

5 Molecular Basis of Inheritance

Fastrack Revision

- ▶ DNA is the genetic material for most of the organisms, except for few exceptions like viruses where RNA is the genetic material.
- ▶ DNA helps in synthesis of RNA, which in turn helps in protein synthesis, and these proteins control traits of individuals.

▶ Structure of Nucleic Acids

- ▶ Nucleic acids are the biomolecules which play a very important role in the process of inheritance.
- ▶ Two types of nucleic acids exist: **DNA (Deoxyribo Nucleic Acid)** and **RNA (Ribo Nucleic Acid)**.
- ▶ DNA has a double-stranded structure. It is a polynucleotide whose monomer units are deoxyribonucleotide. Length of DNA is determined by number of nucleotides in it.
- ▶ RNA has a single-stranded structure. It is also a polymer whose monomer units are ribonucleotide.
- ▶ A nucleotide has three components:

I. Pentose Sugar

- Monosaccharide with five carbon atoms
- Ribose sugar in RNA
- Deoxyribose sugar in DNA

II. Nitrogenous Base

- Nitrogen containing compound with properties of a base
- Two Types: **Purines and Pyrimidines**
 - ◆ **Purine**
 - ✧ Heterocyclic aromatic organic compound
 - ✧ 9-membered ring
 - ✧ **Examples:** Adenine, Guanine
 - ◆ **Pyrimidine**
 - ✧ Heterocyclic aromatic organic compound
 - ✧ 6-membered ring
 - ✧ **Example:** Cytosine, Uracil, Thymine

III. Phosphate Group

- Inorganic salt of phosphorus
- Forms backbone of polynucleotide chain along with the sugar

- ▶ Formation of a polynucleotide takes place using the following linkages:
 - ▶ Nitrogenous base is linked to the pentose sugar through a **N-glycosidic bond** to form a nucleoside.
 - ▶ A phosphate group is linked to 5'-OH of a nucleoside through **phosphoester bond** to form a nucleotide.
 - ▶ Multiple nucleotides are joined together through 3'-5' **phosphodiester bond** to form a polynucleotide.

▶ Structure of DNA

- ▶ DNA polynucleotide chain has two free ends:
 - **5' end:** Free phosphate moiety at 5'-end of ribose sugar.
 - **3' end:** Free 3'-OH group of ribose sugar.

- ▶ **Watson and Crick** were the first to propose the double-helix structure of DNA, based on X-ray diffraction technique.
- ▶ Very soon, Francis Crick proposed the **central dogma** in molecular biology which states that genetic information flows from DNA → RNA → Protein.
- ▶ The flow of information is in reverse direction i.e. RNA to DNA in some viruses.

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If each strand from a DNA (parental DNA) acts as a template for synthesis of a new strand then the two double-stranded DNA (daughter DNA) produced would be identical to the parental DNA molecule.

▶ DNA Double-Helix Model

- ▶ DNA is composed of two polynucleotide chains.
- ▶ Sugar-phosphate forms the backbone.
- ▶ Nitrogenous bases form the interior, paired through H-bonds.
- ▶ Complementary base pairing is an important feature of DNA structure.
- ▶ The two polynucleotide chains have anti-parallel polarity.
- ▶ Two chains are coiled in a right handed fashion forming a right-handed helix.
- ▶ Uniform distance is maintained between the two strands of helix.

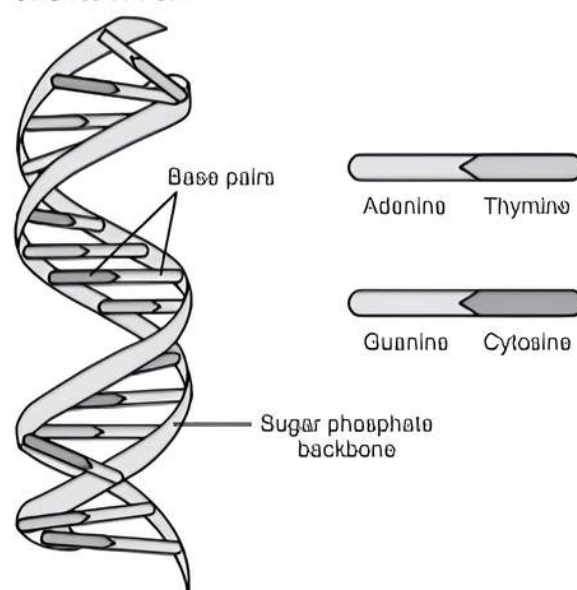


Fig. DNA double helix

▶ Packaging of DNA Helix

- ▶ Length of DNA is found to be far greater than dimension of a typical nucleus.

- Total number of base pairs in a typical mammalian cell is 6.6×10^9 .
- Distance between two base pairs = 0.34 nm.
- Therefore, length of DNA = $0.34 \times 10^{-9} \times 6.6 \times 10^9 = 2.2$ m.
- Size of a nucleus is of the order of 10^{-6} m.
- So, length of DNA is greater than the size of nucleus.
- DNA is packaged very strategically to fit inside the nucleus.
- In prokaryotes, DNA is organised into large loops held by proteins. The region where DNA is present is termed as '**nucleoid**'.
- In **eukaryotes**, there exist positively charged basic proteins called histones.
- DNA wrap around the histone octamer (group of 8 histone proteins) to form a **nucleosome**. Each nucleosome contains 200 base pairs of DNA helix. Nucleosomes in chromatin are seen as 'beads-on-string' under electron microscope.
- Based on different types of DNA packaging, there are two forms of chromatin:

I. Euchromatin

- Less condensed structure with looser DNA packaging.
- Lightly stained when observed under microscope.
- Contains less DNA.
- Transcriptionally active.
- Found in eukaryotes and prokaryotes.

II. Heterochromatin

- Highly condensed structure with tighter DNA packaging.
- Dark stained when observed under microscope.
- Contains more DNA.
- Transcriptionally inactive, as those regions of the genes which need to interact with proteins for transcription is inaccessible.
- Found in eukaryotes.

➤ Search for the Genetic Material

- The study of Genetics started with **Gregor Mendel** who introduced 'factors' for inheritance. **Boveri-Sutton theory** later gave the chromosomal theory of inheritance.
- The concept of inheritance was understood at the level of chromosomes further when Morgan came up with the concept of linkage and recombination at chromosomal level.
- It was taken a step forward in 1926 when experiments were being performed to understand inheritance at a molecular level.
- The search was for the molecule which acts as a genetic material.

➤ Griffith's Experiment (Transforming Principle)

- Griffith experimented with *Streptococcus pneumoniae* bacteria which causes pneumonia. Two strains of this bacterium were used— S-strain and R-strain.

I. S-strain

- Smooth mucous polysaccharide coat
- Resistant to immune system
- Virulent

II. R-strain

- Lacks the coat
- Destroyed by immune system of the host
- Non-virulent

➤ The experiment was performed in multiple steps:

- S-strain (virulent) was injected into mouse. It was found that the mouse died of pneumonia.
- R-strain (non-virulent) was injected into mouse. It was found that the mouse remained alive.
- Heat killed S-strain (S-strain bacteria were killed by heating) was injected into mouse. It was found that the mouse remained alive.
- Heat killed S-strain and live R-strain were injected into mouse. It was found that the mouse died of pneumonia.
- Griffith found that live S-strain bacteria could be recovered from the dead mouse.
- Griffith thus arrived at the following conclusion:
 - Something caused bacteria to change from one type (I) to another type (S).
 - Some 'Transforming principle' transferred from heat-killed S-strain to R-strain and transformed it as virulent.
- However, the biochemical nature of the 'Transforming principle' was still unknown.

➤ Biochemical Nature of Transforming Principle

- Bacteriologists performed a series of experiments to identify the transforming principle which were:
 - Transforming principle precipitated with alcohol. This showed it was not carbohydrate.
 - Transforming principle could not be destroyed with proteases. Thus, it was not protein.
 - Transforming principle could not be destroyed with lipases. This proved it was neither lipid.
 - Transforming principle could not be inactivated with ribonuclease, hence it was not RNA.
 - Transforming principle could be inactivated with deoxyribonuclease.
 - Transforming principle was DNA. Therefore, DNA was the genetic material.

➤ Hershey-Chase Experiment

- Hershey-Chase experiment was performed in 1952 to further confirm that DNA was the genetic material. They experimented with bacteriophages. **Bacteriophages** are the viruses that infect and replicate within bacteria.
- Bacteriophages were grown in two different mediums:
 - Some bacteriophages were grown in radioactive phosphorus medium. It was found that these bacteriophages came up with radioactive DNA but not radioactive protein.
 - Some bacteriophages were grown in radioactive sulfur medium. It was found that these bacteriophages contained radioactive protein but not radioactive DNA because DNA does not contain sulfur.
- Bacteriophages with radioactive DNA were brought in contact with *E.coli* bacteria, and then bacteria got infected.
- They were agitated in a blender to separate phage particles from bacterial cells.
- Centrifugation leaves phage particles as supernatant.
- Bacterial cells were found to be radioactive.
- No radioactivity was detected in the phage particles.
- Bacteriophages with radioactive protein were brought in contact with bacteria.
- Bacteria got infected.

- They were agitated in a blender to separate phage particles from bacterial cells.
- Phage particles were found to be radioactive.
- No radioactivity was detected in the bacterial cells.
- It was, therefore, concluded that it was not the proteins, rather DNA which entered into the bacteria. Therefore, DNA causes the replication of viruses inside the bacteria.
- DNA was, thus, proved to be the genetic material.

► Criteria for Genetic Material

- DNA was found to be the prominent genetic material in most organisms.
- Exceptions were some viruses where RNA was the genetic material.
- The differences between the chemical structures of the DNA and RNA made DNA eligible to be the genetic material, and no other molecules like proteins, carbohydrates etc.
- Important criteria to be fulfilled to be a genetic material are:
 - Capable of replicating itself.
 - Chemically and structurally stable.
 - Provide scope for mutation which can lead to evolution.
 - Capable of expressing itself in the form of 'Mendelian Characters'.
- Most of the other molecules like proteins, carbohydrates, lipids etc. failed to fulfill the above mentioned criteria.
- RNA could also fulfill the criteria but still DNA was a preferred genetic material over RNA because of the following reasons:
 - DNA is structurally more stable than RNA.
 - DNA is chemically more stable than RNA.
 - DNA has double-stranded structure which provides better ability to rectify errors during replication.
 - DNA can't code directly for protein synthesis and thus depends on RNA.
- DNA was thus used for storage of genetic information due to its structural and chemical stability. RNA was used for expression of genetic information as it could directly code for proteins.

► RNA World

- RNA world was a kind of hypothetical world where RNA performed all the activities which are today performed by DNA and proteins. DNA later evolved from RNA with chemical modifications which made it more stable.

► Types of RNA

- There are three major types of RNAs:
 - mRNA (messenger RNA)
 - tRNA (transfer RNA)
 - rRNA (ribosomal RNA)
- All three RNAs are needed to synthesize a protein in a cell.
- The mRNA provides the template, tRNA brings amino acids and reads the genetic code, and rRNAs play structural and catalytic role during translation.

► Structure of tRNA

- The tRNA has a role as an adapter molecule.
- tRNA has an anticodon loop that has bases complementary to the code.

- It has an amino acid acceptor end to which it binds to amino acids.
- The secondary structure of tRNA looks like a clover-leaf.
- In actual structure, the tRNA is a compact molecule which looks like an inverted L.

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tRNA or transfer RNA is also known as soluble (s) RNA, acceptor RNA or adaptor RNA, which consists of AA-binding site lies opposite to the anticodon site.

► Central Dogma of Molecular Biology

- Francis Crick in 1956 proposed the hypothesis of Central Dogma. This explains the flow of genetic information in any biological system.
- Three major classes of biopolymers are involved in this flow: DNA, RNA and proteins.
- With these three categories of biopolymers, a total of nine transfers can be possible which are grouped under the following categories:
 - **General Transfers:** These transfers occur in most of the organisms:
 - DNA → DNA (Replication)
 - DNA → RNA (Transcription)
 - RNA → Proteins (Translation)
 - **Special Transfers:** These occur in viruses where RNA is the genetic material:
 - RNA → RNA
 - RNA → DNA
 - DNA → Proteins
 - **Unknown Transfers:** These transfers might be possible but yet not known:
 - RNA → RNA
 - RNA → DNA
 - DNA → Proteins

► DNA Replication

- **Replication** is the process of reproducing or creating a copy of something. Through replication, DNA creates a copy of itself.
- Various hypotheses were proposed by various scientists regarding the replication model of DNA i.e., how DNA replicates. Some of these were:
 - Semi conservative DNA replication model
 - Conservative DNA replication
 - Dispersive DNA replication

► Meselson-Stahl Experiment

This experiment was performed to prove the semiconservative nature of DNA replication. Matthew Meselson and Franklin Stahl experimented with bacteria *E. coli* in 1958.

► Basis of the Experiment

- If *E. coli* was grown in a medium with N-15 (isotope of nitrogen), the *E. coli* had DNA with N-15 isotope.
- If *E. coli* was grown in a medium with N-14 (more abundant isotope of nitrogen), the *E. coli* had DNA with N-14 isotope.

- It was then observed with centrifugation in a cesium chloride (CsCl) density gradient that DNA with N-15 is heavier than that of N-14.
- Making use of the fact that DNA with N-15 is heavier than DNA with N-14, this experiment was performed.
 - **Step 1.** *E. coli* was grown in a medium with N-15 for several generations.
 - **Step 2.** *E. coli* with only N-15 in their DNA were transferred to a medium with N-14.
- Cells of *E. coli* were allowed to divide. Sample was taken and DNA was extracted periodically as cell division continued to check what type of DNA is being formed now. One replication in *E. coli* takes around 20 minutes. So, generation I was formed in 20 minutes.
- Samples were taken after 20 minutes, then again after 40 minutes, densities of DNA from the sample were measured to reach to results and conclusion.
- **Results**
 - **Generation I:** DNA was found to have intermediate density after first replication.
 - **Generation II:** Equal amounts of DNA with two different densities were found.
- **Conclusion**
 - Presence of a hybrid/Intermediate density excluded conservative hypothesis.
 - Presence of N-14 DNA in generation II excluded dispersive hypothesis.
 - Semiconservative hypothesis could explain the entire experimental result. Separation of strands concept could explain the outcomes of generation I and II.
 - It was proved that DNA replication is semiconservative in nature.
- **Machinery and Enzymes for Replication**
 - Enzymes play an important role acting as catalysts during the process of DNA replication. Some of the important enzymes are: DNA polymerase, helicase, primase, DNA ligase.
 - Deoxyribonucleoside triphosphates act as substrates and provide energy for polymerisation reaction.
- **DNA Polymerase**
 - DNA polymerase creates DNA from nucleotides. It reads the existing DNA strands to create two new strands that match the existing ones. This enzyme is needed everytime a cell divides so that one copy of DNA can be passed to each daughter cell.
 - DNA polymerase is a highly efficient enzyme, as it can replicate a large number of base pairs in a very short time. Rate of replication or rate of polymerisation is approx 2000 bp per second. A total of 4.6×10^6 base pairs are replicated within 18 minutes. DNA polymerase also catalyse with high degree of accuracy. Any mistake made once in every 1 billion base pairs gets copied. DNA polymerase proof reads to check for errors. However, these errors if remain can cause mutations.
- **Helicase:** Enzyme helicase unwinds DNA from tightly double-stranded structure. Only after the strands are separated, DNA polymerase can do its job of creating the new strands. This enzyme separates the strands by breaking the hydrogen bonds between the bases of the two strands.
- **Primase:** This enzyme creates a short fragment of RNA (primer) paired with the template DNA strand. This enzyme initiates the process of creation of new strands. DNA polymerase cannot initiate the process on its own. Therefore, primase initiates the same.
- **Process of DNA Replication**
 - Replication cannot be initiated in any random part of DNA. Region in a DNA where replication initiates is termed as '**Origin of Replication**'.
 - **Step 1:** Enzyme helicase breaks hydrogen bonds, thus separating the two strands of DNA. **Replication fork** structure is formed.
 - **Step 2:**
 - **Continuous synthesis** takes place in the leading strand. In this strand, DNA is synthesized in the same direction as the growing replication fork.
 - **Discontinuous synthesis** takes place in the lagging strand. Synthesis in this strand is more complicated than the leading strand. DNA polymerase can add new free nucleotides to the 3' end of the new strand. In the lagging strand, no free 3'-OH end is available. Therefore, DNA polymerase is unable to initiate the process. Enzyme primase initiates the process by creating a small RNA fragment called **primer**. DNA polymerase then extends the primed segments adding free nucleotides. RNA primers are replaced with DNA. Thus, we have DNA fragments in which the direction of synthesis in lagging strand is opposite to the direction of growing replication fork. DNA Ligase now joins the DNA fragments and forms a complete DNA.
 - These DNA fragments are termed as 'Okazaki fragments' after the name of the scientist who first described the process of discontinuous synthesis on lagging strand.
 - The entire process of DNA replication occurs during S-phase of cell cycle in eukaryotes. Research is still going on for more detail on the replication process.
- **Transcription**
 - The process of copying genetic information from one strand of the DNA into RNA is termed as **transcription**.
 - In transcription, only a segment of DNA and only one of the strands is copied into RNA because of the following reasons:
 - If both strands act a template, they would code for RNA molecule with different sequences and the sequences of amino acids in the coded protein would be different.
 - If two RNA molecules are produced simultaneously, they would be complementary to each other and would form a double-stranded RNA which would prevent translation.
- **Transcription Unit**
 - A transcription unit in DNA consists of the following regions:
 - A Promoter
 - The Structural gene
 - A Terminator
 - The two strands of the DNA in the structural gene of a transcription unit is termed as template strand and coding strand.

- The strand that has the polarity 3'→5' acts as a template and is referred as **template strand**.
- The other strand which has the polarity 5'→3' is referred as **coding strand**.

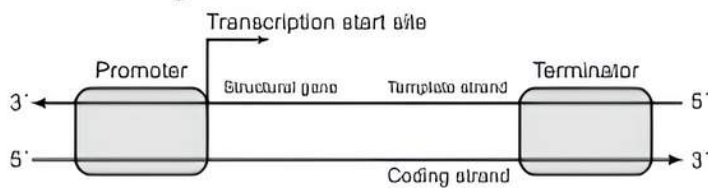


Fig. Structure of a transcription unit

- The **promoter** and **terminator** flank the structural gene in a transcription unit.
- The promoter is located towards 5'-end (upstream) of the structural gene which provides binding site for RNA polymerase.
- The terminator is located towards 3'-end (downstream) of the coding strand which defines the end of the process of transcription.

➤ Process of Transcription

- In prokaryotes, transcription takes place in three steps:

I. Initiation

- RNA polymerase binds to promoter and initiates transcription.
- Initiation factor or sigma (σ) recognises the promoter of the DNA.

II. Elongation

- RNA polymerase facilitates opening of the helix and continues elongation.
- RNA polymerase uses nucleoside triphosphates as substrate and polymerises in a template dependent fashion following the rule of complementarity.
- Only a short stretch of RNA remains bound to the enzyme.

III. Termination

- Once the polymerase reaches the terminator region, RNA polymerase binds with the **termination-factor** (ρ) to terminate transcription.
- The nascent RNA falls off with the RNA polymerase which results in termination of transcription.
- The transcription and translation can be coupled in bacteria as the mRNA does not require any processing to become active, and also transcription and translation take place in the same compartment.

- In eukaryotes, there are two additional complexities:

1. The first complexity is that there are at least three RNA polymerases in the nucleus.

- The RNA polymerase I transcribes **rRNAs** (28S, 18S, and 5.8S).
- The RNA polymerase III is responsible for transcription of **tRNA**, **5srRNA** and **snRNAs** (small nuclear RNAs).
- The RNA polymerase II transcribes precursor of mRNA, the **heterogeneous nuclear RNA (hnRNA)**.

2. The second complexity is that the primary transcripts contain both the exons and the introns and are non-functional.

- Primary transcripts are subjected to a process called **splicing** where the introns are removed and exons are joined in a defined order.

- **hnRNA** undergo two additional processing called as **capping** and **tailing**.

- In capping, an unusual nucleotide (methyl guanosine triphosphate) is added to the 5'-end of **hnRNA**.

- In tailing, adenylate residues (200-300) are added at 3'-end in a template independent manner and the fully processed **hnRNA** is called **mRNA**.

- **mRNA** is transported out of the nucleus for translation.

➤ Significance of Complexities

- The split-gene arrangements represent probably an ancient feature of the genome.
- The presence of introns is reminiscent of antiquity, and the process of splicing represents the dominance of **RNA world**.

➤ Genetic Code

- The sequence of nucleotides on DNA which determines the sequence of amino acids in a polypeptide chain is termed as **genetic code**.

- The process of translation requires transfer of genetic information from a polymer of nucleotides to a polymer of amino acids but there is no complementarity between nucleotides and amino acids. This led to the proposition of a genetic code that could direct the sequence of amino acids during synthesis of proteins.

- The salient features of genetic code are as follows:

- The codon is triplet, 61 codons code for amino acids and three codons do not code for any amino acids, hence they function as **stop codons**.
- One codon codes for only one amino acid thus it is **unambiguous** and **specific**.
- Some amino acids are coded by more than one codon, hence the code is **degenerate**.
- The codon is read in mRNA in a contiguous fashion and there are no punctuations.
- The code is nearly **universal**. For example, from bacteria to human UUU would code for Phenylalanine (phe).
- AUG has dual functions, it codes for Methionine (met), and it also acts as **initiator** codon.

➤ Mutation and Genetic Code

The relationships between genes and DNA are best understood by mutation studies. The two kinds of mutation are:

- **Point Mutation:** It is the insertion or deletion of a single gene in the structural gene.

Example: Point mutation is a change of single base pair in the gene for beta globin chain that results in the change of amino acid residue glutamate to valine, which results into a diseased condition called as **sickle-cell anaemia**.

- **Frameshift mutation** is the insertion and deletion of three or its multiple bases which insert or delete one or multiple codon, hence one or multiple amino acids and reading frame remains unaltered from that point onwards.

Example: Cystic fibrosis.

➤ Translation

- Translation refers to the process of polymerisation of amino acids to form a polypeptide.

- ▶ The order and sequence of amino acids are defined by the sequence of bases in the *mRNA* and the amino acids are joined by a bond which is known as a **peptide bond**.
- ▶ Formation of a peptide bond requires energy and thus amino acids are activated in the presence of ATP and linked to their cognate *tRNA* by the process of **charging of *tRNA* or aminoacylation of *tRNA***.
- ▶ If charged *tRNAs* are brought close enough, a peptide bond forms which is enhanced by the presence of a catalyst such as ribosome.
- ▶ Ribosome in its inactive state exists as two subunits—a large subunit and a small subunit.
- ▶ There are two sites in the large subunit for subsequent amino acids to bind to and thus become close enough to each other for the formation of a peptide bond.
- ▶ A translational unit in *mRNA* is the sequence of RNA that is flanked by the start codon (AUG) and the stop codon and codes for a polypeptide.
- ▶ An *mRNA* also has some additional sequences that are not translated and are referred as **Untranslated Regions (UTR)**.
- ▶ The UTRs are present at both 5'-end (before start codon) and at 3'-end (after stop codon) which are required for efficient translation process.
- ▶ After activation of amino acids, translation starts with its three steps:
 - I. Initiation**
 - For initiation, the ribosome binds to the *mRNA* at the start codon (AUG) that is recognised only by the Initiator *tRNA*.
 - II. Elongation**
 - The ribosome proceeds to the elongation phase of protein synthesis.
 - During elongation stage, complexes composed of an amino acid linked to *tRNA*, sequentially bind to the appropriate codon in *mRNA* by forming complementary base pairs with the *tRNA* anticodon.
 - The ribosome moves from codon to codon along the *mRNA*.
 - Amino acids are added one by one, translated into polypeptide sequences dictated by DNA and represented by *mRNA*.
 - III. Termination**
 - At the end, a **release factor** binds to the stop codon, terminating translation and releasing the complete polypeptide from the ribosome.
- ▶ **Regulation of Gene Expression**
 - ▶ Gene expression results in the formation of a polypeptide and it can be regulated at several levels such as:
 - transcriptional level (formation of primary transcript),
 - processing level (regulation of splicing),
 - transport of *mRNA* from nucleus to the cytoplasm,
 - translational level.
 - ▶ It is the metabolic, physiological or environmental conditions that regulate the expression of genes.
 - ▶ In prokaryotes, control of the rate of transcriptional initiation is the predominant site for control of gene expression.
- ▶ In a transcription unit, the activity of RNA polymerase at a given promoter is in turn regulated by interaction with accessory proteins which can act both positively (activators) and negatively (repressors).
- ▶ Regulation of gene expression can be studied with the help of ***Lac operon***.
- ▶ ***Lac Operon***
 - ▶ *Lac* refers to lactose in *lac operon*.
 - ▶ The *lac operon* consists of one regulatory gene *i*-gene which codes for the repressor of the *lac operon* and three structural genes (*z*, *y* and *a*).
 - The *z*-gene codes for beta-galactosidase (β -gal), which hydrolyses disaccharide, lactose into galactose and glucose.
 - The *y*-gene codes for permease, which increases permeability of the cell to β -galactosides.
 - The *a*-gene encodes a transacetylase.
 - ▶ Lactose is termed as **inducer** as lactose is the substrate for the enzyme beta-galactosidase and it regulates switching on and off of the operon.
- ▶ **In the absence of inducer**
 - ▶ The repressor of the operon is synthesised (all-the-time – constitutively) from the *i*-gene.
 - ▶ The repressor protein binds to the operator region of the operon and prevents RNA polymerase from transcribing the operon.
- ▶ **In the presence of inducer**
 - ▶ The repressor is inactivated by interaction with the inducer which allows RNA polymerase access to the promoter and transcription proceeds.
 - ▶ Regulation of *Lac operon* by repressor is referred to as **negative regulation**.
- ▶ **Human Genome Project**
 - ▶ The scientific project which deals with the study of base sequences of DNA molecules of complete set of chromosomes is called **Human Genome Project**.
 - ▶ HGP was closely associated with the rapid development of a new area in biology called as **bioinformatics** and was called a mega project.
- ▶ **Goals of Human Genome Project**
 - ▶ Identify all the approximately 20,000-25,000 genes in human DNA.
 - ▶ Determine the sequences of the three billion chemical base pairs that make up human DNA.
 - ▶ Store this information in databases.
 - ▶ Improve tools for data analysis.
 - ▶ Transfer related technologies to other sectors, such as industries.
 - ▶ Address the Ethical, Legal and Social Issues (ELSI) that may arise from the project.
- ▶ **Methodologies of HGP**
 - ▶ Two major approaches involved are:
 - Identifying all the genes that are expressed as RNA also referred to as **Expressed Sequence Tags (ESTs)**.
 - Simply sequencing the whole set of genome that contained all the coding and non-coding sequence, and later assigning different regions in the sequence with functions called as **sequence annotation**.
 - ▶ The total DNA from a cell is isolated and converted into random fragments of relatively smaller sizes and cloned in suitable host using specialised vectors.

- The cloning resulted into amplification of each piece of DNA fragment.
- The commonly used vectors are **BACs** (Bacterial Artificial Chromosomes), and **YACs** (Yeast Artificial Chromosomes).
- The fragments were sequenced using automated DNA sequencers.
- Specialised computer based programmes were developed for the alignment of the sequences.
- The sequences were subsequently annotated and were assigned to each chromosome.
- **Salient Features of Human Genome**
 - The human genome contains 3164.7 million nucleotide bases.
 - The average gene consists of 3000 bases with the largest known human gene being **dystrophin** at 2.4 million bases.
 - The total number of genes is estimated at 30,000.
 - 9% nucleotide bases are exactly the same in all people.
 - The functions are unknown for over 50% of discovered genes.
 - Less than 2% of the genome codes for proteins.
 - Repeated sequences make up very large portion of the human genome.
 - Repetitive sequences are stretches of DNA sequences that are repeated many times.
 - Chromosome 1 has most genes (2968), and the Y has the fewest (231).
 - Scientists have identified about 1.4 million locations where single base DNA differences (**SNPs – Single Nucleotide Polymorphism**) occur in humans.
- **Applications of HGP**
 - All the genes in a genome can be studied together.
 - HGP helps to understand how tens of thousands of genes and proteins work together in interconnected networks.
 - HGP helps to diagnose and treat genetic diseases.
- **DNA Fingerprinting**
 - The process of comparison of DNA from different sources to establish the identity is called **DNA fingerprinting**.
- DNA fingerprinting involves identifying differences in some specific regions in DNA sequence called as **repetitive DNA**.
- Repetitive DNA are separated from bulk genomic DNA as different peaks during density gradient centrifugation.
- The bulk DNA forms a major peak and the other small peaks are referred to as **satellite DNA**.
- Satellite DNA is of two types based on base composition, length of segment, and number of repetitive units:
 - Micro-satellites
 - Mini-satellites
- Satellite DNA sequences normally do not code for any proteins, but they form a large portion of human genome.
- Satellite DNA sequences show high degree of polymorphism and form the basis of DNA fingerprinting.
- An inheritable mutation occurring in a population at high frequency is referred to as **DNA polymorphism**.
- Repeated nucleotide sequences in the non-coding DNA of an individual is called **Variable Number of Tandem Repeats (VNTRs)**.
- VNTR involved Southern blot hybridisation using radiolabelled VNTR as a probe.
- The size of VNTR varies in size from 0.1 to 20 kb.
- DNA fingerprinting technique includes the following steps:
 - Isolation of DNA.
 - Digestion of DNA by restriction endonucleases.
 - Separation of DNA fragments by electrophoresis.
 - Transferring (blotting) of separated DNA fragments to synthetic membranes, such as nitrocellulose or nylon.
 - Hybridisation using labeled VNTR probe.
 - Detection of hybridised DNA fragments by autoradiography.
- **Applications**
 - In identification of criminals.
 - In determining population and genetic diversities.
 - In solving parental disputes.



Practice Exercise



Multiple Choice Questions

- Q 1. In some viruses, DNA is synthesised by using RNA as template. Such a DNA is called:
- A-DNA
 - B-DNA
 - cDNA
 - rDNA
- Q 2. If a double stranded DNA has 20% of cytosine, what will be the percentage of adenine in it?
- 20%
 - 40%
 - 30%
 - 60%
- Q 3. A short piece of DNA, having 20 base pairs, was analysed to find the number of nucleotide bases in each of the polynucleotide strands. Some of the results are shown in the table.

	Number of nucleotide bases			
	Adenine	Cytosine	Guanine	Thymine
Strand 1	4	4		
Strand 2		5		

How many nucleotides containing Adenine were present in strand 2? (CBSE SQP 2023-24)

- 2
- 4
- 5
- 7

- Q 4. RNA is the genetic material in:
- prokaryotes
 - eukaryotes
 - Tobacco Mosaic Virus (TMV)
 - E. coli*

Q 5. Which one among the following was the first genetic material?

- a. DNA
- b. RNA
- c. Protein
- d. Nuclein

Q 6. Polycistronic messenger RNA (mRNA) usually occurs in:

- a. bacteria
- b. prokaryotes
- c. eukaryotes
- d. Both a. and b.

Q 7. Methyl guanosine triphosphate is added to the 5' end of hnRNA in a process of:

- a. splicing
- b. capping
- c. tailing
- d. None of these

Q 8. A codon is a 'triplet of bases' was suggested by:

(CBSE 2021, Term-1)

- a. Marshall Nirenberg
- b. Har Gobind Khorana
- c. George Gamow
- d. Francis Crick

Q 9. The correct feature of double-helical structure of DNA as given by Watson and Crick is:

(CBSE 2021, Term-1)

- a. Right handed helix, pitch is 3.4 nm
- b. Left handed helix, pitch is 3.8 nm
- c. Right handed helix, pitch is 3.8 nm
- d. Left handed helix pitch is 3.4 nm

Q 10. Charging of tRNA during translation is necessary for:

(CBSE 2021, Term-1)

- a. Binding of anticodons of tRNA to the respective codons of mRNA.
- b. Peptide bond formation between two amino acids.
- c. Movement of ribosomes from codon to codon.
- d. Binding of ribosomes to the mRNA.

Q 11. Total number of nucleotide sequences of DNA that codes for a hormone is 1530. The proportion of different bases in the sequence is found to be Adenine = 34%, Guanine = 19%, Cytosine = 23%, Thymine = 19%.

Applying Chargaff's rule, what conclusion can be drawn?

(CBSE SQP 2021, Term-1)

- a. It is a double-stranded circular DNA.
- b. It is a single-stranded DNA.
- c. It is a double-stranded linear DNA.
- d. It is a single-stranded DNA coiled on histones.

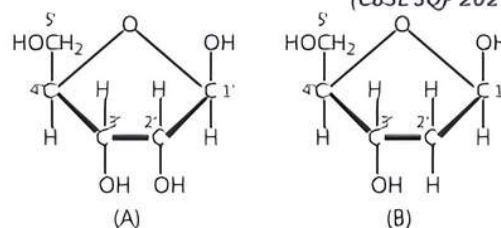
Q 12. A stretch of an euchromatin has 200 nucleosomes. How many bp will there be in the stretch and what would be the length of the typical euchromatin?

(CBSE SQP 2021, Term-1)

- a. 20,000 bp and $13,000 \times 10^{-9}$ m
- b. 10,000 bp and $10,000 \times 10^{-9}$ m
- c. 40,000 bp and $13,600 \times 10^{-9}$ m
- d. 40,000 bp and $13,900 \times 10^{-9}$ m

Q 13. Observe structures A and B given below. Which of the following statements are correct?

(CBSE SQP 2021, Term-1)



- a. A is having 2'-OH group which makes it less reactive and structurally stable, whereas B is having 2'-H group which makes it more reactive and unstable.
- b. A is having 2'-OH group which makes it more reactive and structurally unstable, whereas B is having 2'-H group which makes it less reactive and structurally stable.
- c. A and B both have -OH groups which make it more reactive and structurally stable.
- d. A and B both are having -OH groups which make it less reactive and structurally stable.

Q 14. First experimental proof for semiconservative DNA replication was shown in:

- a. *Streptococcus pneumoniae*
- b. *Escherichia coli*
- c. *Neurospora crassa*
- d. *Rattus rattus*

Q 15. Which of the following phenomena was experimentally proved by Meselson and Stahl?

- a. Transformation
- b. Transduction
- c. Semiconservative DNA replication
- d. Central dogma

Q 16. If Meselson and Stahl's experiment is continued for sixth generations in bacteria, the ratio of Heavy strands $^{15}\text{N}/^{15}\text{N}$: Hybrid $^{15}\text{N}/^{14}\text{N}$: light $^{14}\text{N}/^{14}\text{N}$ containing DNA in the sixth generation would be:

(CBSE SQP 2021, Term-1)

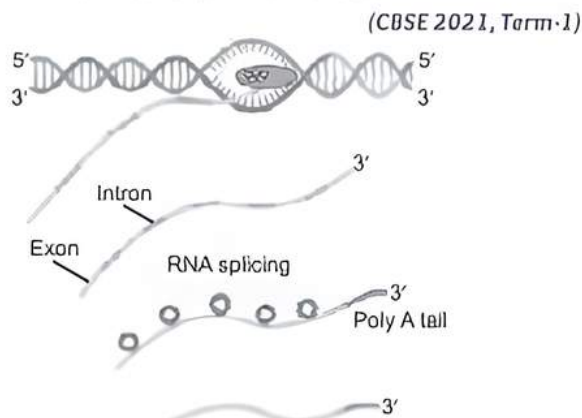
- a. 1 : 1 : 1
- b. 0 : 1 : 7
- c. 0 : 1 : 15
- d. 0 : 1 : 31

Q 17. If *E. coli* were allowed to grow in the culture medium for 80 minutes by Matthew Meselson and Franklin Stahl in their experiments, the proportion of light and hybrid density DNA molecule would have been:

(CBSE 2021, Term-1)

- a. 87.5% of light density DNA and 12.5% of hybrid density DNA.
- b. 75.0% of light density DNA and 25% of hybrid density DNA.
- c. 50% of light density DNA and 50% of hybrid density DNA.
- d. 12.5% of light density DNA and 87.5% of hybrid density DNA.

- Q 18. A diagrammatic illustration of the process of transcription by RNA polymerase-II in eukaryote is given below. Choose the most appropriate statement with respect to the fate of the precursor of mRNA transcribed that will be:



- a. Translation will take place once the precursor of mRNA leaves the nucleus.
 b. Translation on mRNA will not take place once the precursor of mRNA leaves the nucleus.
 c. Translation will take place in the nucleus.
 d. The precursor of mRNA has to be processed further in next step before being translated.
- Q 19. Transcription unit is represented in the diagram given below: (CBSE SQP 2021, Term-1)



Identify site (i), factor (ii) and enzyme (iii) responsible for carrying out the process.

- a. (i) Promoter site, (ii) Rho factor, (iii) RNA polymerase
 b. (i) Terminator site, (ii) Sigma factor, (iii) RNA polymerase
 c. (i) Promoter site, (ii) Sigma factor, (iii) RNA polymerase
 d. (i) Promoter site, (ii) Sigma factor, (iii) DNA polymerase
- Q 20. What is the smallest part of a DNA molecule that can be changed by a point mutation?

- (CBSE SQP 2023-24)
- a. Oligonucleotide b. Codon
 c. Gene d. Nucleotide

- Q 21. Variations caused due to mutations are:

- (CBSE SQP 2023-24)
- a. random and directionless
 b. random and directional
 c. random and small
 d. random, small and directional

- Q 22. The promoter site and the terminator site for transcription are located at: (CBSE SQP 2021, Term-1)

- a. 3' (downstream) end and 5' (upstream) end, respectively of the transcription unit.
 b. 5' (upstream) end and 3' (downstream) end, respectively of the transcription unit.

- c. the 5' (upstream) end of the transcription unit.
 d. the 3' (downstream) end of the transcription unit.

- Q 23. Which of the following is correct about mature RNA in eukaryotes? (CBSE SQP 2021, Term-1)

- a. Exons and introns do not appear in the mature RNA.
 b. Exons appear, but Introns do not appear in the mature RNA.
 c. Introns appear, but exons do not appear in the mature RNA.
 d. Both exons and Introns appear in the mature RNA.

- Q 24. A region of coding strand of DNA has the following nucleotide sequence. (CBSE 2021, Term-1)

5' -TACGCCG-3'

The sequence of bases on mRNA transcribed by this would be :

- a. 5'-UACGCCG-3' b. 3'-UACGCCG-3'
 c. 5'-ATCGGGC-3' d. 3'-ATCGGGC-3'

- Q 25. A DNA molecule is 160 base pairs long. If it has 20% adenine, how many cytosine bases are present in this DNA molecule? (CBSE 2021, Term-1)

- a. 48 b. 64 c. 96 d. 192

- Q 26. A template strand in a bacterial DNA has the given base sequence : (CBSE 2021, Term-1)

5'-AGGTTTAACG-3'

What would be the RNA sequence transcribed from this template strand?

- a. 5'-CGUUAACCU-3' b. 5'-AGGUUUUUCG-3'
 c. 5'-TCCAAATTGC-3' d. 5'-AGGTTTAACG-3'

- Q 27. Given below is a sequence of bases in mRNA of a bacterial cell. Identify the amino acid that would be incorporated at codon position 3 and codon position 5 during the process of its translation:

3' AUCAGGUUUGUGAUGGUACGA 5' (CBSE 2023)

- a. Phenylalanine, Methionine
 b. Cysteine, Glycine
 c. Alanine, Proline
 d. Serine, Valine

- Q 28. In *E. coli*, the *lac* operon gets switched on when:

(CBSE SQP 2021, Term-1)

- a. lactose is present and it binds to the repressor.
 b. repressor binds to operator.
 c. RNA polymerase binds to the operator.
 d. lactose is present and it binds to RNA polymerase.

- Q 29. Which of the following cannot act as inducer?

- a. Glucose b. Lactose
 c. Galactose d. Both a. and c.

- Q 30. In the presence of allolactose, the *lac* repressor in the operon of *E. coli*. (CBSE 2021, Term-1)

- a. binds to the operator
 b. cannot bind to the operator
 c. binds to the promoter
 d. binds to the regulator

Q 31. Taylor and colleagues performed experiments on using radioactive to prove that the DNA in chromosomes replicate semiconservatively.

(CBSE 2021, Term-1)

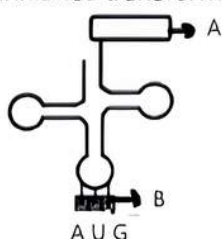
- a. *Vicia faba*, Uridine b. *E. coli*, Uridine
c. *Vicia faba*, Thymidine d. *E. coli*, Thymidine

Q 32. Oswald Avery, Colin MacLeod and Maclyn McCarty used enzymes to purify biochemicals such as proteins, DNA and RNA from the heat-killed S cells to see which ones could transform live R cells into S cells in Griffith's experiment. They observed that:

(CBSE SQP 2021, Term-1)

- a. Proteases and RNases affected transformation
b. DNase inhibited transformation
c. Proteases and Lipases affected transformation
d. RNases inhibited transformation

Q 33.



AUG on the mRNA will result in the activation of which of the following RNA having correct combination of amino acids: (CBSE SQP 2021, Term-1)

	Site A	Site B
a.	UAC	Methionine
b.	Methionine	UAC
c.	Methionine	AUG
d.	AUG	Methionine

Q 34. Short stretches of DNA used to identify complementary sequence in a sample are called:

(CBSE SQP 2021, Term-1)

- a. probes b. markers c. VNTRs d. primers

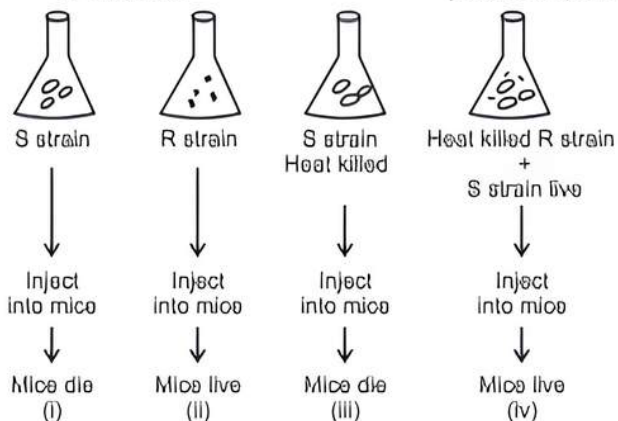
Q 35. The reactive hydroxyl group in the nucleotide of RNA is:

(CBSE 2021, Term-1)

- a. 5' OH b. 4' OH c. 3' OH d. 2' OH

Q 36. Study the given diagrammatic representation of Griffith's experiment to demonstrate transformation in bacteria.

(CBSE 2021, Term-1)



Select the option which is incorrectly representing the experiment :

- a. (i) and (iii) b. (ii) and (iii)
c. (iii) and (iv) d. (ii) and (iv)

Q 37. Which cellular process is shown below?

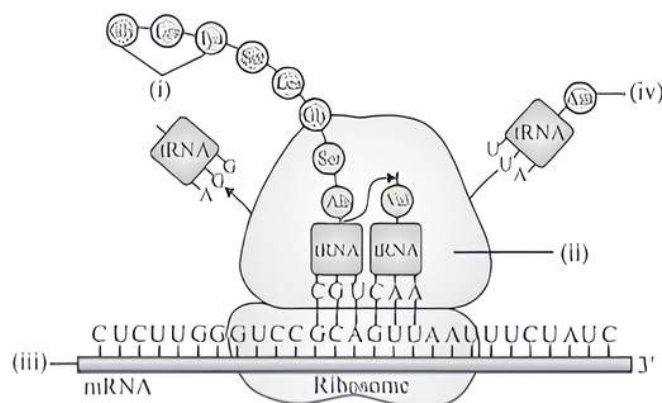


(CBSE SQP 2021, Term-1)

- a. DNA replication
b. Translation – Initiation
c. Translation – Elongation
d. Translation – Termination

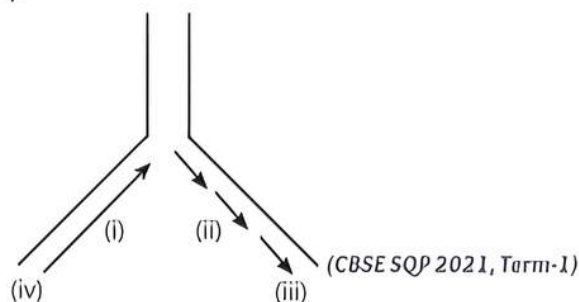
Q 38. In the given figure of translation machinery of eukaryotes, select the correct labellings for (i), (ii), (iii) and (iv).

(CBSE 2021, Term-1)



- a. (i) Codon, (ii) Anticodon, (iii) tRNA, (iv) 3' end of mRNA
b. (i) Anticodon, (ii) Codon, (iii) 3' end of mRNA, (iv) 5' end of mRNA
c. (i) Polypeptide chain, (ii) large subunit of ribosome, (iii) 5' end of mRNA, (iv) tRNA
d. (i) Ribozyme, (ii) Polypeptide chain, (iii) tRNA, (iv) 5' end of tRNA

Q 39. Origin of replication of DNA in *E. coli* is shown below. Identify the labelled parts (i), (ii), (iii) and (iv).

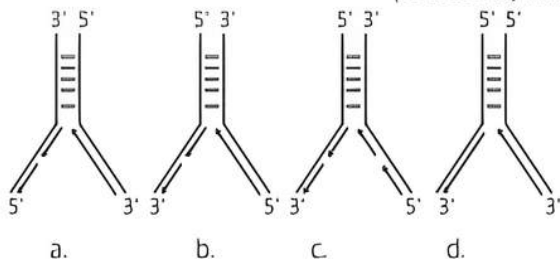


- a. (i) discontinuous synthesis, (ii) continuous synthesis (iii) 3' end (iv) 5' end

- b. (i) continuous synthesis, (ii) discontinuous synthesis (iii) 5' end (iv) 3' end
 c. (i) discontinuous synthesis, (ii) continuous synthesis (iii) 5' end (iv) 3' end
 d. (i) continuous synthesis, (ii) discontinuous synthesis (iii) 3' end (iv) 5' end

Q 40. Which one of the following diagram correctly represents DNA replication in eukaryotes?

(CBSE 2021, Term-1)



Q 41. Identify the correct pair of codon with its corresponding pair of amino acid:

(CBSE 2021, Term-1)

- a. UAA : Leucine
 b. UGA : Serine
 c. AUG : Histidine
 d. UUU : Phenylalanine

Q 42. Two important RNA processing events lead to specialised end sequences in most human mRNAs:(i)..... at the 5' end, and (ii) at the 3' end. At the 5' end the most distinctive specialized end nucleotide, (iii) is added and a sequence of about 200(iv) is added to the 3' end.

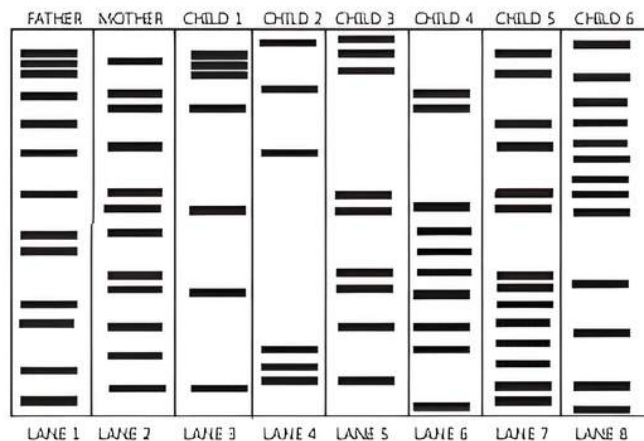
(SQP 2021, Term-1)

- a. (i) Initiator codon (ii) Promoter (iii) Terminator codon (iv) Release factors.
 b. (i). Promoter (ii) Elongation (iii) Regulation (iv) Termination.
 c. (i) Capping (ii) Polyadenylation (iii) mG_{ppp} (iv) Poly(A).
 d. (i) Repressor (ii) Co-repressor (iii) Operon (iv) Release factors.

Q 43. What are minisatellites? (CBSE SQP 2021, Term-1)

- a. 10-40 bp sized small sequences within the genes.
 b. Short coding repetitive region on the eukaryotic genome.
 c. Short non-coding repetitive sequence forming large portion of eukaryotic genome.
 d. Regions of coding strands of the DNA.

Q 44. There was a mix-up at the hospital after a fire accident in the nursery division. Which of these children belong to the parents?



LANE 1 LANE 2 LANE 3 LANE 4 LANE 5 LANE 6 LANE 7 LANE 8

(CBSE SQP 2021, Term-1)

- a. All of the children
 b. Children 2, 3 and 6
 c. Children 1 and 3
 d. Children 2 and 4



Assertion & Reason Type Questions

Directions (Q. Nos. 45-50): Each of the following questions consists of two statements, one is Assertion (A) and the other is Reason (R). Select the correct answer to these questions from the codes a, b, c and d as given below.

- a. Both Assertion and Reason are true and Reason is the correct explanation of Assertion.
 b. Both Assertion and Reason are true but Reason is not the correct explanation of Assertion.
 c. Assertion is true but Reason is false.
 d. Assertion is false but Reason is true.

Q 45. Assertion (A): Sequences of bases in one polynucleotide chain of DNA can determine the sequence of bases in the other chain.

Reason (R): In a DNA, amount of adenine equals that of thymine and amount of guanine equals that of cytosine, i.e., $A = T$ and $C = G$.

Q 46. Assertion (A): tRNA acts as an adapter molecule.

Reason (R): tRNA recognizes codon sequence of mRNA during translation.

Q 47. Assertion (A): Same tRNA can recognise more than one codons differing only at the third position.

Reason (R): The specificity of a codon is particularly determined by the first two bases.

Q 48. Assertion (A): Ribosomal RNA is synthesised in the nucleus of the cell.

Reason (R): It is translated with the enzyme RNA polymerase-III. (CBSE SQP 2023-24)

Q 49. Assertion (A): UAA, UAG and UGA terminate protein synthesis.

Reason (R): They are not recognised by tRNA.

Q 50. Assertion (A): Ribosomes attached to endoplasmic reticulum release proteins into lumen of ER.

Reason (R): Such proteins are used for formation of hydrolytic enzymes or are modified.

Answers

1. (c) cDNA

Complimentary DNA (cDNA) is DNA synthesised from a single-stranded RNA template in a reaction catalysed by the enzyme reverse transcriptase. RNA of viruses first synthesises complementary DNA (cDNA) through reverse transcription. DNA then transfers information to RNA which takes part in the translation of coded information to form a polypeptide.

2. (c) 30%

According to Chargaff's rule, the amount of adenine is always equal to that of thymine and the amount of guanine is always equal to that of cytosine, i.e., $A = T$ and $G = C$.

If double-stranded DNA has 20% cytosine, then according to the law, it would have 20% of guanine. The remaining 60% represents both A + T molecule. Since, adenine and guanine are always present in equal numbers, the percentage of adenine molecule is 30%.

3. (d) 7

4. (c) Tobacco Mosaic Virus (TMV)

5. (b) RNA

6. (d) Both a. and b.

7. (b) capping

Methyl guanosine triphosphate is associated with capping. Capping occurs at the beginning of transcription in the nucleus. It consists of the addition of a 7-methylated guanosine cap at the 5' end of the mRNA. Capping offers protection to the mRNA against phosphatases and other nucleases.

8. (c) George Gamow

George Gamow attempted to solve the problem of how the order of the four different kinds of bases (A, T, G and C) in DNA chains could control the synthesis of proteins from amino acids. Gamow suggested that the twenty of the combinations of four DNA bases taken three at a time corresponded to twenty amino acids used to form proteins.

9. (a) Right handed helix, pitch is 3.4 nm

10. (b) Peptide bond formation between two amino acids.

11. (b) It is a single-stranded DNA.

According to the Chargaff's rules, the DNA from any cell of all organisms should have a 1 : 1 ratio (base Pair Rule) of purine bases (for the DNA cytosine, thymine and for the RNA uracil) and pyrimidine bases (guanine and adenine for RNA and DNA). The amount of guanine should be equal to cytosine and the amount of adenine should be equal to thymine. From the given data, it is concluded that it is a single-stranded DNA.

12. (c) 40,000 bp and $13,600 \times 10^{-9}$ m

Nucleosomes are fundamental organisational units of chromatin which appear as 'beads-on-a-string' arrangement. Each bead of nucleosome has 200 bp of DNA which is wound 1.65 times around histone octamer. The bead plus linker DNA (20-40 bp; average 20 bp) leads to the next bead and form the nucleosomes. Therefore, a 'beads on string' structure

with 200 beads contains $200 \times 200 = 40,000$ bp DNA on an average.

The length of typical euchromatin is calculated by multiplying the total number of bp with distance between two consecutive bp, that is, $(40,000 \text{ bp} \times 0.34 \times 10^{-9} \text{ m/bp})$.

So, length = $40,000 \times 0.34 \times 10^{-9} = 13,600 \times 10^{-9} \text{ m}$.

So, there will be 40,000 bp in the stretch and the length of the typical euchromatin would be $13,600 \times 10^{-9} \text{ m}$.

13. (b) A is having 2'-OH group which makes it more reactive and structurally unstable, whereas B is having 2'-H group which makes it less reactive and structurally stable.

14. (b) *Escherichia coli*

15. (c) Semiconservative DNA replication

16. (d) 0 : 1 : 31

The ratio of Heavy strands $^{15}\text{N}/^{15}\text{N}$: Hybrid $^{15}\text{N}/^{14}\text{N}$: Light $^{14}\text{N}/^{14}\text{N}$ containing DNA in the sixth generation will be 0 : 1 : 31.

17. (a) 87.5% of light density DNA and 12.5% of hybrid density DNA.

18. (d) The precursor of mRNA has to be processed further in next step before being translated.

19. (c) (i) Promoter site (ii) Sigma factor (iii) RNA polymerase

20. (d) Nucleotide

21. (a) random and directionless

22. (b) 5' (upstream) end and 3' (downstream) end, respectively of the transcription unit.

The promoter site and the terminator site for transcription are located at 5' (upstream) end and 3' (downstream) end, respectively of the transcription unit.

23. (b) Exons appear, but Introns do not appear in the mature RNA.

Eukaryotic transcripts possess extra segments called Introns or Intervening sequences or noncoding sequences. they do not appear in mature or processed RNA. The functional coding sequences are called exons. Splicing is removal of Introns and fusion of exons to form functional RNA.

24. (a) 5'-UACGCCG-3'

25. (a) 48

Total number of base pairs (bp) in given

$$\text{DNA} = 160 \text{ bp}$$

Percentage of adenine (A) = 20%

$$\text{Amount or number of bp in A} = 160 \times \frac{20}{100} = 32 \text{ bp}$$

We know that A is equal to T

So, total amount of bp of A and T = $32 + 32 = 64$

Total bp in DNA = 160

bp in A and T = 64

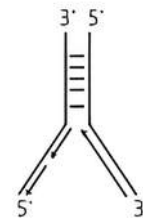
Remaining bp = 160 - 64 = 96

We also know that cytosine (C) is equal to guanine (G) and here C + G = 96

So, Cytosine = $\frac{96}{2} = 48$.

26. (a) 5'-CGUUAACCU-3'
27. (a) Phenylalanine, Methionine
28. (a) lactose is present and it binds to the repressor. The repressor of the operon is synthesised (all-the-time-constitutively) from the *i* gene. The repressor protein binds to the operator region of the operon and prevents RNA polymerase from transcribing the operon. In the presence of an inducer, such as lactose or allolactose, the repressor is inactivated by interaction with the inducer. This allows RNA polymerase access to the promoter and transcription proceeds. Thus, the *lac* operon gets switched on.
29. (d) Both a. and c.
30. (b) cannot bind to the operator
31. (c) *Vicia faba*, Thymidine
32. (b) DNase inhibited transformation
Prior to the work of Oswald Avery, Colin MacLeod and Maclyn McCarty (1933-44), the genetic material was thought to be a protein. They worked to determine the biochemical nature of 'transforming principle' in Griffith's experiment. They purified biochemicals (proteins, DNA, RNA, etc.) from the heat-killed S cells to see which ones could transform live R cells into S cells. They discovered that DNA alone from S bacteria caused R bacteria to become transformed. They also discovered that protein-digesting enzymes (proteases) and RNA-digesting enzymes (RNases) did not affect transformation, so the transforming substance was not a protein or RNA. Digestion with DNase did inhibit transformation, suggesting that the DNA caused the transformation.
33. (b) Site A- Methionine, Site B-UAC
RNA has the right combination of amino acids as methionine at site A and UAC at site B.
34. (a) probes
A probe is a single-stranded sequence of DNA or RNA used to search for its complementary sequence in a sample genome. The probe is placed into contact with the sample under conditions that allow the probe sequence to hybridize with its complementary sequence.
35. (d) 2' OH
36. (c) (iii) and (iv)
37. (c) Translation - Elongation
38. (c) Polypeptide chain, (ii) large subunit of ribosome, (iii) 5' end of mRNA, (iv) tRNA
39. (d) (i) continuous synthesis (ii) discontinuous synthesis (iii) 3' end (iv) 5' end

40. (a)



41. (d) UUU : Phenylalanine
42. (c) (i) Capping (ii) Polyadenylation (iii) mG_{ppp} (iv) Poly(A)
Two important RNA processing events lead to specialized end sequences in most human mRNA capping at the 5' end, and polyadenylation at the 3' end. At the 5' end, the most distinctive specialized end nucleotide, mG_{ppp} is added and a sequence of about 200 poly(A) is added to the 3' end.
43. (c) Short non-coding repetitive sequence forming large portion of eukaryotic genome.
44. (c) Children 1 and 3
The a DNA fingerprints of children 1 and 3 are matching with those of parents so, they are probably their children.
45. (b) Both Assertion and Reason are true but Reason is not the correct explanation of Assertion.
Although A \equiv T and C \equiv G, there is no any restriction or sequence of bases in one polynucleotide chain. Since A is always linked to T and C go G as determined from the above evidences, sequence of bases in one of polynucleotide should determine the sequence of bases in the other polynucleotide of the double helix.
46. (b) Both Assertion and Reason are true but Reason is not the correct explanation of Assertion.
tRNA is an adaptor molecule because it adapts amino acid to bring it to protein synthesis site in activated form and not because it recognises the codon on mRNA.
47. (a) Both Assertion and Reason are true and Reason is the correct explanation of Assertion.
It has been shown, for instance that the same tRNA can recognise more than one codons differing only at the third position. This pairing is not very stable and is allowed due to wobbling in base pairing at this third position. This kind of wobbling allows economic of the number of tRNA molecules, since several codons meant for same amino acid are recognised by same tRNA. For instance, anticodon CGC can recognise codons GCU, GCC and GCA.
48. (c) Assertion is true but Reason is false.
49. (a) Both Assertion and Reason are true and Reason is the correct explanation of Assertion.
Synthesis of polypeptide terminates when a nonsense codon of mRNA reaches the A-site. There are three nonsense codons—UAA, UAG and UGA. These codons are not recognised by any of the tRNAs. Therefore, no more aminoacyl tRNA reaches the A-site. The P-site tRNA is hydrolysed and the completed polypeptide is released in the presence of release factor. Thus termination occurs.

50. (b) Both Assertion and Reason are true but Reason is not the correct explanation of Assertion.

Polyribosomes attached to membranes of endoplasmic reticulum produce proteins which either pass into their lumen or become integrated into the membranes. The proteins released into the lumen generally reach Golgi apparatus for modifications like formation of hydrolytic enzymes and glycosylation (addition of sugar residues). The modified proteins are packed in vesicles for export or formation of lysosomes, cell wall, enzymes, plasma membrane, etc.



Case Study Based Questions

Case Study 1

Nucleic Acids

Deoxyribonucleic Acid (DNA) and Ribonucleic Acid (RNA) are the two types of nucleic acids found in the living systems. DNA acts as the genetic material in most of the organisms. Although RNA also acts as a genetic material in some organisms.

- Q 1. In which of the following organisms, RNA acts as a genetic material?

a. *Escherichia coli* b. QB Bacteriophage
c. Tobacco Mosaic virus d. Both b. and c.

- Q 2. What is the reason for the additional stability of DNA in comparison to RNA?

a. Presence of thymine
b. Presence of uracil
c. Presence of OH group
d. Presence of deoxyribose sugar

- Q 3. Which of the following criteria a molecule must fulfill to act as a genetic material?

a. It should be able to generate its replica.
b. It should be stable chemically and structurally.
c. It should be able to express itself in the form of Mendelian character.
d. All of the above

- Q 4. Read the given statement and select the option that correctly fill in the blanks.

Pyrimidines present in DNA are: (i) and (ii) while pyrimidines present in RNA are: (iii) and (iv)

a. (i) Adenine, (ii) Guanine, (iii) Cytosine, (iv) Thymine
b. (i) Cytosine, (ii) Thymine, (iii) Cytosine, (iv) Uracil
c. (i) Cytosine, (ii) Uracil, (iii) Adenine, (iv) Guanine
d. (i) Cytosine, (ii) Uracil, (iii) Cytosine, (iv) Thymine

- Q 5. Assertion (A): RNA is liable and easily degradable.

Reason (R): The 2'-OH group present at every nucleotide in RNA is a reactive group.

a. Both Assertion and Reason are true, and Reason is the correct explanation of Assertion.
b. Both Assertion and Reason are true, but Reason is not the correct explanation of Assertion.

- c. Assertion is true, but Reason is false.
d. Assertion is false but Reason is true.

Answers

1. (d) 2. (a) 3. (d) 4. (b) 5. (a)

Case Study 2

DNA Double Helix

In prokaryotes, DNA is circular and present in the cytoplasm but in eukaryotes, DNA is linear and mainly confined to the nucleus. DNA or deoxyribonucleic acid is a long polymer of nucleotides. In 1953, the first correct double helical structure of DNA was worked out by Watson and Crick. Based on the X-ray diffraction data produced by Maurice Wilkins and Rosalind Franklin, it is composed of three components *i.e.*, a phosphate group, a deoxyribose sugar and a nitrogenous base. Different forms of DNA are B-DNA, Z-DNA, A-DNA, C-DNA and D-DNA.

- Q 1. Name the linkage present between the nitrogen base and pentose sugar in DNA.

a. Phosphodiester bond
b. Glycosidic bond
c. Hydrogen bond
d. None of the above

- Q 2. The double helix structure of DNA was proposed by:

a. James Watson and Francis Crick
b. Erwin Chargaff
c. Frederick Griffith
d. Hershey and Chase

- Q 3. The double chain of B-DNA is coiled in a helical fashion. The spiral twisting of B-DNA duplex produces:

a. right and left part
b. major and minor grooves
c. upper and lower sides
d. linear and circular part.

- Q 4. Which of the following describes the structure of B-DNA?

Polynucleotide chains	Number of base pairs per Complete turn of helix
a. Parallel	5
b. Anti-parallel	10
c. Parallel	15
d. Anti-parallel	20

- Q 5. Assertion (A): The two strands of DNA helix have uniform distance between them.

Reason (R): A large sized purine is always paired opposite to a small sized pyrimidine.

a. Both Assertion and Reason are true, and Reason is the correct explanation of Assertion.

- b. Both Assertion and Reason are true, but Reason is not the correct explanation of Assertion.
 c. Assertion is true, but Reason is false.
 d. Assertion is false but Reason is true.

Answers

1. (b) 2. (a) 3. (b) 4. (b) 5. (a)

Case Study 3

Translation

Translation is the process of polymerisation of amino acids to form a polypeptide. The order and sequence of amino acids are defined by the sequence bases in the mRNA. The amino acids are joined by a bond called peptide bond. Ribosome is the site of protein synthesis.

- Q 1. Which ion is essential for association of both units of ribosome at the time of protein formation?**
 a. Mg^{2+} b. Mn^{2+} c. Cl^- d. Ca^{2+}
- Q 2. During translation, how many initiation factors are required in eukaryotes for initiation reactions?**
 a. 3 b. 6 c. 7 d. 9
- Q 3. Which part of mRNA contains Untranslated Regions (UTR)?**
 a. 3' end b. 5' end
 c. Either 3' or 5' end d. Both 5' end and 3' end
- Q 4. Name the enzyme that helps in combining amino acid to its particular RNA.**
 a. Activating enzyme
 b. Amino-acyl tRNA-synthetase
 c. Peptidyl transferase
 d. Both a. and b.
- Q 5. From the given list, select the translation machinery.**
 1. mRNA
 2. Ribosomes
 3. Amino acids
 4. tRNAs
 5. Amino acyl tRNA synthetase
 6. Peptidyl transferase
 7. Pyrophosphatase
 a. (1), (2), (3), (4) and (6)
 b. (1), (2), (3), (4) and (5)
 c. (1), (2), (3), (4), (5) and (6)
 d. (1), (2), (3), (4), (5), (6) and (7)

Answers

1. (a) 2. (d) 3. (d) 4. (c) 5. (a)

Case Study 4

DNA Replication

DNA replication is a complex multistep process that requires enzymes, protein factors and metal ions. DNA replication in eukaryotes occurs in the nucleus during the S-phase of the cell

cycle. It is semi-discontinuous in eukaryotes. In prokaryotes, replication takes place in the cytoplasm. DNA replication in bacteria occurs prior to fission. Nucleoid or viral chromosome is a single molecule of nucleic acid, it may be linear or circular. Nucleic acid in a virus is either DNA or RNA but never both.

Read the given passage carefully and give the answer of the following questions:

- Q 1. In viral DNA, how many origins of replication are present?**

Ans. Single origin of replication is present in viral DNA.

- Q 2. Select the main enzyme involved in DNA of these replications.**

Ans. The main enzyme involved in DNA of these replication is DNA dependent DNA polymerase.

- Q 3. What does the DNA strand built up of Okazaki fragments called?**

Ans. DNA strand built up of okazaki fragments is called leading strand.

OR

Which enzyme acts over the Ori site and unwinds the two strands of DNA by destroying hydrogen bonds?

Ans. Helicase enzyme acts over the Ori site.

Case Study 5

Transcription

The process of copying genetic information from template strand of DNA into RNA is called transcription. It is mediated by RNA polymerase. Transcription takes place in the nucleus of eukaryotic cells. In transcription, only a segment of DNA and only one of the strands is copied into RNA.

Read the given passage carefully and given the answer of the following questions:

- Q 1. What do you mean by transcription?**

Ans. Transcription is the process by which the information in a strand of DNA is copied into a new molecule of messenger RNA (mRNA).

- Q 2. What are regions of transcription unit in a DNA molecule?**

Ans. The regions of transcription unit in a DNA molecule are promoter structural gene and terminator.

OR

In which organisms monocistronic structural genes are found?

Ans. Monocistronic structural genes are found in eukaryotes.

- Q 3. Which enzyme helps in tailing or polyadenylation?**

Ans. Poly-A polymerase helps in tailing or polyadenylation.



Very Short Answer Type Questions

Q 1. Write the dual purpose served by deoxyribonucleoside triphosphates in polymerisation. (CBSE 2018)

Ans. Deoxyribonucleoside triphosphate acts as a substrate and provide energy (from the terminal two phosphates) in polymerisation.

Q 2. Write the central dogma of molecular biology.

Ans. Central dogma of molecular biology states that the genetic information flows unidirectionally from DNA → RNA → Protein.



Q 3. How many base pairs would a DNA segment of length 1.36 mm have? (CBSE 2017)

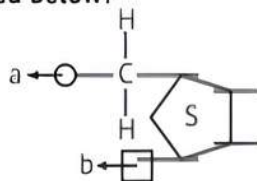
Ans. Distance between two base pairs ≈ 0.34 nm or 0.34×10^{-6} mm. Number of base pairs in 1.36 mm DNA segment

$$= \frac{1}{0.34 \times 10^{-6}} \times 1.36 \approx 4 \times 10^6 \text{ bp (base pairs)}$$

Q 4. Write the role of histone protein in packaging of DNA in eukaryotes. (CBSE 2017)

Ans. Histones are positively charged basic proteins. The negatively charged DNA is wrapped around the positively charged histone octamer to form nucleosome.

Q 5. What are 'a' and 'b' in the nucleotide with purine represented below?



Ans. 'a' is phosphate group and 'b' is nitrogenous base i.e., purine (adenine/guanine).

Q 6. How does the flow of genetic information in HIV deviate from the 'central dogma' proposed by Francis Crick?

Ans. In HIV, single-stranded RNA is converted to double stranded DNA.

Q 7. Name the negatively charged and positively charged components of a nucleosome. (CBSE 2015)

Ans. In a nucleosome, the negatively charged component is DNA and positively charged component is histone octamer.

Q 8. Name the enzyme and state its property that is responsible for continuous and discontinuous replication of the two strands of a DNA molecule.

Ans. The enzyme is DNA dependent DNA polymerase. It catalyses polymerisation in 5' → 3' direction only.

Q 9. Name the transcriptionally active region of chromatin in a nucleus. (CBSE 2015)

Ans. Euchromatin or exon is the transcriptionally active region of chromatin in a nucleus.

Q 10. Mention the two additional processings which *hnRNA* needs to undergo after splicing so as to become functional.

Ans. Capping and tailing are the two additional processings.

Q 11. When and at what end does the 'tailing' of *hnRNA* take place?

Ans. 'Tailing' of *hnRNA* takes place during conversion of *hnRNA* into functional *mRNA* after transcription. It takes place at the 3'-end.

Q 12. At which ends do 'capping' and 'tailing' of *hnRNA* occur, respectively?

Ans. Capping occurs at 5'-end and tailing occurs at 3'-end.

Q 13. What is cistron? (CBSE 2015)

Ans. A cistron is a segment of DNA coding for a polypeptide.

Q 14. How does a degenerate code differ from an unambiguous one? (CBSE 2015)

Ans. Degenerate code means that one amino acid can be coded by more than one codon. Unambiguous code means that one codon codes for only one amino acid.

Q 15. Mention two functions of the codon AUG.

Ans. Two functions of the codon AUG are:
(i) It acts as a start codon during protein synthesis.
(ii) It codes for the amino acid methionine.

Q 16. Mention the role of the codons AUG and UGA during protein synthesis.

Ans. The codon AUG initiates protein synthesis whereas the codon UGA stops protein synthesis.

Q 17. Write the function of RNA polymerase II.

Ans. RNA polymerase II transcribes precursor of *mRNA* or *hnRNA*. (CBSE 2015)

Q 18. Give an example of a codon having dual function.

Ans. AUG acts as an initiation codon and also codes for methionine. (CBSE 2016)

Q 19. Mention how does DNA polymorphism arise in a population.

Ans. DNA polymorphism in a population arises due to presence of inheritable mutations at high frequency.

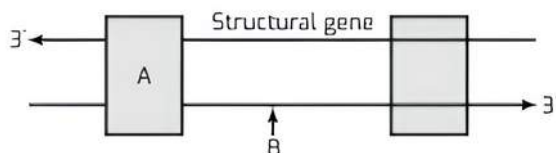
Q 20. Suggest a technique to a researcher who needs to separate fragments of DNA. (CBSE 2016)

Ans. Gel electrophoresis is used to separate DNA fragments.

Q 21. Mention one difference to distinguish an exon from an intron.

Ans. Exon is the coded or expressed sequence of nucleotides in *mRNA*. Whereas, intron is the intervening sequence of nucleotides not appearing in processed *mRNA*.

Q 22. Name the parts 'A' and 'B' of the transcription unit given below: (CBSE 2016)



Ans. 'A' is promoter sequence of DNA and 'B' is coding strand.

Q 23. A region of a coding DNA strand has the following nucleotide sequence:

– A T G C –

What shall be the nucleotide sequence in:

(i) sister DNA segment it replicates, and

(ii) mRNA polynucleotide it transcribes?

Ans. (i) – T A C G –
(ii) – U A C G –

COMMON ERROR

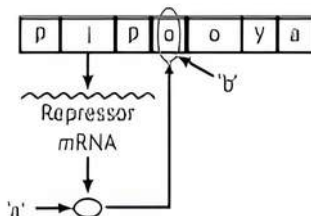
There may be confusion in writing nucleotide sequence so practice them carefully.

Q 24. Why *hnRNA* is required to undergo splicing?

(CBSE 2019)

Ans. *hnRNA* undergoes splicing in order to remove introns which are intervening or non-coding sequences and exons are joined to form functional mRNA.

Q 25. Given below is a schematic representation of a *lac* operon in the absence of an inducer. Identify 'a' and 'b' in it. (CBSE 2017)



Ans. a–Repressor, b–Repressor bound to the operator that prevents transcription of structural genes.

Q 26. Mention the contribution of genetic maps in human genome project.

Ans. The contribution of genetic maps is as follows:

- Genetic maps have played an important role in sequencing of genes.
- DNA fingerprinting and in tracing human history.
- Chromosomal location for disease associated sequences.

Q 27. Calculate the length of the DNA of bacteriophage lambda that has 48502 base pairs.

Ans. Distance between two consecutive base pairs
 $\approx 0.34 \times 10^{-9} \text{ m}$

The length of DNA in bacteriophage lambda

$$\approx 48502 \times 0.34 \times 10^{-9} \text{ m}$$

$$\approx 16.49 \times 10^{-6} \text{ m}$$



Short Answer Type Questions

Q 1. Draw a schematic representation of dinucleotide.

Label the following:

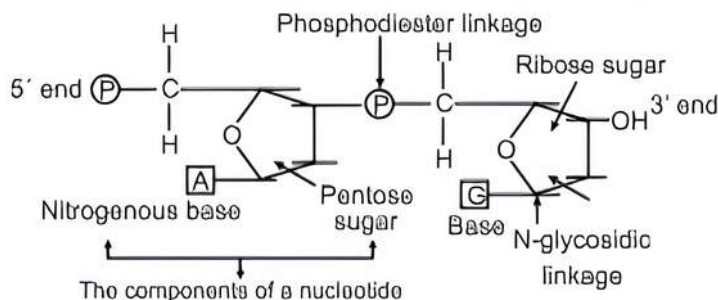
(i) The components of a nucleotide

(ii) 5' end

(iii) N-glycosidic linkage

(iv) Phosphodiester linkage

Ans. Nucleotide = Ribose sugar + Base + Phosphate group.



TIP

Practice making the dinucleotide linkage along with the labelling of its components.

Q 2. How do histones acquire positive charge?

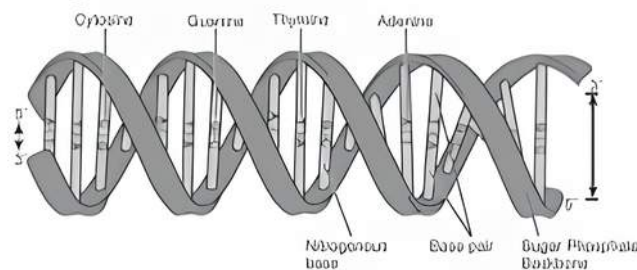
Ans. Histones are rich in the basic amino acid residues lysines and arginines, which carry positive charges in their side chains. Therefore, histones are positively charged.

Q 3. Although a prokaryotic cell has no defined nucleus, yet DNA is not scattered throughout the cell. Explain. (CBSE 2018)

Ans. DNA is negatively charged and positively charged proteins hold it in places in large loops (in a region termed as nucleoid).

Q 4. Draw a schematic diagram of a part of double-stranded dinucleotide DNA chain having all the four nitrogenous bases and showing the correct polarity.

Ans. Diagram of double-stranded dinucleotide DNA chain:



Q 5. Explain the two factors responsible for conferring stability to double helix structure of DNA.

(CBSE 2017)

Ans. Factors responsible for conferring stability to double helix structure are presence of hydrogen bonds, the plane of one base pair stacks over the other and complementary presence of thymine in place of uracil.

Q 6. Why do you see two different types of replicating strands in the given DNA replication fork? Explain. Name these strands.

Ans. The DNA-dependent DNA polymerase catalyses polymerisation only in one direction i.e., $5' \rightarrow 3'$. Therefore, in one strand with polarity $3' \rightarrow 5'$, continuous replication takes place whereas the other strand with polarity $5' \rightarrow 3'$ carries out discontinuous replication.

The strand with polarity $3' \rightarrow 5'$ is called leading strand and the strand with polarity $5' \rightarrow 3'$ is called lagging strand.

Q 7. State the dual role of deoxyribonucleoside triphosphates during DNA replication.

Ans. The dual role is as under:

(i) Deoxyribonucleoside triphosphates act as substrates for polymerisation.

(ii) These provide energy for polymerisation reaction.

Q 10. Differentiate between a template strand and a coding strand of DNA.

Ans.

S.No.	Basis of difference	Template Strand	Coding Strand
(i)	Definition	The DNA strand that has the polarity and act as a template for transcription is known as template strand.	The strand which does not code anything and has polarity is called coding strand.
(ii)	Nucleotide sequence	Nucleotide sequence is <u>complementary to the one present in RNA</u> .	The nucleotide sequence is the <u>same to the one present in mRNA</u> except for the presence of thymine instead of uracil.

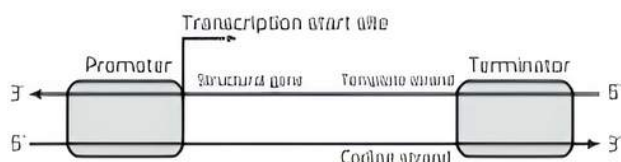
Q 11. Explain the role of ^{35}S and ^{32}P in the experiments conducted by Hershey and Chase.

Ans. Viruses grown in the medium containing ^{32}P contained radioactive DNA but not radioactive protein because DNA contains phosphorus but proteins do not contain phosphorus.

Similarly, viruses grown on radioactive sulphur ^{35}S contained radioactive protein but not radioactive DNA because DNA does not contain sulphur.

Q 12. Draw a labelled schematic diagram of a transcription unit. (CBSE 2015)

Ans. Diagram of transcription unit:



Q 13. What is amino acylation? State its significance.

Ans. Amino acylation of tRNA or charging of tRNA is the activation of amino acids in the presence of ATP and their linkage to their cognate tRNA.

If two such charged tRNAs are brought close enough, the formation of peptide bond between them would be favoured energetically.

Q 8. A DNA segment has a total of 1500 nucleotides, out of which 410 are Guanine containing nucleotides. How many pyrimidine bases this DNA segment possesses?

Sol. According to Chargaff's rule,

$$\frac{A}{G} = \frac{T}{C} = 1$$

$G = C$, $G = 410$, hence $C = 410$

$$G + C = 410 + 410 = 820$$

$$\text{So, } A + T = 1500 - 820 = 680$$

$$\therefore A = T, \text{ so } T = \frac{680}{2} = 340$$

So, pyrimidines $= C + T = 410 + 340 = 750$

Q 9. A template strand is given below. Write down the corresponding coding strand and the mRNA strand that can be formed, along with their polarity.

$3' \text{ ATGCATGCATGCATGCATGC } 5'$

Ans. Coding strand: $5' \text{ TACGTACGTACGTACGTACGTACG } 3'$
mRNA strand: $5' \text{ UACGUACGUACGUACGUACGUACG } 3'$

Q 14. What is a cistron? Why is the structural gene in a transcription unit of eukaryotes called monocistronic and that in prokaryotes/bacteria called polycistronic? Give reasons.

Ans. Cistron is a segment of DNA coding for a polypeptide. In eukaryotes, the transcriptional units have interrupted coding sequences—exons and introns. It codes for only one polypeptide, so it is called monocistronic.

In prokaryotes structural genes have many coding sequences, so it is called polycistronic.

Q 15. (i) Name the scientist who suggested that the genetic code should be made of a combination of three nucleotides.

(ii) Explain the basis on which he arrived at this conclusion.

Ans. (i) George Gamow.

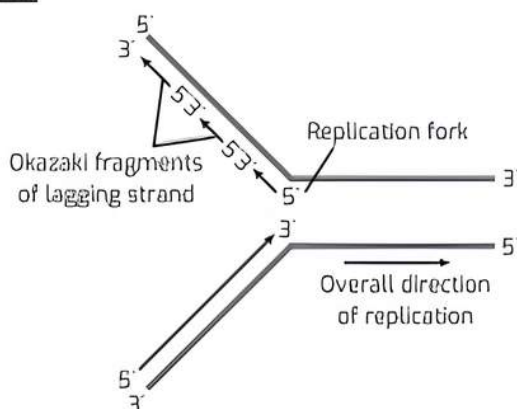
(ii) He proposed that there are four bases and 20 amino acids. So, there should be at least 20 different genetic codes for these 20 amino acids.

The only possible combinations that would meet the requirement is combinations of 3 bases that will give 64 codons.

(iii) Okazaki fragments are short DNA segments on the lagging strand, formed in the 5' → 3' direction, starting from RNA primers. A separate RNA primer is needed for the synthesis of each Okazaki fragment. These discontinuously synthesised fragments are later joined by the enzyme DNA ligase.

(iv) ori stands for Origin of replication. This site has the highly conserved sequence of DNA among various species. The replication of DNA starts here because this site attracts some proteins which help in the opening and unwinding of DNA and this leads to the initiation of replication.

Role: The function of DNA Ligase is to join the two nucleotides. During the DNA replication process, it joins the Okazaki fragments of the daughter DNA to form the complete DNA molecule on the lagging strand.



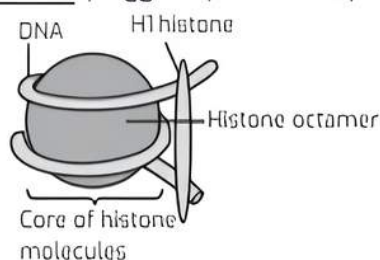
Q 2. A typical mammalian cell has 22 metres long DNA molecule whereas the nucleus in which it is packed measures about 10–6 m. Explain how such a long DNA molecule is packed within a tiny nucleus in the cell.

OR

Describe the structure of a nucleosome. (CBSE 2019)

Ans. Packaging of DNA in eukaryotes:

- (i) The proteins associated with DNA are of two types—basic proteins (histone and protamine) and acidic Non-Histone Chromosomal (NHC) proteins.
- (ii) The negatively charged DNA molecule wraps around the positively charged histone proteins to form a structure called nucleosome.
- (iii) The nucleosome core is made up of four types of histone proteins—H2A, H2B, H3 and H4—occurring in pairs.
- (iv) 200 bp of DNA helix wrap around the nucleosome by $1\frac{3}{4}$ turns, plugged by H1 histone protein.



Q 3. (i) A DNA segment has a total of 1000 nucleotides, out of which 240 of them are adenine containing nucleotides. How many pyrimidine bases this DNA segment possesses?

(ii) Draw a diagrammatic sketch of a portion of DNA segment to support your answer.

Ans. (i) We have $A = T$, $A = 240$, hence $T = 240$

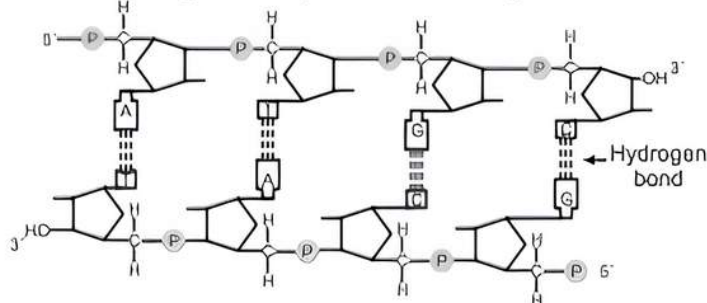
$$A + T = 240 + 240 = 480$$

$$\text{So, } G + C = 1000 - 480 = 520$$

$$G = C, \text{ so } C = \frac{520}{2} = 260$$

$$\text{So, pyrimidines} = C + T = 260 + 240 = 500$$

(ii) Diagram of a portion of DNA segment:



TiP

Students should learn the formula and practice numericals based on it. Also revise the diagram of DNA segment.

Q 4. Describe Frederick Griffith's experiment on *Streptococcus pneumoniae*. Discuss the conclusion he arrived at.

OR

Describe the experiment with *Streptococcus pneumoniae* that demonstrated the existence of some "transforming principle".

Ans. Frederick Griffith's Transforming Principle

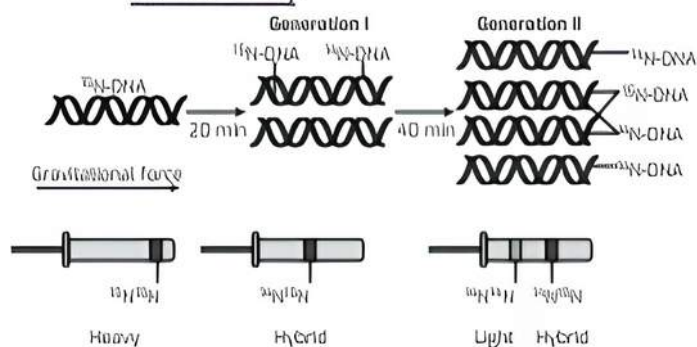
- (i) Frederick Griffith (1928) conducted experiments with *Streptococcus pneumoniae* (bacterium causing pneumonia).
- (ii) He observed two strains of this bacterium—one forming smooth shiny colonies (S-type) with capsule, while other forming rough colonies (R-type) without capsule.
- (iii) When live S-type cells were injected into mice, they died due to pneumonia.
- (iv) When live R-type cells were injected into mice, they survived.
- (v) When heat-killed S-type cells were injected into mice, they survived and there were no symptoms of pneumonia.
- (vi) When heat-killed S-type cells were mixed with live R-type cells and injected into mice, they died due to unexpected symptoms of pneumonia and live S-type cells were obtained from mice.
- (vii) He concluded that heat-killed S-type bacteria caused a transformation of the R-type bacteria into S-type bacteria but he was not able to understand the cause of this bacterial transformation.

Q 5. Describe the experiments that established the identity of 'transforming principles' of Griffith.

(CBSE 2017)

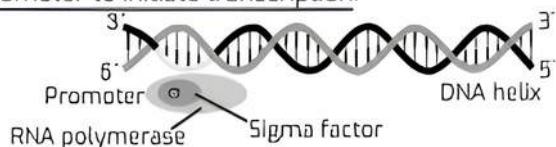
Ans. Experimental proof for Griffith's transforming principle:

- (i) Matthew Meselson and Franklin Stahl in 1958 performed experiments on *E. coli* to prove that DNA replication is semiconservative.
- (ii) They grew *E. coli* in a medium containing $^{15}\text{NH}_4\text{Cl}$ (in which ^{15}N is the heavy isotope of nitrogen) for many generations.
- (iii) As a result, ^{15}N got incorporated into newly synthesised DNA.
- (iv) This heavy DNA can be differentiated from normal DNA by centrifugation in caesium chloride (CsCl) density gradient.
- (v) Then they transferred the cells into a medium with normal $^{14}\text{NH}_4\text{Cl}$ and took the samples at various definite time intervals as the cells multiplied.
- (vi) The extracted DNAs were centrifuged and measured to get their densities.
- (vii) The DNA extracted from the culture after one generation of transfer from the ^{15}N medium to ^{14}N medium (i.e., after 20 minutes; *E. coli* divides every 20 minutes) showed an intermediate hybrid density.
- (viii) The DNA extracted from culture after two generations (i.e., after 40 minutes) showed equal amounts of light DNA and hybrid DNA.
- (ix) Similar experiment was performed by Taylor and colleagues in 1958, on *Vicia faba* to prove that the DNA in chromosome also replicate semi-conservatively.



Q 6. Describe the initiation process of transcription in bacteria. (CBSE 2015)

Ans. In bacteria, the transcription of all the three types of RNA (mRNA, tRNA, rRNA) is catalysed by single DNA-dependent enzyme called the RNA polymerase. The RNA polymerase has cofactors that catalyse the process. During initiation, σ (sigma) factor recognises the start signal and promoter region on DNA which then along with RNA polymerase binds to the promoter to initiate transcription.



Q 7. Describe the elongation process of transcription in bacteria. (CBSE 2018)

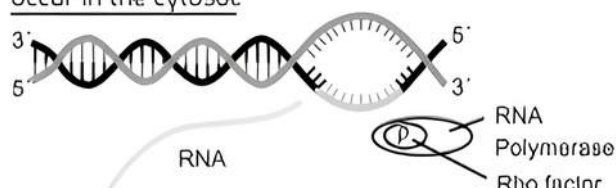
Ans. After initiation, RNA polymerase loses the σ factor but continues the polymerisation of ribonucleotides

to form RNA. It uses nucleoside triphosphates as substrate and polymerises in a template-dependent fashion, following the rule of complementarity.



Q 8. Describe the termination process of transcription in bacteria. (CBSE 2017)

Ans. Once the RNA polymerase reaches the termination region of DNA, the RNA polymerase is separated from DNA-RNA hybrid, as a result nascent RNA separates. This process is facilitated by a termination factor ρ (rho). In prokaryotes, mRNA does not require any processing, so transcription and translation both occur in the cytosol.



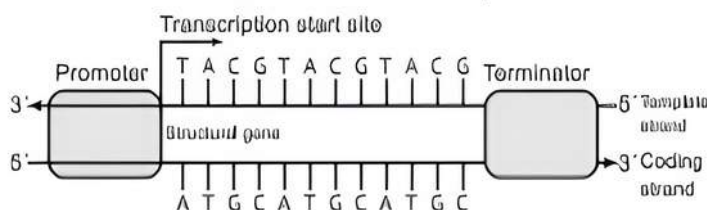
Q 9. Construct and label a transcription unit from which the RNA segment given below has been transcribed. Write the complete name of the enzyme that transcribed this RNA. (CBSE 2019)



Ans. Here, the RNA segment given is having Thymine which is not possible. Hence, the question is wrong. The solution can be possible by taking U (Uracil) instead of T (Thymine) in the given strand.

RNA Polymerase is the enzyme which is used during transcription.

Schematic structure of a transcription unit:



Q 10. How is hnRNA processed to form mRNA?

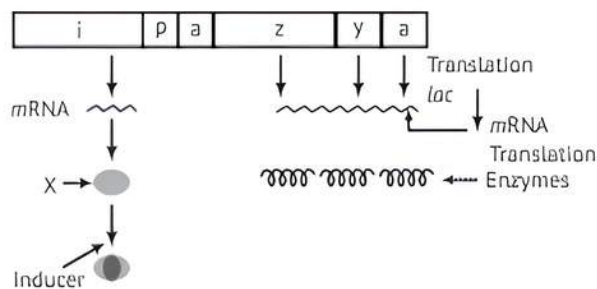
Ans. The hnRNA undergoes the following processes to form mRNA:

- (i) **Capping:** Addition of methyl guanosine triphosphate at 5'-end.
- (ii) **Tailing:** Addition of 200-300 adenylate residues at 3'-end.
- (iii) **Splicing:** Removal of introns and rejoining of exons.

Q 11. (i) Name the molecule 'X' synthesised by 'i' gene. How does this molecule get inactivated?

(ii) Which one of the structural genes codes for β -galactosidase?

(iii) When will the transcription of this gene stop?



- Ans. (i) The molecule 'X' is repressor. It gets inactivated when lactose (inducer) binds with the repressor molecule.
- (ii) z gene codes for β -galactosidase.
- (iii) Transcription of the gene stops when lactose is absent and thus repressor is free to bind with the operator.



TIP

Students must go through the concept of lac operon and understand the gene coding.

Q 12. Human Genome Project (HGP) was a mega project launched in the year 1990 with some important goals.

- Enlist any four prime goals of HGP.
- Name any one common non-human animal model organism which has also been sequenced thereafter. (CBSE 2023)

- Ans. (i) The prime goals of HGP are given below:
- Identify all the approximately 20,000-25,000 genes in human DNA.
 - Determine the sequences of the 3 billion chemical base pairs that make up the human DNA.
 - Creating genome sequence databases to store the data.
 - Improve tools for data analysis.
- (ii) *Caenorhabditis elegans* (a free living non-pathogenic nematode).

Q 13. (i) Expand VNTR and describe its role in DNA fingerprinting.

(ii) List any two applications of DNA fingerprinting technique. (CBSE 2018)

- Ans. (i) VNTR: Variable Number of Tandem Repeat(s)
It is used as a probe (because of its high degree of polymorphism) in DNA fingerprinting.
- (ii) The applications of DNA fingerprinting technique are:
- Forensic science/criminal investigation
 - Determine population and genetic diversities
 - Paternity testing/maternity testing/study of evolutionary biology.



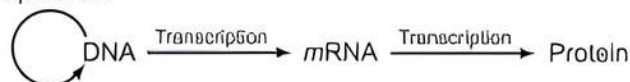
Long Answer Type-II Questions

- Q 1. (i) State the 'central dogma' as proposed by Francis Crick. Are there any exceptions to it? Support your answer with a reason and an example.

- (ii) Explain how the biochemical characterisation (nature) of 'Transforming Principle' was determined, which was not defined from Griffith's experiments. (CBSE 2018)

Ans. (i) **Central Dogma:** The principle was proposed by Francis Crick. This states that the genetic information always flows indirectly from DNA to mRNA (Transcription) and then from mRNA to protein (Translation).

Replication



Yes, in some viruses flow of information is in reverse direction/reverse transcription, e.g., any Retrovirus / HIV.

- (ii) The biochemical characterisation of Transforming Principle, was determinant in the following way:

- Protein, DNA and RNA were purified from heat killed S strain / smooth *Streptococcus* / *Diplococcus pneumoniae*.
- Protein + Protease \rightarrow transformation occurred (R cell to S type)
- RNA + RNA ase \rightarrow transformation occurred (R cell to S type)
- DNA + DNA ase \rightarrow transformation inhibited
Hence, DNA alone is the transforming material.

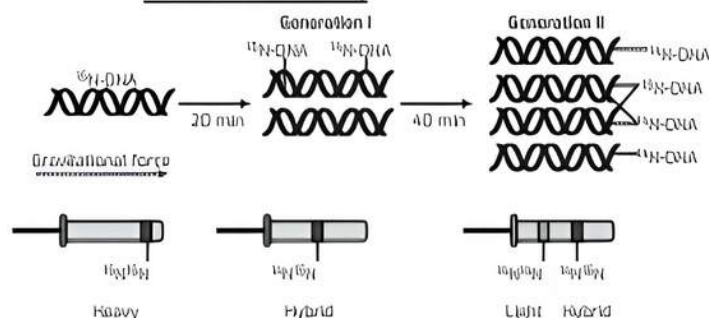
Q 2. (i) Explain the observations of Meselson and Stahl when:

- they cultured *E. coli* in a medium containing for a few generations and centrifuged the content.
- they transferred one such bacterium to the normal medium of?

(ii) What does the above experiment prove?

(iii) Which is the first genetic material identified?

- Ans. (i) Observations of Meselson and Stahl:
- Meselson and Stahl observed that in the *E. coli* bacterium, the DNA becomes completely labelled with N medium by centrifugation for few generations.
 - After two generations, density changed and showed equal amount of light DNA (^{14}N) and dark hybrid DNA (N-N).
 - The given experiment proved that DNA replicates semiconservatively.

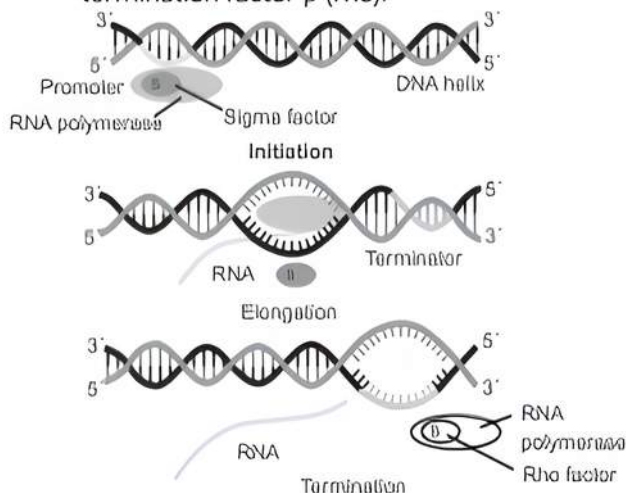


- (iii) Ribonucleic Acid (RNA) was the first genetic material identified.

Q 3. Explain the process of transcription in prokaryotes. How is the process different in eukaryotes?

Ans. Process of Transcription in Prokaryotes is as follows:

- (i) **Initiation:** σ (sigma) factor recognises the start signal and promoter region on DNA which then along with RNA polymerase binds to the promoter to initiate transcription.
- (ii) **Elongation:** The RNA polymerase after Initiation of RNA transcription loses the σ factor but continues the polymerisation of ribonucleotides to form RNA.
- (iii) **Termination:** Once the RNA polymerase reaches the termination region of DNA, the RNA polymerase is separated from DNA-RNA hybrid, as a result, nascent RNA separates. This process is called termination which is facilitated by a termination factor ρ (rho).



Process of Transcription in Eukaryotes is as follows:

- (i) The structural genes are monocistronic in eukaryotes.
- (ii) The process of transcription is similar to that in prokaryotes.
- (iii) It takes place in the nucleus.
- (iv) Coding gene sequences called exons form the part of mRNA and non-coding sequence called introns are removed during RNA splicing.
- (v) In eukaryotes, three types of RNA polymerases are found in the nucleus:
 - (a) RNA polymerase I transcribes rRNAs (28S, 18S, and 5.8S).
 - (b) RNA polymerase II transcribes the precursor of mRNA (called heterogeneous nuclear RNA or hnRNA).
 - (c) RNA polymerase III transcribes tRNA, 5S rRNA and snRNAs (small nuclear RNAs).

Q 4. Given below is a stretch of DNA showing the coding strand of a structural gene of a transcription unit:
 5'—ATG ACC GTA TTT TCT GTA GTG CCC GTA CTT CAG GCA TAA—3'

- (i) Write the corresponding template strand and the mRNA strand that will be transcribed, along with its polarity.

- (ii) If GUA of the transcribed mRNA is an intron, depict the sequence involved in the formation of mRNA/the mature processed hnRNA strand.
 - (a) In a bacterium
 - (b) In humans
- (iii) Upon translation, how many amino acids will the resulting polypeptide have? Justify.

(CBSE SQP 2023-24)

Ans. 5'—ATG ACC GTA TTT TCT GTA GTG CCC GTA CTT CAG GCA TAA—3' = Coding

(i) 3'—TAC TGG CAT AAA AGA CAT CAC GGG CAT GAA GTC CGT ATT — 5' = Template

5'—AUG ACC GUA UUU UCU GUA GUG CCC GUA CUU CAG GCA UAA—3'

- (ii) (a) In a bacterium

5'—AUG ACC GUA UUU UCU GUA GUG CCC GUA CUU CAG GCA UAA—3'

- (b) In humans

5'—mGpppAUG ACC UUU UCU GUG CCC CUU CAG GCA UAA— Poly A tail—3'

- (iii) There are 9 amino acids in the resulting polypeptide because UAA is stop or terminator codon and does not code for any amino acid.

COMMON ERROR

Students often make mistakes in pairing nitrogenous bases while writing the template strand.

Q 5. Protein synthesis requires the services of all three types of RNAs, namely tRNA, mRNA and rRNA. Explain the role of each of them during the process of protein synthesis in prokaryotes. (CBSE 2023)

Ans. The role of all the three types of RNAs during the process of protein synthesis in prokaryotes are as follows:

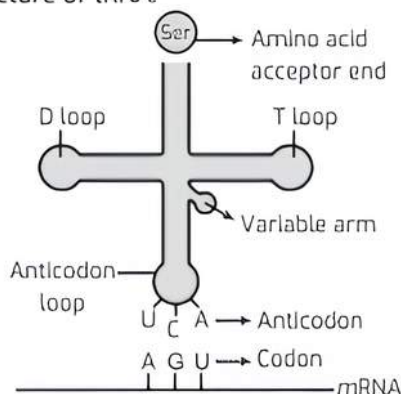
- (i) **mRNA:** Messenger RNA, helps in making protein i.e., codes for amino acids, obtained from DNA.
- (ii) **tRNA:** Transfer RNA, helps in transporting amino acid molecules that form the polypeptide chain in protein synthesis. It has anticodons that help read and deposit the amino acids at the right place.
- (iii) **rRNA:** Ribosomal RNA, form the small and large subunits of ribosomes that help in running through the mRNA sequence and possess different sites and enzymes for completing the polypeptide synthesis.

Q 6. (i) Describe the structure and function of a tRNA molecule. Why is it referred to as an adapter molecule?

- (ii) Explain the process of splicing of hnRNA in a eukaryotic cell. (CBSE 2016)

Ans. (i) tRNA (transfer RNA) reads the genetic code on one hand and transfers amino acids on the other hand, so it is called as adapter molecule by Francis Crick. It is also called as soluble RNA (sRNA).

Structure of tRNA:



The secondary structure of tRNA is clover leaf like but the 3-D structure is inverted L-shaped. tRNA has five arms or loops:

- Anticodon loop:** It has bases complementary to the code.
- Amino acid acceptor end:** It is the end to which amino acid binds.
- T-loop:** It helps in binding to ribosome.
- D-loop:** It helps in binding amino acyl synthetase.
- Variable loop:** It has function known.

- In a eukaryotic cell the primary transcript formed are non-functional, containing the coding region, exon and non-coding region, intron in RNA and are called heterogeneous RNA or hnRNA. hnRNA undergoes a process where the introns are removed and exons are joined to form mRNA (functional) by the process called splicing.

- Q 7.** (i) Explain the process of aminoacylation of tRNA and its role in the process of translation.
 (ii) How does initiation of the translation process occur in prokaryotes? Explain.
 (iii) Where are the untranslated regions located on mRNA and why? (CBSE 2023)

- Ans.** (i) Aminoacylation is the process by which amino acids become activated by binding with its aminoacyl tRNA synthetase in the presence of ATP. If two charged tRNAs come close during translation process, the formation of peptide bond between them is energetically favourable.
 (ii) In bacteria, translation initiation occurs co-transcriptionally with the RNA polymerase (RNAP) and the ribosome physically interacting with each other. The ribosome binds to the ribosome binding site of the mRNA as soon as it emerges from the RNAP.
 (iii) mRNA has some additional sequences that are not translated and are referred as untranslated regions (UTRs). The UTRs are present at both the ends, i.e., 5'-end (before the start codon) and the 3'-end (after the stop codon). They are required for an efficient translation process.

- Q 8.** (i) How and why is charging of tRNA essential in the process of translation?
 (ii) State the function of ribosome as a catalyst in bacteria during the process of translation.
 (iii) Explain the process of binding of ribosomal units to mRNA during protein synthesis.

(CBSE 2023)

- Ans.** (i) The amino acids are activated in the presence of ATP and linked to their cognate tRNA. This process is called charging of tRNA or aminoacylation of tRNA. When two such charged tRNAs are brought close enough, the formation of peptide bond between the corresponding amino acids would be favoured energetically. The presence of a catalyst would enhance the rate of peptide bond formation.

- The ribosome is universally responsible for **synthesizing proteins by translating the genetic code transcribed in mRNA into an amino acid sequence.** Ribosomes use cellular accessory proteins, soluble transfer RNAs, and metabolic energy to accomplish the initiation, elongation and termination of peptide synthesis.
- During translation, ribosomal subunits assemble together like a sandwich on the strand of mRNA, where they proceed to attract tRNA molecules tethered to amino acids. A long chain of amino acids emerges as the ribosome decodes the mRNA sequence into a polypeptide or a new protein.

- Q 9.** (i) Explain the expression of lac operon genes in *E. coli* growing in lactose containing culture medium.
 (ii) Name the types of cells and the process by which hnRNA is formed. Describe the processing mechanism it undergoes before it becomes functional. (CBSE 2020)

- Ans.** (i) The lac operon is an operon required for the transport and metabolism of lactose in *E. coli*. The mechanism is as follows:
 (a) When lactose is added to the growth medium, the lac genes are expressed because allolactose binds to the lac repressor protein and keeps it from binding to the lac operator. Allolactose is an isomer of lactose.
 (b) Small amounts of allolactose are formed when lactose enters into *E. coli*. Allolactose binds to the repressor protein and causes the conformational change. As a result of this, the repressor can no longer bind to the operator region and falls off.
 (c) RNA polymerase can then bind to the promoter and transcribe the lac genes.
 (d) After some time, when the level of lactose decreases as it is completely metabolised by enzymes, it causes synthesis of the repressor from the regulator gene.
 (e) This repressor binds to the operator gene and prevents RNA polymerase from transcribing the operon and the transcription is stopped. This type of regulation is known as negative regulation.
 (ii) hnRNA is formed in eukaryotic cells. During transcription.

Processing Mechanism: Primary transcript contains both exon and intron. Intron is non-functional and it is subjected to splicing. Where introns are removed, exons are joined in a defined order. hnRNA undergoes capping with nucleotide (methyl guanosine triphosphate)

being added to the 5'-end of *hnRNA*. In tailing, adenylate residues (200-300) are added at 3'-end in a template independent manner.

Q 10. Write the different components of a *lac* operon in *E.coli*. Explain its expression while in an 'open' state. (CBSE 2017)

Ans. The concept of operon was first proposed in 1961, by Jacob and Monod.

Components of *lac* operon:

- (i) **Structural gene:** It is the fragment of DNA which transcribe *mRNA* for polypeptide synthesis.
- (ii) **Promoter:** It is the sequence of DNA where RNA polymerase binds and initiates transcription.
- (iii) **Operator:** The sequence of DNA adjacent to promoter is called operator.
- (iv) **Regulator gene:** It is the gene that codes for repressor protein which binds to operator due to which operon is switched 'OFF'.
- (v) **Inducer:** Lactose is inducer which helps in switching 'ON' of operon. *lac* operon consists of three structural genes (α , γ , β), operator (o), promoter (p), regulatory gene (i).
- (vi) **Expression in open state:** Lactose/inducer binds to the repressor protein, makes it inactive so it cannot bind with operator, allows RNA polymerase access to the promoter and transcription proceeds. Thus, β -galactosidase, permease, transacetylase are formed by translation process for lactose metabolism.

Q 11. Name and describe the steps involved in the technique widely used in forensics that serves as the basis of paternity testing in case of disputes. (CBSE 2023)

Ans. The technique widely used in forensics that serves as the basis of paternity testing in case of disputes is DNA profiling or DNA fingerprinting. The steps involved in this technique are as follows:

- (i) **Sample collection:** The first step in DNA profiling is to collect a biological sample from the individuals involved in the paternity dispute. This can include blood, saliva, hair or other tissue samples.
- (ii) **DNA extraction:** The DNA is then extracted from the biological sample using various methods such as phenol-chloroform extraction or commercial DNA extraction kits.
- (iii) **Polymerase Chain Reaction (PCR):** The next step is to amplify the DNA using the Polymerase Chain Reaction (PCR) technique. Specific regions of the DNA, such as Short Tandem Repeats (STRs), are targeted for amplification.
- (iv) **Gel electrophoresis:** The PCR products are then

separated using gel electrophoresis, which separates DNA fragments based on their size. The resulting DNA fragments are visualized on the gel using a stain or fluorescent dye.

- (v) **DNA analysis:** The DNA fragments are then analyzed to determine the unique genetic profile of each individual. The number and size of the amplified fragments at specific loci are compared between the individuals involved in the dispute. A match in the genetic profile between the child and the alleged father provides evidence of paternity, while a mismatch indicates exclusion. Overall, DNA profiling is a highly accurate and reliable technique for determining paternity and is widely used in forensic investigations and legal disputes.

Q 12. Which methodology is used while sequencing the total DNA from a cell? Explain it in detail. (CBSE 2015, 17, 18)

Ans. Methodology of HGP is used while sequencing the total DNA from a cell.

- (i) The method involves two major approaches:
 - (a) **Expressed Sequence Tags (ESTs):** This method focuses on identifying all the genes that are expressed as RNA.
 - (b) **Sequence Annotation:** It is an approach of simply sequencing the whole set of genome that contains all the coding and non-coding sequences, and later assigning different regions in the sequence with functions.
- (ii) For sequencing, the total DNA from cell is first isolated and broken down in relatively small sizes as fragments.
- (iii) These DNA fragments are cloned in suitable host using suitable vectors. When bacteria is used as vector, they are called Bacterial Artificial Chromosomes (BAC) and when yeast is used as vector, they are called Yeast Artificial Chromosomes (YAC).
- (iv) Frederick Sanger developed a principle according to which the fragments of DNA are sequenced by automated DNA sequences.
- (v) On the basis of overlapping regions on DNA fragments, these sequences are arranged accordingly.
- (vi) For alignment of these sequences, specialised computer-based programmes were developed.
- (vii) Finally, the genetic and physical maps of the genome were constructed by collecting information about certain repetitive DNA sequences and DNA polymorphism, based on endonuclease recognition sites.



Chapter Test

Multiple Choice Questions

- Q 1. A nucleoside differs from a nucleotide. It lacks the:**
- a. base
 - b. sugar
 - c. phosphate group
 - d. hydroxyl group

- Q 2. In one political strand of a DNA molecule, the ratio of A + T/G + C is 0.3. What is the A + G/T + C ratio of the entire DNA molecule?**

- a. 0.3
- b. 0.6
- c. 1.2
- d. 1

Q 3. Pyrimidines are:

- a. monocyclic
- b. dicyclic
- c. tetracyclic
- d. tricyclic

Assertion and Reason Type Questions

Directions (Q.Nos. 4-5): Each of the following questions consists of two statements, one is Assertion (A) and the other is Reason (R). Select the correct answer to these questions from the codes a, b, c and d as given below.

- a. Both Assertion and Reason are true and Reason is the correct explanation of Assertion.
- b. Both Assertion and Reason are true but Reason is not the correct explanation of Assertion.
- c. Assertion is true but Reason is false.
- d. Both Assertion and Reason are false.

Q 4. **Assertion (A)** : If the sequence of bases of one DNA strand is known then the sequence of other strand can be predicted.

Reason (R) : Both the strands of DNA are complementary to each other.

Q 5. **Assertion (A)** : The genetic code is degenerate.

Reason (R) : For a particular amino acid, more than one codon can be used.

Case Based Questions

Case Study 1

Q 6. RNA or ribonucleic acid is a single chain polyribonucleotide which functions as carrier of coded genetic or hereditary information from DNA to cytoplasm for taking part in protein and enzyme synthesis. Six types of RNAs are ribosomal, transfer, messenger, genomic, small nuclear and small cytoplasmic RNA. Out of these, rRNA, mRNA and RNA are major classes of RNAs that are involved in gene expression.

(i) Which one is referred to a soluble RNA?

- a. mRNA
- b. tRNA
- c. rRNA
- d. hnRNA

(ii) The RNA that picks up specific amino acid from amino acid pool in the cytoplasm in ribosome during protein synthesis is:

- a. rRNA
- b. hnRNA
- c. mRNA
- d. tRNA

(iii) Which of the following is found in both DNA and messenger RNA?

- a. Double helix structure
- b. Ribose
- c. Sugar-phosphate chain
- d. Thymine

(iv) Which of the following statements regarding RNA is correct?

- a. Messenger RNA carries coded information for synthesis of polypeptide.
- b. Ribosomal RNA binds with tRNA to catalyse the formation of phosphodiester bonds.
- c. Genomic RNA is always single-stranded.

d. Synthesis of rRNA occurs in cytoplasm by RNA polymerase III.

Case Study 2

Q 7. The Meselson and Stahl experiment was an experiment to prove that DNA replication was semiconservative and it was first shown in *Escherichia coli* and subsequently in higher organism, such as plants and human cells. Semiconservative replication means that when the double-stranded DNA helix was replicated, each of the two double-stranded helices consisted of one strand coming from the parental helix and one is newly synthesised.

Read the given passage carefully and give the answer of the following questions:

- (i) Who is Meselson and Stahl?
- (ii) Name the heavy isotope used by Meselson and Stahl for proving the semiconservative mode of DNA.
- (iii) Heavy DNA can be differentiated from normal DNA by which centrifugation technique?
- (iv) Name the radioisotope used by Taylor in his experiment.

Very Short Answer Type Questions

- Q 8. What conclusion was drawn from the blender experiment performed by Hershey and Chase?
- Q 9. Differentiate between DNA and DNase.
- Q 10. How is repetitive/satellite DNA separated from bulk genomic DNA for various genetic experiments?

Short Answer Type Questions

- Q 11. How is the length of DNA usually calculated?
- Q 12. Why hnRNA is required to undergo splicing?

Long Answer Type-I Question

- Q 13. The base sequence in one of the strands of DNA is TAGCATGAT.
 - (i) Give the base sequence of the complementary strand.
 - (ii) How are these base pairs held together in a DNA molecule?
 - (iii) Explain the base complementarity rule. Give the name of the scientist who framed this rule.

Long Answer Type-II Question

- Q 14. (i) Explain the role of DNA dependent RNA polymerase in initiation, elongation and termination during transcription in bacterial cell.
- (ii) How is transcription a more complex process in eukaryotic cells? Explain