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Lecture – 16

Nature & Structure of DNA

by

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- ❑ The progeny of organism develops characters similar to that organism
- ❑ The resemblance of offspring to their parents depends on the precise transmission of principle component from one generation to the next
- ❑ That component is- **The Genetic Material**

Four requirements for a genetic material

- Must **carry information**
 - Cracking the genetic code

- Must self **replicate**
 - DNA replication

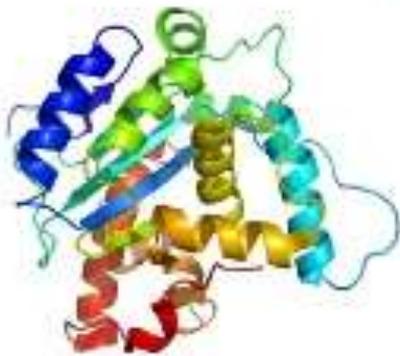
- Must allow for information to **change**
 - Mutation

- Must govern the **expression** of the phenotype
 - Gene function

What is genetic material?

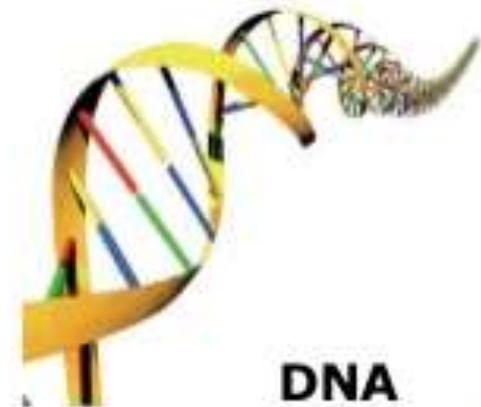
Protein, RNA and **DNA** were thought as genetic material. But many experiments suggest DNA as genetic material rather than protein and RNA

50% of total dry weight of cell



Protein

RNA



DNA



Identification of genetic material:

- The process of identification of genetic material began in **1928 with experiments of Griffith** and concluded in **1952 with the studies of Hershey and Chase.**
- Between these two experiments other three scientists, **Avery, Macloed and McCarty** were did an experiment to identify the genetic material.





The discovery of DNA as genetic material

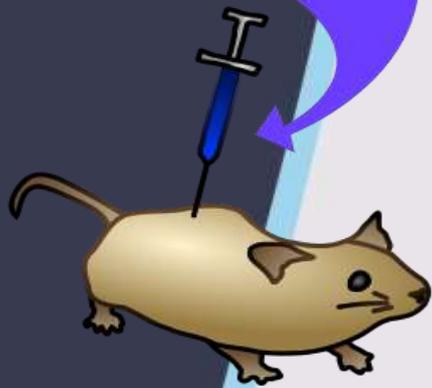
- ❖ One of the first study that ultimately led to the identification of DNA as genetic material was done by **Frederick Griffith** involving the bacterium ***Streptococcus pneumoniae*** in **1928**.
- ❖ This bacterium, which causes pneumonia in humans, is normally lethal in mice.
- ❖ Griffith used two strains that are distinguishable by the appearance of their colonies when grown in laboratory cultures. In one strain, a normal virulent type, the cells are enclosed in a polysaccharide capsule, giving colonies a **smooth appearance**; this strain is **labelled S**. In the other strain, a mutant nonvirulent type that is not lethal, the polysaccharide coat is absent, giving colonies a **rough appearance**; this strain is called **R**.



**rough strain
(nonvirulent)**

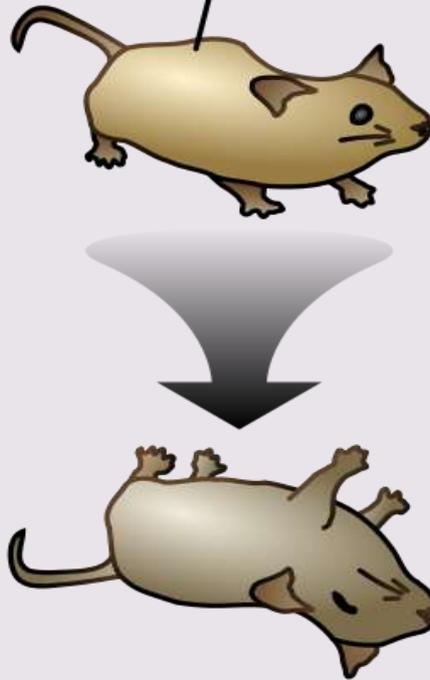
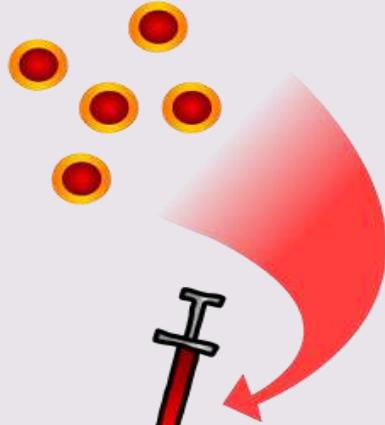
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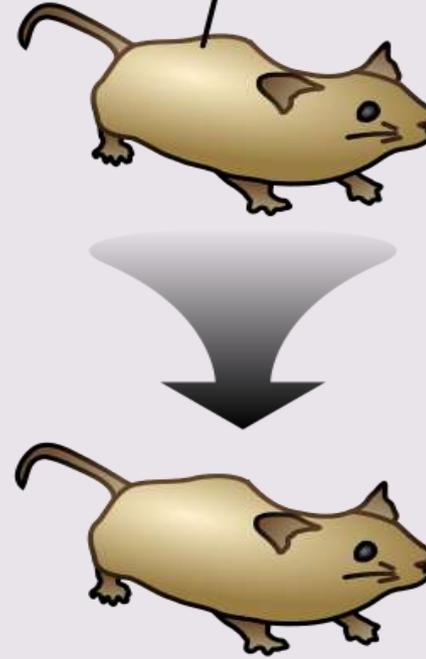
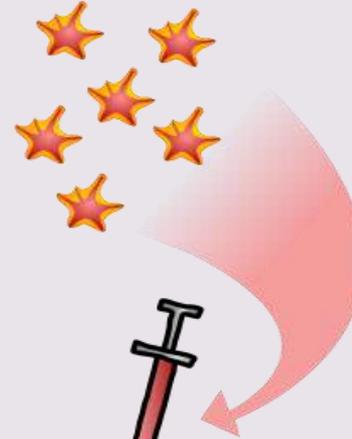
mouse lives

**smooth strain
(virulent)**



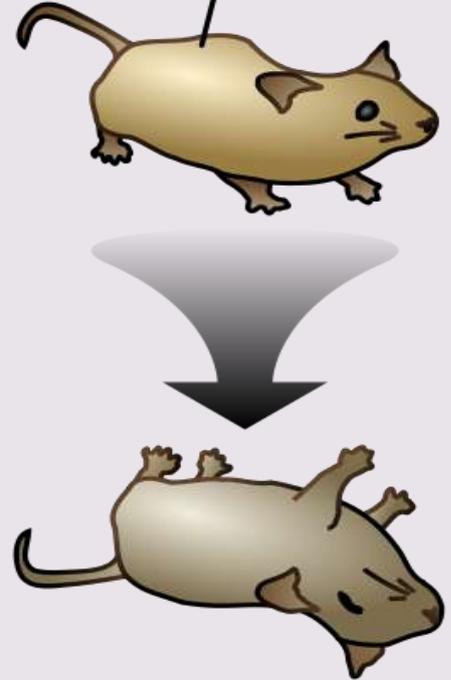
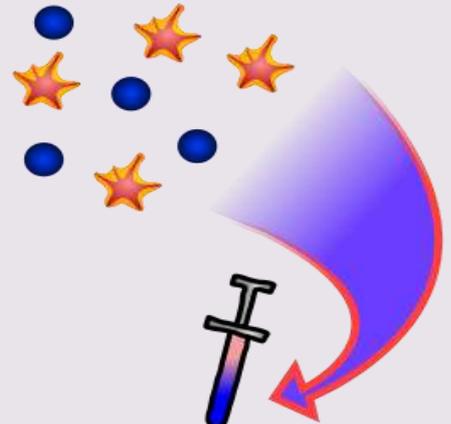
mouse dies

**heat-killed
smooth strain**



mouse lives

**rough strain &
heat-killed
smooth strain**



mouse dies



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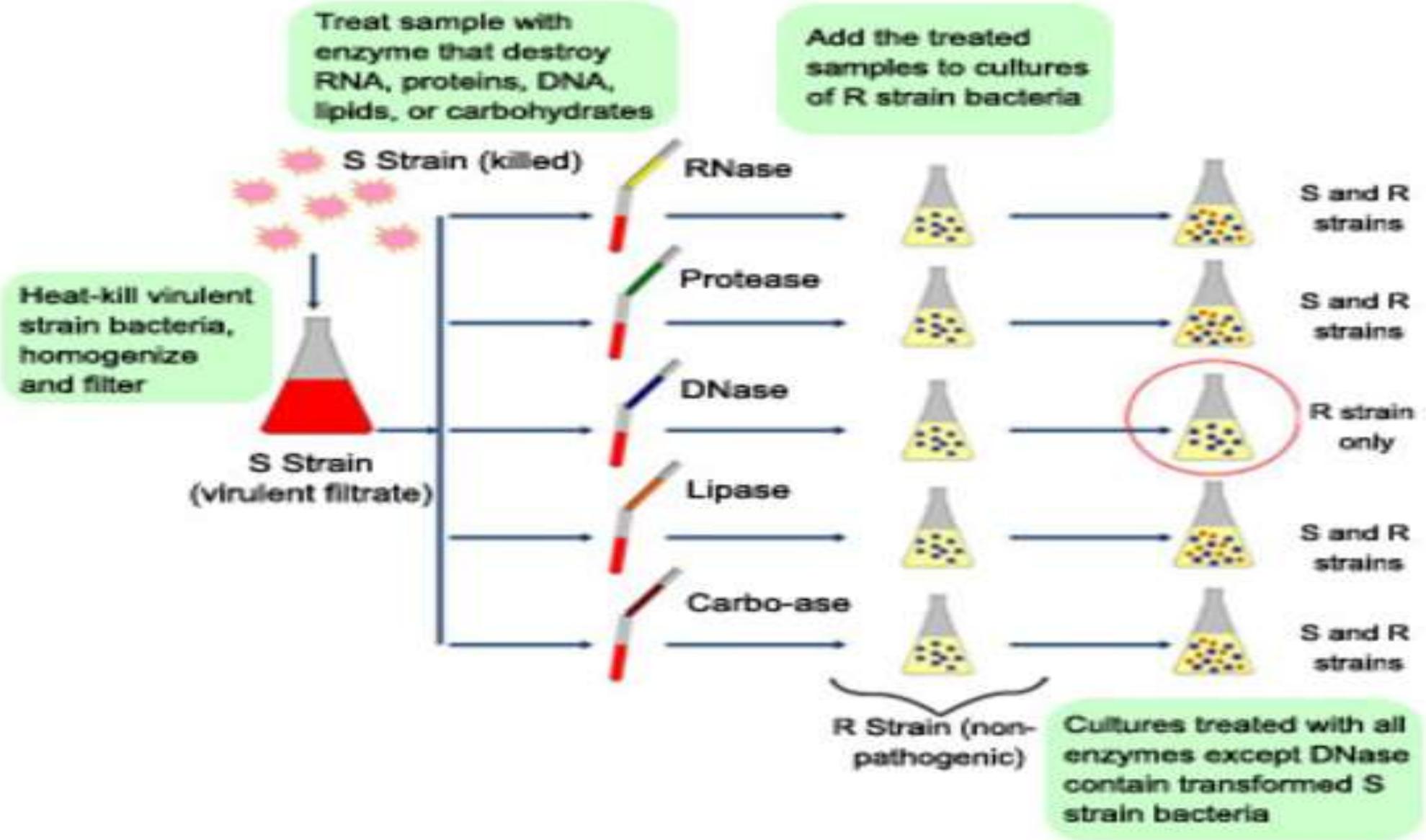
The mice injected with a mixture of heat-killed virulent cells and live nonvirulent cells did die. Live cells could be recovered from the dead mice; these cells gave smooth colonies and were virulent on subsequent injection.

Griffith's Conclusion

- Based on these observations he concluded that some of the cells of type R had changed into type S due to influence of dead S cells
- He called this phenomenon as **transformation**
- Principle Component of S cells which induced the conversion of R cells into S was named **transforming principle**.



Oswald Avery, C. M. MacLeod, and M. McCarty (1944) Experiment





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❖ In 1944, Oswald Avery, C. M. MacLeod, and M. McCarty separated the classes of molecules found in the debris of the dead S cells and tested them for transforming ability, one at a time. These tests showed that the polysaccharides themselves do not transform the rough cells.

❖ In screening the different groups, it was found that only one class of molecules, DNA, induced the transformation of R cells. DNA is the agent that determines the polysaccharide character and hence the pathogenic character. It seemed that providing R cells with S DNA was equivalent to providing these cells with S genes.

Demonstration that DNA is the transforming agent. DNA is the only agent that produces smooth (S) colonies when added to live rough (R) cells.



Hershey-Chase experiment

- ❖ In 1952 Alfred Hershey and Martha Chase used bacteriophage (virus) T 2 to show that DNA is the genetic material. Most of the phage structure is protein, with DNA contained inside the protein sheath of its “head.”
- ❖ They reasoned that phage infection must entail the introduction (injection) into the bacterium of the specific information that dictates viral reproduction.



Hershey and Chase incorporated the radioisotope of phosphorus (^{32}P) into phage DNA and that of sulfur (^{35}S) into the proteins of a separate phage culture. P is not found in proteins but is an integral part of DNA; S is present in proteins but never in DNA.



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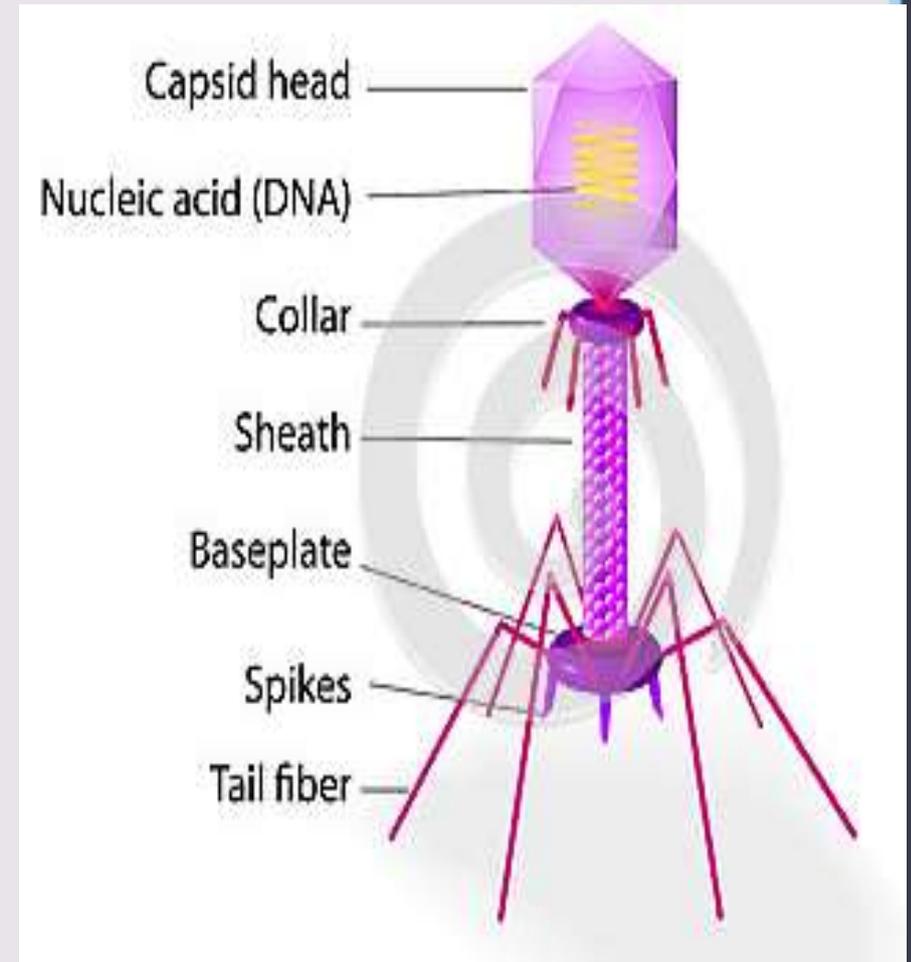
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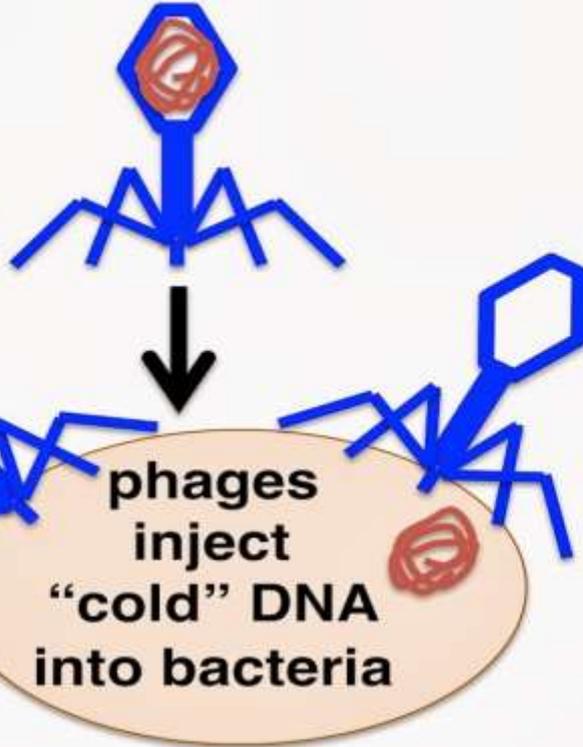
Bacteriophage

- ❖ Bacteriophage: a virus that infects bacteria.
- ❖ When Bacteriophages infect bacterial cells they produce more viruses.
- ❖ The viruses are released when the bacterial cells rupture.



The Hershey-Chase experiment, which demonstrated that the genetic material of phage is DNA, not protein.

phage with
radioactive
protein (^{35}S)



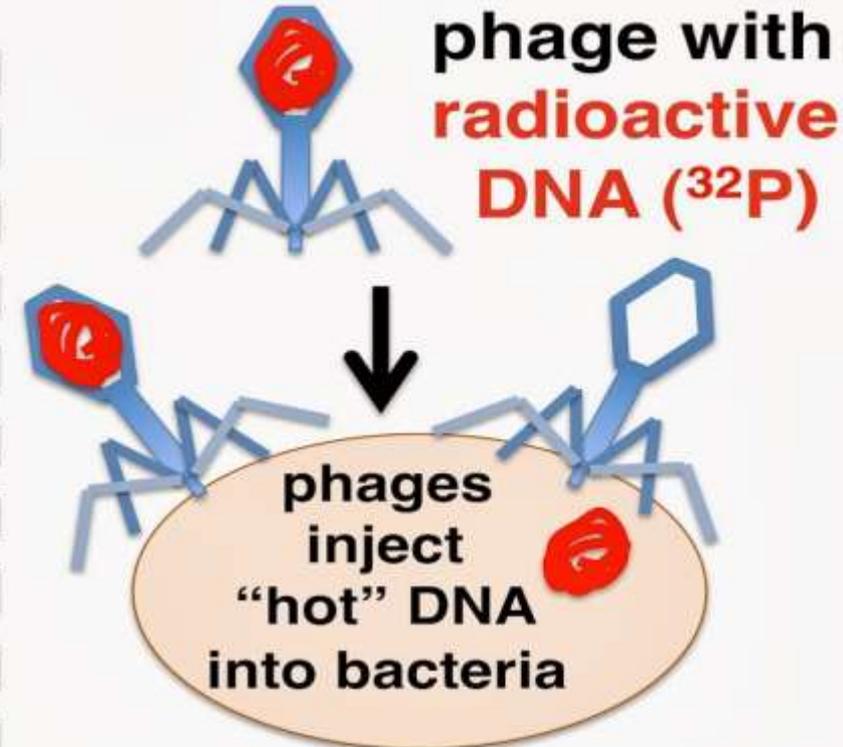
infection

blender, then
centrifuge



no
radioactive ^{35}S
inside cells

phage with
radioactive
DNA (^{32}P)



radioactive ^{32}P
inside cells



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DEOXY RIBOSE NUCLEIC ACID (DNA)

- ❑ In **1869**, **Friedrich Meischer** was the first person who separated cell nuclei from the cytoplasm and extracted an acidic material, **nuclein**, from the nuclei of pus cells. He found that the acidic material contained unusually large amounts of phosphorous and no sulphur.
- ❑ Later on, in **1889**, **Richard Altmann** used the **term nucleic acid in place of nuclein**.
- ❑ DNA is the genetic material in most of the organisms. RNA acts as genetic material only in some viruses.
- ❑ DNA is mainly found in the chromosomes in the nucleus, while RNA is mostly found in the ribosomes in the cytoplasm.



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Nucleic Acid Structure

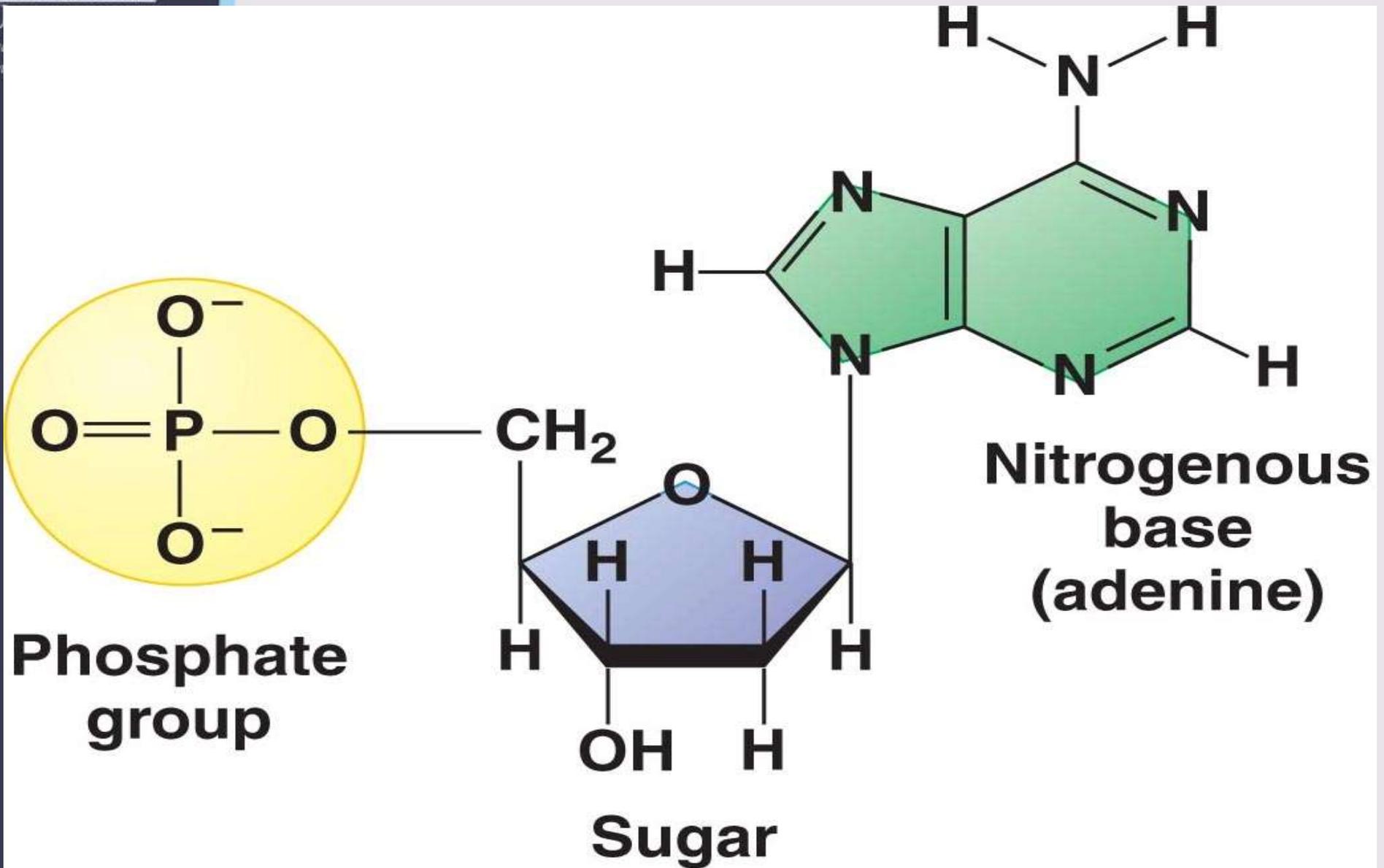
- ❖ What structural features do DNA and RNA share?
- ❖ Nucleotides are the building block of DNA
- ❖ Polymers of nucleotides
- ❖ Each nucleic acid contains 4 different nucleotides



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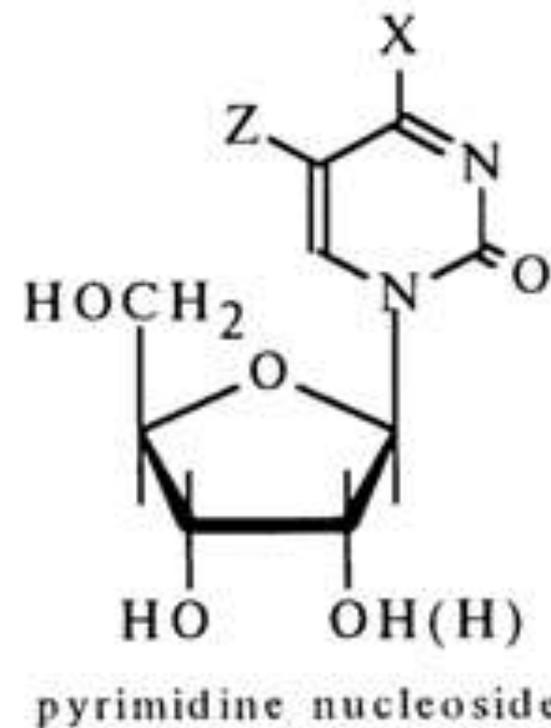
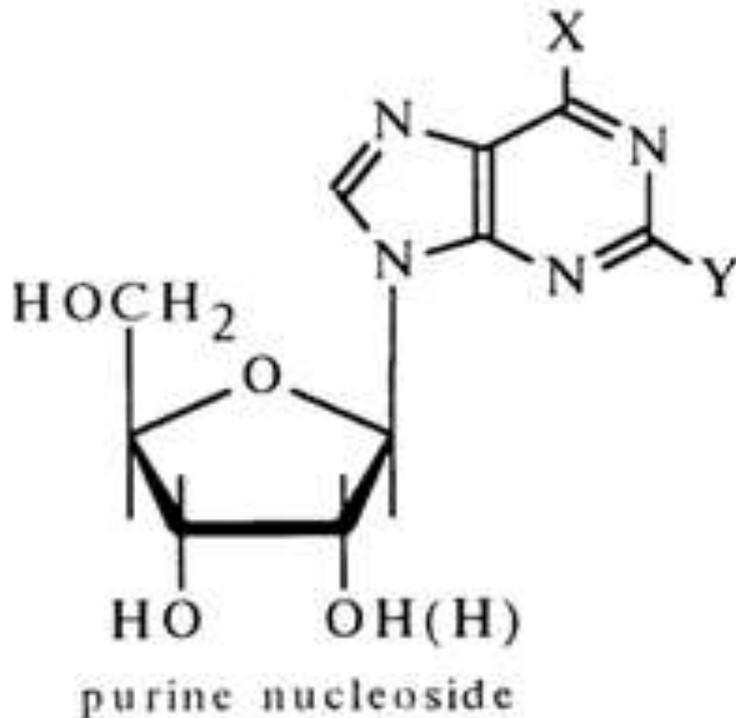
U
Sh
Em

Nucleotide= sugar + phosphate + nitrogen containing base





Nucleoside= sugar + nitrogen containing base

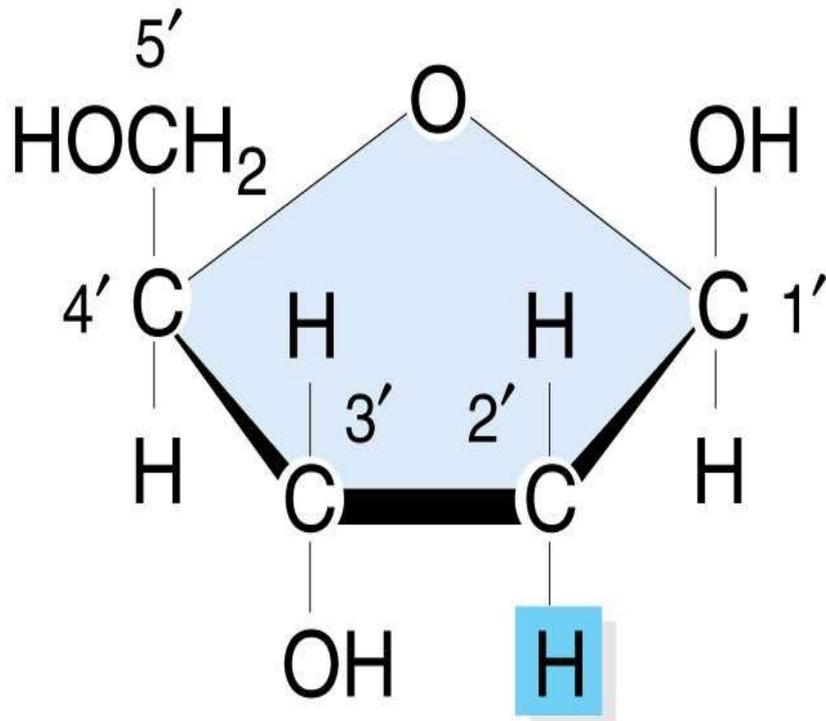


$X = \text{OH or NH}_2$; $Y = \text{H, OH or NH}_2$; $Z = \text{H or CH}_3$

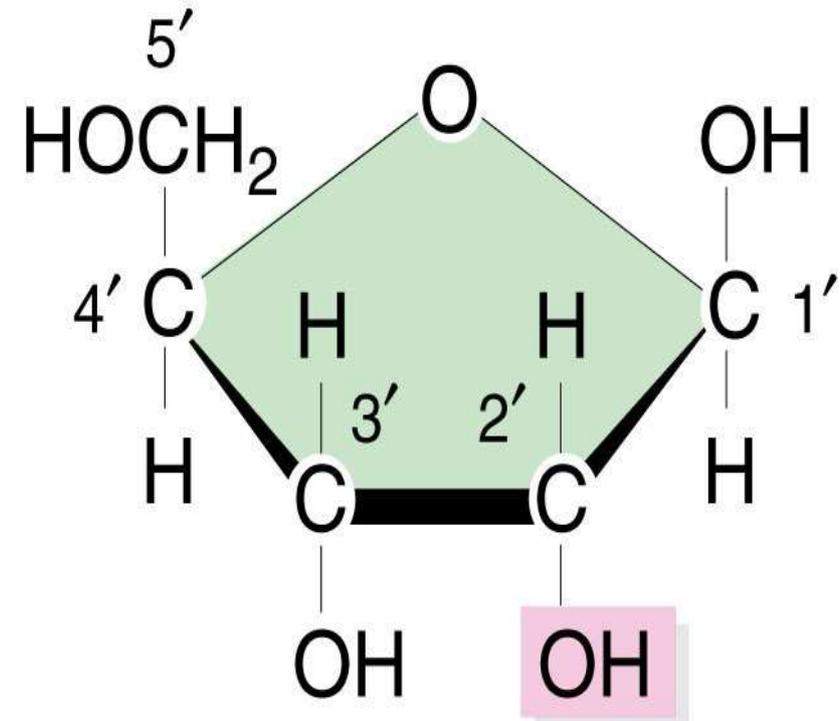
Hence, Nucleotide= Nucleoside + Phosphate



Pentose sugar



Deoxyribose
(2' Deoxyribose)



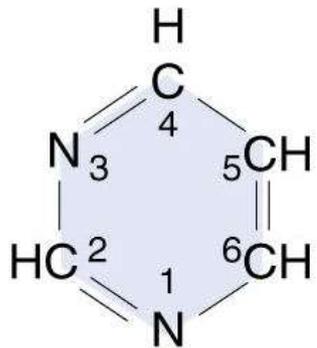
Ribose

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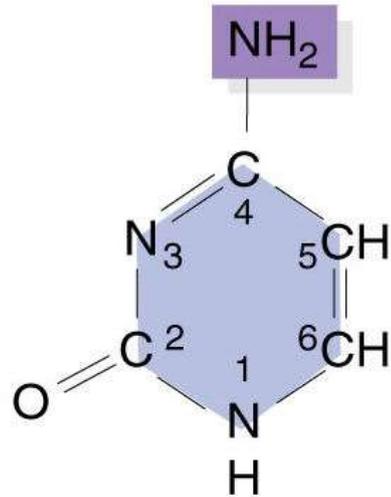
- ❑ Pentose sugar is the basis of nomenclature of nucleic acid (RNA or DNA)
- ❑ Each carbon atom of ring designated by a number with prime sign



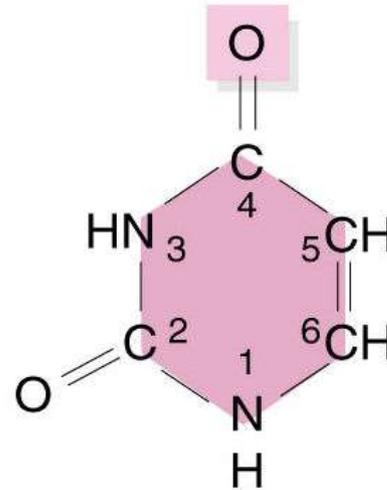
NTROGENOUS BASES



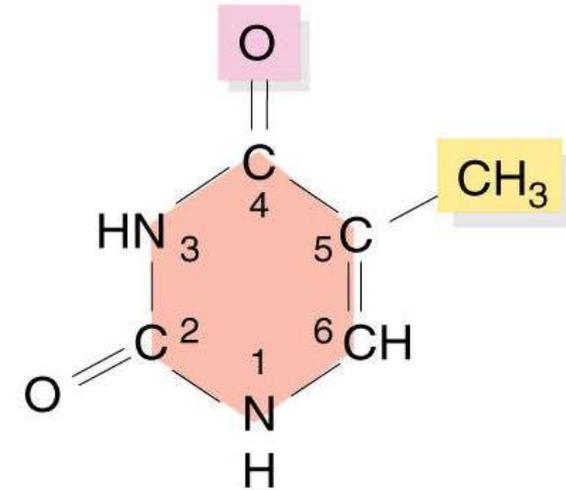
Pyrimidine



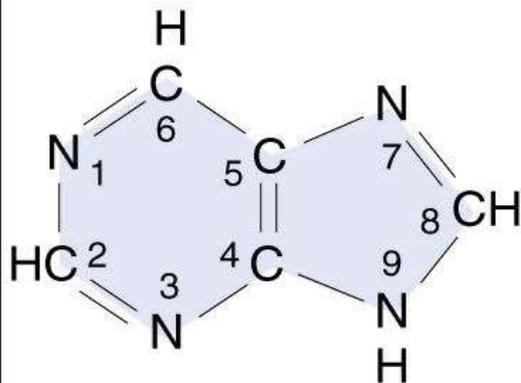
Cytosine (C)



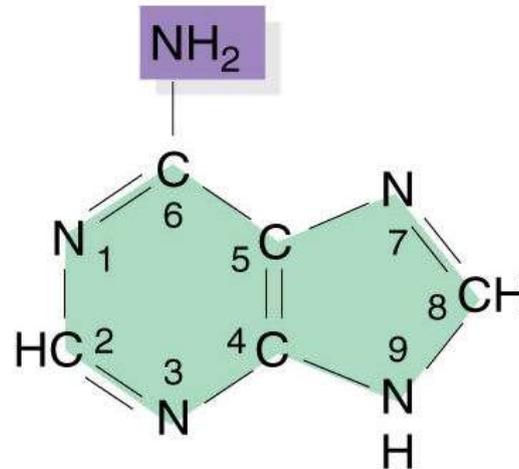
Uracil (U)
(found in RNA)



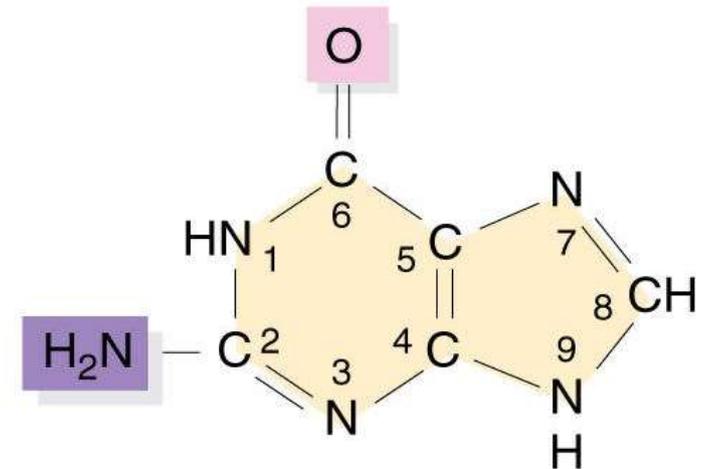
Thymine (T)
(found in DNA)



Purine



Adenine (A)



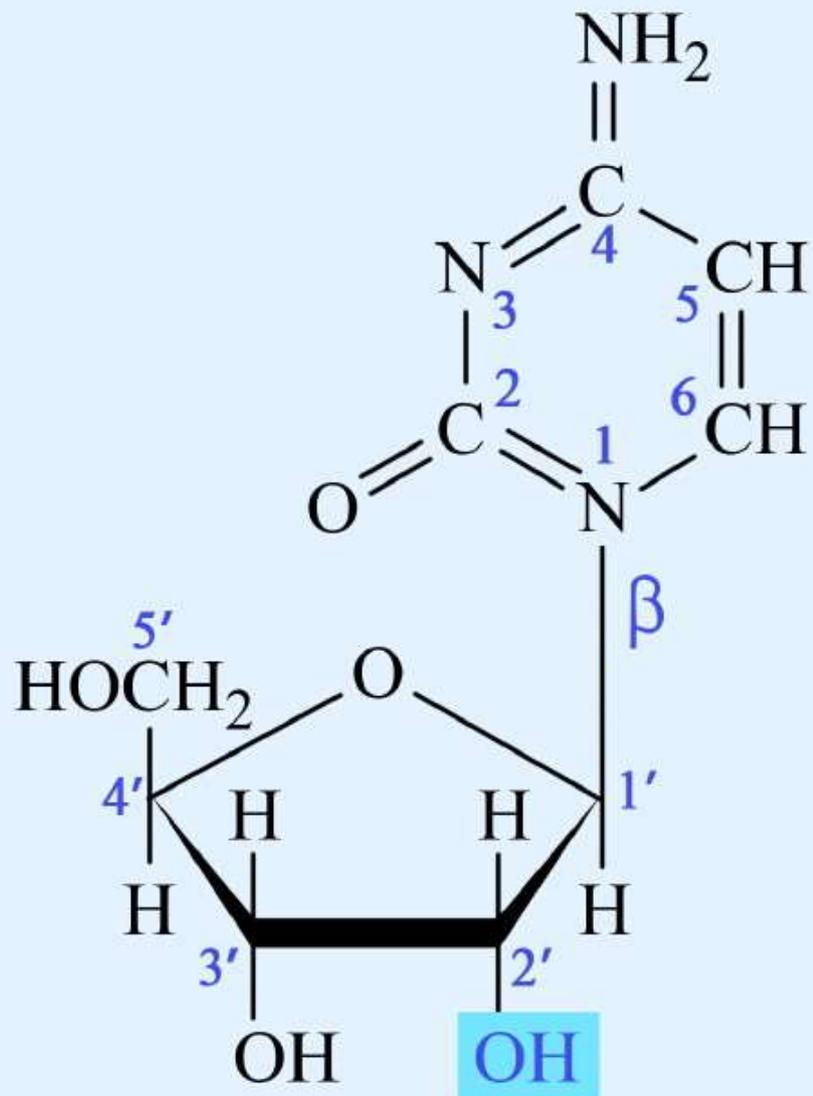
Guanine (G)



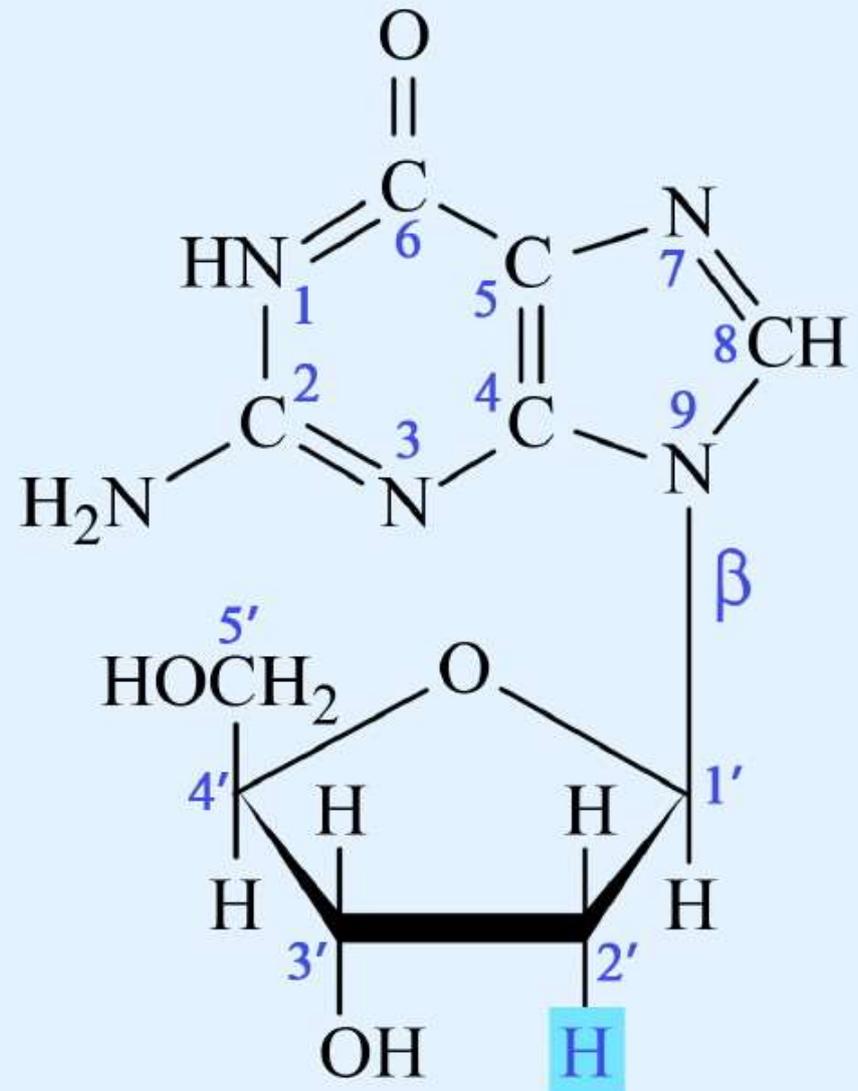
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Bonding among the components of nucleoside and nucleotide and their nomenclature in DNA and RNA

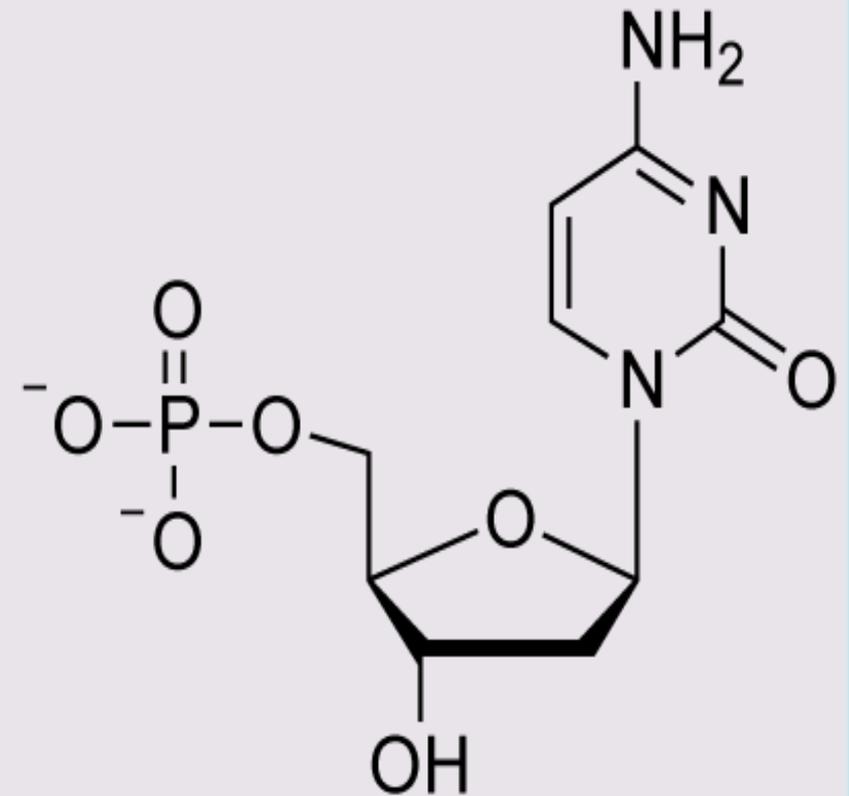
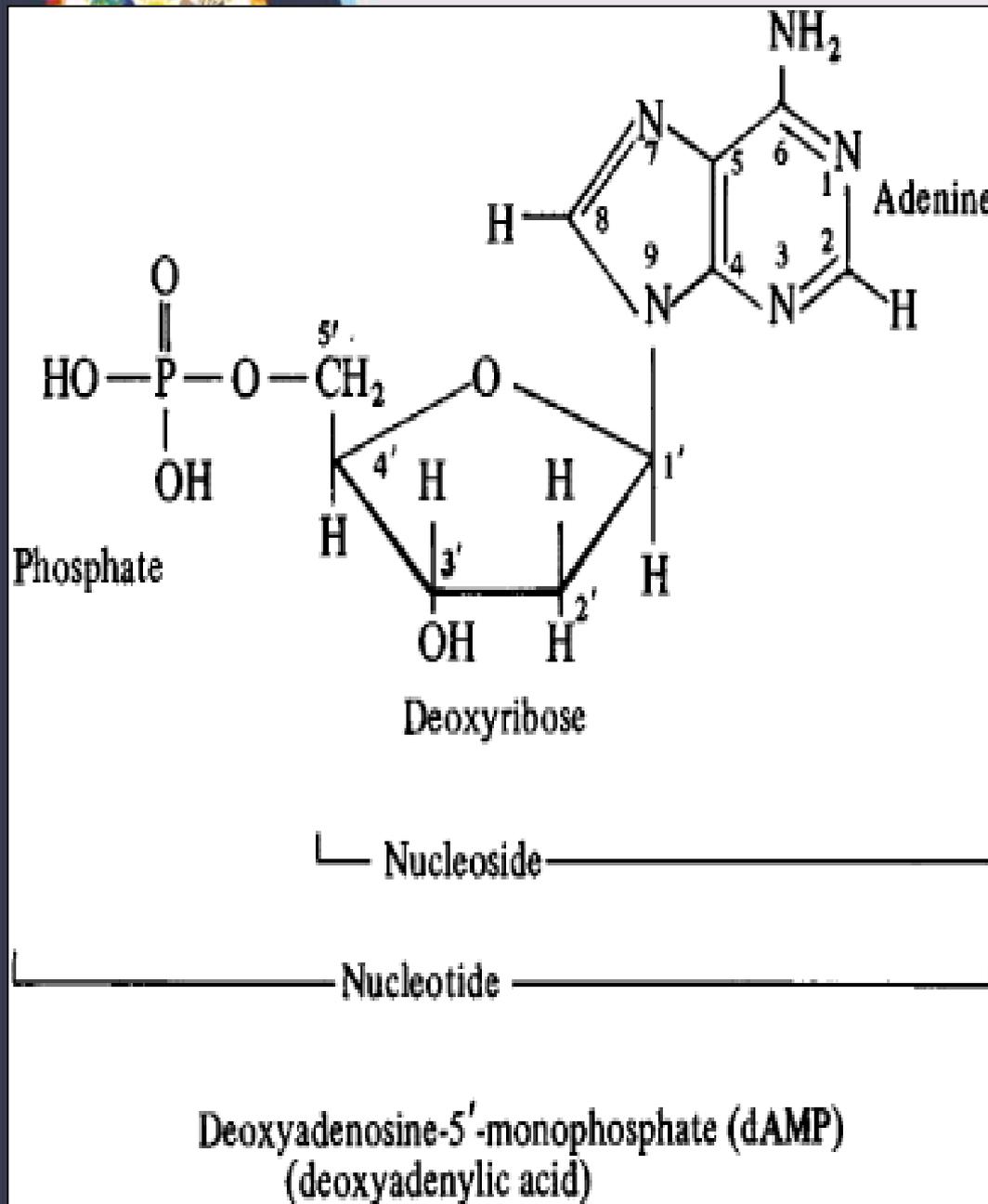
- Bonding among the components of nucleoside and nucleotide is highly specific.
- The C-1' atom of sugar is involved in chemical linkage to the Nitrogenous base.
 - In Purine- N-9 atom
 - In Pyrimidine- N-1 atom
- Phosphate group bound to C-2', C-3' or C-5' atom of sugar . But C-5' bonding of phosphate most prevalent in biological system.



Cytidine
A ribonucleoside



Deoxyguanosine
A deoxyribonucleoside

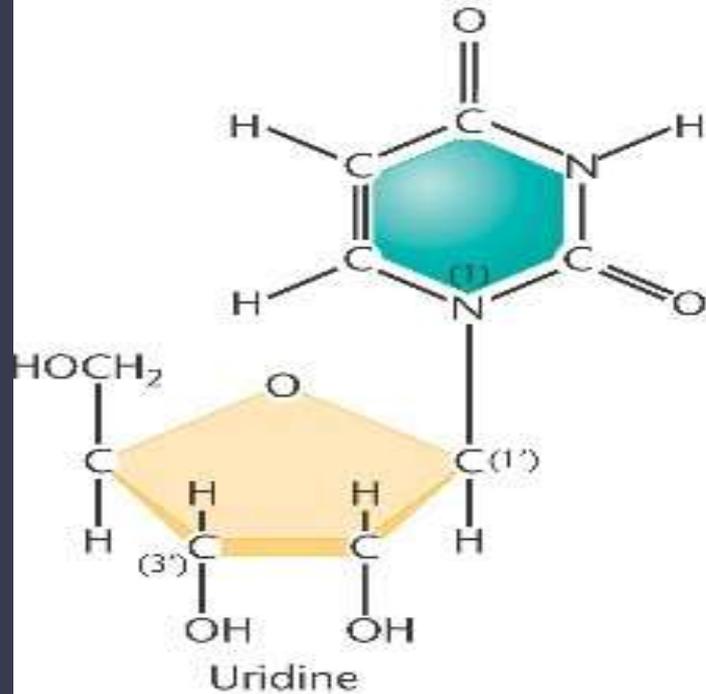


2'-deoxycytidine-
5'-monophosphate
(a nucleotide)

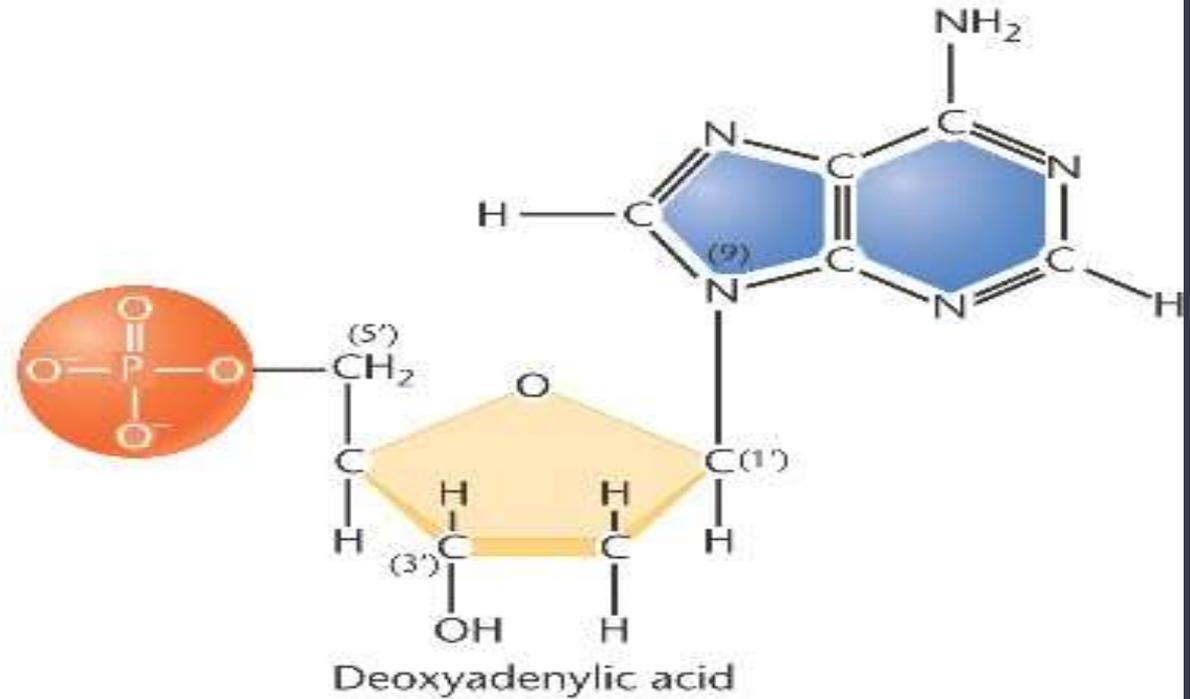


Nomenclature

Nucleoside



Nucleotide



Ribonucleosides

Adenosine
Cytidine
Guanosine
Uridine

Ribonucleotides

Adenylic acid
Cytidylic acid
Guanylic acid
Uridylic acid

Deoxyribonucleosides

Deoxyadenosine
Deoxycytidine
Deoxyguanosine
Deoxythymidine

Deoxyribonucleotides

Deoxyadenylic acid
Deoxycytidylic acid
Deoxyguanylic acid
Deoxythymidylic acid



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Polynucleotide

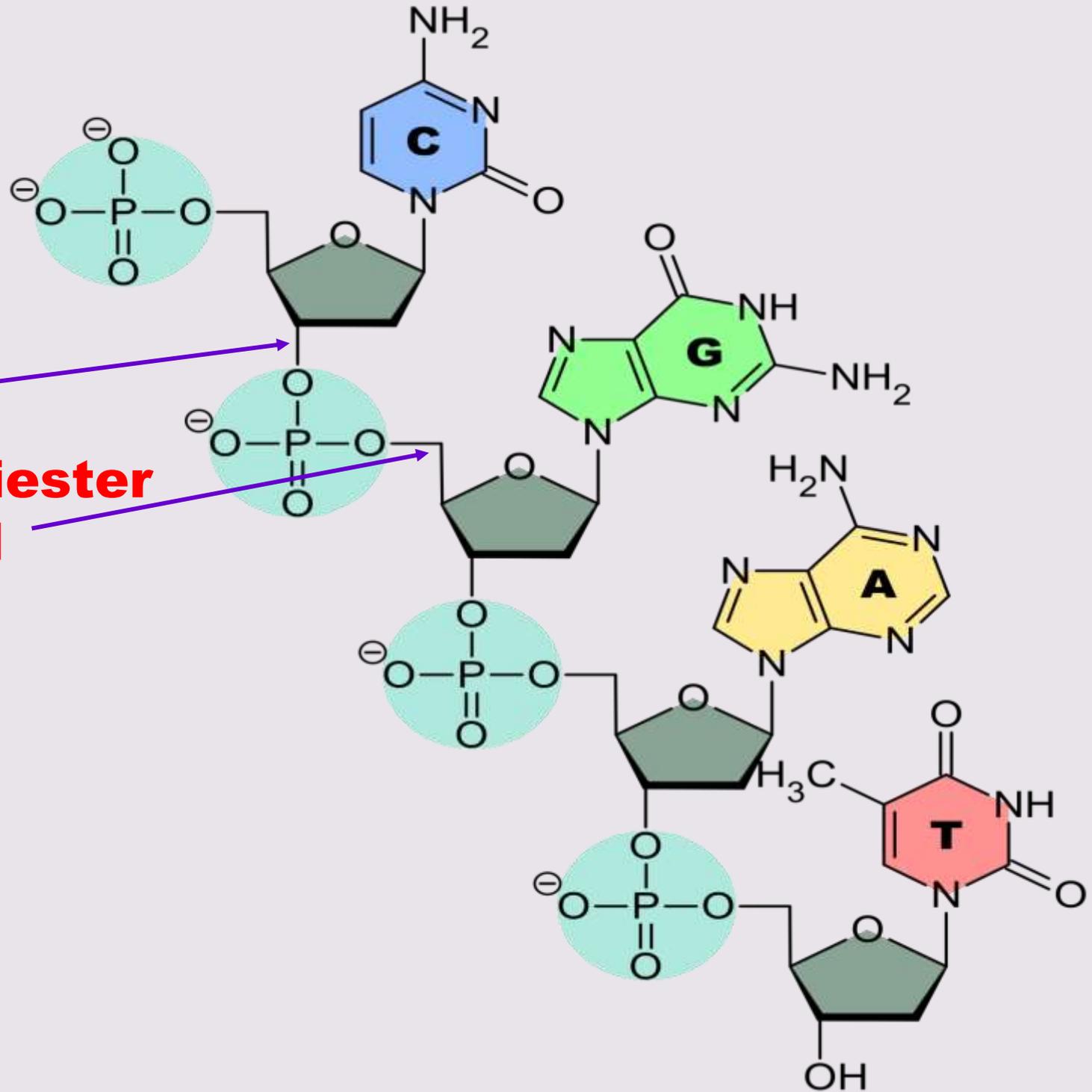
- ❖ A nucleotide having phosphate at 5' C will have a free –OH at 3' C such a nucleotide is called 5'-nucleotide or 5' P 3' OH and if situation is reverse the nucleotide called 3'-nucleotide or 3' P 5' OH
- ❖ The linkage between mono-nucleotide consist of phosphate group linked to two sugar.
- ❖ A phosphodiester bond join two mono-nucleotide (both in DNA & RNA)- C5'- C3'.
- ❖ If each nucleotide position in this long chain occupied by any one of four nucleotide, extraordinary variation is possible. For example a polynucleotide having 1000 nucleotide can be arranged in 4^{1000} **different ways** each one different from all othe possible sequences.



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3'-5'
Phosphodiester
Bond





Structure of DNA

- In 1953 James Watson and Francis Crick proposed the double helix model of DNA
- Published in Journal '**Nature**' (pg. 235) and which was recounted in Watson's book 'The Double Helix'.
- In 1962 got Nobel prize along with **M.H.F. Wilkins**



Francis Harry
Compton Crick
(1916-2004)



James Dewey
Watson
(1928 -)



Maurice Hugh
Frederick Wilkins
(1916-2004)



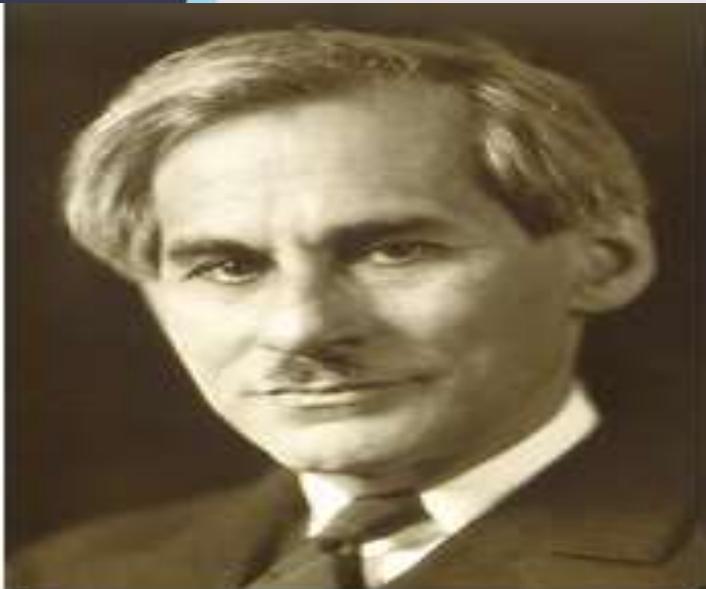
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Key Source of Watson and Crick double helix model of DNA

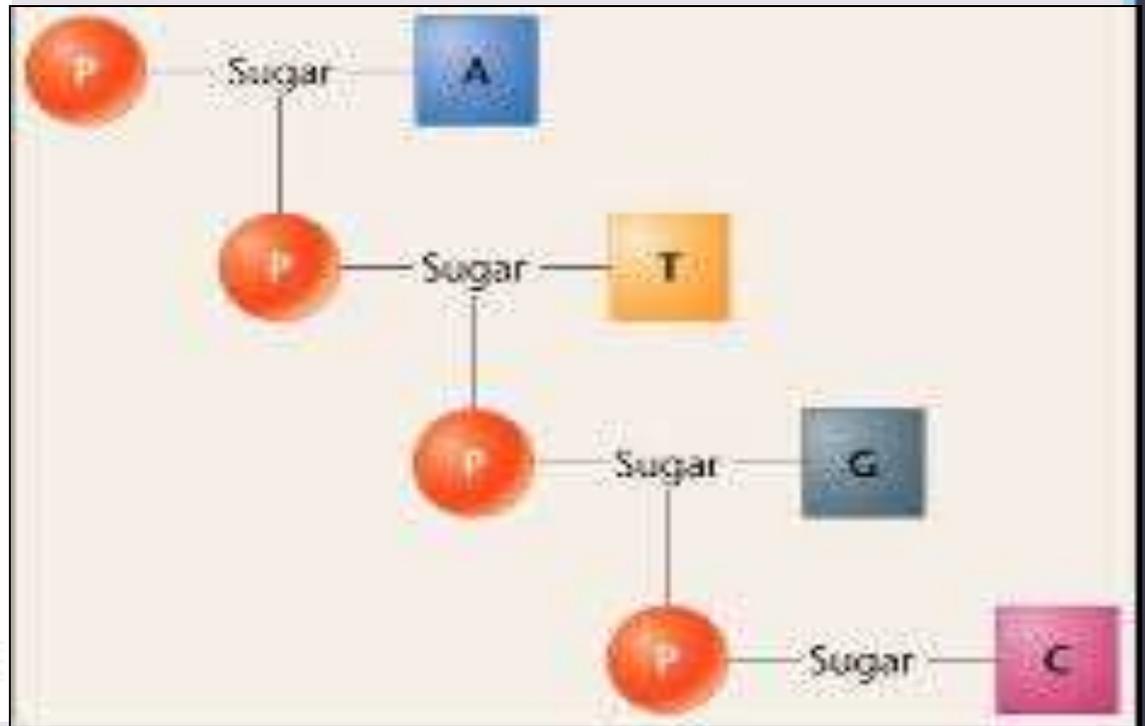
1. Tetranucleotide sequence:

Levene (1931) proposed that each of the deoxy-ribonucleotides was present in equal amounts and connected together in chains in which each of the four different nucleotides was regularly repeated in a tetranucleotide sequence (AGCT, AGCT etc.).



Phoebus Aaron Theodor Levene

Courtesy of the Rockefeller Archives Center.
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2. Base composition analysis of hydrolysed sample of DNA:

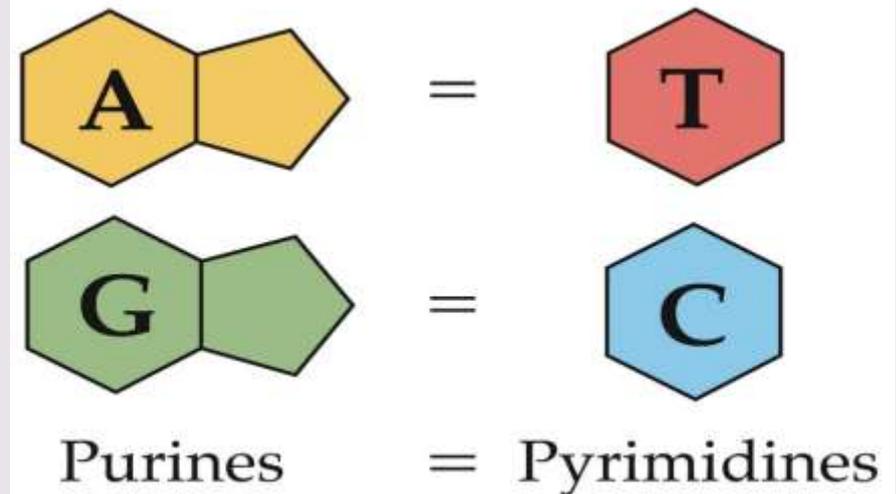
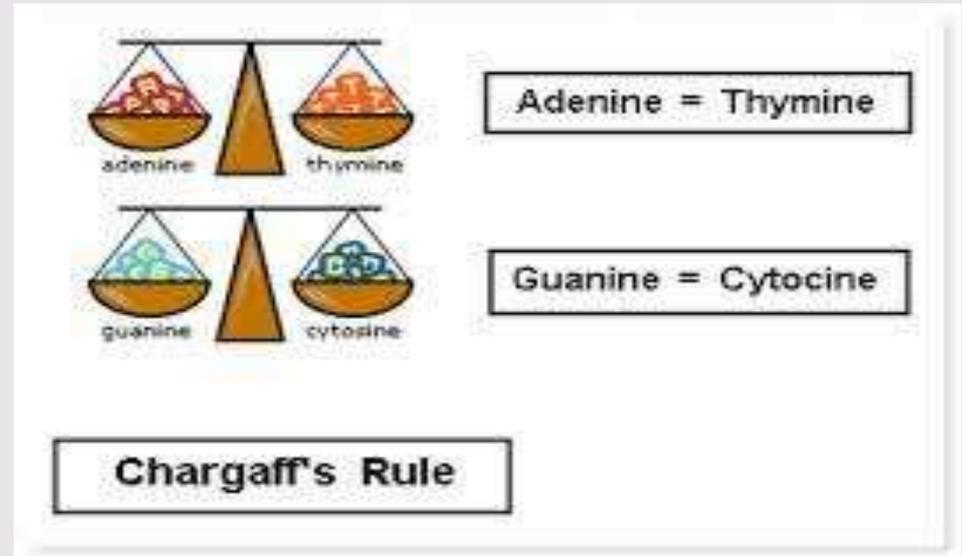
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Erwin Chargaff (1940s) used paper chromatographic method to separate the 4 bases in DNA sample from various organism and drawn following conclusion.

- ❖ Amount of A and G residues is proportional to amount of T and C residues.

i.e. $A = T$ and $G = C$ and $A/T = 1$ and $G/C = 1$





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Sum of purine (A+ G)= Sum of pyrimidine (T+ C)

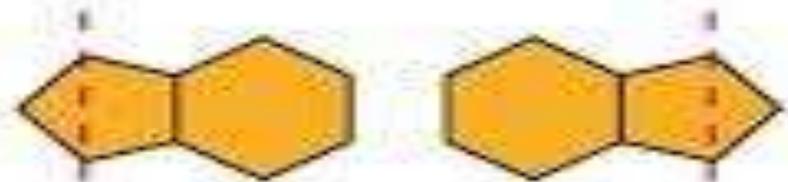
The percentage of A+T does not necessarily equal to the percentage of G+C and its ratio varies from species to species

i.e. $A+T / G=C \neq 1$

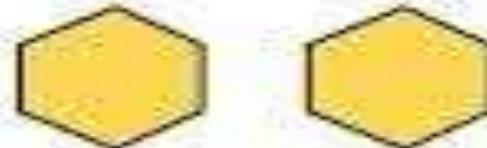
The Race to Discover DNA's



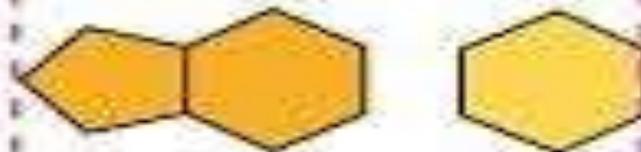
Erwin Chargaff



Purine + Purine = Too wide



Pyrimidine + Pyrimidine = Too Narrow



Purine + Pyrimidine = Perfect Fit from X-ray data

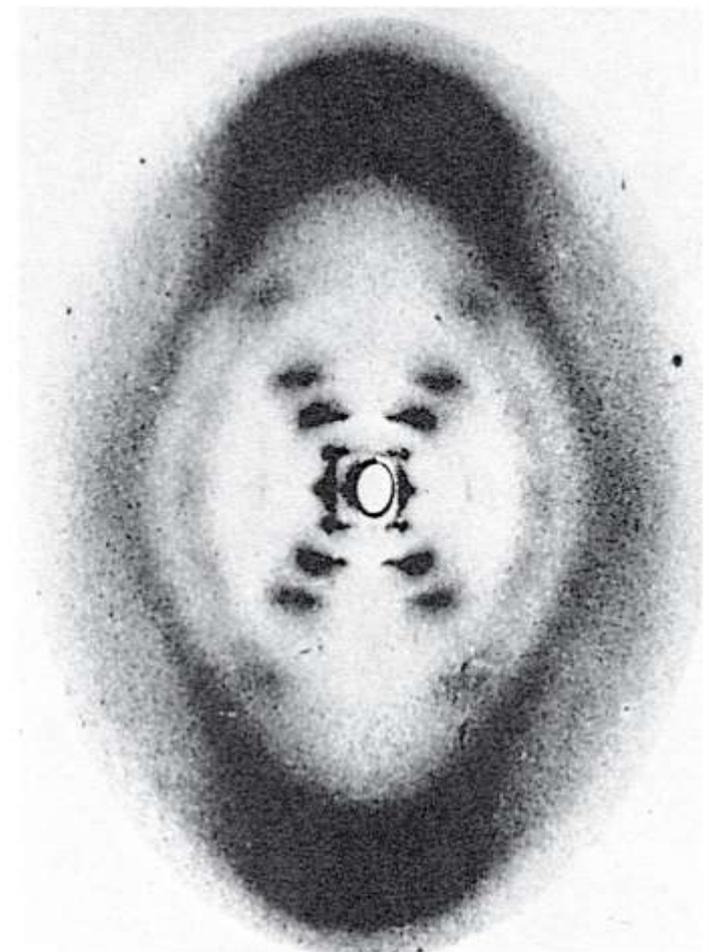


3. X- rays diffraction analysis:

Rosalind Franklin and Wilkins (1953) studied the X-ray crystallography of purified DNA and concluded that a well-organized multiple stranded fibre of about 22\AA in diameter that was also characterized by the presence of groups or bases spaced, 3.4\AA apart along the fibre and occurrence of a repeating unit at every 34\AA .



Rosalind Franklin



Franklin's X-ray diffraction photograph of DNA

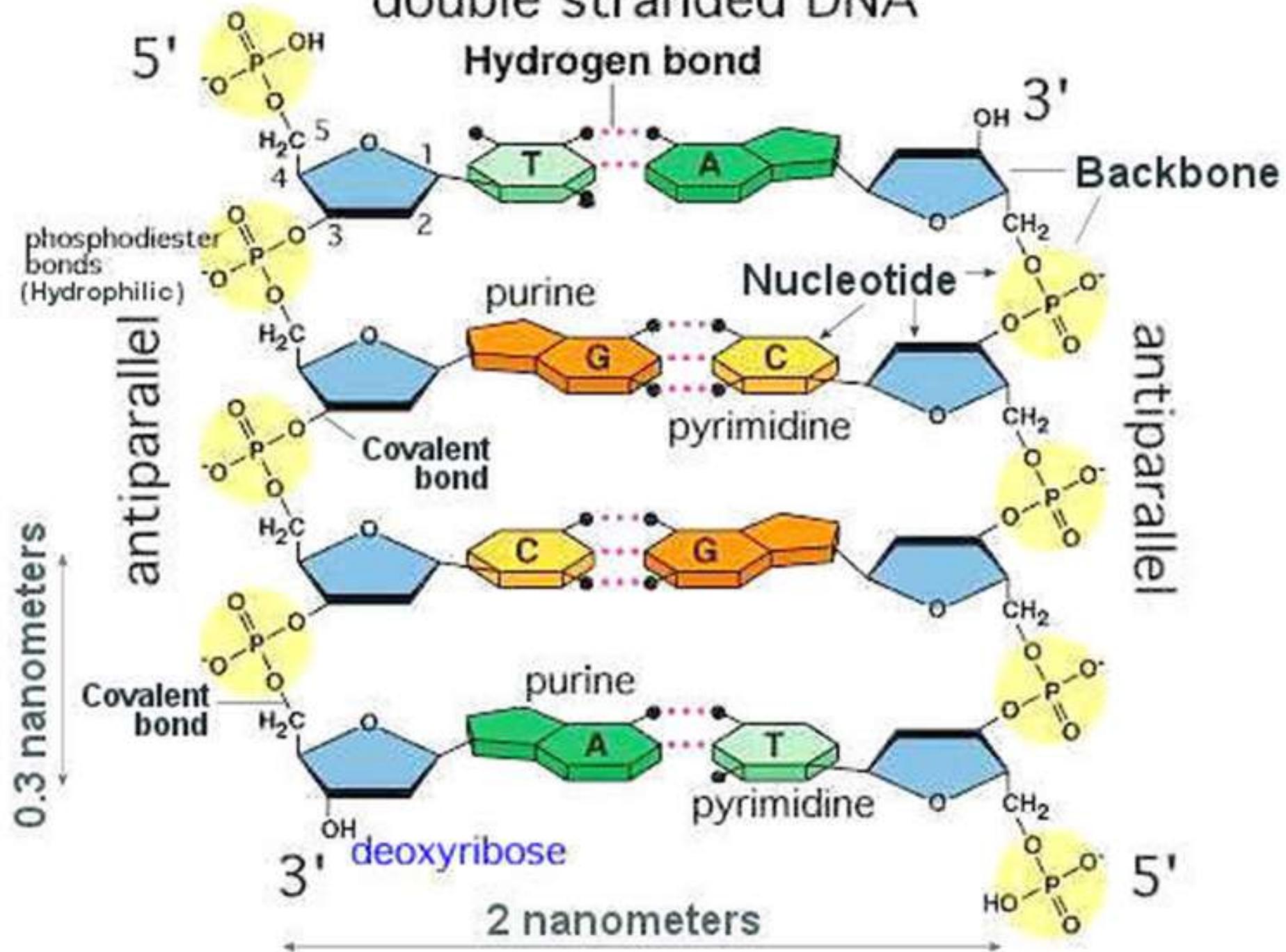


Watson and Crick model of DNA

Using the above sources Watson and Crick in 1953 proposed a “double helix” structure of DNA. The salient features of double helix structure of DNA are

- ❖ The DNA molecule consists of two polynucleotide chains wound around each other in a right-handed double helix.
- ❖ The two strands of a DNA molecule are oriented anti-parallel to each other i.e. the 5' end of one strand is located with the 3' end of the other strand at the same end of a DNA molecule.
- ❖ Each polydeoxyribonucleotide strand is composed of many deoxyribonucleotides joined together by phosphodiester linkage between their sugar and phosphate residues and the sugar phosphate backbones are on the outsides of the double helix with the nitrogen bases oriented toward the central axis.

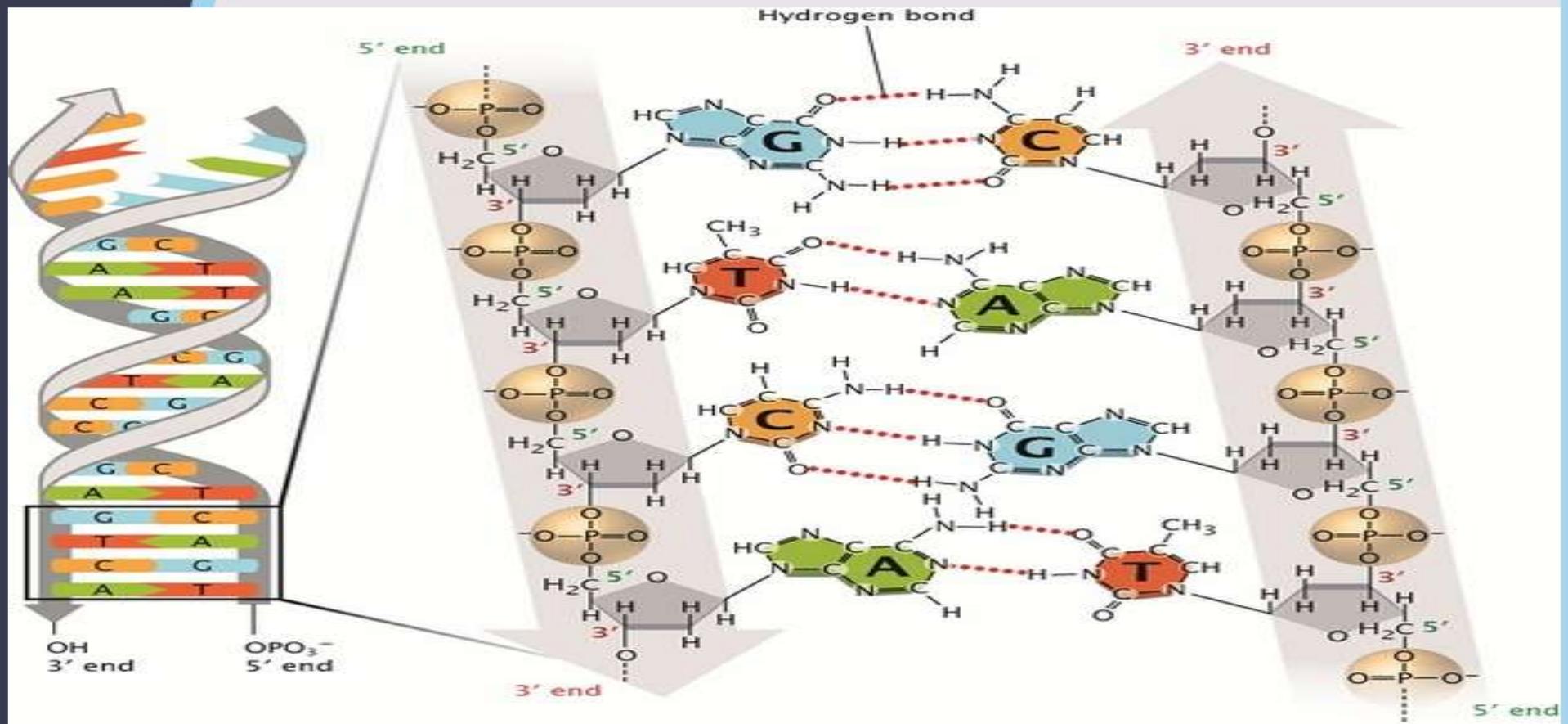
double stranded DNA





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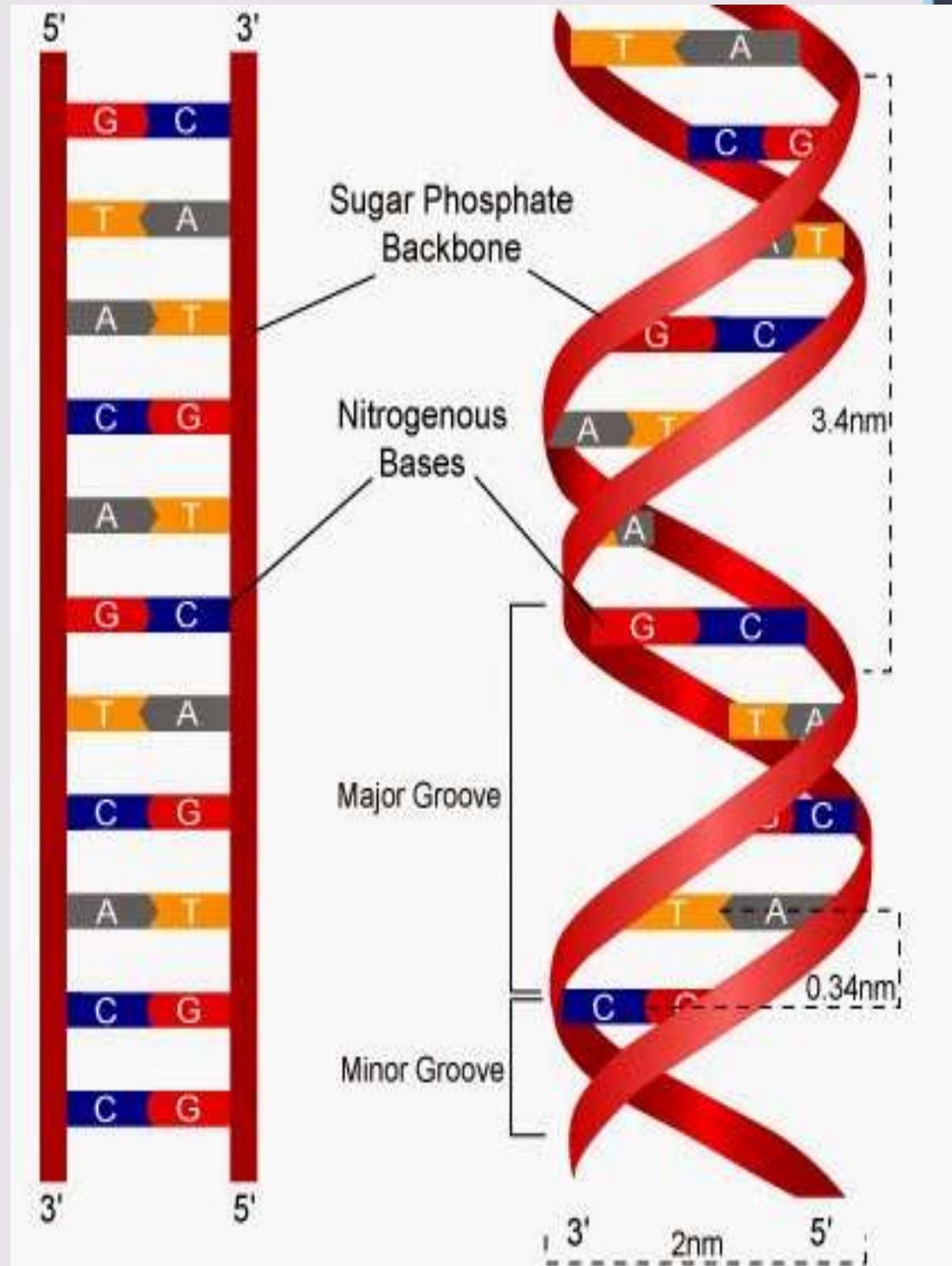
- ❖ The half steps of one strand extend to meet half steps of the other strand and the base pairs are called **complementary base pairs**. The adenine present in one strand of a DNA molecule is linked by two hydrogen bonds with the thymine located opposite to it in the second strand, and vice-versa. Similarly, guanine located in one strand forms three hydrogen bonds with the cytosine present opposite to it in the second strand, and vice-versa. **The pairing of one purine and one pyrimidine maintains the constant width of the DNA double helix.**





❖ The bases are connected by hydrogen bonds. Although the hydrogen bonds are weaker, the fact that so many of them occur along the length of DNA double helix provides a high degree of stability and rigidity to the molecule.

❖ The diameter of this helix is 20\AA , while its pitch (the length of helix required to complete one turn) is 34\AA . In each DNA strand, the bases occur at a regular interval of 3.4\AA so that about 10 base pairs are present in one pitch of a DNA double helix.





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- ❖ The helix has two external grooves, a deep wide one, called major groove and a shallow narrow one, called minor groove. Both these grooves are large enough to allow protein molecules to come in contact with the bases.
- ❖ This DNA structure offers a ready explanation of how a molecule could form perfect copies of itself. During replication, the two strands of a DNA molecule unwind and the unpaired bases in the single-stranded regions of the two strands by hydrogen bonds with their complementary bases present in the cytoplasm as free nucleotides. These nucleotides become joined by phospho-diester linkages generating complementary strands of the old ones with the help of appropriate enzymes.



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Types of DNA

- ❑ The double helix described by Watson and Crick has right handed helical coiling and is called B-DNA.
- ❑ It is a biologically important form of DNA that is commonly and naturally found in most living systems.
- ❑ This double helical structure of DNA exists in other alternate forms such as A-form, C-form etc. which differ in features such as the number of nucleotide base pairs per turn of the helix.
- ❑ The B-form contains ~ 10 (range 10.0 – 10.6) base pairs per turn.
- ❑ The B-DNA is the most stable form and it can change to another form depending upon the humidity and salt concentration of the sample.
- ❑ The A- form is also a right-handed helix, but it has 11 base pairs per turn.
- ❑ The C-form of DNA has 9.3 base pairs per turn, while the D-form of DNA, which is rare form, has 8 base pairs per turn.

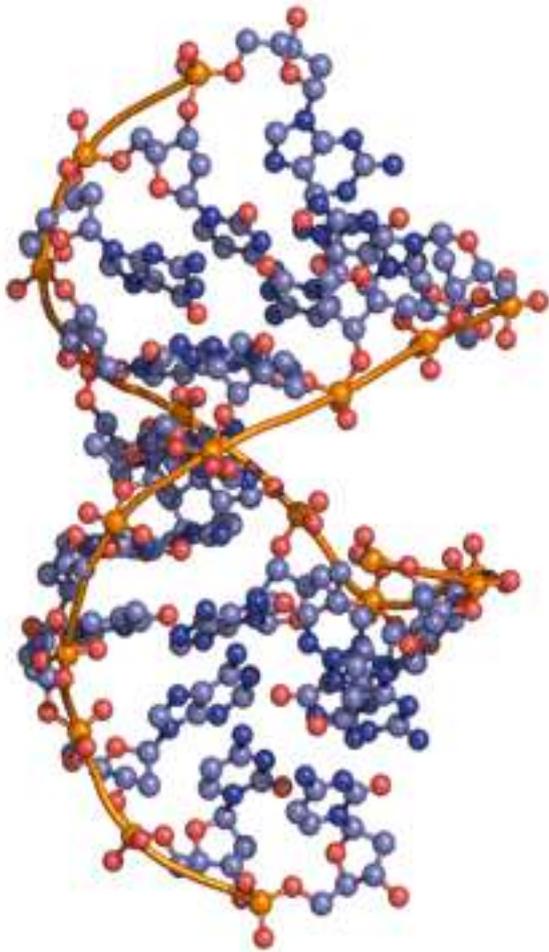


- ❑ Another form of DNA, in which the helix is left-handed, called Z-DNA was discovered by Rich.
- ❑ In Z-DNA sugar and phosphate linkages follow a zigzag pattern. Z-DNA plays a role in the regulation of the gene activity.

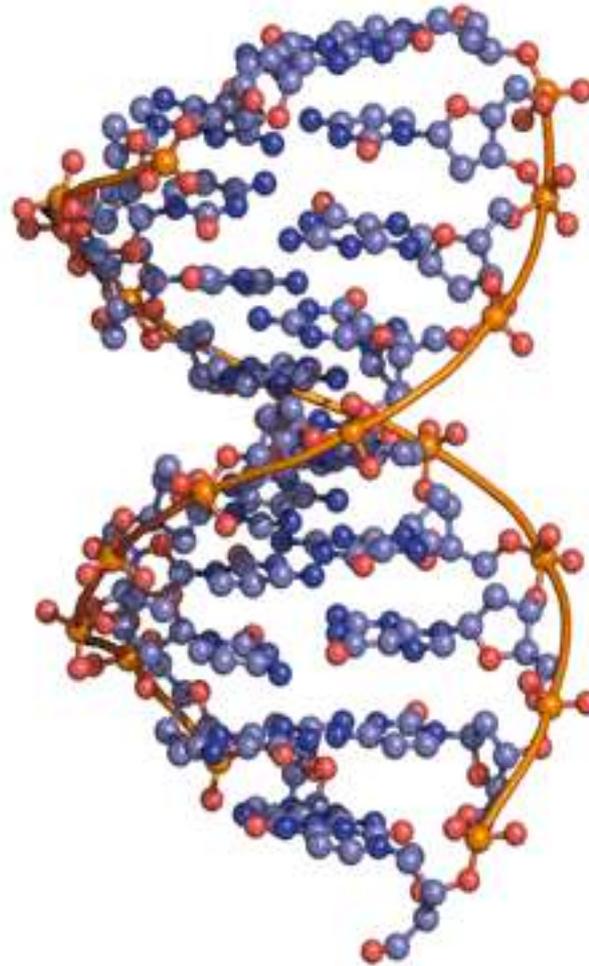
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Structural forms of DNA

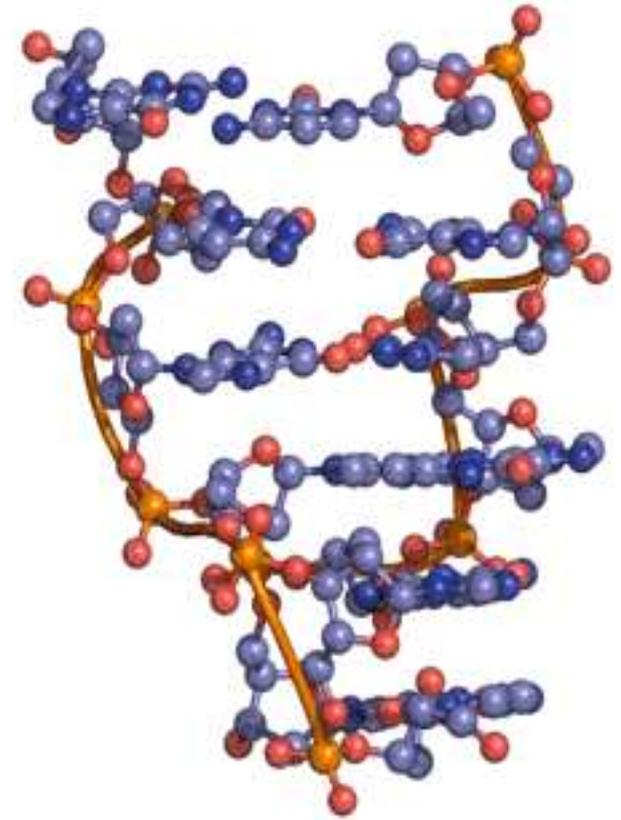
Property	A-DNA	B-DNA	Z-DNA
Helix Handedness	Right	Right	Left
Base Pairs per turn	11	10.4	12
Rise per base pair along axis	0.23nm	0.34nm	0.38nm
Pitch	2.46nm	3.40nm	4.56nm
Diameter	2.55nm	2.37nm	1.84nm
Conformation of Glycosidic bond	anti	anti	Alternating anti and syn
Major Groove	Present	Present	Absent
Minor Groove	Present	Present	Deep cleft



A-DNA



B-DNA



Z-DNA

Thus, the essential functions of DNA are the storage and transmission of genetic information and the expression of this information in the form of synthesis of cellular proteins.



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RNA (Ribose nucleic acid), Structure and function

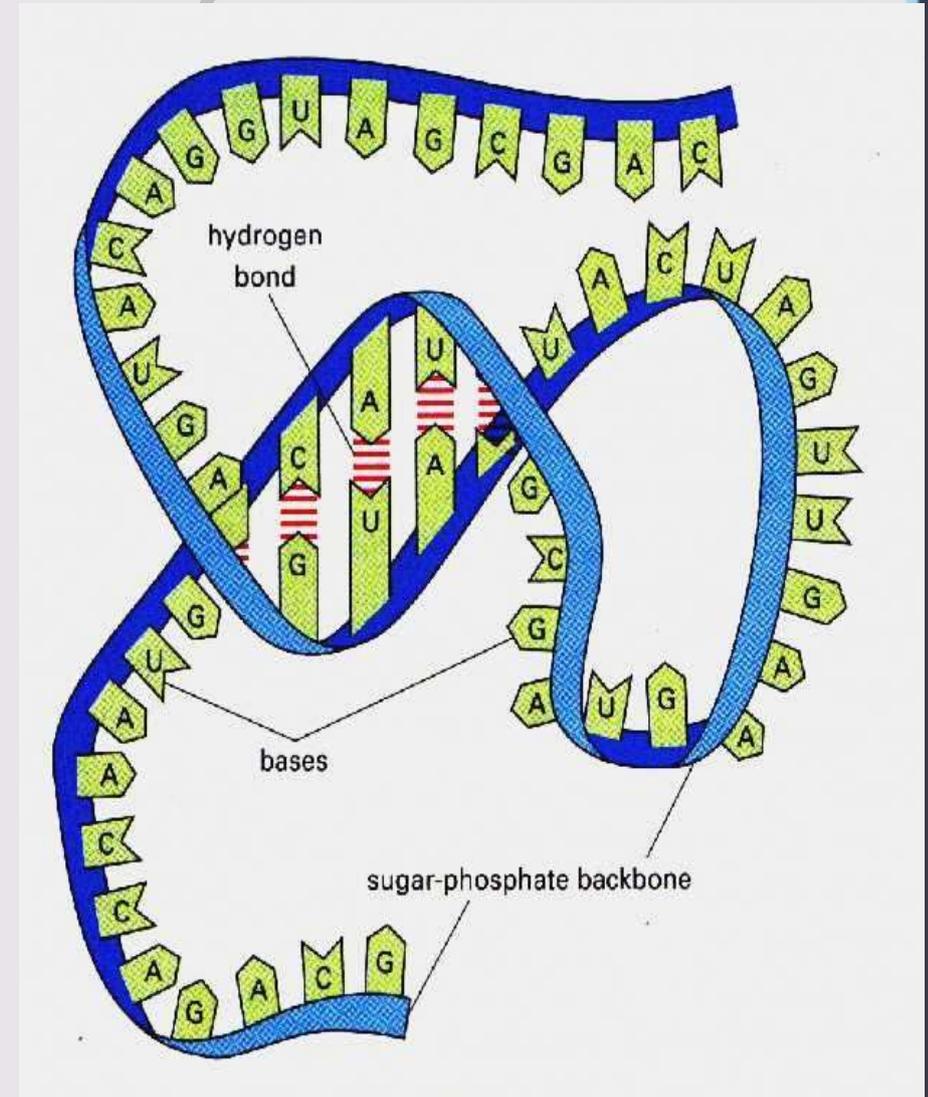
RNA like DNA is a polynucleotide. RNA nucleotides have ribose sugar, which participate in the formation of sugar phosphate backbone of RNA.

- ❖ Thymine is absent and is replaced by Uracil.
- ❖ Usually RNA is a single stranded structure. Single stranded RNA is the genetic material in most plant viruses Eg. TMV.
- ❖ Double stranded RNA is also found to be the genetic material in some organisms. Eg.: Plant wound and tumour viruses.
- ❖ RNA performs non-genetic function.

There are three main types or forms of RNA.

1. messenger RNA (m-RNA):

- It constitutes about 5-10% of the total cellular RNA.
- It is a **single stranded** base for base complimentary copy of one of the DNA strands of a gene.
- It provides the information for the amino acid sequence of the polypeptide specified by that gene.





2. ribosomal RNA (r – RNA):

- ❖ Occur in association with proteins and is organized into special bodies of about 200⁰A diameter called ribosomes.
- ❖ The size of ribosomes is expressed in terms of 'S' units, based on the rate of sedimentation in an ultracentrifuge.
- ❖ It constitutes about 80% of the total cellular RNA.
- ❖ The function of rRNA is binding of mRNA and tRNA to ribosomes.

Ribosome



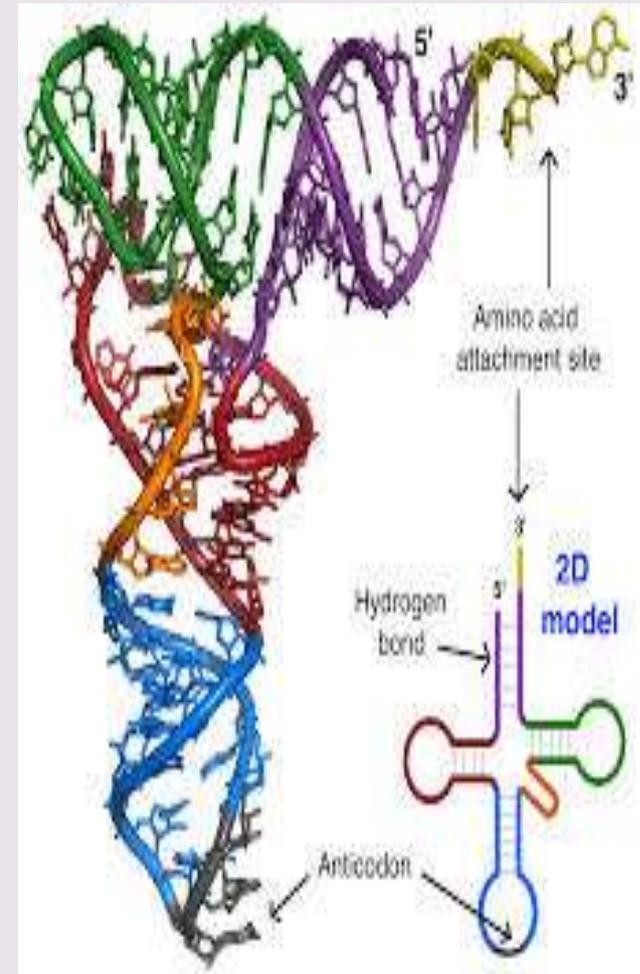
Ribosomal RNA



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transfer RNA (t- RNA):

- ❑ It is also known as **soluble RNA(sRNA)**.
- ❑ It constitutes about 10-15% of total RNA of the cell. It is a class of RNA which is of small size of 3S type and generally have 70 – 80 nucleotides. The longest t – RNA has 87 nucleotides.
- ❑ Its main function is to carry various types of amino acids and attach them to mRNA template for synthesis of protein.
- ❑ Each t- RNA species has a specific anticodon which base pairs with the appropriate m – RNA codon



The nucleotide sequence of the first tRNA (yeast alanyl tRNA) was determined by Robert Holley (1965), who proposed the clover leaf model of secondary structure of tRNA. Each tRNA is specific for each amino acid.



❖ tRNA molecule contains the sequence of CCA at the 3' end, which is called amino acid attachment site.

➤ At the CCA end, it is joined to the single amino acid molecule for which that tRNA is specific. For example, a tRNA molecule specific for lysine cannot bind to the arginine.

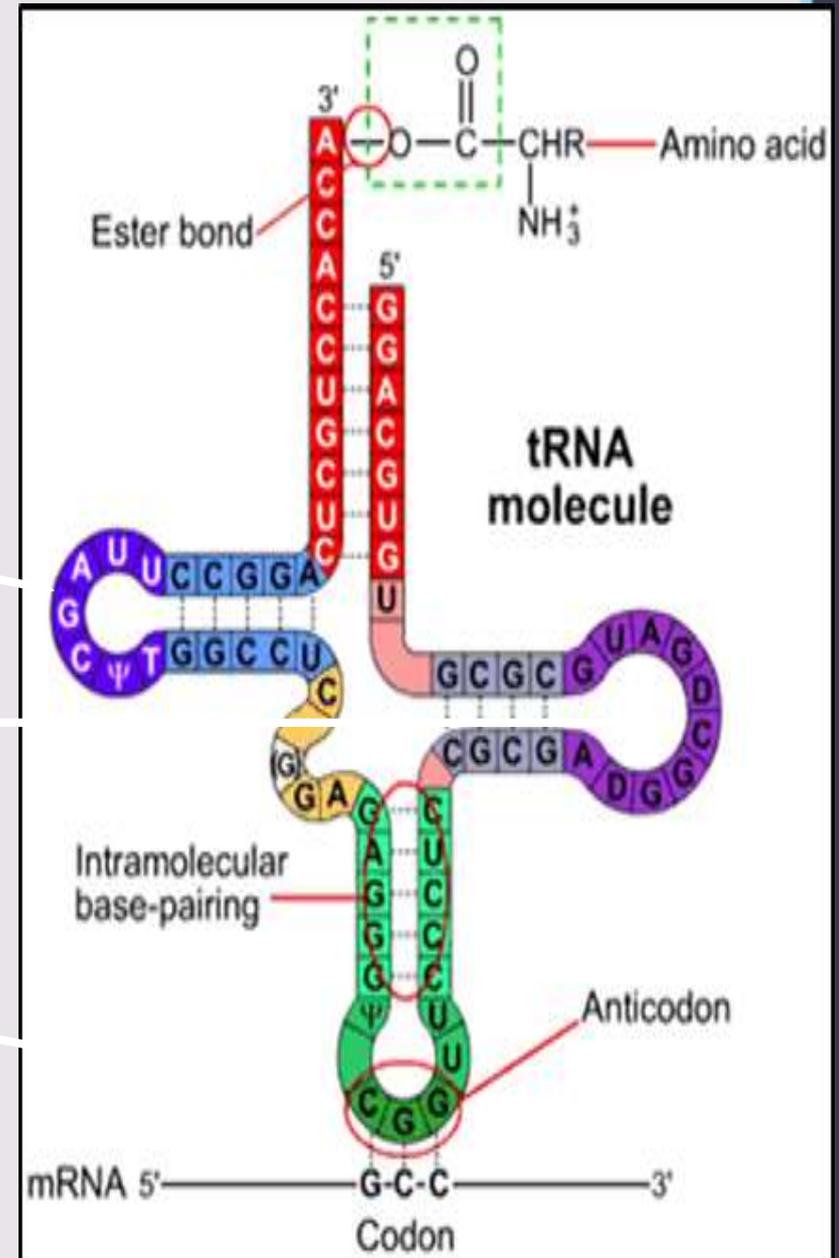
➤ tRNA consists of three loops

(a) DHU-loop or D-loop (aminoacyl recognition region),

(b) thymine loop (ribosome attachment region). and

(c) anticodon loop

➤ Anticodon loop contains a short sequence of bases, which permits temporary complementary pairing with the codons of mRNA.

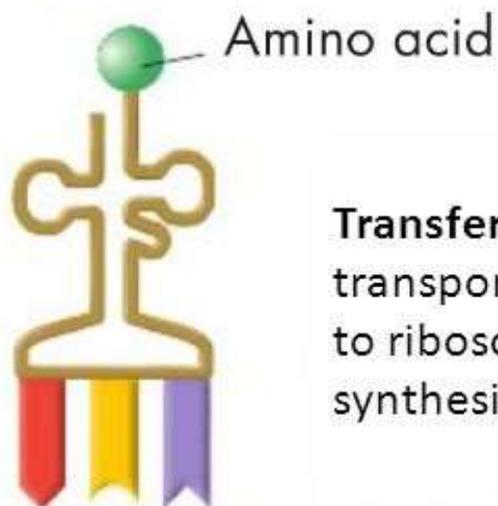


3 types of RNA

Messenger RNA (mRNA) – carries code from DNA to ribosome for protein synthesis



Ribosomal RNA (rRNA) – assembles amino acids brought by tRNA in a specific order from mRNA to make proteins; made of RNA by the nucleolus



Transfer RNA (tRNA) – transports specific amino acid to ribosome for protein synthesis

DIFFERENCES BETWEEN DNA AND RNA

SL. No.	Particulars	DNA	RNA
1	Strands.	Usually two, rarely one.	Usually one, rarely two.
2	Sugar.	Deoxyribose.	Ribose.
3	Bases.	Adenine, guanine, cytosine and thymine.	Adenine, guanine, cytosine and uracil.
4	Pairing.	AT and GC.	AU and GC.
5	Location.	Mostly in chromosomes, some in mitochondria and chloroplasts.	In chromosomes and ribosomes.
6	Replication.	Self-replicating.	Formed from DNA. Self replication only in some viruses.
7	Size.	Contains up to 4.3 million nucleotides.	Contains up to 12,000 nucleotides.
8	Function,	Genetic role.	Protein synthesis, genetic in some viruses.
9	Types.	There are several forms of DNA.	Three types, viz., mRNA, tRNA and rRNA.



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