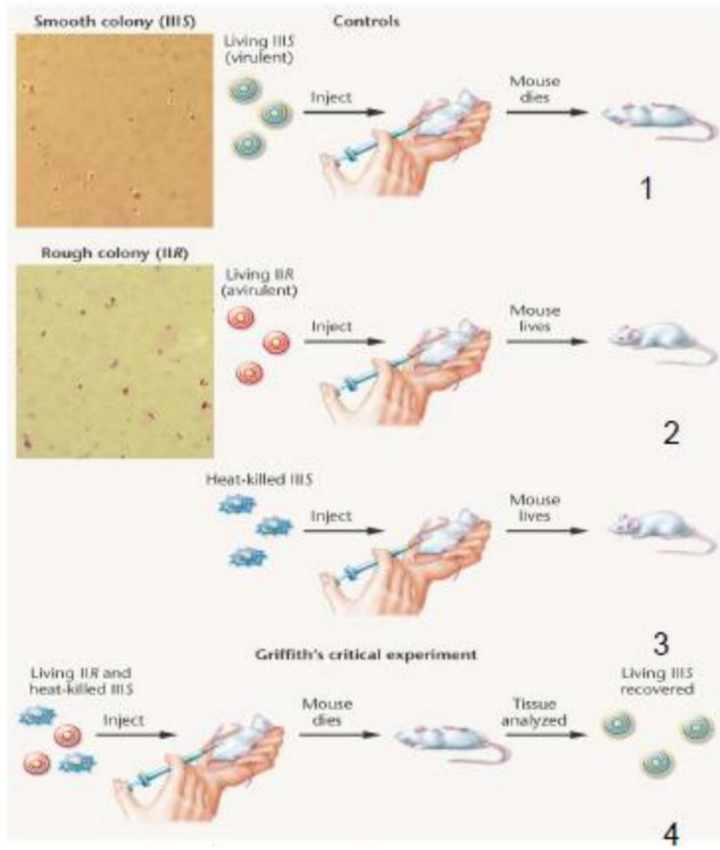


1 LIVE SIII   2 LIVE RII   3 H K S III   4 H K S III & LIVE RII

Strains of Diplococcus pneumoniae injected to mice

Griffith's Experiment

RII → SIII transformation takes place in step 4 give clue for DNA as genetic material

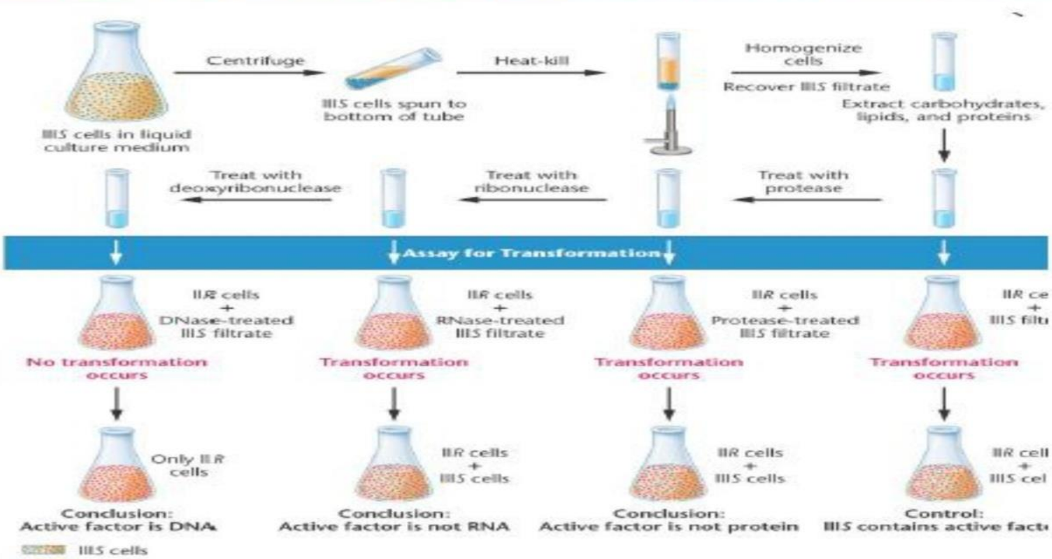


STEPS AND RESULTS OF GRIFFITH'S EXPERIMENT

S N	STEPS	RESULT
I	Mouse injected with SIII strain	Mouse died √
II	Mouse injected with RII strain	Mouse survived
III	Mouse injected with Heat Killed SIII strain	Mouse survived
IV	Mouse injected with Heat Killed SIII & living R II strain	Mouse died & from its blood live SIII √ strain bacteria recovered
V	Mouse injected with Heat Killed SIII+ living RII strain + DNase enzyme	Mouse survived
VI	Mouse injected with Heat Killed SIII+ living RII strain + Protease enzyme	Mouse died of √ Pneumonia

Avery, MacLeod, & McCarty Conclusion

- Avery, MacLeod, & McCarty, 1944 repeated Griffith's experiment of transformation using purified cell extracts.
- He concluded that removal of all protein from the transforming material did not destroy its ability to transform R strain cells.
- DNA-digesting enzymes destroyed all transforming ability
- The transforming material is DNA.



Avery, MacLeod, & McCarty observation

Hershey AND Chase Experiment

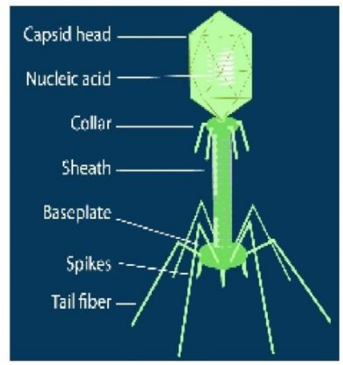
- Alfred Hershey and Martha Chase, 1952 investigated bacteriophages: viruses that infect bacteria.
- Bacteriophage was composed of only DNA and protein. They wanted to determine which of these molecules is the genetic material that enters into the bacteria.

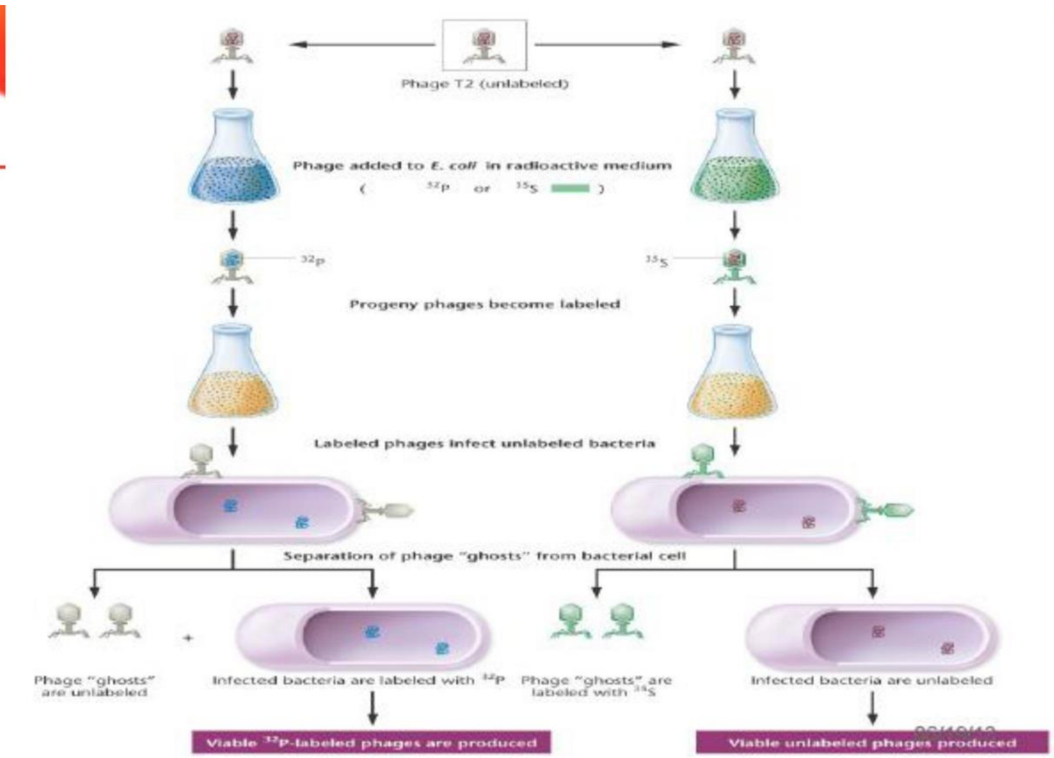
Experiment with T2 Bacteriophage

- In culture I Bacteriophage was grown in medium containing Radioactive Phosphorus (32P))To make DNA Radioactive.
- In culture II Bacteriophage was grown in medium containing radioactive Sulphur (35S) To make proteins Radioactive. Both kinds of Bacteriophage particles were allowed to infect Bacteria.
- The infected bacteria were observed for radioactivity. Radioactive Phosphorus was found with bacterial cells

Experiment with T2 Bacteriophage

- Radioactive Sulphur was not traced in bacterial cells (Only in Ghosts)
- Bacteriophage progeny carried only radioactive phosphorus and not radioactive sulphur.





HERSHAY & CHASE CONCLUSION

- As ghosts, Bacteriophage were not labelled with 32P and only with 35S. The results of experiment clearly indicate that only DNA and not the proteins enter the bacterial cell.
- Protein coat is left outside. The DNA entering the host cell carries all the genetic information for synthesis of new phage particle.
- It proves that DNA is the genetic material in Bacteriophage and not proteins.

GENETIC CODE

What is GENETIC CODE?

- The genetic information which is coded and stored in the form of nucleotide sequence.
- This sequence is a triplet i.e. a base sequence comprising of three nucleotides in mRNA which acts as code for particular amino acid which is called Genetic code.
- All four nucleotide bases present in mRNA in different combination form 64 such triplet codes.
- Unit of three nucleotides = a **codon**

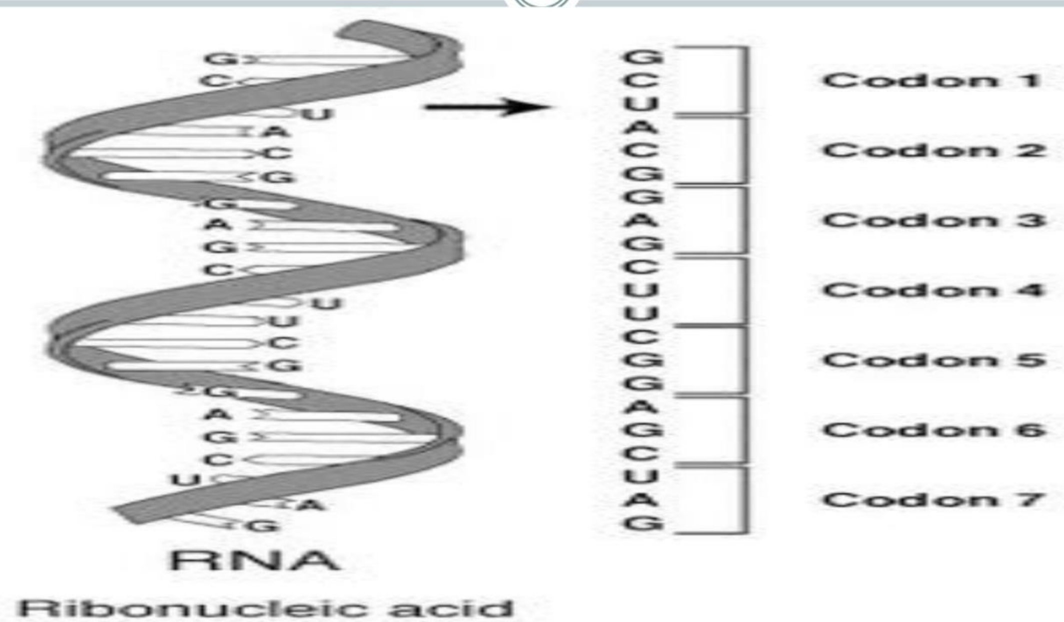
Triplet code or Genetic code

First letter	Second letter: U	C	A	G	Third letter
U	UUU } Phe	UCU } Ser	UAU } Tyr	UGU } Cys	U
	UUC	UCC	UAC	UGC	C
	UUA } Leu	UCA	UAA Stop	UGA Stop	A
	UUG	UCG	UAG Stop	UGG Trp	G
C	CUU } Leu	CCU } Pro	CAU } His	CGU } Arg	U
	CUC	CCC	CAC	CGC	C
	CUA	CCA	CAA } Gln	CGA	A
	CUG	CCG	CAG	CGG	G
A	AUU } Ile	ACU } Thr	AAU } Asn	AGU } Ser	U
	AUC	ACC	AAC	AGC	C
	AUA	ACA	AAA } Lys	AGA } Arg	A
	AUG Met	ACG	AAG	AGG	G
G	GUU } Val	GCU } Ala	GAU } Asp	GGU } Gly	U
	GUC	GCC	GAC	GGC	C
	GUA	GCA	GAA } Glu	GGA	A
	GUG	GCG	GAG	GGG	G

Introduction of Genetic Code

- The genetic code is the set of rules by which a linear sequence of nucleotides specifies the linear sequence of a polypeptide.
- It specify how the nucleotide sequence of an mRNA is translated into the amino acid sequence of a polypeptide.
- Relationship between the nucleotide sequence of the mRNA and the amino acid sequence of the polypeptide is the genetic code.
- The nucleotide sequence is read as triplets called codons.

Representation of codon



RNA codon table

Amino acids biochemical properties	nonpolar	polar	basic	acidic	Termination: stop codon

Standard genetic code

1st base	2nd base U		2nd base C		2nd base A		2nd base G		3rd base
U	UUU	(Phe/F) Phenylalanine	UCU	(Ser/S) Serine	UAU	(Tyr/Y) Tyrosine	UGU	(Cys/C) Cysteine	U
	UUC		UCC		UAC		UGC		C
	UUA	(Leu/L) Leucine	UCA		UAA	Stop (*Ochre*)[B]	UGA	Stop (*Opal*)[B]	A
	UUG[A]		UCG		UAG	Stop (*Amber*)[B]	UGG	(Trp/W) Tryptophan	G
C	CUU		CCU	(Pro/P) Proline	CAU	(His/H) Histidine	CGU	(Arg/R) Arginine	U
	CUC		CCC		CAC		CGC		C
	CUA		CCA		CAA	(Gln/Q) Glutamine	CGA		A
	CUG[A]		CCG		CAG		CGG		G
A	AUU	(Ile/I) Isoleucine	ACU	(Thr/T) Threonine	AAU	(Asn/N) Asparagine	AGU	(Ser/S) Serine	U
	AUC		ACC		AAC		AGC		C
	AUA		ACA		AAA	(Lys/K) Lysine	AGA	(Arg/R) Arginine	A
	AUG[A]	(Met/M) Methionine	ACG		AAG		AGG		G
G	GUU	(Val/V) Valine	GCU	(Ala/A) Alanine	GAU	(Asp/D) Aspartic acid	GGU	(Gly/G) Glycine	U
	GUC		GCC		GAC		GGC		C
	GUA		GCA		GAA	(Glu/E) Glutamic acid	GGA		A
	GUG		GCG		GAG		GGG		G

What are codons and Anticodons?

- A **codon** is found on the coding strand of double-stranded DNA and in the (single-stranded) mRNA.
- The **anticodon** is found on the tRNA and is the part that base-pairs with the **codon** (on the mRNA) in order to bring the appropriate amino acid to the ribosome to be added to the growing peptide chain.

Characteristics of Genetic code

- Basic characteristics of genetic code are:-

a) Universality
b) Specificity
c) Non Overlapping
d) Degenerate
e) Comma less
f) Non-ambiguity
g) Polarity

Universality

- Universality of the code means that the same sequences of 3 bases encode the same amino acids in all life forms from simple microorganisms to complex, multicelled organisms such as human beings.
- Although the code is based on work conducted on the bacterium *Escherichia coli* but it is valid for other organisms.
- The genetic code applies to all modern organisms with only minor exceptions, such as the yeast, mitochondria, and the *Mycoplasma*.

Specificity

- A code always codes for a particular amino acid which is specific for it.
- Same code can not stand for any other amino acid.

Non Overlapping

- The genetic code is no overlapping, i.e., the adjacent codons do not overlap.
- A no overlapping code means that the same letter is not used for two different codons. In other words, no single base can take part in the formation of more than one codon.

Degenerate

- The code is degenerate which means that the same amino acid is coded by more than one base triplet.
- Degeneracy does not imply lack of specificity in protein synthesis.
- It merely means that a particular amino acid can be directed to its place in the peptide chain by more than one base triplets.
- The code degeneracy is basically of 2 types: partial and complete.

Degenerate

- In partial degeneracy, the first two nucleotides are identical but the third (i.e., 3′ base) nucleotide of the degenerate codon differs; for example, CUU and CUC code for leucine.
- Complete degeneracy occurs when any of the 4 bases can take third position and still code for the same amino acid; for example, UCU, UCC, UCA and UCG all code for serine.

Comma less

- The genetic code is comma less (or comma-free). There is no signal to indicate the end of one codon and the beginning of the next.
- There are no intermediary nucleotides (or commas) between the codons.

Non-ambiguity

- Non-ambiguous code means that there is no ambiguity(the quality of being open to more than one interpretation) about a particular codon.
- A particular codon will always code for the same amino acid.
- While the same amino acid can be coded by more than one codon (the code is degenerate), the same codon shall not code for two or more different amino acids (non-ambiguous).

Polarity

- The genetic code has polarity, that is, the code is always read in a fixed direction, i.e., in the $5' \rightarrow 3'$ direction.
- It is apparent that if the code is read in opposite direction (i.e., $3' \rightarrow 5'$), it would specify 2 different proteins, since the codon would have reversed base sequence.

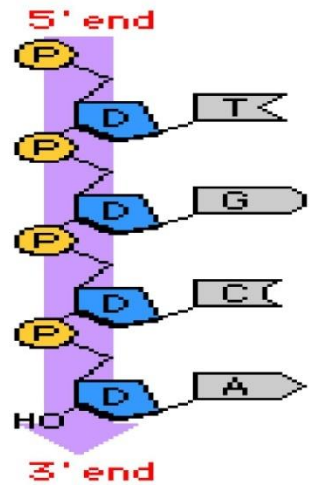
HIERARCHY OF DNA STRUCTURE

Introduction to Nucleoside

- A **nucleoside** consists simply of a nucleobase (also termed a nitrogenous base) and a five-carbon sugar ribose whereas a nucleotide is composed of a nucleobase, a five-carbon sugar, and one or more phosphate groups.
- A linear polymer whose molecule is composed of many nucleotide units, constituting a section of a nucleic acid molecule.
- A **polynucleotide** is made when a polymerase enzyme joins nucleotides together. The strand has two different ends, which we call 3' and 5'

Difference in the 3' end and the 5' end of a polynucleotide chain

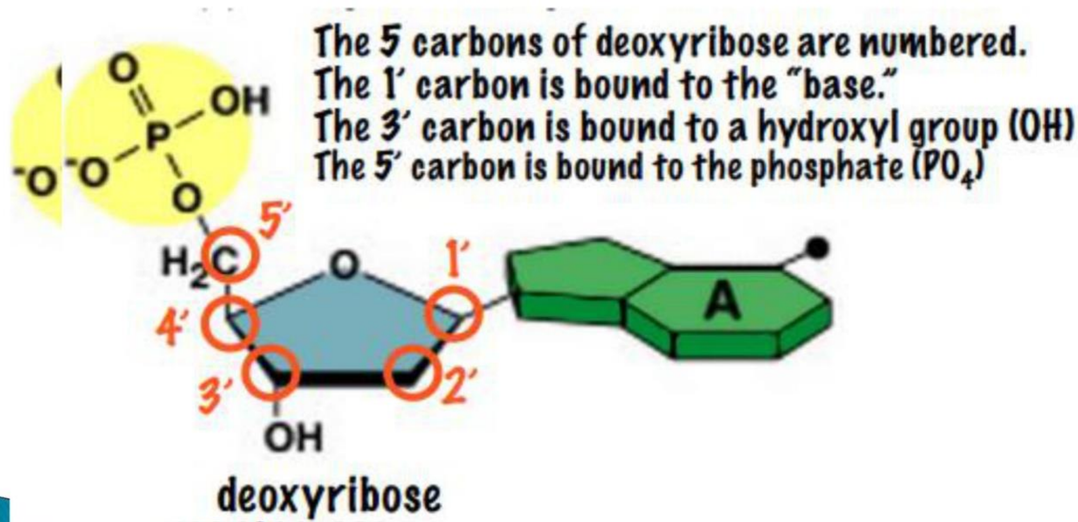
- One **end** of the **chain ends** with a phosphate linked to the **5'** carbon of the sugar and is called the **5' end**. The other **end** of the **chain ends** with an hydroxyl group linked to the **3'** carbon of the sugar and is called the **3' end**.
- DNA replication goes in the **5' to 3'** direction because DNA polymerase (enzyme that synthesis DNA molecule) acts on the **3'**-OH of the existing strand for adding free nucleotides.



Why is it called 5 and 3?

- The **5' and 3'** mean "five prime" and "**three** prime", which indicate the carbon numbers in the DNA's sugar backbone. The **5'** carbon has a phosphate group attached to it and the **3'** carbon a hydroxyl (-OH) group. This asymmetry gives a DNA strand a "direction“
- Carbon atoms in the deoxyribose sugar are then numbered 1', 2', 3', 4', and 5' (shown in red in the figure below).
- Phosphate groups are attached to the 5'- and 3'-carbon atoms of each sugar to form the backbone chain of DNA.

Diagrammatically representation of 5' and 3' in nucleotide



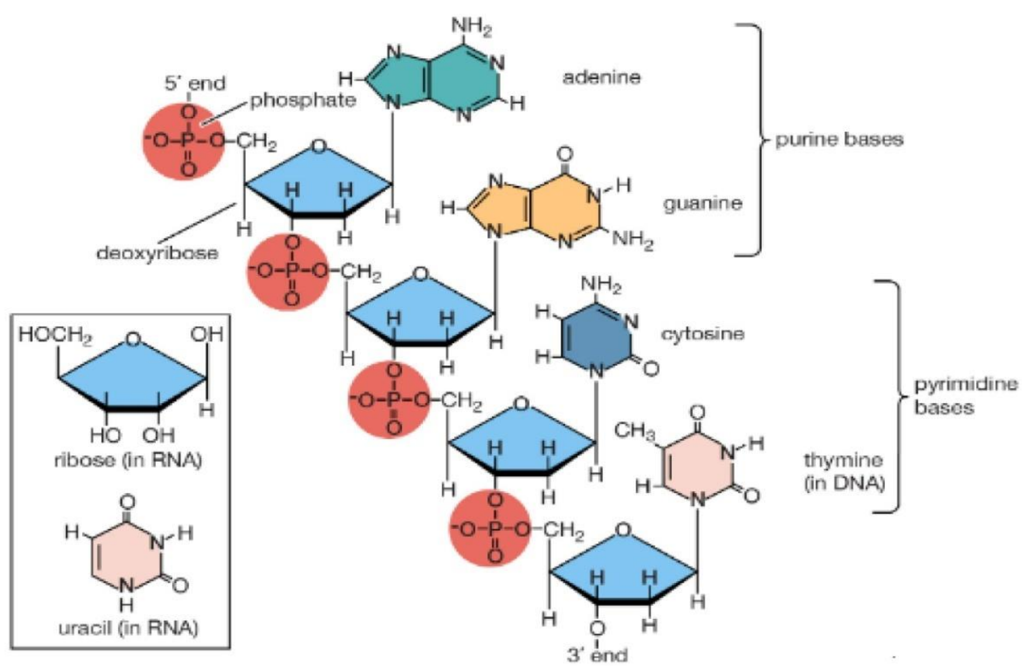
Hierarchal Structure of DNA

- Hierarchal structure of DNA are broadly classified as:-
  a) Primary or 1° Structure
  b) Secondary or 2° Structure
  c) Tertiary or 3° Structure
  d) Quaternary or 4° Structure

Primary or 1° Structure

- **Primary structure** consists of a linear sequence of nucleotides that are linked together by phosphodiester bonds(linkage between the 3' carbon atom of one sugar molecule and the 5' carbon atom of another).
- It is this linear sequence of nucleotides that make up the Primary structure of DNA or RNA.
- Single stranded polynucleotide chain formed represent primary structure.

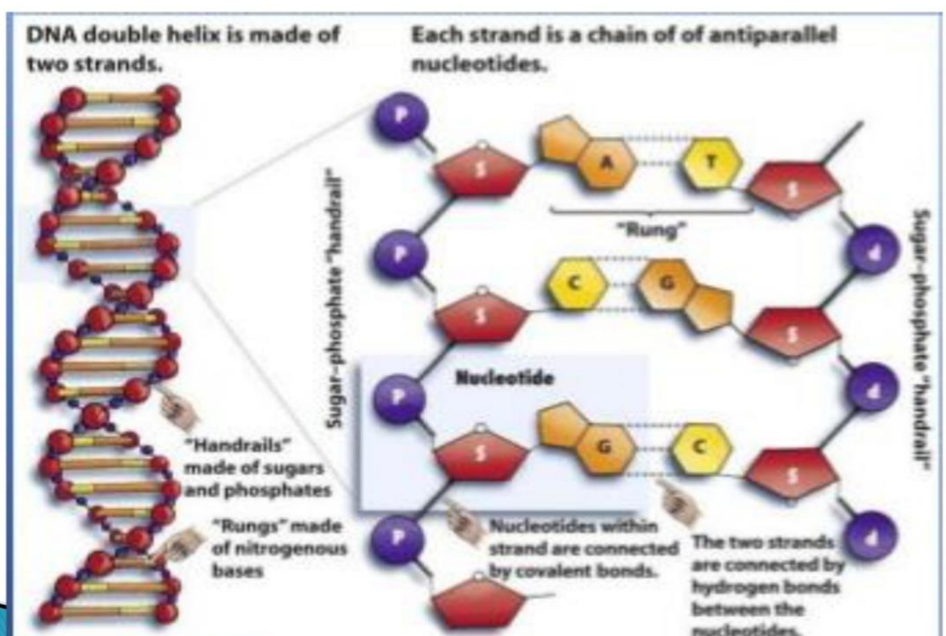
Diagram of primary structure



Secondary or 2° Structure

- **Secondary structure** is the set of interactions between bases, i.e., which parts of strands are bound to each other.
- In DNA double helix, the two strands of DNA are held together by hydrogen bonds. The nucleotides on one strand base pairs with the nucleotide on the other strand.
- The secondary structure is responsible for the shape that the nucleic acid assumes.
- DNA's secondary structure is predominantly determined by base-pairing of the two antiparallel polynucleotide chains wound around the same axis which can be explained by Watson and crick model.

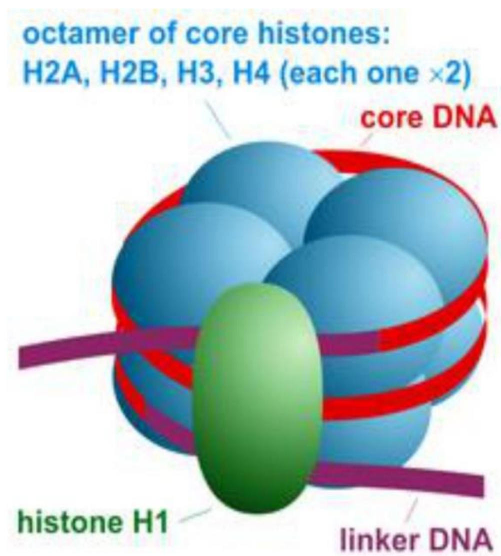
Diagram of secondary structure



Tertiary or 3° Structure

- **Tertiary structure** refers to the locations of the atoms in three-dimensional space, taking into consideration geometrical and steric constraints.
- It is a higher order than the secondary structure, in which large-scale folding in a linear polymer and the entire chain is folded into a specific 3-dimensional shape.
- The tertiary arrangement of DNA's double helix in space includes B-DNA, A-DNA and Z-DNA.

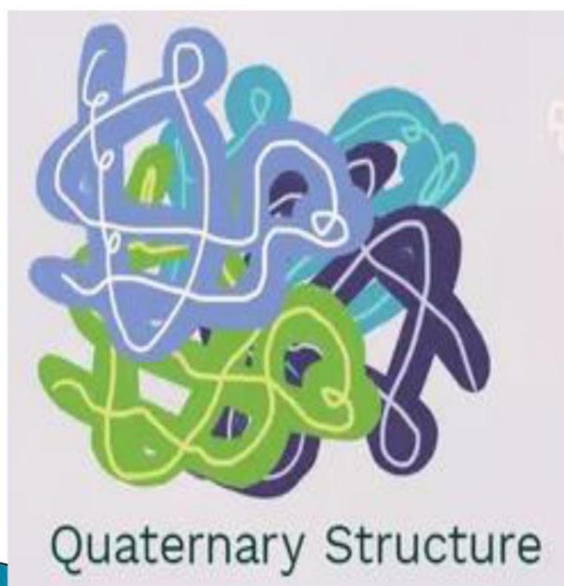
Diagram of tertiary structure

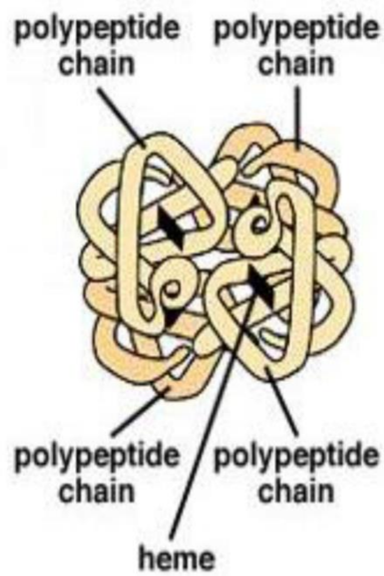


Quaternary or 4° Structure

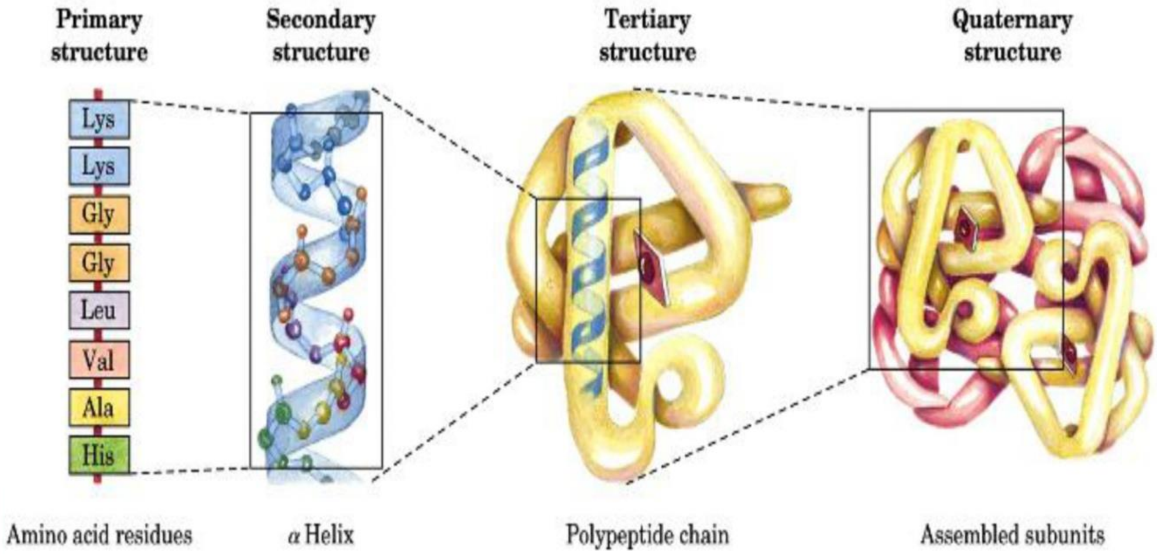
- **Quaternary structure** is the interaction of two or more folded polypeptides. Many proteins require the assembly of several polypeptide subunits before they become active.
- The three-dimensional **structure** consisting of the aggregation of two or more individual polypeptide chains (subunits) which operate as a single functional unit (multimer).
- The resulting multimer is **stabilized** by the same non-covalent interactions and disulfide bonds as in tertiary **structure**.

Diagram of quaternary structure





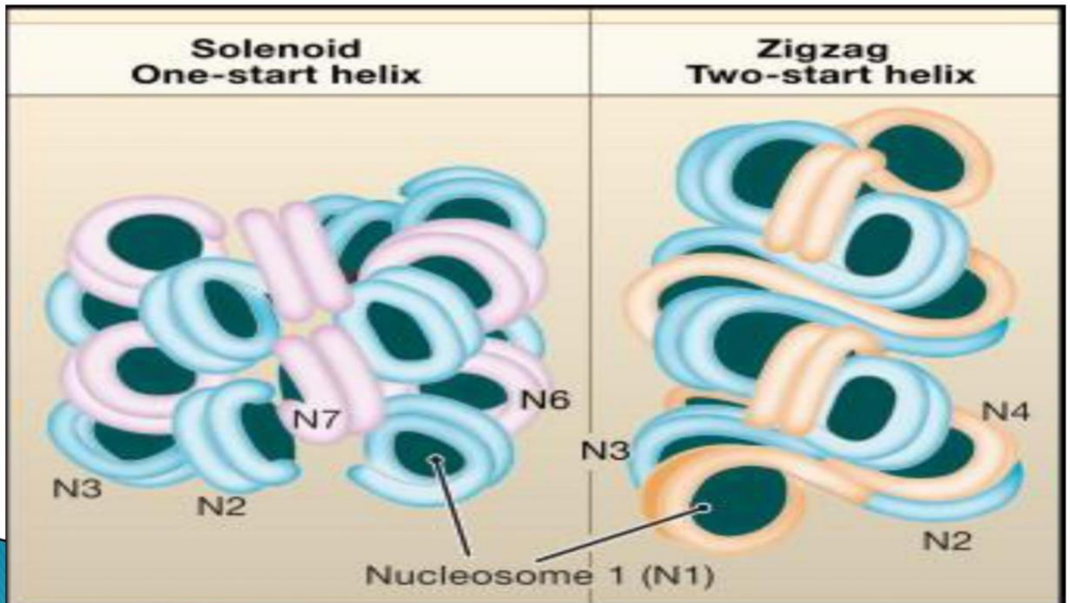
Connection between various structures



Models for Quaternary structure

- **Solenoid model** is characterized by interactions between consecutive nucleosomes (n, n + 1; a,b),
- **Zigzag model** implies interactions between alternate nucleosomes (n, n + 2; c,d).
- The two **models** also differ in the trajectory and degree of bending of the DNA that connects two nucleosomes (linker DNA).

Structural difference between models



Molecular Basis of Information Transfer

- Entire pathway of information flow involves two main steps:-
  a) Transcription
  b) Translation
- Both have 3 sub types under each named as Initiation, Elongation & Termination.

Central Dogma

Information is transferred from polynucleotide sequence to amino acid sequence(Unidirectional)

NUCLEIC ACIDS

WHAT IS NUCLEIC ACID ?

- **Nucleic acids** are large molecules where genetic information is stored.
- The nucleic acids are made of nucleotides. A nucleotide is made of a nitrogenous base, sugar with five carbon atoms and a phosphate group.
- They are composed of nucleotides, which are the monomers made of three components: a 5-carbon sugar, a phosphate group and a nitrogenous **base**.
- If the sugar is a compound ribose, the polymer is **RNA** (**ribonucleic acid**); if the sugar is derived from ribose as deoxyribose, the polymer is DNA (deoxyribonucleic acid).

TYPES OF **NUCLEIC ACIDS**

- The two main types of nucleic acids are:-

  1) Deoxyribonucleic **acid**, better known as DNA:- Transmits the genetic information via orderly sequence of subunits called nucleotides.

  2) Ribonucleic **acid**, better known as RNA:- Responsible for number of metabolic activities involving gene expression as well as carrying genetic information

FUNCTION OF NUCLEIC ACIDS

- They are the repository(a place where things may be stored) of the genetic information responsible for the transmission of inherited characteristics from parents to children and from one cell to another.
- They guide cell protein synthesis and are responsible for the correct assembly of amino acids in defined sequences.
- Ultimately, the morphological and functional uniqueness of each living being are determined by the information contained in its nucleic acids.

DNA (DEOXY RIBONUCLEIC ACID)

- It's a long polymer of nucleotides stored in the nucleus in super coiled and condensed form called chromatin network.
- Gene is the smallest part of DNA which contains and convey a genetic information or protein.
- The information in **DNA** is stored as a code made up of four chemical bases: adenine (A), guanine (G), cytosine (C), and thymine (T).
- The main role of **DNA** in the cell is the long-term storage of information.

RNA (RIBONUCLEIC ACID)

- Is a linear molecule **composed of** four types of smaller molecules called ribonucleotide bases: adenine (A), cytosine (C), guanine (G), and Uralic (U).
- found mainly in the **cytoplasm** of the **cell** although it is usually synthesized in the **nucleus**.
- **RNA** is present in **human body** , and mainly involved in protein synthesis.

TYPES OF RNA

- It is divided into 3 types:
  - a) Messenger RNA (m RNA)
  - b) Transfer RNA (t RNA)
  - c) Ribosomal RNA (r RNA)

MESSENGER RNA (MRNA)

- **Messenger RNA** (mRNA) is a single-stranded **RNA** molecule that corresponds to the genetic sequence of a gene and is read by the ribosome in the process of producing a protein.
- The primary **function of mRNA** is to act as an intermediary between the genetic information in DNA and the amino acid sequence of proteins. **mRNA** contains codons that are complementary to the sequence of nucleotides on the template DNA and direct the formation of amino acids through the action of ribosome's and **tRNA**.

TRANSFER RNA (TRNA)

- **Transfer RNA** (tRNA) is small **RNA** molecule that participates in protein synthesis. Each tRNA molecule has two important areas: a tri-nucleotide region called the anticodon and a region for attaching a specific amino acid.
- Transfer ribonucleic acid (tRNA) is a type of RNA molecule that helps decode a messenger RNA (mRNA) sequence into a protein.

RIBOSOMAL RNA (RRNA)

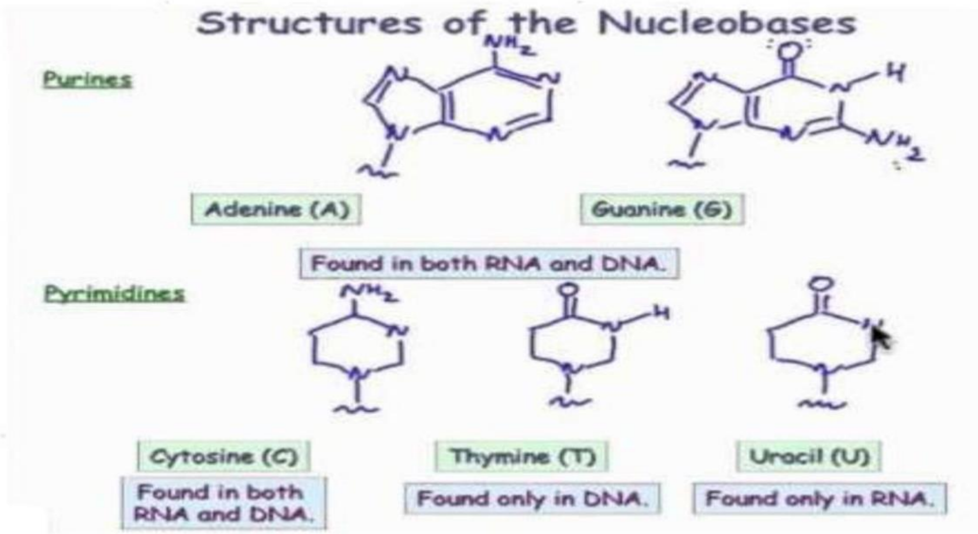
- **Ribosomal RNA** (**rRNA**), molecule in cells that forms part of the protein-synthesizing organelle known as a **ribosome** and that is exported to the cytoplasm to help translate the information in messenger **RNA** (mRNA) into protein.
- Ribosome's are responsible for translation, or the process our cells use to make **proteins**. rRNA are responsible for reading the order of **amino acids** and linking **amino acids** together. They do this through a highly complex sequence.

Difference between DNA & RNA		
Sr.No.	DNA	RNA
1	It is a Double Stranded molecule	It is a Single Stranded Molecule
2	The sugar present is Deoxy ribose sugar which have five membered carbon ring.	Sugar present is five membered carbon ring
3	Four nitrogenous base present are Thymine, Cytosis, Adenine,Guanine.	It has Uracil base instead of Thmine. While remaining base remains same.
4	Sum total of purine base is always equal to pyrimidine base i.e. A+G = C+T	Sum of purine and pyrimidine bases is not equal.
5	Exist in one form or type in an organism	Exists in three main types:- mRNA, rRNA and tRNA
6	Involved in transfer of genetic information from one generation to other	Involved in transfer and expression of genetic information
7	Do not degrade in the cell	Degrade in the cell by nucleases.

PURINES VERSUS PYRIMIDINES

PURINES	PYRIMIDINES
Purines are heterocyclic aromatic organic compounds, consisting of a pyrimidine ring fused to an imidazole ring	Pyrimidines are heterocyclic aromatic organic compounds
Contain two carbon-nitrogen rings and four nitrogen atoms	Contain a single carbon-nitrogen ring and 2 nitrogen atoms
Contain comparatively high melting and boiling points	Contain comparatively low melting and boiling points
Synthesized by Traube Purine Synthesis	Synthesized by Biginelli Reaction
Catabolism produces uric acid	Catabolism produces beta amino acids, carbon dioxide, and ammonia

PURINE VS PYRIMIDINE



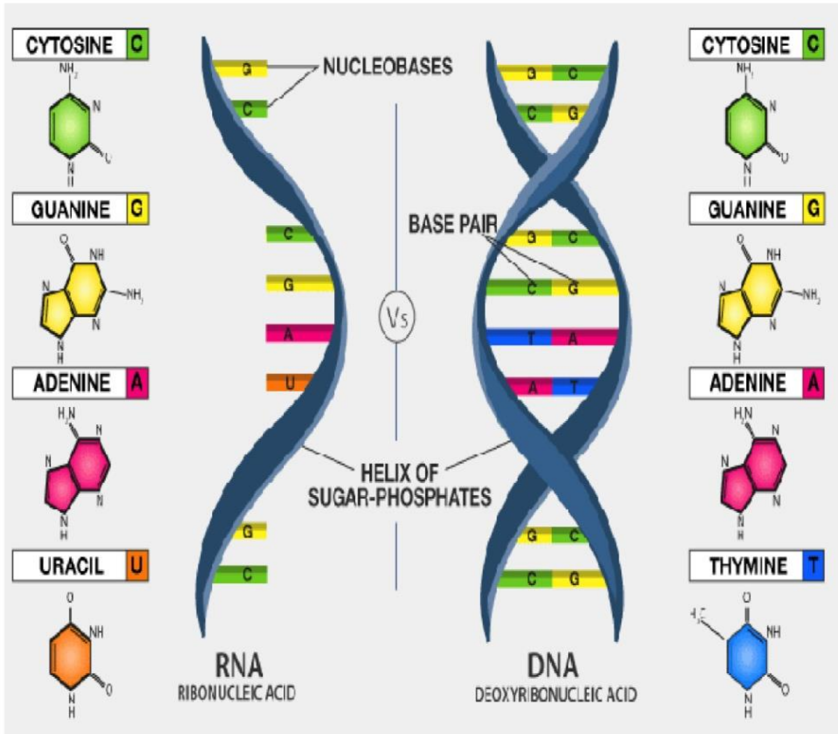
CHEMICAL STRUCTURE OF NUCLEIC ACID

- Both DNA & RNA are linear polymers of nucleotides(**Nucleotides** are the building blocks of nucleic acids).
- They are composed of three sub unit molecules:

1) A nitrogenous base (also known as nucleobase)

2) A Pentose Sugar/ five-carbon sugar (ribose or deoxyribose)

3) At least one phosphate group.



Difference between DNA and RNA