ADVANCED LEVEL – INHERITANCE AND EVOLUTION NOTES

Learning outcomes

a) A learner analyses the structural and functional significance of nucleic acids in meiosis and mitosis, their role in cellular functions, and how mutations in nucleotide sequences can contribute to disease (cancer).

Introduction

Inheritance refers to the transfer of traits from generations to generations or from parents to the offspring through genes.

A **gene** is a section of DNA that codes for a functional protein, DNA is a part of chromosomes, and belongs to special series of chemicals of life called nucleic acids

Chromosomes are thread like structures in the nucleus of a cell that contain the genetic information of the organisms

Genetic information is the hereditary material, primarily found in DNA that determines the characteristics and traits of an organism and is passed down from parents to offspring.

Chromatin refers to a complex mixture of DNA and proteins that form the chromosomes found in the cells of humans and other higher organisms.

Chromatid refers to one of the two identical halves of a chromosome that has been replicated in preparation for cell division. The two "sister" chromatids are joined at a constricted region of the chromosome called the centromere.

Evolution refers to a long-term process in which the population of organisms change from primitive forms to more advanced ones.

NUCLEIC ACIDS

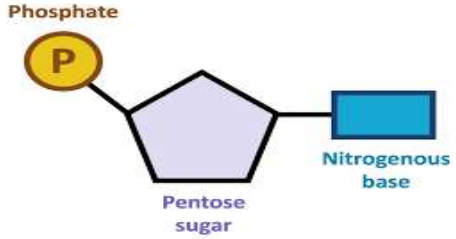
These are polymers consisting of long chains of individual units called nucleotides. Nucleic acids carry the genetic code that determines the order of amino acids in proteins. It stores information, can be replicated, and also undergoes mutations.

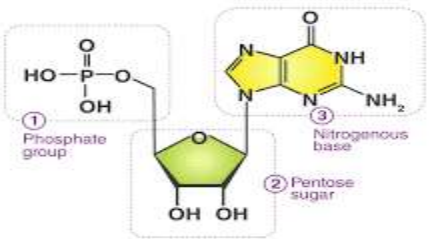
There are two types of nucleic acids which differ in nitrogenous base and pentose sugar as well as number of chains or strands. i.e.

- DNA (Deoxyribo-Nucleic Acid)
- RNA (Ribo Nucleic Acid)

NUCLEOTIDES

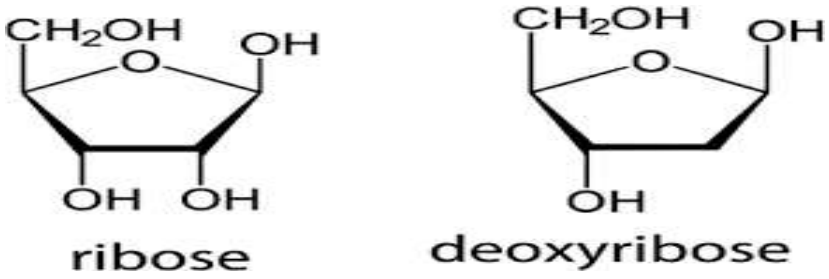
These are building blocks of nucleic acids comprising of a phosphate group, a pentose sugar and a nitrogen containing organic group.





Components of a nucleotide.

a) **Pentose sugar**; this may be Ribose for RNA or deoxyribose for DNA

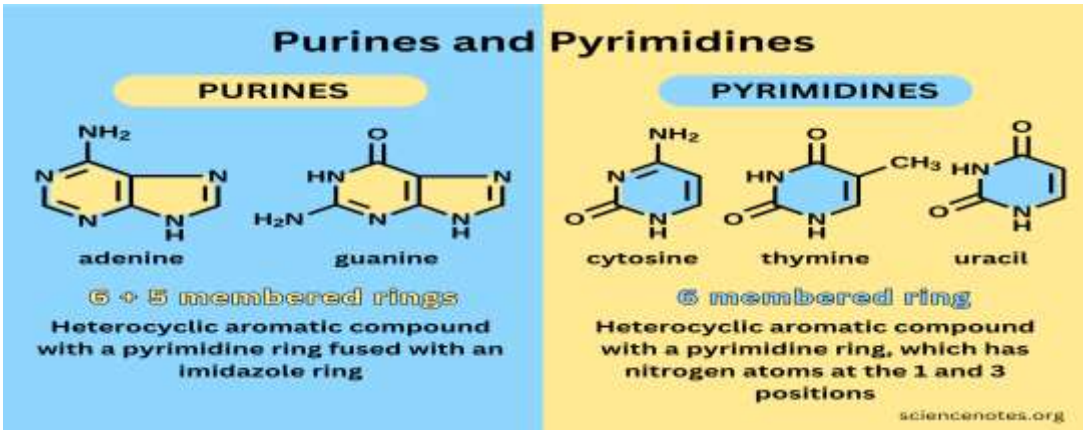


b) Nitrogenous base/nitrogen base/ organic base.

This is a nitrogen containing cyclic base consisting of two types, i.e.

- **Purines** (adenine and guanine) which contain a single ring
- **Pyrimidines** (cytosine, thymine, and uracil) which contain two fused rings

All the nitrogen bases can be found in both DNA and RNA except uracil which is found only in RNA and never in DNA and thymine which is found in DNA only and never in RNA. In **DNA**, adenine pairs with thymine and guanine pairs with cytosine; in **RNA**, adenine pairs with uracil instead.



(Details of the structure not needed)

c) Phosphate group

This gives the nucleic acids their acidic character, it tells the reason why nucleic acids are acidic yet they contain nitrogen bases. Some nucleotides exist singly (mononucleotides) e.g. ATP, AMP ADP may contain one or more phosphate groups.

DNA (DEOXYRIBONUCLEIC ACID)

DNA has been called the "molecule of life" as it plays a key role in genetic inheritance and protein synthesis; resulting into gene expression; thus influences all the physical and behavioral characteristics of organisms.

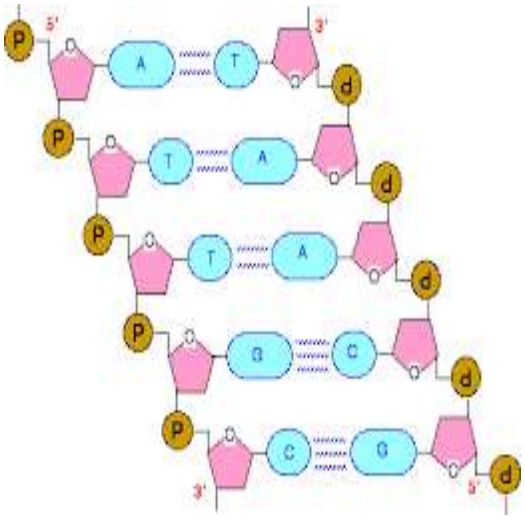
DNA; is made up of deoxyribose sugar; adenine (A), thymine (T), guanine (G), and cytosine (C) as the nitrogen bases together with phosphate groups.

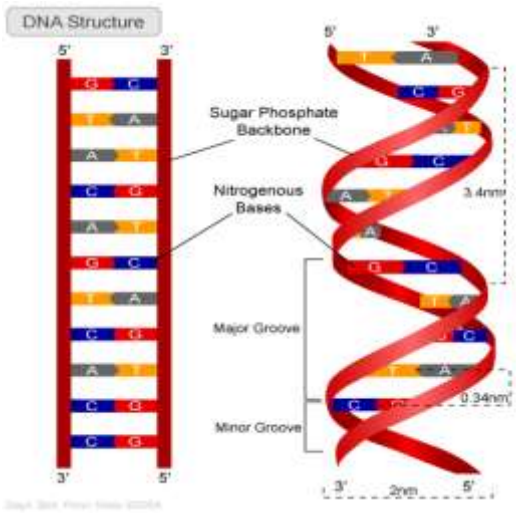
Structure of DNA

DNA molecule consists of two polynucleotide strands each coiled in a right-handed spiral helix. The polynucleotide strands run anti parallel to each other.

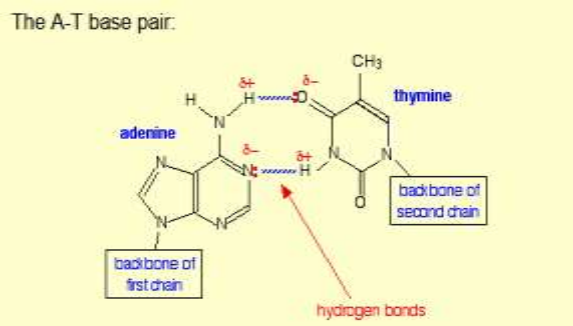
The two strands coil around each other to form a double helix are held together by hydrogen bonding found between the nitrogenous bases of adjacent nucleotides. Adenine pairs with thymine, and guanine with cytosine; the adenine-thymine pair has two hydrogen bonds while the guanine-cytosine pair has 3 hydrogen bonds.

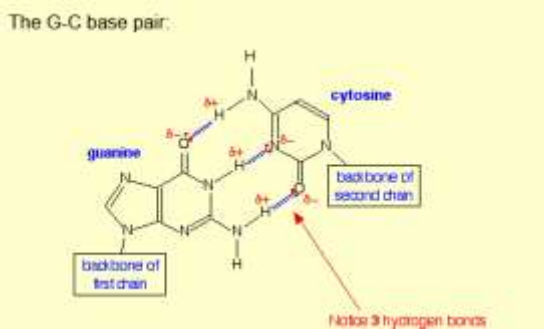
Along the axis of the molecule the base pairs are 0.34nm apart. For each complete twist of the double helix there are 10 pairs of nucleotides





The complementary base pairing in DNA (Details of structure not needed)





Adaptations of DNA as a hereditary material

- It's location in the nucleus protects it from being affected by cytoplasmic chemicals and enzymes.
- It's extremely large to carry vast information and instructions inform of base sequences.
- The two strands are joined by weak hydrogen bonds which can separate easily during DNA replication and formation of mRNA for protein synthesis.
- It can replicate hence can be transferred from generation to generation without change.
- It's highly coiled to fit in the small space with in the nucleus
- Complementary base pairing ensures accuracy during DNA replication and protein synthesis.

RIBONUCLEIC ACID (RNA)

This usually contains a single polynucleotide chain (strand); coiled into an alpha-helix; its sugar phosphate backbone has ribose as its pentose sugar; the nitrogen bases are similar to those in DNA except thymine which is replaced by uracil.

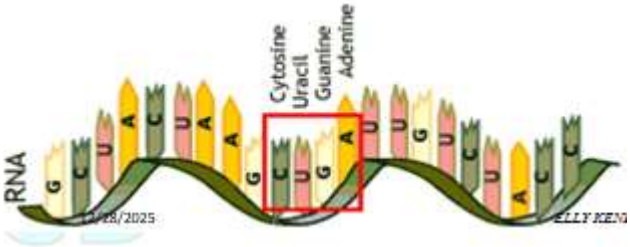
RNA occurs in three main forms; these differ in length, shape and function, though they have the same basic structure i.e.

- Messenger RNA (mRNA)
- Ribosomal RNA (rRNA)
- Transfer RNA (tRNA)

Messenger RNA (mRNA)

It accounts for about 3%-5% of the total RNA molecules in a cell. The molecules of mRNA are single, helical strands made of up to several thousand nucleotides. Messenger

RNA is made in the nucleus from a single strand of DNA through transcription where only one strand of the DNA molecule is copied. From there it passes through the nuclear membrane pores to the ribosomes where triplets of bases in the mRNA act as codons in the synthesis of proteins. Most mRNA exists within the cell for a short time



Transfer RNA (tRNA)

Transfer RNA makes up between 10 and 15 % of a cell's RNA content. The single strand of 75-90 nucleotides which make up a tRNA molecule is wound into a double helix which usually has three prominent bulges to form a clover-leaf arrangement.

One of the free ends of every tRNA molecule ends with nucleotides containing the following order of bases ACC where the amino acid binds.

There are at least twenty different kinds of tRNA and differ in the sequence of base triplets making up the anticodons by which tRNA binds to the codons of mRNA during the synthesis of proteins

Base pairing occurs in certain regions of the molecule. The 3 unpaired bases at the bottom loop (anti codon) pair with mRNA

Amino Acid attachment site

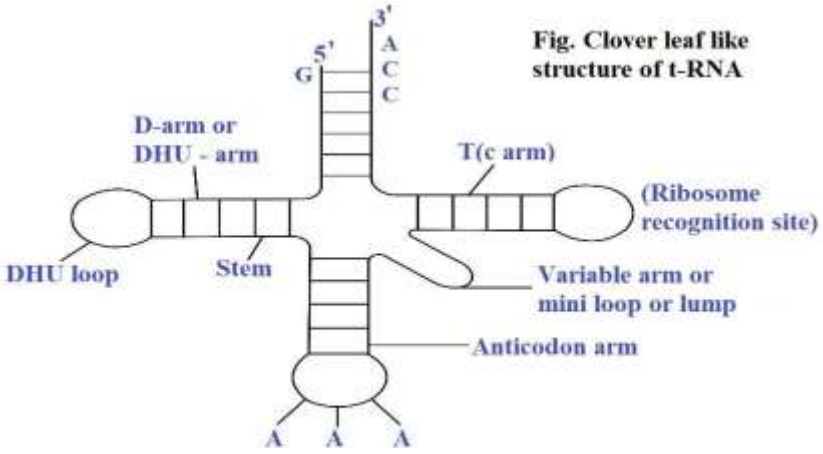


Fig. Clover leaf like structure of t-RNA

Codon recognition site

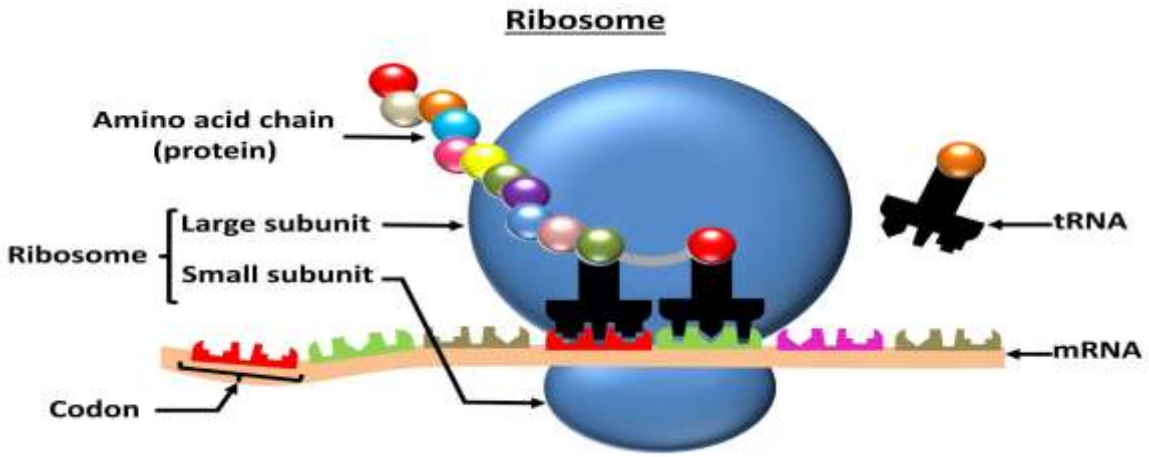
Ribosomal RNA (rRNA)

The many thousands of nucleotides which make up a molecule of rRNA are wound into a complex structure consisting partly of single and partly of double helices.

Ribosomal RNA is made in the nucleus under the control of the nucleoli. It enters the cytoplasm and binds with protein molecules to become ribosomes.

Over half the mass of a ribosome consists of rRNA and it makes up more than 80 % of the total RNA in a cell. Even so, the precise function of rRNA is still not known.

It is synthesized by genes present on the DNA of several chromosomes found within a region of the nucleolus known as the nucleolar organizer. It is found in the cytoplasm where it is associated with protein molecules.



Comparison of the structure of RNA and DNA.

Feature	DNA (Deoxyribonucleic Acid)	RNA (Ribonucleic Acid)
Full Name	Deoxyribonucleic Acid	Ribonucleic Acid
Sugar	Deoxyribose sugar	Ribose sugar
Nitrogen Bases	Adenine (A), Thymine (T), Cytosine (C), Guanine (G)	Adenine (A), Uracil (U), Cytosine (C), Guanine (G)
Structure	Always double-stranded helix	Usually single-stranded
Location in Cell	Mainly in the nucleus	Nucleus and cytoplasm
Function	Stores genetic information	Helps in protein synthesis
Stability	More stable	Less stable
Length	Very long strands	Relatively short strands
Base Pairing	A–T, C–G	A–U, C–G
Types	One primary type	Three main types: mRNA, tRNA, rRNA

Assignment: Outline the similarities between DNA and RNA

DNA AS A HEREDITARY MATERIAL

DNA is described as a hereditary molecule, as it contains information that is responsible for physical and behavioral characteristics of all organisms (genes); these are passed on from

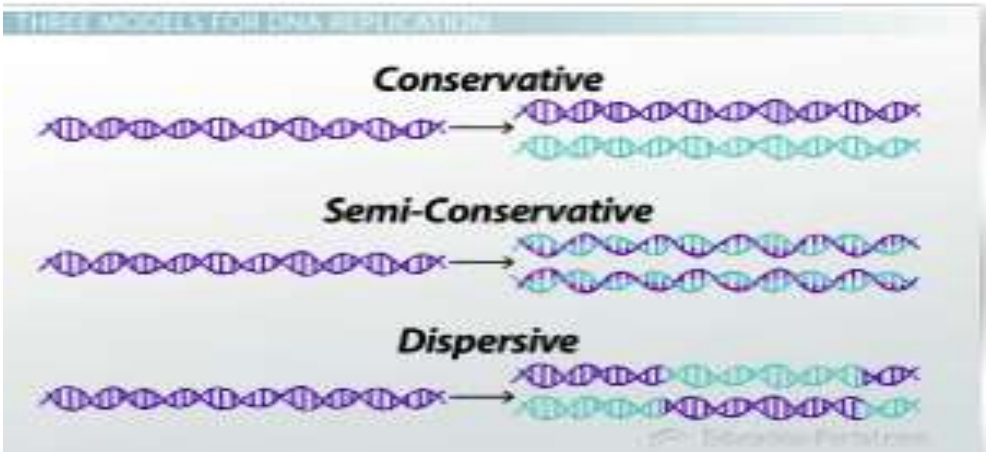
generation to generation (inheritance), the information is in form of codes; sequences of nitrogen bases.

Transfer of DNA to the offspring follows DNA replication during gamete formation in meiosis as well as during mitosis; this is possible due to complementary base pairing; as there are many nucleotides in the nucleus; when the hydrogen bond are broken, the attracted nucleotides complementary pair with those on single strands forming new exact copies of the parent DNA molecule.

DNA REPLICATION

DNA replication refers to the process by which a cell makes an identical copy of its DNA before cell division. It occurs during the S-phase of the cell cycle and ensures that each daughter cell receives the same genetic information as the parent cell.

DNA replication can be described to be semi-conservative when only one of the strands in the new DNA molecule is the parental strand and the other; is the newly synthesized strand. Conservative when the parental DNA molecule is retained and the new DNA molecule comprises of only the newly synthesized strands as a result of rejoining of the template strands and the joining of the two newly synthesized strands. Dispersive; in which the new DNA molecule has some sections having completely the parental strands and the other sections having only sections of the synthesized strands; as a result of breaking the parental DNA molecule and randomly mixing it with fragments of the newly synthesized DNA fragments



The semi – conservative DNA replication process.

DNA replication occurs within the nucleus of a non – dividing cells and is controlled by a number of enzymes including;

- DNA Helicase
- DNA Ligase
- Primase
- Topoisomerase
- DNA polymerase.

The histone proteins coat peels off, **DNA helicase** enzyme attaches itself to the parent DNA molecule at points called replication origin. This causes the DNA to **split by breaking the hydrogen bonds** between base pairs, forming a replication fork. The hydrogen bonds between base pairs are completely broken down, forming **two separate strands** of the parent DNA molecule. These strands act as template strands or molds over which new strands are copied.

One of the parent strands is partly broken by the enzyme **topoisomerase,** to prevent the strands from rejoining, and it rejoins after unwinding is complete. The unwinding process requires

energy and therefore uses ATP. The separated strands are maintained by **DNA binding proteins.**

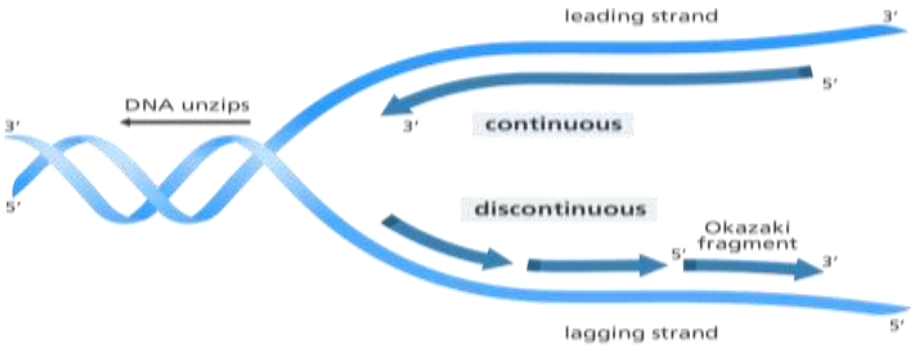
Synthesis of new strands begins with primers formed by the **Primase** enzyme. These primers are short fragments that are later removed by the polymerase enzyme.

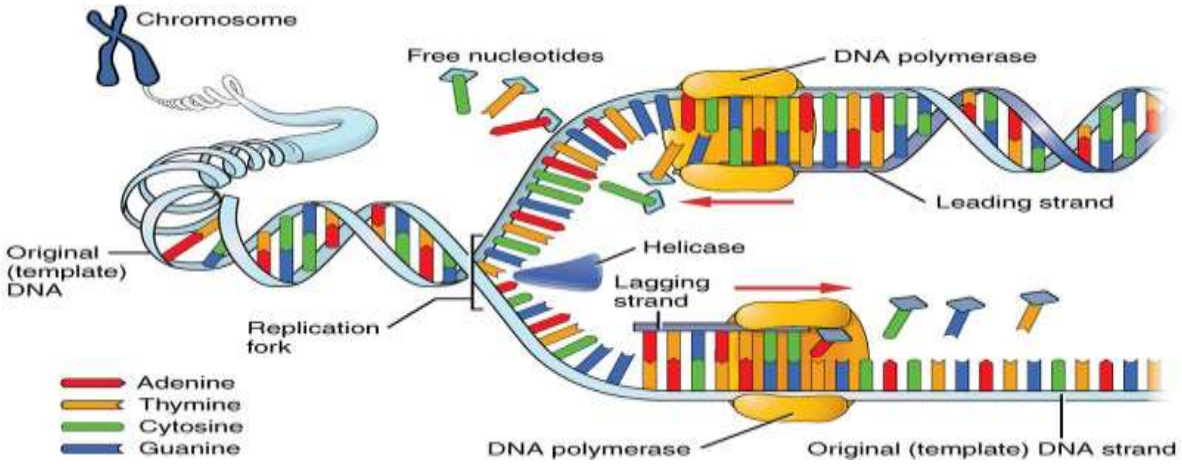
During the assembly of the leading strand, **DNA polymerase** attaches itself to the template strand that runs in **the 3′–5′ direction**. It assembles a complementary strand **continuously** as it moves along the parallel template strands, activated free DNA nucleotides join up the exposed bases on the template. The synthesized strand is called the leading strand and runs in the 5′–3′ direction because DNA polymerase moves in the same direction as the unwinding enzyme and the replication fork.

During the assembly of the lagging strand, since DNA polymerase works only in the 5′–3′ direction, the antiparallel parental strand that runs in the 5′–3′ direction is copied in small fragments. These fragments run in the 5′–3′ direction and are called **Okazaki fragments**, named after Reiji Okazaki. These fragments are later joined together by **DNA ligase** to form a continuous strand.

As the new strands are synthesized, free nitrogen bases from the nucleus are attracted to the complementary bases on the template strand. DNA polymerase holds them in position until hydrogen bonds form between them, followed by the formation of phosphodiester bonds to create the sugar-phosphate backbone.

Finally, DNA replication is completed by removing mismatched nucleotides and replacing them with the correct ones, a process carried out by DNA polymerase **(Proof – reading)**





How the structural properties of DNA allows for replication.

Weak hydrogen bonds between the base pairs which is easily broken allowing the two strands to separate exposing the bases on the template strands.

Complementary base pairing allows each strand to be used as a molecular mould to synthesize complementary strand.

THE GENETIC CODE

DNA stores information in genes and gives instructions for which amino acids to be synthesized basing on the genetic code. Each of the 20 amino acids has a specific code referred to as a triplet code in DNA and or Codon mRNA.

Features of the Genetic Code.

Triplet. Each of the 20 amino acids used to make proteins is coded for by three bases e.g. UGG codes for tryptophan.

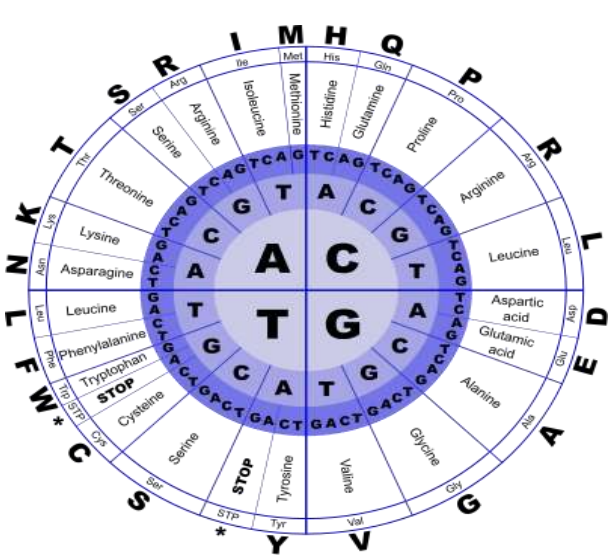
Degenerate. A single amino acid can be coded for by more than one codon e.g. GAU and GAC code for aspartic acid. Degeneracy prevents the effect of mutation produced as substitution of one DNA base may not alter the amino acid code for.

Non – overlapping. Each base in the sequence is only read once. E.g. CUGAGC is read as GUC – AGC not CUG – UGA – GAG – AGC, where each codon overlaps the previous one by two bases. Overlapping would allow more information to be provided by a given sequence but limits flexibility.

Universal. Same codons code for the same amino acids in all organisms.

Punctuated. The start and the end of coding sequence is determined by specific codons. The start codon is usually AUG which codes for Methionine that initiates the polypeptide chain and stop or nonsense codons e.g. UGA, UAG and UAA which do not code for any amino acid and thus marks the endpoint of a gene

Linear. Always read from the starting point to a finishing point in the 5'→ 3' direction.



Second Letter

1st letter	U		C		A		G		3rd letter
U	UUU	Phe	UCU	Ser	UAU	Tyr	UGU	Cys	U
	UUC		UCC		UAC		UGC		C
	UUA	Leu	UCA		UAA	Stop	UGA	Stop	A
	UUG		UCG		UAG	Stop	UGG	Trp	G
C	CUU	Leu	CCU	Pro	CAU	His	CGU	Arg	U
	CUC		CCC		CAC		CGC		C
	CUA		CCA		CAA	Gln	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU	Ile	ACU	Thr	AAU	Asn	AGU	Ser	U
	AUC		ACC		AAC		AGC		C
	AUA		ACA		AAA	Lys	AGA	Arg	A
	AUG	Met	ACG		AAG		AGG		G
G	GUU	Val	GCU	Ala	GAU	Asp	GGU	Gly	U
	GUC		GCC		GAC		GGC		C
	GUA		GCA		GAA	Glu	GGA		A
	GUG		GCG		GAG		GGG		G

PROTEIN SYNTHESIS

This is the process by which the coded information is transferred from DNA on chromosomes in the nucleus to the ribosomes in the cytoplasm to make the proteins. The central Dogma of molecular biology describes that DNA makes RNA and RNA makes protein. Protein synthesis involves the process by which a polypeptide is formed from amino acids following the instructions from the genetic code.

The sequence in which the amino acids are assembled during the formation of the protein is based on the arrangement of the codons on mRNA which is formed from a section of DNA known as the gene. Therefore the process of protein synthesis can also be called gene expression.

There are two main stages in the formation of a protein namely i.e.

- Transcription
- Translation

a. TRANSCRIPTION.

Transcription is the mechanism by which the base sequence of a section of DNA representing a gene is converted into the complementary base sequence of mRNA.

Transcription occurs in the nucleus where the gene that codes for a particular protein is located on the DNA molecule. The DNA double helix unwinds and the hydrogen bonds between complementary bases break, exposing the nucleotide sequence of one strand called the **template strand**.

The enzyme **RNA polymerase** attaches to the promoter region of the gene and moves along the template strand of DNA. Free RNA nucleotides in the nucleus align with complementary bases on the DNA template strand according to base pairing rules: adenine pairs with uracil, thymine pairs with adenine, cytosine pairs with guanine, and guanine pairs with cytosine. RNA polymerase then catalyzes the formation of phosphodiester bonds between adjacent RNA nucleotides, forming a single-stranded molecule of **messenger RNA (mRNA)**.

Once the entire gene has been copied, the mRNA strand detaches from the DNA and the DNA rewinds back into its double helix structure. In eukaryotic cells, the mRNA may undergo processing before it leaves the nucleus; this involves removal of introns these are nucleotide base sequences that do not code for a protein; but are part of the cistron. The remaining nucleotide base sequences of the cistron that codes for the functional protein are the exons; these are joined together (spliced together) to form a mature mRNA. The mature mRNA then leaves the nucleus through nuclear pores and enters the cytoplasm.

b. TRANSLATION

Translation is the second stage of protein synthesis in which the genetic information carried by messenger RNA (mRNA) is decoded to form a specific polypeptide chain that later folds into a functional protein. It occurs in the cytoplasm on ribosomes, either free in the cytosol or attached to the rough endoplasmic reticulum. During translation, the sequence of bases in the mRNA is read in groups of three nucleotides called codons, each codon specifying a particular amino acid according to the genetic code.

Before translation begins, amino acids must first be activated and attached to their corresponding tRNA molecules in a process known as **amino acid activation**. Each amino acid is recognized by a specific enzyme called aminoacyl-tRNA synthetase, which catalyzes the attachment of the amino acid to its appropriate tRNA molecule. This reaction requires energy from ATP. The amino acid becomes linked to the 3′ end of the tRNA, forming an aminoacyl-tRNA complex. Each tRNA molecule possesses a three-base sequence known as an anticodon that is complementary to a specific codon on the mRNA molecule. This ensures that the correct amino acid is delivered to the ribosome according to the genetic code.

The first stage of translation is **initiation**. During this stage, the small ribosomal subunit binds to the mRNA molecule near its **5′** end. The ribosome moves along the mRNA until it recognizes the start codon, which is usually **AUG**. This codon codes for the amino acid methionine and marks the beginning of protein synthesis. A tRNA carrying methionine binds to this start codon through complementary base pairing between its anticodon **(UAC)** and the codon on the mRNA. After this pairing occurs, the large ribosomal subunit joins the small subunit to form a complete functional ribosome. The ribosome has two main binding sites for tRNA molecules: the P site (peptidyl site), which holds the tRNA carrying the growing polypeptide chain, and the A site (aminoacyl site), where the incoming aminoacyl-tRNA binds.

The second stage is **elongation**, during which the polypeptide chain grows as amino acids are added sequentially. A second aminoacyl-tRNA carrying another specific amino acid enters the A site of the ribosome and pairs with the next codon on the mRNA through complementary base pairing between the codon and anticodon. Once the correct pairing has occurred, the ribosome catalyzes the formation of a peptide bond between the amino acid in the P site and the amino acid in the A site. This reaction is catalyzed by the enzyme **peptidyl transferase**, which is part of the ribosomal structure. As a result, the growing polypeptide chain becomes attached to the tRNA located in the A site. The ribosome then moves along the mRNA by one codon in a process called translocation. During translocation, the tRNA that was previously in the P site leaves the ribosome and returns to the cytoplasm, while the tRNA carrying the polypeptide chain moves from the A site to the P site. The A site becomes vacant and ready to receive another aminoacyl-tRNA. This cycle repeats many times, leading to the progressive elongation of the polypeptide chain according to the sequence of codons on the mRNA.

The final stage of translation is **termination**. Termination occurs when the ribosome reaches a stop codon on the mRNA, such as UAA, UAG, or UGA. These codons do not code for any amino acid and therefore do not have corresponding tRNA molecules. Instead, special proteins known as release factors bind to the ribosome at the stop codon. The binding of these release factors causes the completed polypeptide chain to be released from the tRNA in the P site. The ribosomal subunits then dissociate from the mRNA molecule, and the mRNA, ribosomal subunits, and tRNA molecules are free to be reused in further rounds of protein synthesis.

After translation, the newly synthesized polypeptide chain moves through the lumen of rough endoplasmic reticulum (RER); into the Golgi apparatus; where it is modified. The polypeptide may fold into a specific three-dimensional structure due to interactions among its amino acids, such as hydrogen bonds, ionic bonds, and disulfide bridges. In some cases, additional modifications such as the addition of carbohydrate groups, phosphate groups, or lipid groups occur. The completed protein is then transported to the part of the cell where it performs its specific biological function such as antibacterial resistance by beta lactamase enzyme.

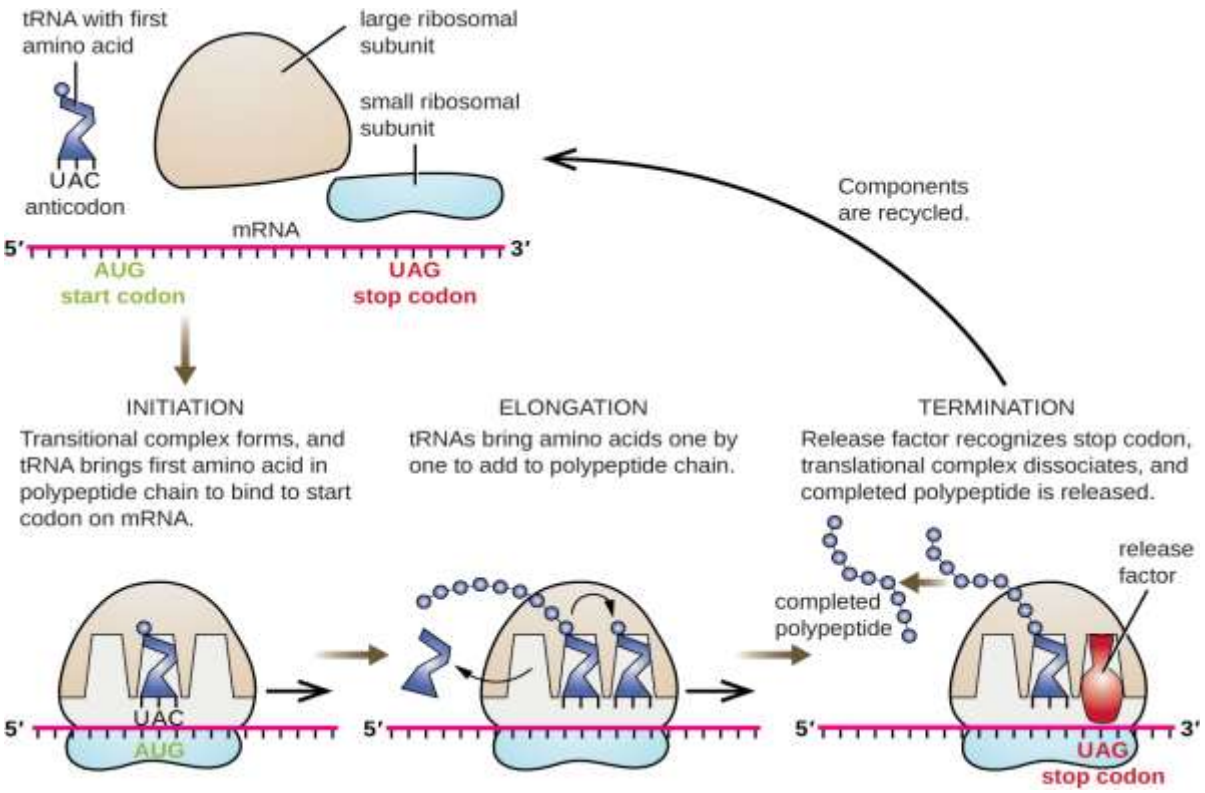


Figure Showing the Process of Translation

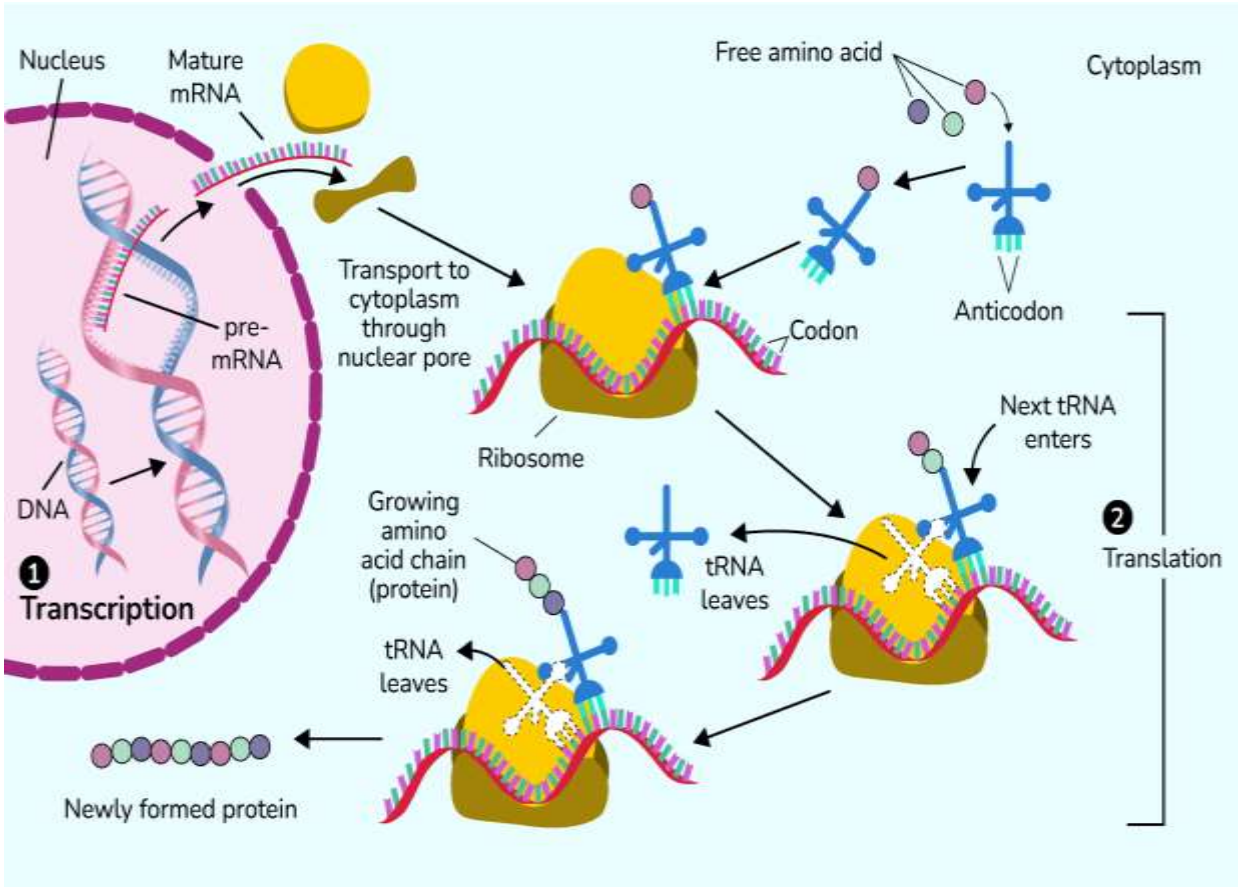


Figure Showing the Process of Protein Synthesis