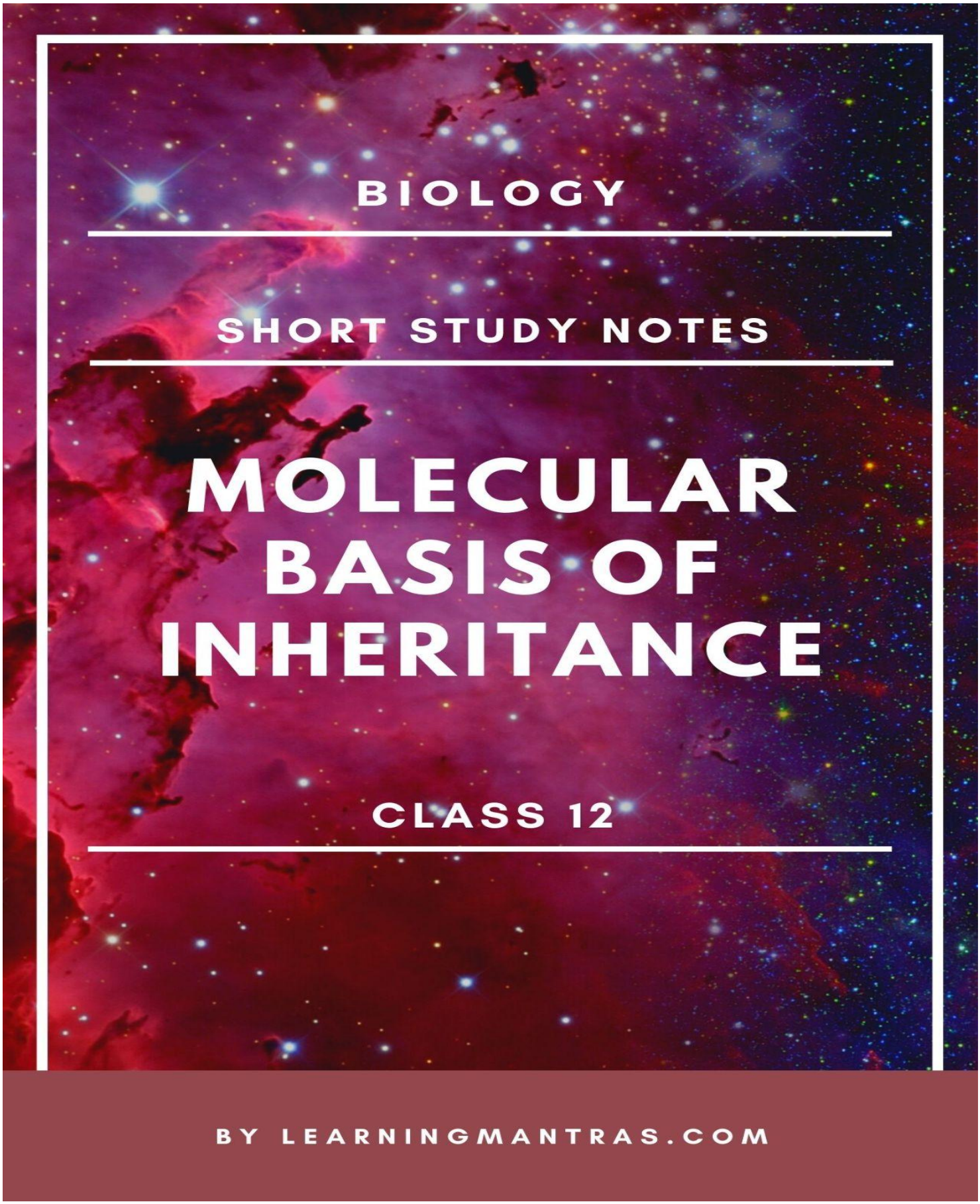

BIOLOGY
SHORT STUDY NOTES
MOLECULAR BASIS OF INHERITANCE
CLASS 12
BY LEARNINGMANTRAS.COM

Molecular Basis of Inheritance

Molecular basis of inheritance involves the study of genes, genetic variations and heredity. It explains how an offspring looks similar to the parents. DNA, RNA and genetic code form the basis of the molecular basis of inheritance. They transmit the hereditary genes from the parents to the offspring.

There are two types of Nucleic Acid – DNA and RNA.

- DNA: Deoxyribonucleic Acid
- RNA: Ribonucleic Acid

Deoxyribonucleic Acid (DNA)

Deoxyribonucleic acid (DNA) is a molecule that contains the biological instructions that make each species unique. DNA, along with the instructions it contains, is passed from adult organisms to their offspring during reproduction.

- Bacteriophage ΦX174 has a genome of 5,386 nucleotides.
- Bacteriophage λ has 48,502 base pairs in length.
- E Coli has 4 x 10^6 base pairs.
- Haploid cells of human DNA have 3.3 x 109 base pairs.

Structure of Polynucleotide Chain

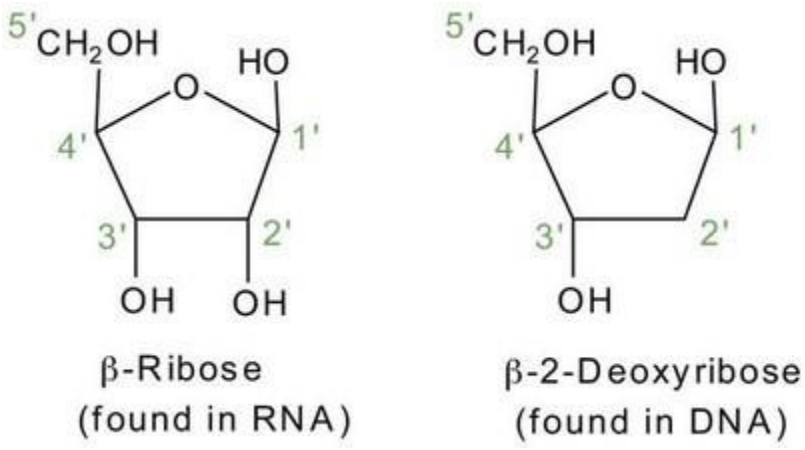
1. What are Nucleotides?

It is a base unit of the polynucleotide chain of DNA and RNA.

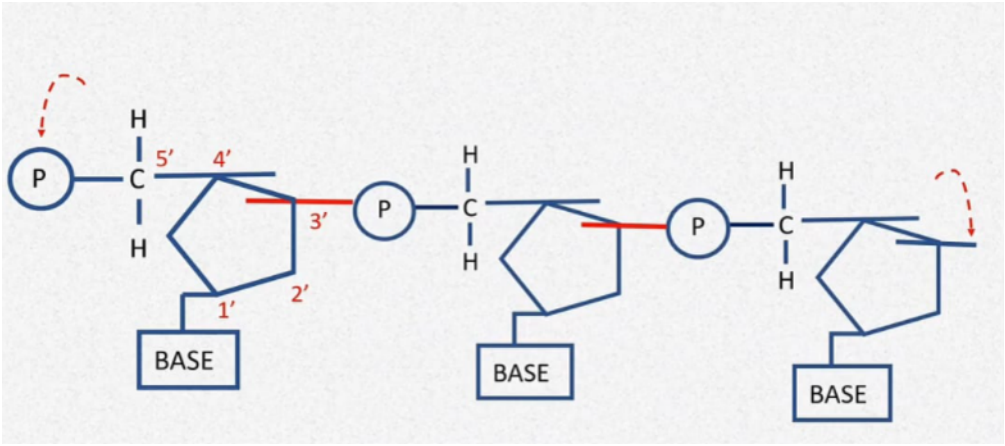
2. Name the main components of each Nucleotides?

Main components are:

- Nitrogenous Base
- Sugar - Either ribose sugar or deoxyribose sugar
- Phosphate Group
- **Nitrogenous Base**
- **Purines:** Adenine, Guanine
- **Pyrimidines:** Cytosine Thymine (in DNA), Cytosine Uracil (in RNA)
- Nitrogenous bases are connected to the pentose sugar by nitrogen glycosidic bonds.



- When a phosphate group is attached to the 5' carbon of a nucleoside (without phosphate), a nucleotide is formed.
- Two nucleotides join together through 3'-5'carbon phosphodiester linkage dinucleotide is formed.

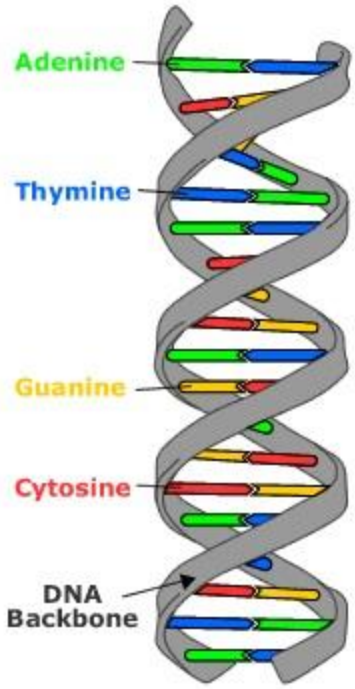


Features of Deoxyribonucleic Acid (DNA)

- DNA is made up of two polynucleotide chains, where the backbone is made up of sugar and phosphate groups and nitrogenous base projecting towards the center.
- There is a complementary base pairing between the two strands.
- The two strands are coiled in right-handed fashion and anti-parallel in orientation. One chain has a 5′→3′ polarity while the other has 3′→5′ polarity.
- The diameter of the strand is always constant due to the pairing of purine and pyrimidine. (A – T and G – C)
- The distance between the two base pairs in the helix is 0.34 nm and both the strands are right handed coiled.

Double Helical Structure of DNA

The 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. Each DNA strand within the double helix is a long, linear molecule made of smaller units called nucleotides that form a chain.

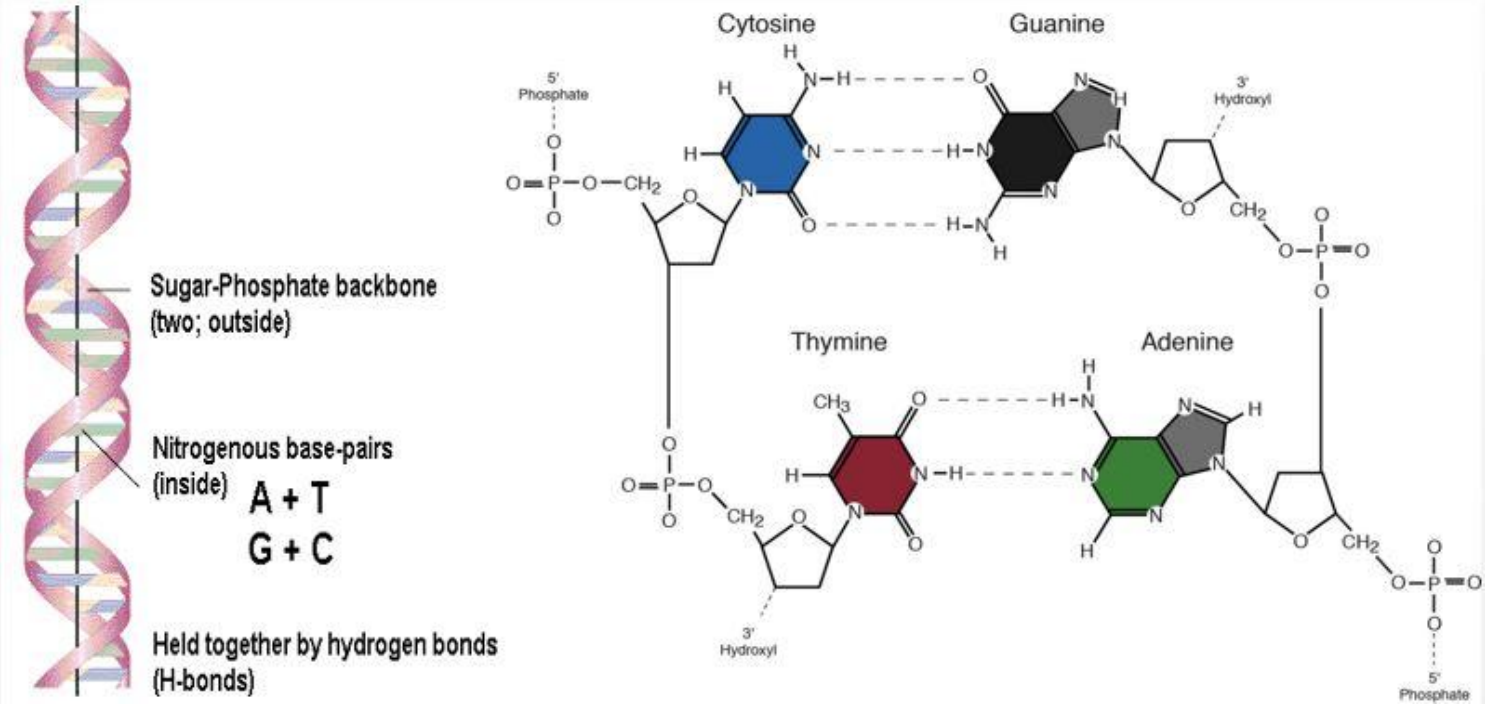


Watson-Crick Structure of DNA

They discovered the double helix structure of DNA and proposed an X-Ray diffraction pattern.

Important features of this model was:

- Complementary base pairing between two strands of polynucleotide chains.
- Data for this pattern was produced by Maurice Wilkins and Rosalind Franklin.



Chargaff's rule

- It states that the amount of guanine should be equal to cytosine and the amount of adenine should be equal to thymine.

$$[A] = [T] \quad [G] = [C]$$

- Adenine with Thymine and Guanine with Cytosine are always joined by hydrogen bonds.
- The ratio of Adenine and Guanine to that of Thymine and Cytosine is always equal to one.

$$[A + G] / [T + C] = 1$$

Central Dogma

Francis Crick proposed the Central Dogma of molecular biology which states the genetic information flows from DNA to MRNA (transcription) and then from MRNA to proteins (translation) this is a unidirectional process. Central Dogma is bidirectional in some viruses and this process is called reverse transcription.

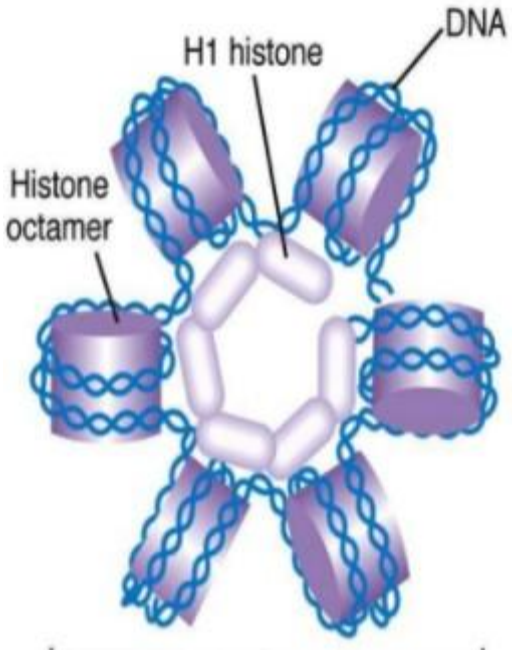
Packaging of Deoxyribonucleic Acid (DNA)

- Roger Kornberg in 1974 reported that chromosomes are made up of DNA and proteins.
- Later, Beadle and Tatum reported that chromatin fibers look like beads on the string, where beads are repeated units of proteins.
- The proteins associated with DNA are true type – basic proteins (histone and protamine) and acidic non-histone chromosomal proteins.

- The negatively charged DNA molecule wraps around the positively charged histone proteins to form a structure called nucleosomes and nucleosomes are made up of four types of histone proteins H2A, H2B, H3 and H4 occurring in pairs.
- 200 BP of DNA helix is wrapped around the nucleosome by 1 1/3 turns plugged by H1 histone protein.
- Repeating units of nucleosome from chromatin (thyroid like) in nucleus.
- When chromatin is packed it from a solenoid structure of 30 nm in diameter and father supercoiling forms chromatin films (chromatin) which condense and coil during metaphase to form chromosomes.
- In prokaryotic cells (which do not have a defined nucleus) such as E coli DNA (being negatively charged) is held with some proteins (that have positive charge) in a region called a nucleoid. The DNA nucleoid is organized in large loops held by proteins.

Core of Histone Molecules

Histone proteins play essential structural and functional roles in the transition between active and inactive chromatin states. Although histones have a high degree of conservation due to constraints to maintain the overall structure of the nucleosomal octameric core, variants have evolved to assume diverse roles in gene regulation and epigenetic silencing. Histone variants, post-translational modifications and interactions with chromatin remodeling complexes influence DNA replication, transcription, repair and recombination. The authors review recent findings on the structure of chromatin that confirm previous interparticle interactions observed in crystal structures.



Search of Deoxyribonucleic Acid (DNA)

- Frederick Griffith in 1928 performed a series of experiments using Streptococcus pneumoniae bacteria and mice.
- When Streptococcus pneumoniae are grown in a cultural plate, some produce smooth shiny colonies (S) while others produce rough colonies (R).

- Mice infected with S-strain die from pneumoniae whereas mice infected with R-strain does not.
- Griffith then killed the bacteria by heating them.
- Now when S-strain (heat-killed) were injected in mice they lived whereas when R lived and S killed were injected the mice died.
- He concluded that R-strain bacteria had somehow been transformed by the heat killed S-strain bacteria, i.e. some transforming material must be transferred from S-strain to R-strain that enabled the R-strain to synthesis smooth polysaccharides coat and become urilest.

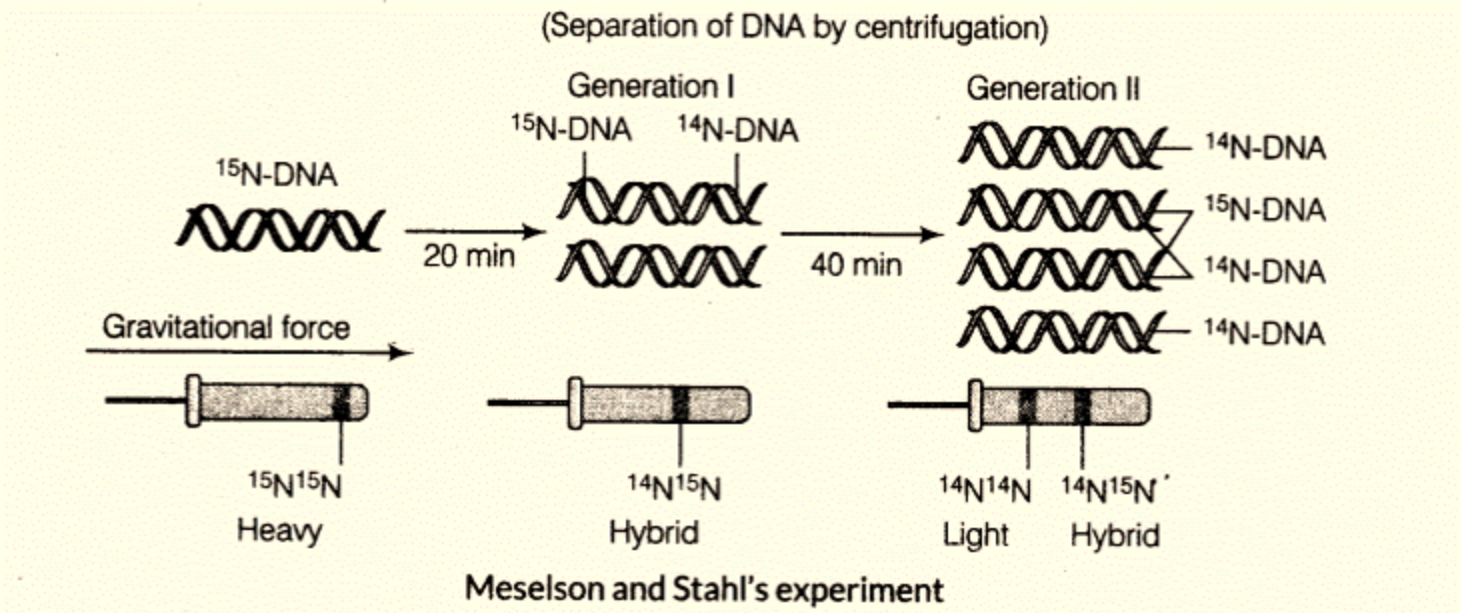
Replication

- Watson and Crick suggested that the replication of DNA is semiconservative.
- Meselson and Stahl in 1958 experimentally proved that the DNA replicates semi conservatively.
- Taylor et al in another experiment on fava beans (Vicia faba) using radioactive thymidine proved that the replication on DNA is semiconservative.
- Enzyme DNA polymerase catalyses DNA replication. It can polymerise only in 5'→3' direction.
- Replication is initiated at the origin of replication.
- Deoxyribonucleoside triphosphate provides energy for the polymerisation reaction and also acts as a substrate.
- A small part of DNA opens up making a replication fork, where replication occurs.
- Replication is continuous in a strand with 5'→3' direction, called leading strand, where the template strand has 3'→5' polarity, called leading strand template.
- Replication is discontinuous in the other strand, where the template strand has 5'→3' polarity, called lagging strand template.
- The discontinuous fragments, called Okazaki fragments are joined together by the enzyme DNA ligase.
- In eukaryotic cells, the replication takes place during s-phase of the cell cycle.
- If cell division doesn't occur after the replication, it results in polyploidy of chromosomes.

Experimental proof that DNA replicates semi-conservatively

- E. coli was grown in a medium containing 15NH4C1 as the only nitrogen source for many generations. 15N got incorporated into newly synthesised DNA (and other nitrogen containing compounds). This heavy DNA molecule could be distinguished from the normal DNA by centrifugation in a cesium chloride (CsCl) density gradient.
- They then transferred the cells into a medium with normal 14NH4Cl and took samples at various definite intervals as the cells multiplied and extracted the DNA that remained as double stranded helices. DNA samples were separated independently on CsCl gradients to measure DNA densities.

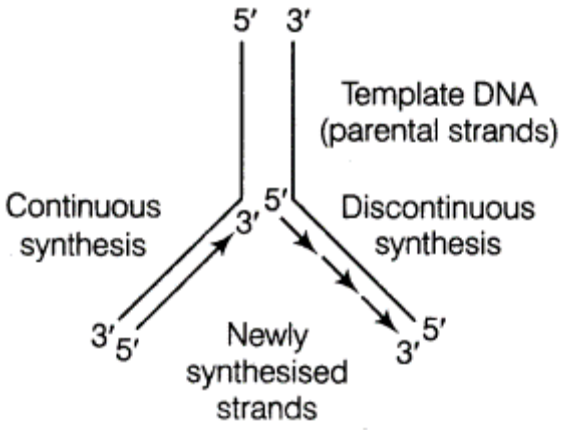
- The DNA that was extracted from the culture, one generation (after 20 min) after the transfer from 15 N to 14N medium had a hybrid or intermediate density. DNA extracted from the culture after another generation (after 40 min) was composed of equal amounts of this hybrid DNA and of light DNA.
- Very similar experiments were carried out by Taylor and Colleagues on Vicia faba (faba beans) using radioactive thymidine and the same results, i.e. DNA replicates semiconservatively, were obtained as in earlier experiments.



Meselson and Stahl's experiment

DNA Replication Machinery and Enzymes

- DNA replication machinery and enzymes process of replication requires a set of catalysts (enzymes).
- The main enzyme is DNA-dependent DNA polymerase, since it uses a DNA template to catalyse the polymerisation of deoxynucleotides. The average rate of polymerisation by these enzymes is approximately 2000 bp/second.
- These polymerases have to catalyse the reaction with a high degree of accuracy because any mistake during replication would result in mutations.
- DNA polymerisation is an energy demanding process, so deoxyribonucleoside triphosphates serve dual purposes, i.e. act as substrates and provide energy for polymerisation reaction.
- Many additional enzymes are also required in addition to DNA-dependent DNA polymerase.
- Replication in DNA strands occurs within a small opening of the DNA helix, known as replication fork.
- DNA-dependent DNA polymerases catalyse polymerisation only in one direction, i.e. 5′ -> 3. It creates additional complications at the replication fork. Consequently, on one strand (template 3′-5′), the replication is continuous, while on the other strand (template 5′-3′), it is discontinuous. The discontinuously synthesised fragments called Okazaki fragments are later joined by DNA ligase.
- DNA polymerases cannot initiate the process of replication on their own. Also, replication does not initiate randomly at any place in DNA. So, there is a definite region in E.coli DNA where the replication originates. The region is termed as the origin of replication.
- Due to this requirement, a piece of DNA, if needed to be propagated during recombinant DNA procedures, requires a vector. The vectors provide the origin of replication.



Replicating fork of DNA

Difference between Euchromatin and Heterochromatin

Heterochromatin	Euchromatin
• It is a form of DNA in the chromosome that has the characterization of tight packing.	• It is a form of DNA in the chromosome that has the characterization of loose packing.
• It has a dark stain.	• It has a light stain.
• It has a high density of DNA.	• It has a low density of DNA.
• Little or no transcriptional activity here.	• There is active participation in the transcriptional process here.
• They exist at the periphery of the nucleus. Furthermore, they exist only in eukaryotic cells.	• They exist in the nucleus's inner body. Furthermore, they exist in eukaryotic as well as prokaryotic cells.
• Coiling is compact, regions are sticky, there is no change in the phenotype of an organism, gene expression regulation is possible, and maintenance of the cell's structural integrity.	• Coiling is loose, regions are non-sticky, variation may occur due to the effect in DNA at the time of the genetic process, genetic variations are possible, and genetic transcription takes place.

Genetic Code

- It is the sequence of bases in mRNA that codes for a particular amino acid in the protein synthesis.
- Each code is made up of three nucleotides called a triplet. codons are nearly universal, except for some protozoans and mitochondrial codons.
- More than one triplet codon code for the same amino acid, so the code is degenerate.
- There are a total of 64 codons, of which 61 code for amino acids.
- 3 codons do not code for any amino acids, they are called stop codons- UAA, UAG, UGA.
- AUG is the start codon as well as codes for the amino acid methionine.

DNA is the Genetic Material

- Alfred Hershey and Martha Chase (1952) gave unequivocal proof that DNA is the genetic material.
- In their experiments, bacteriophages (viruses that infect bacteria) were used.
- They grew some viruses on a medium that contained radioactive phosphorus and some others on sulphur containing radioactive medium.
- Viruses grown in the presence of radioactive phosphorus contained radioactive DNA but not radioactive protein because DNA contains phosphorus but protein does not. In the same way, viruses grown on radioactive sulphur contained radioactive protein, but not radioactive DNA because DNA does not contain sulphur.
- Radioactive phages were allowed to attach to E. coli bacteria. As the infection proceeded, viral coats were removed from the bacteria by agitating them in a blender. The virus particles were separated from the bacteria by spinning them in a centrifuge.
- Bacteria which were infected with viruses that had radioactive DNA were radioactive, indicating that DNA was the material that passed from the virus to the bacteria.
- Bacteria that were infected with viruses that had radioactive proteins were not radioactive. This indicated that the proteins did not enter the bacteria from viruses. It proved that DNA is a genetic material that is passed from virus to bacteria.

Properties of Genetic Material

- It became established that DNA is the genetic material from the Hershey-Chase experiment.
- In some viruses, RNA was also reported as genetic material, e.g. Tobacco mosaic viruses, QB bacteriophage, etc.
- According to the above mentioned rules, both the nucleic acids (DNA and RNA) have the ability to direct duplications.
- Stability can be explained in DNA as the two strands being complementary if separated by heating come together in appropriate conditions.
- The 2′ — OH group present at every nucleotide in RNA is a reactive group and makes RNA labile and easily degradable, hence it is reactive.
- DNA is chemically less reactive and structurally more stable when compared to RNA. Thymine also confers additional stability to DNA. So, among the two nucleic acids, the DNA is a predominant genetic material.
- Both RNA and DNA are able to mutate. Viruses having RNA genome and having shorter life span mutate and evolve faster.

- DNA is dependent on RNA for protein synthesis, while RNA can directly code for it. The protein synthesising machinery has evolved around RNA. This concluded that the DNA being more stable is suitable for storage of genetic information, while for the transmission of genetic information, RNA is suitable.

Characteristics of a Genetic Material

- It should be able to replicate.
- It should be chemically and structurally stable.
- It should provide scope for slow changes (mutation) that are required for evolution.
- It should be able to express itself in the form of 'Mendelian characters'.

Ribonucleic acid (RNA)

- RNA was the first genetic material.
- Essential life processes (such as metabolism, translation, splicing, etc.) evolved around RNA.
- RNA acts as genetic material as well as a catalyst.
- RNA being a catalyst was reactive and hence unstable. Therefore, DNA has evolved from RNA with chemical modifications that make it more stable.
- DNA being double stranded and having complementary strands resist changes by evolving a process of repair.

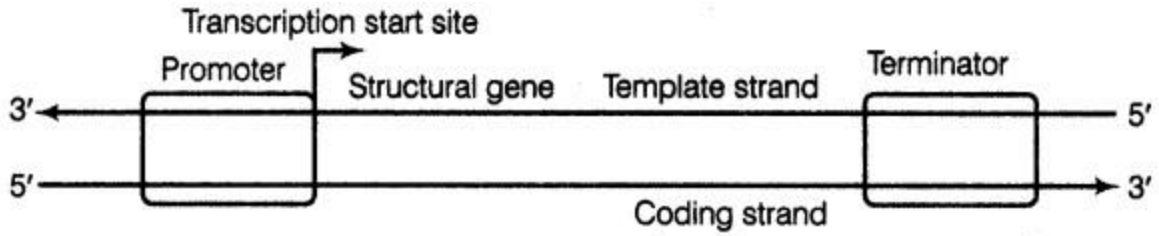
Transcription

- Transcription is the process of copying genetic information from one strand of the DNA into RNA. The principle of complementarity governs the process of transcription, except the adenosine now forms base pair with uracil instead of l thymine.
- In transcription, only a segment of DNA is duplicated and on Iv one of the strands is copied into RNA. Both the strands are not copied.
- A transcription unit in DNA is defined by three regions in the DNA which are as follows:
  (a) A promoter: It is the building size for RNA polymerase for initiation of transcription.
  (b) The structural gene: It codes for enzymes or proteins for structural functions.
  (c) A terminator: It is the region where transcription ends.
- The two strands of DNA have opposite polarity and the DNA-dependent RNA polymerase also catalyse the polymerisation in only one direction that is 5′ -» 3′.
- The strand that has the polarity 3′-» 5′ acts as a template and is referred to as template strand. The other strand which has the polarity (5′ -> 3′) and the sequence same as RNA (T at the place of U) is displaced during transcription. This strand is called a coding strand.
- The promoter and terminator flank the structural gene in a transcription unit.
- The promoter is located towards the 5′ end (upstream) of the structural gene.
- It is the DNA sequence that provides binding sites for RNA polymerase and the presence of a promoter defines the template and coding strands. By switching its position with terminator, the definition of coding and template strands could be reversed.

- The terminator is located towards the 3f-end (downstream) of the coding strand and it usually defines the end of the process of transcription.
- There are additional regulatory sequences that may be present further upstream or downstream to the promoter.

Transcription Unit and the Gene

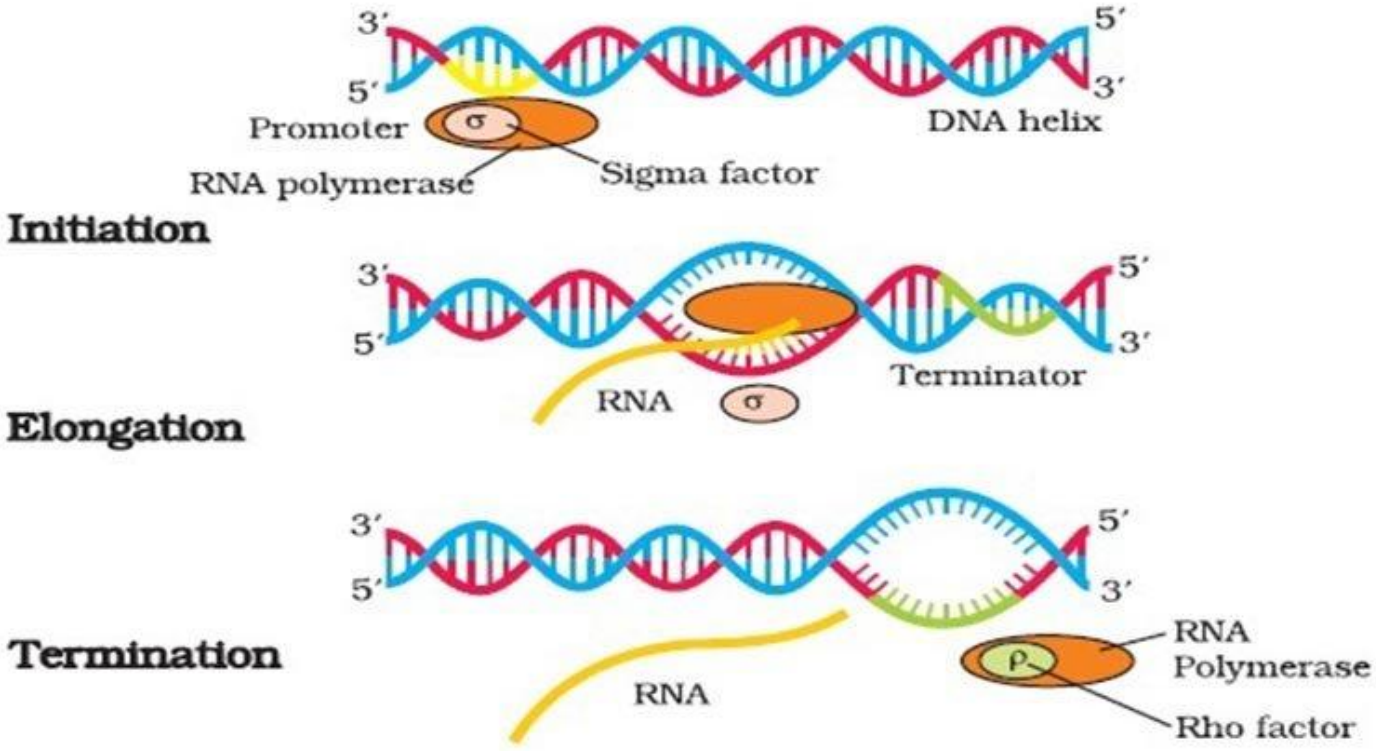
- A gene can be defined as the functional unit of inheritance.
- A cistron is a segment of DNA coding for a polypeptide.
- The structural gene in a transcription unit could be said as monocistronic (mostly in eukaryotes) or polycistronic (mostly in bacteria or prokaryotes).
- The coding sequences or expressed sequences are defined as exons. Exons appear in mature or processed RNA. The exons are interrupted by introns.
- Introns or intervening sequences do not appear in mature or processed RNA.
- Sometimes, the regulatory sequences are loosely defined as regulated even though these sequences do not code for any RNA or protein.



Schematic structure of a transcription unit

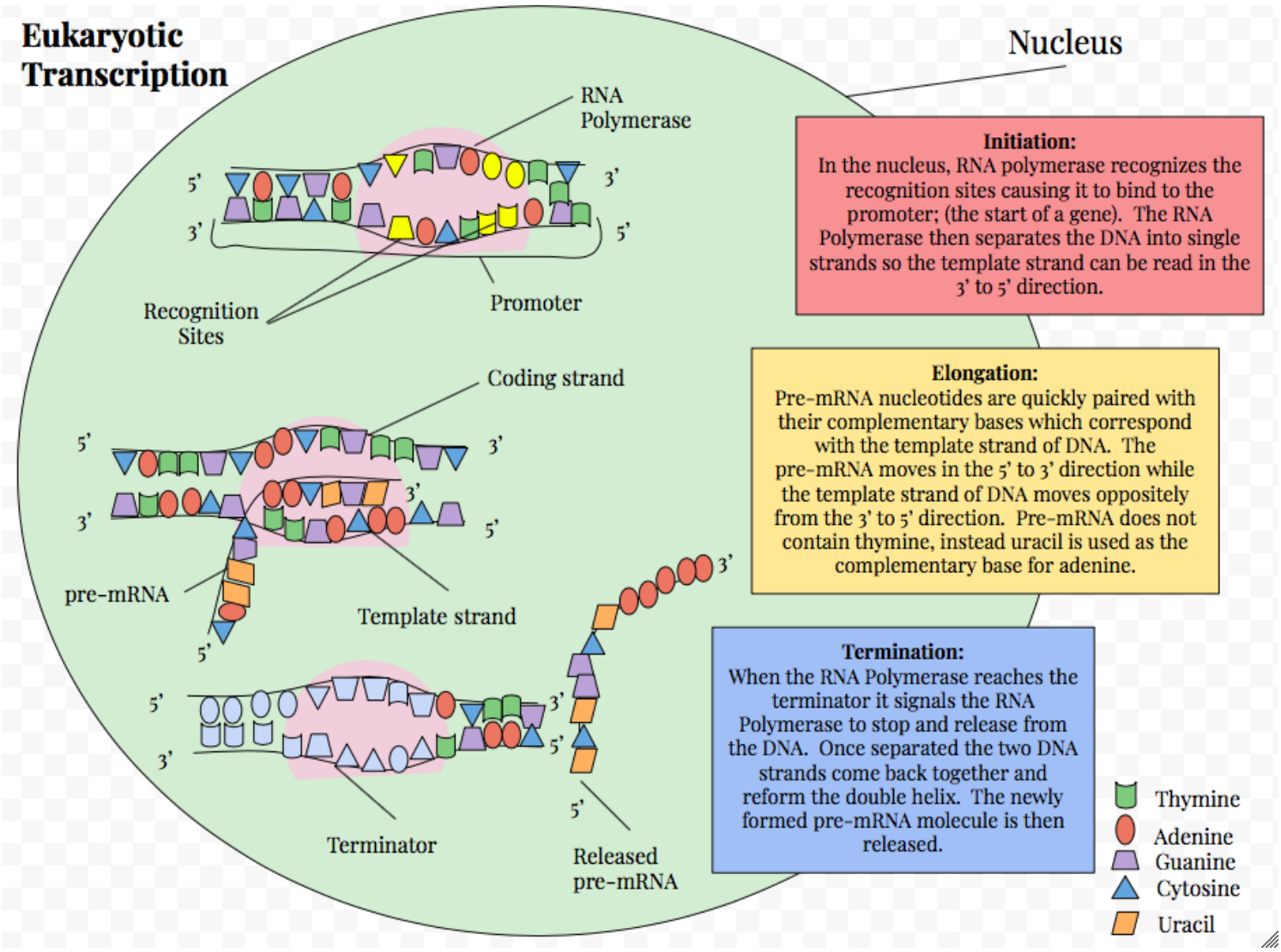
Transcription in Prokaryotes

- The process of synthesis of RNA by copying the template strand of DNA is called transcription.
- During replication the entire genome is copied but in transcription only the selected portion of the genome is copied.
- The enzyme involved in transcription is RNA polymerase. Unlike DNA polymerase it can initiate transcription by itself, it does not require primase. More exactly it is a DNA dependent RNA polymerase.
- The steps of transcription completes in three major steps
    - **Initiation:** RNA polymerase attaches to the DNA molecule and moves along the DNA strand until it recognises a promoter sequence. These are known as the transcription start sites. The DNA double helix then unwinds and all the bases on each of the DNA strands are exposed. This acts as a template for a new mRNA strand.
    - **Elongation:** Ribonucleotides are added to the template strand that enables the growth of mRNA growth.
    - **Termination:** RNA polymerase encounters a terminator sequence and the transcription stops. RNA polymerase then releases the DNA template.



Transcription in Eukaryotes

- The structural genes are monocistronic in eukaryotes.
- The process of transcription is similar to prokaryotes.
- It takes place in the nucleus.
- Coding gene sequences called exons form the part of mRNA and non-coding sequences called introns, are removed during RNA splicing and exons are joined in a defined order.



Difference between DNA & RNA

DNA	RNA
• It occurs inside the nucleus of a cell and some cell organelles but it is present in mitochondria and plant cells.	• It is found in the cytoplasm of the cell but very little is found inside the nucleus.
• It occurs inside the nucleus of a cell and some cell organelles but it is present in mitochondria and plant cells.	• It is found in the cytoplasm of the cell but very little is found inside the nucleus.

• It stores and transfers genetic information to generate new cells and organisms.	• It is used to transfer genetic code from nucleus to the ribosomes to make proteins and carries DNA blueprint's guidelines.
• It has two nucleotide strands consisting of a phosphate group, five carbon sugar (stable deoxyribose 2) and four nitrogen bases.	• It is single stranded consisting of a phosphate group, five carbon sugars (less stable ribose) and four nitrogen bases.
• DNA is self replicating	• RNA is synthesised from DNA when needed.
• The DNA helix geometry is in the form of B and can be damaged by exposure of ultraviolet rays.	• The RNA helix geometry is in the form of A. It is more resistant to damage by ultraviolet rays.
• Nitrogen base pairs are Adenine links to Thymine (A-T) and Cytosine links to Guanine (C-G)	• Here nitrogen base pairs are Adenine links to Uracil (A-U) and Cytosine links to Guanine (C-G).
• DNA is a long polymer chain.	• RNA is a shorter polymer chain.
• DNA produces regular helix i.e. it is spirally twisted.	• RNA produces secondary helix or pseudo helix as its stranded may get folded at places.
• It occurs in the form of chromosomes or chromatin fibres.	• It occurs in ribosomes or forms association with ribosomes.
• Quantity of DNA is fixed for cells.	• The quantity of RNA for a cell is variable.
• It is of two types: intra-nuclear and extranuclear.	• It is of four types: m-RNA, t-RNA and r-RNA.

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